

TROPICAL JOURNAL OF NEPHROLOGY

The Official Journal of the Nigerian Association of Nephrology

AIMS and SCOPE

The aims and scope include the following:

1. *To provide a medium of exchange of ideas and knowledge of nephrology in the tropics through publication of research works, clinical experiences and relevant articles.*
2. *To promote nephrology education, clinical practice and research through publication of original research works, innovative clinical experience and authoritative review articles on topical issues.*
3. *To provide an avenue for global dissemination of consensus positions on issues of concern in tropical nephrology through publication of proceedings of consensus meetings, dedicated conferences and commissioned reviews.*
4. *To serve as a scientific link between the Nigerian Association of Nephrology and other such International Organizations all over the world.*

Publication Details

The Tropical Journal of Nephrology is owned by the Nigerian Association of Nephrology and published by Samd Davies Publishers, His Grace Villa, Plot 4, Adenekan-Oyejide Street, Olorunredo Layout, Kuelu, Oloode, New Ife Road, Ibadan, P. O. Box 27411, Agodi, Ibadan, Nigeria. *Tel:* 234 8023451177, 07034885019, 08084878480.

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Subscription request should be sent to the Managing Editor. Subscription prices (2 issues) for individuals in Africa is N3,000.00 and \$50 for outside Africa. Institutional rate is N4,500.00 for African countries and \$60 for countries outside Africa.

Manuscripts should be submitted at <https://tjn-online.com/index.php/tjn/login>. Authors should first register on the website before submission. If there are difficulties the Editor could be contacted at The Editor, Dr. Samuel Ajayi, Department of Medicine, College of Medicine, University of Ibadan, Ibadan, Nigeria. *E-mail:* tropicaljournal_2005@yahoo.com. Website: www.tjn-ng.com.

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ISSN 2006-49 OX

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The Official Journal of the Nigerian Association of Nephrology

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Guidelines for the Detection and Management of Chronic Kidney Disease 2022 Revision

**Nigerian Association of Nephrology
October 2022**

TROPICAL JOURNAL OF NEPHROLOGY

The Official Journal of the Nigerian Association of Nephrology

FOREWORD

The Nigerian Association of Nephrology, affiliated with the International Society of Nephrology (ISN) and the African Association of Nephrology (AFRAN), has, since her establishment 34 years ago, been at the forefront of fighting kidney disease in Nigeria through preventive, curative and training programmes. With the increasing incidence and prevalence of kidney disease worldwide and end-stage kidney disease (ESKD) now assuming epidemic proportion in high-income as well as low and middle-income countries, and the need for a uniform management strategy, that should address the general and specific national issues in Nigeria, a Guidelines Committee was set up that produced the first guideline on the management of chronic kidney disease (CKD) 11 years ago. The current guideline is the second.

Although a National Renal Registry is yet to be fully established in Nigeria, the burden of CKD is high in Nigeria as available hospital data revealed that CKD accounts for about 10% of medical admissions. This extrapolation puts the prevalence figure between 200-300 patients per million population. This is an under-estimation as many of these patients do not have access to a hospital where a definitive diagnosis could be made before death. In view of this persistent burden of CKD and the current evidence-based findings in this field in the past decade, a revised and updated guideline was embarked on.

Important causes of CKD and ESKD in Nigeria include chronic glomerulonephritis and hypertension (the most common causes), diabetic nephropathy (which is rapidly increasing in prevalence), obstructive nephropathy and interstitial nephritis, which account for the significant other causes received greater attention. All the management strategies were discussed, and recommendations were made. Also updated are the very important complications of CKD such as Anaemia and CKD– mineral and bone disorder (MBD). APOL 1 genetic mutation and its import on transplantation caught attention, in addition.

Each subject was first introduced, and then the recommendations and the advised practice points were given based on the strength of available evidence and the grading of evidence using the GRADE system.

In conclusion, we are confident that this guideline will be beneficial for the management of CKD in our setting. We are grateful to the Guidelines Committee, ably led by Professor Olugbenga Awobusuyi, to the reviewers and all those who contributed towards making this document a reality.

Dr. Adanze O. Asinobi

President, Nigerian Association of Nephrology

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Guidelines for the Detection and Management of Chronic Kidney Disease

INTRODUCTION

In 2010, the Nigerian Association of Nephrology (NAN) published the Guidelines for the Detection and Management of Chronic Kidney Disease (CKD) [1], which was aimed at improving awareness of CKD by all practicing medical doctors, standardizing the practice of nephrology and encourage research relevant to nephrology practice in Nigeria. Over the past decade, evolving knowledge, and the development of newer concepts in the field of Nephrology worldwide have led to remarkable changes in the practice of the discipline. Responding to these changes, in the first quarter of 2020, the NAN Executive Committee recognized the need to update these guidelines to improve patient care quality, improve health outcomes, and reduce the morbidity and mortality attributable to CKD.

To update the guidelines, a Guideline Revision Committee was set up with the responsibility of revising the existing guidelines, updating the recommendations in the guidelines based on the best available evidence, and contextualizing them in relation to specific renal care requirements of day-to-day clinical practice in the country.

The updated guidelines are intended to rely on scientific evidence from published literature, with the overriding objective of improving the quality of health care delivery to patients with CKD in Nigeria's context of human, infrastructural and financial resources.

It is hoped that the updated Guidelines will improve the consistency of renal care across the country regardless of where or by whom such care is delivered.

Scope of the Revised Guidelines

The committee's principal aim is to revise and update the previous guidelines following current research evidence, with recommendations in the context of prevailing clinical practice and experience in Nigeria. These revised guidelines cover all five sections in the 2010 guidelines: CKD definition and screening, management of CKD, haemodialysis therapy, peritoneal dialysis, and kidney transplantation.

The guideline recommendations cover CKD detection and management in paediatric and adult patients. Also, recommendations on special populations such as pregnant women and elderly patients are included where applicable.

The guidelines are intended for use by nephrologists, resident doctors, medical practitioners interested in renal care medicine, hospital administrators, and policymakers.

Method

Guideline Development Method

The process for revising the guidelines was extensively discussed at the Committee's inaugural meeting. The committee reviewed the appraisal of the 2010 NAN guidelines for the detection and management of chronic kidney disease guidelines conducted by independent experts commissioned by Cochrane Nigeria under the auspices of the Effective Healthcare Research Consortium at the Liverpool School of Tropical Medicine. They used the international Appraisal of Guidelines, Research and Evaluation II (AGREE II) tool, which was presented at the NAN Conference of Nephrology in Calabar in January 2015. A survey was conducted among members to assess the validity of the issues raised in the appraisal in the six domains evaluated by the reviewer. There was general agreement on the validity of the reviewer's conclusions, and the appraisal was then used to guide the revision process.

The options considered were the adoption of an existing guideline, an adaptation of an existing guideline using the ADAPTE process, and a review of recommendations in the 2010 NAN guidelines guided by utilization of internationally recognized clinical practice guidelines (CPGs) such as KDIGO guidelines,(2) NICE guidelines(3) and others that have similar purposes to the intended revision. After extensive deliberation on the options, the Committee finally decided on a revision process based on the review of recommendations in the 2010 NAN guidelines guided by the utilization of international CPGs that have similar purposes to the intended revision.

The guidelines were written collaboratively. Members were divided into five groups to review the five sections of the 2010 NAN guidelines. Each sectional group evaluated the recommendations of the guidelines in terms of relevance, currency, and need for contextualization.

The first drafts of the recommendation statements and rationale were written by members of the sectional groups, and preliminary discussions on the recommendations were held by the groups. Presentation of the drafts to the other committee members was done at the regular committee meetings, during which consensus was reached on the guideline recommendations. The recommendations were contextualized appropriately in relation to the human, infrastructural and financial resources available in Nigeria. Due to the COVID-19 pandemic, the Committee's meetings were held on-line.

Grading of the Quality of Evidence and Strength of Recommendations

The committee adopted the Grading of Recommendations, Assessment, Development, and Evaluation system (GRADE) for the categorization of the levels of evidence and strength of recommendations.^(5,6) Quality of evidence is presented as high, moderate, low, or very low, while the strength of recommendation is indicated as either strong or weak. An additional category, "Not Graded," is used to provide guidance based on the expert opinion of committee members in areas where scientific evidence is lacking.

Strong recommendations are given in instances where the committee is confident that the recommendation can be implemented in our current setting and that the positive effects of adhering to the recommendation outweigh the negative effects of doing so. A weak recommendation is given when the committee believes that the advantages of following a recommendation outweigh the disadvantages, but this is not certain.

Consensus practice points are included in Section II to instruct users on specific care aspects. They represent the Committee's accepted views in these areas, applicable in the context of routine clinical practice in our setting, and deemed appropriate as guides to patient care. Practice points are a new addition to KDIGO guidelines and may be organized as a table, a figure or an algorithm. They are consensus statements about a specific aspect of care, and supplement recommendation for which a larger quality of evidence was identified. Practice points in this updated guideline represent the expert opinion of the Guidelines Review Team and are based on our limited evidence in this environment.

Declaration of Conflict of Interest

None relevant to the guidelines development

Acknowledgments

The committee would like to express its gratitude to Professors Evelyn Unuigbo, Solomon Kadiri, and Rasheed Balogun for their insightful reviews of the draft guideline document. In addition, we also appreciate the consultants and Residents responsible for extracting and organizing the recommendations in the previous guidelines for use in the revision process.

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Guideline Committee Composition

In the first quarter of 2020, the Executive Committee of NAN constituted the guidelines revision committee by inviting ten experienced members of the Association from various institutions in the country. This committee was subsequently increased to twenty-six to enable completion of the revision process within the time frame for completion decided on by the committee members.

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How to cite this document

Awobusuyi JO, Arogundade FA, Asinobi OA, Bamgboye EL, Amira CO, Aliyu A, Effa EE, Ifebunandu NA, Esezobor IC, Okaka EI, Raji YR, Alao MA, Waziri B, Busari AA, Ibrahim OR, Ajjiyan Y, Solarin AU, Johnson BO, Odeyemi A, Ezeugonwa RS, Sulaiman MM, Umezudike T, Okwuonu CG, Olatise OO, Adebawale DA and Oguntola SO. Guidelines for the detection and Management of Chronic Kidney Disease -2022 Revision. Trop J Nephrol. 2023 Jan; Suppl. 1(1): 5-153

SECTION I: CKD DEFINITION AND SCREENING

Introduction

Chronic kidney disease (CKD) is a significant contributor to the global burden of disease and a common chronic complication of highly prevalent diseases such as hypertension and diabetes mellitus. In Africa, it is estimated to affect 15.8% of the one billion people.¹ The estimates of CKD for Nigeria ranges from 2.5% to 26% with a median of 11.4%.² With reducing burden of infectious diseases and increasing life expectancy in Nigeria, an increase in non-communicable diseases such as hypertension and diabetes mellitus is expected. Also, more pre-term newborns surviving the neonatal period will translate to more children living with reduced nephron mass. These two observations above will with time contribute to the rising burden of CKD in Nigeria.

1.1 Definition of CKD

Background

Having myriads of definitions for the same condition endangers collaboration, communication, and data collection. In contrast, clear, practical, and widely accepted definition fosters research and drives decision making.

Supporting Evidence

Until 2002, CKD was defined variably in the literature with most definitions focusing on dialysis-requiring forms and severe forms. In 2002, the Kidney Disease Outcomes Quality Initiative of the National Kidney Foundation in USA published its definition which shifted the focus to milder forms. The new definition was based on the accumulated body of evidence which showed that mildly decreased glomerular filtration rate and/or albuminuria was associated with increased mortality, and adverse kidney and cardiovascular outcomes.³⁻⁶ In 2012, the Kidney Disease: Improving Global Outcomes further refined the definitions to include implication for health.⁷

Recommendations

- 1.1.1 We recommend that CKD should be defined as "as abnormalities in kidney structure or function lasting more than 3 months with health implications."^{3,7}

Quality of evidence - Low

Recommendation- Strong

- 1.1.2 We recommend that CKD in practice should be diagnosed when one or more of the following is present for three months or longer.

- Persistent albuminuria or proteinuria
- Persistent haematuria
- Electrolyte or other abnormalities due to tubular disorders
- Abnormality in kidney structure on imaging or histology
- History of kidney transplantation.
- Glomerular filtration rate <60 ml/min/1.73 m²

Quality of evidence - High

Recommendation- Strong

1.2 CKD Staging

Background

Due to the fact that CKD is a progressive disease and modifiable predictors of progression are known, staging of CKD should routinely be done when initial CKD diagnosis is made. Accurate staging of CKD allows for anticipatory care and timely discussion of the management and prognosis with the patient and their family.

Supporting Evidence

Large observational studies including meta-analyses consistently report that albuminuria and/or reduced GFR are associated with adverse outcomes including increased mortality and adverse cardiovascular events.⁴⁻⁶ Some of these studies showed a dose-gradient association between albuminuria and decreasing glomerular filtration rate and adverse outcomes.

Recommendations

1.2.1. We recommend that CKD should be staged using GFR, albuminuria and the underlying cause of the CKD.

Quality of evidence - Moderate

Recommendation- Strong

The staging should be as in table 1:

Table 1: GFR Staging: [4-6,8]

Stage	GFR (mL/min/1.73 m ²)	Interpretation
1	≥90	Requires evidence of kidney damage to qualify as CKD
2	89-60	Mildly decreased kidney function. Requires evidence of kidney damage to qualify as CKD
3a	59-45	Mildly to moderately decreased kidney function
3b	44-30	Moderately to severely decreased kidney function
4	29-15	Severely decreased kidney function
5	<15	Also known as end stage kidney disease; requires chronic dialysis or kidney transplantation to maintain life

Table 2: Albuminuria Staging [4-6]

Category	AER (mg/24 hours)	ACR (mg/mg)	PCR (mg/mg)	Dipstick	Interpretation
A1	<30	<0.03	0.15	0 to trace	Normal to mildly increased
A2	30-300	0.03-0.3	0.15-0.50	Trace to 1+	Moderately increased
A3	>300	>0.3	>0.50	>1+	Severely increased

Classification based on the cause of CKD

Examples of some of the classes include:

Glomerular causes: diabetic glomerulopathy, SLE, focal segmental glomerulosclerosis, sickle cell disease. Tubulointerstitial causes: chronic interstitial nephritis, nephronophthisis.

Vascular causes: atherosclerosis, hypertension, ANCA vasculitis.

Congenital causes: posterior urethral valves, bilateral renal hypodysplasia.

In general CKD caused by glomerular diseases progresses faster to ESKD than CKD caused by tubulointerstitial diseases.

1.3 Measuring albuminuria

Background

Excretion of albumin or protein in urine varies remarkably throughout the day. Furthermore, albumin or protein concentration in urine is inversely related to the concentration of the urine, which in turn is dependent on the fluid status of the person.

Supporting Evidence

Persistent albuminuria or proteinuria irrespective of how measured is associated with adverse kidney and cardiovascular outcomes. The associations with these adverse outcomes are more profound and more precise with albuminuria compared to proteinuria and with albuminuria/proteinuria when measured using timed collection of urine or expressed in relation to urine creatinine concentration in first morning urine voids. These associations are more profound and precise when:

- a) Albuminuria rather than proteinuria levels are used
- b) Timed urine samples are used for measurement of albuminuria or proteinuria
- c) First or early urine samples are used and results expressed in urine albumin/creatinine.^{5,9,10}

Albuminuria is AER ≥ 30 mg/24 hours, ACR ≥ 0.03 mg/mg, while proteinuria is PER > 150 mg/24 hours, protein-creatinine ratio (≥ 0.15 mg/mg) or dipstick proteinuria $\geq 1+$

Recommendations

- 1.3.1 We recommend that albuminuria should be determined using (1.) either albumin excretion rate (AER) in timed urine or (2.) albumin-creatinine ratio (ACR) in first morning urine sample.

Quality of evidence - Moderate

Recommendation - Strong

- 1.2.1 When this is not feasible, we recommend that albuminuria should be determined using spot urine ACR, protein-creatinine ratio or dipstick proteinuria.

Quality of evidence - Moderate

Recommendation- Strong

1.4 Estimation of GFR

Background

Although the gold standard for measuring GFR is inulin clearance, this is not feasible in routine clinical practice. The impractical nature of inulin clearance has spurred quest for other means of determining GFR. One of such means is creatinine clearance which entails collection of urine over 24 hours. Others include the use of estimation formulae. In adults the common formulae include Cockcroft-Gault (CG) equation, 4-variable Modification of Diet in Renal Disease (MDRD) and the recent Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation. In children aged < 18 years the bedside Schwartz formula is the most used.

Supporting Evidence

The 2009 CKD-EPI formula shows less bias, better precision and higher accuracy than the 4-variable MDRD formula especially in those with eGFR > 60 ml/1.73 m². The better performance of the CKD-EPI formula over the CG and MDRD formulae has been demonstrated in North America, Europe, among Korean and in Black Africans.^{1,11,12} An observational study without a gold standard measure of GFR in Nigeria showed that the 4-variable MDRD formula underestimated GFR compared with the CKD-EPI formula.¹³

Recommendations

- 1.4.1 We recommend that in both children and adults serum creatinine should be transformed to estimated GFR using the appropriate formula when diagnosing and classifying severity of CKD.

Quality of evidence - Moderate

Recommendation - Strong

- 1.4.2 We recommend that GFR should be calculated using the CKD-EPI formula In adults ¹¹, rather than assessing kidney function using the serum creatinine values only

Quality of evidence - Moderate

Recommendation - Strong

CKD-EPI creatinine formula:

$$eGFR = 141 \times \min(S_{Cr}/K, 1)^{-1.209} \times 0.993^{Age} \times 1.018 [\text{if female}] \times 1.159 [\text{if Black}]$$

Where K = 0.7 (females) or 0.9 (males); $\alpha = -0.329$ (females) or -0.411 (males); min = indicates the minimum of S_{Cr}/K or 1; max = indicates the maximum of S_{Cr}/K or 1

- 1.4.3 We recommend that the GFR should be calculated using the Schwartz formula¹⁴ in children aged 0-18 years rather than using the serum creatinine values only. Furthermore, we recommend that a constant, k, of 0.413 should be used for all children irrespective of age or sex.

Quality of evidence - Low

Recommendation - Strong

Schwartz formula:

$$eGFR = 0.413 \times (\text{height}/S_{Cr}) \text{ if height is expressed in centimetre OR } 41.3 \times (\text{height}/S_{Cr}) \text{ if height is expressed in meter}$$

(Serum Cr in mg/dl)

1.5 Screening of for CKD

Background

In most cases, the onset of CKD is insidious until significant kidney function has been lost. When clinical features of kidney damage manifest, opportunities to halt or reverse progression of the kidney disease have substantially diminished. Screening for CKD in any adult/at-risk population is advocated and deemed cost effective when CKD is common, it is a significant cause of morbidity and mortality, has a long latency period before severe stages manifest and has potential for reversibility or halting the progression exists. Chronic kidney disease in Nigeria satisfies all the characteristics above; indeed, the benefits of screening may be higher in Nigerians where access to therapies for advanced stages of CKD are expensive and beyond the reach of many who do not have health insurance coverage. Most people with CKD in Nigeria are only detected when kidney function has been severely depleted. The late detection means lost opportunity to halt further progression and inadequate plan for renal replacement therapy.

Supporting Evidence

Although the US Prevention Task Force posited that there is no randomized controlled trial to support the benefit of screening for CKD in the general population, several large observational studies indicate that CKD screening in the general adult population and those at risk of CKD offer some cost-effective benefits.^{15,16} In contrast to the USA, mass or targeted screening for CKD and adverse cardiovascular events are common in Europe. A major argument against screening for CKD is cost.

How should CKD be Screened?

- 1.5.1 We recommend that in at-risk person, screen for CKD by checking for albuminuria, haematuria and estimating GFR from serum creatinine value

Quality of evidence - Low

Recommendation- Strong

- 1.5.2 We recommend that pregnant women should have late second trimester foetal anomaly scan with comments on the kidneys, bladder and amniotic volume.

Quality of evidence- Moderate

Recommendation- Strong

- 1.5.3 We recommend screening for diabetes mellitus and hypertension in adults

Quality of evidence- Moderate

Recommendation- Strong

Who should be Screened for CKD?

- 1.5.4 We recommend that all persons aged >18 years should be screened for CKD

Quality of evidence- Very low

Recommendation- Weak

- 1.5.5 We recommend that all persons with diabetes mellitus or hypertension, previous history of AKI stage II or III, family history of CKD, SCD, SLE, HIV, HBV or HCV infection irrespective of age, should be screened for CKD

Quality of evidence - Moderate

Strong recommendation

- 1.5.6 We recommend that the following categories of children should be screened for CKD: those born before gestational age of 36 weeks; those born with birth weight <2500 g; those with antenatal diagnosis of CAKUT; or those with perinatal asphyxia, and other at-risk individuals.

Quality of evidence - Low

Weak recommendation

- 1.5.7 We recommend that adults with obesity should be screened for CKD

Quality of evidence - Low

Weak recommendation

How Frequently should CKD Screening be Performed?

- 1.5.8 We recommend that in adults, CKD screening should be done every 1-3 years if the last one was negative

Quality of evidence - Low

Weak recommendation

1.6 Haematuria

Background

Haematuria is a common finding in progressive glomerulonephritis and together with proteinuria is a strong marker of glomerular damage. However, dipstick urinalysis for blood tests for the presence of globin in the urine. Hence, myoglobin and hemoglobin will equally give a positive blood test on urine dipstick even in the absence of haematuria.

Recommendation

- 1.6.1 We recommend that haematuria detected by urine dipstick should be confirmed by microscopy of freshly voided urine sample

Quality of evidence - Low

Weak recommendation

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SECTION II: MANAGEMENT OF CHRONIC KIDNEY DISEASE

Introduction

The aim of this section is to provide guidelines on the management of pre-dialysis CKD mainly those in KDIGO stages G3 - G5 not on dialysis. The guidelines specifically cover the evaluation, management of progression and complications of CKD recommend institution of measures that will retard the progression of CKD. It also covers timing of referral to a Nephrologist, multi-disciplinary approach to care, patient education and preparation for renal replacement therapy. Early diagnosis of CKD is not made and institution of measures to retard its progression are not in place in most of our patients because of late presentation. Bearing these in mind, this section highlights all the important aspects of what constitutes conservative management of CKD.

Practice points are a new addition to KDIGO guidelines and may be organized as a table, a figure or an algorithm. They are consensus statements about a specific aspect of care, and supplement recommendation for which a larger quality of evidence was identified. Practice points in this updated guideline represent the expert opinion of the Guidelines Review Team and are based on our limited evidence in this environment.

GOALS OF CONSERVATIVE MANAGEMENT OF CKD

- Educate patient about the aetiology and natural history of the disease
- Education on strategies to prevent progression of the disease
- Preparation for renal replacement therapy

2.1 Patient counselling and psychosocial issues

Background

It is important that the patients and their carers have access to reliable and relevant information about the disease and treatment options. This enables them to participate fully in the decision-making processes, and to make informed choices about kidney replacement therapy (KRT); these educational programmes should take place in specialized clinics.[1] Timely referral to the nephrologist is very important as it provides the opportunity to monitor the progression of CKD, institute measures to retard progression, proper management of complications such as anaemia, hypertension, dyslipidemia, glycaemic control, nutrition, CKD-MBD, as well as allowing for planning of RRT.

Supporting Evidence

The available evidence suggests that, in addition to improving patient knowledge and understanding [2-5], pre-dialysis education confers many additional advantages such as: an improved sense of well-being, enhanced mood, reduced levels of anxiety and better physical functioning⁶. Regular clinical reviews are recommended by most guidelines as there is evidence that progression of CKD may be prevented or slowed significantly with frequent measurement of serum creatinine, instituting strict blood pressure control, strict glycaemic control in patients with diabetes mellitus and the use of RAS blockers in patients with proteinuria.

Recommendations

- 2.1.1 We recommend that all patients in CKD stages 3 - 5, together with their families and carers, should be offered an appropriate educational programme aimed at improving their knowledge and understanding of their condition, and to help them choose from the options for treatment. The educational information should be relevant to the person, in terms of the cause of the disease, stage of the disease and the treatment options available to them
Quality of evidence - Moderate Recommendation - Strong

- 2.1.2 We recommend that this educational programme should be extended to all those who commence

CATEGORIES OF PATIENTS FOR EARLY REFERRAL TO NEPHROLOGIST

- Patients with acute kidney injury (AKI) or abrupt or sustained fall in GFR (acute on chronic)
- Patients with $\text{eGFR} < 60 \text{ ml/min/1.73m}^2$ i.e. **GFR stages G3-G5**
- Patients with significant albuminuria (overt proteinuria) $\text{ACR} \geq 300 \text{ mg/g}$ ($\geq 30 \text{ mg/mmol/L}$ or $\text{AER} \geq 300 \text{ mg/24 hours}$)
- Individuals with progression of CKD (see definition of progression)
- Individuals with abnormalities of serum potassium
- Hereditary kidney disease e.g. ADPKD, CAKUT
- Individuals with recurrent kidney stones or extensive stone disease

renal replacement therapy in an unplanned fashion (Crashlanders)

Quality of evidence - Low

Recommendation - Strong

- 2.1.3 We recommend that the following class of people should be referred early to the Nephrologist for specialist care:
Quality of evidence - Moderate Recommendation - Strong

Definition: Rapidly deteriorating renal function is defined as a reduction in eGFR of $> 5 \text{ ml/min/1.73m}^2$ per year

- 2.1.4 We recommend that patients with $\text{eGFR} < 30 \text{ ml/min/1.73m}^2$ should undergo regular clinical review at least every 1-3 months; the reviews should include measurement of eGFR , ACR (or urine dipstick in situation where ACR is not readily available or accessible), haemoglobin, serum calcium, phosphate, potassium, bicarbonate and dietary assessment. Serum parathyroid hormone should be assessed annually. Frequency of monitoring should be individualized as this will guide therapeutic decisions.
Not graded

- 2.1.5 The frequency of nephrology follow-up should be increased when eGFR has fallen $< 15 \text{ ml/min/1.73m}^2$ if dialysis treatment has not commenced. These short follow-up visits will allow for close monitoring and initiation of dialysis at the appropriate time
Quality of evidence - Very low Recommendation - Weak

2.2 General Conservative Management of CKD

Background

This section describes the key recommendations and guidance for institution of measures to delay progression of CKD and commencement of conservative management. General lifestyle recommendations are provided including care for patients with diabetes. Cardiovascular risk reduction strategies including management of hypertension, dyslipidemia, and hyperuricemia are further addressed. A multi-disciplinary team approach is ideal. It is important to institute general lifestyle modification practices in people with CKD so that they may gain the benefit of these in addition to more kidney-specific strategies. Often these general measures are overlooked or disregarded in people with CKD, thus their utility is underscored here.

Supporting Evidence

The goal of conservative management of CKD is to retard progression, prevent and treat complications and delay the initiation of KRT for as long as possible. Observation studies and systematic reviews and meta-analysis have demonstrated the benefits and cost saving approach of the conservative management of CKD [7,8]. The institution of low protein diet of high biological values tailored to individual patients' requirement have been shown to retard CKD progression and prevent early development of uraemic symptoms[9]. Adequate control of hypertension, dyslipidaemia and lifestyle modifications have also been shown to retard CKD progression [10].

GENERAL CONSERVATIVE MANAGEMENT OF CKD

- Identify and treat underlying cause if possible and intercurrent illness
- Weight management
- Optimize nutrition in undernourished patients to achieve ideal BMI
- Cessation of smoking
- Avoidance of nephrotoxic agents such as NSAIDs, COXIBs, aminoglycosides, radiocontrast agents and herbal preparations
- Adjust doses of all medications as appropriate for patients' GFR
- Dynamic exercise such as brisk walking/treadmill, jogging, swimming, cycling for 30-45 minutes at least 3 times a week
- Low salt diet (2g daily)
- Low protein diet (0.6-0.8g/Kg body weight per day)
- Control of hypertension to target as per guidelines
- Control of blood glucose in diabetics to target
- Treatment of hyperlipidemia to target as per guidelines

Recommendations

- 2.2.1 We recommend that clinicians should take into account GFR when prescribing medications in CKD patient. The doses of all medications should be adjusted as appropriate for patients' GFR.
Quality of evidence - High Recommendation - Strong
- 2.2.2 We recommend that all potentially nephrotoxic drugs and those excreted via the kidneys should be monitored/avoided in patients with GFR < 60ml/min/1.73m²(CKD stage 3a - 5). These agents include but not limited to NSAIDs, COXIBs, aminoglycosides and other nephrotoxic drugs
Quality of evidence - Low Recommendation - Strong
- 2.2.3 We recommend that patients with CKD should not use herbal remedies/medications.
Quality of evidence - Moderate Recommendation - Strong
- 2.2.4 We suggest that the risk of acute kidney injury due to contrast agent use should be weighed against the diagnostic value and therapeutic implications of the investigation (Risk-benefit ratio)
Not graded

- 2.2.5 We recommend that all patients with $\text{GFR} < 60 \text{ ml/min/1.73 m}^2$ (CKD stages 3a - 5), undergoing elective investigation or procedure involving the administration of iodinated radiocontrast media should be managed according to standard guidelines for prevention of contrast-induced AKI as shown in the box below.
- Avoidance of high osmolar agents
Quality of evidence - Moderate Recommendation - Strong
 - Adequate hydration with saline before, during and after the procedure
Quality of evidence - Moderate Recommendation - Strong
 - Withdrawal of any potentially nephrotoxic agents before, during and after the procedure
Quality of evidence - Moderate Recommendation - Strong
 - Measurement of GFR 48 -96 hours after the procedure
Quality of evidence - Low Recommendation - Strong
 - Use the lowest possible radiocontrast dose Not graded
- 2.2.6 We recommend that Gadolinium-containing contrast media should not be used in patients with $\text{GFR} < 15 \text{ ml/min/1.73 m}^2$ unless there is no alternative appropriate test.
Quality of evidence - Moderate Recommendation - Strong
- 2.2.7 We suggest that patients with a $\text{GFR} < 30 \text{ ml/min/1.73 m}^2$ (GFR categories G4-G5) who require gadolinium containing contrast media are preferentially offered a macrocyclic chelate preparation.
Quality of evidence - Moderate Recommendation - Weak
- 2.2.8 We recommend that oral phosphate-containing bowel preparations should not be used in patients with a $\text{GFR} < 60 \text{ ml/min/1.73 m}^2$ (GFR categories G3a-G5).
Quality of evidence - High Recommendation - Strong.
- 2.2.9 We recommend lower salt intake to $< 90 \text{ mmol} (< 2 \text{ g})$ per day of sodium (corresponding to 5 g of sodium chloride) in adults, unless contraindicated.
Quality of evidence - Moderate Recommendation - Strong.

PRACTICE POINT ON SALT RESTRICTION FOR BP CONROLS

Salt restriction is usually not appropriate for patients with salt-losing nephropathy e.g. chronic tubulointerstitial diseases. Furthermore, anecdotal observation from some centres have revealed that an increasing number of patients with kidney failure coming with severe symptomatic hyponatremia. Therefore, this recommendation should be individualized.

- 2.2.10 We recommend that CKD patients should maintain a healthy weight ($\text{BMI } 20 - 25 \text{ kg/m}^2$)
Quality of evidence - Very low Recommendation - Strong
- 2.2.11 We suggest that patients with high BP and CKD should undertake moderate-intensity physical activity (such as brisk walking, dancing, and other aerobic exercises) for a total duration of at least 150 minutes per week, (30 minutes 5 times a week) or to a level compatible with their cardiovascular and physical tolerance

Quality of evidence - Low

Recommendation - Weak

PRACTICE POINTS ON EXERCISE RECOMMENDATION FOR PATIENTS WITH CKD

In making this recommendation, it is important to consider the followings:

- The cardio-respiratory fitness of the patient (i.e. how fit the patient is)
- If there are any physical limitations (disabilities)
- Any risk of falls
- Cognitive function
- The form and intensity of the physical activity should be individualized.

- 2.2.12 We recommend that individuals with CKD receive expert dietary advice and information in the setting of an education program, tailored to the severity of CKD and the need to intervene on salt, phosphate, potassium, and protein intake where indicated.

Quality of evidence - Moderate

Recommendation - Strong

Areas that require further research

1. The role of locally available protein of high biological values (e.g., Soya Beans) in CKD.
2. Role of physiotherapy in retarding CKD progression.

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2.3 Identification and treatment of primary disease and underlying cause of chronic kidney disease

2.3.1 Glomerulonephritis

Background

The glomerulonephritides are a group of renal disorders characterised by intra-glomerular inflammation due

to cytopathic, immunologic, or mixed renal injuries that manifest clinically as haematuria, proteinuria, hypertension, oedema, azotaemia or a combination of these manifestations [1]. Glomerulonephritis (GN) remains a leading cause of chronic kidney disease (CKD) in children and is among the top three leading causes of CKD in adults in Nigeria [2]. Glomerulonephritis can be primary or secondary, and the spectrum of clinical manifestations varies from asymptomatic haematuria \pm proteinuria to rapidly progressive renal failure. Irrespective of the pattern of renal injury, focused clinical evaluation with careful selection of investigations is key to early diagnosis for prompt and appropriate intervention in settings where management of end-stage renal disease is a daunting task [3,4]. This section provides an update on the NAN 2010 clinical practice guidelines on the management of glomerulonephritis.

Supporting Evidence

The evidence bases for the definition of terms, flow charts and recommendations were from multicentre randomized control trials including but not limited to the Euro-Lupus Nephritis Trial, Aspreva Lupus Management Study (ALMS), the MAITAIN nephritis trial, observational studies, the 2012 KDIGO guidelines on management of CKD, a combination of paediatric guidelines and Ibadan consensus guidelines for management of childhood nephrotic syndrome. Also, evidence obtained from systematic reviews and meta-analysis as referenced in the appropriate sections provided bases for the contextualized synthesis of information to upgrade this section of the 2011 NAN guidelines for CKD management.

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Definition of terms and evaluation of glomerulonephritis

Table 1a. Definition of terms

Terms	Definition
Haematuria	A dipstick urinalysis of trace or more confirmed by the presence >5 red blood cell per high power field (RBC/hpf).
Nephrotic-range proteinuria	Children : UPr/UCr ≥ 200 mg/mmol (2 mg/mg) in first morning void or 24 h urine sample ≥ 1000 mg/m ² /day or >50 mg/kg/day, or >40 mg/m ² /hr corresponding to 3+ or 4+ by urine dipstick Adult: proteinuria ≥ 3.5 g/d, UPr/UCr ≥ 300 mg/mmol (3mg/mg)
Nephrotic syndrome	Children: Nephrotic-range proteinuria and either hypoalbuminemia (serum albumin <25 g/l or < 30 g/l) or oedema when serum albumin level is not available with or without hyperlipidaemia (Cholesterol >220 mg/dl)
Steroid sensitive nephrotic syndrome:	Complete remission within 4 weeks of prednisone or prednisolone at the standard dose (60 mg/m ² /day or 2 mg/kg/day, maximum 60 mg/day).
Steroid resistant nephrotic syndrome:	Lack of complete remission 6-8 weeks of treatment with prednisolone at the standard dose

Complete remission:	UPr/UCr (based on first morning void or 24 h urine sample) \leq 20 mg/mmol (0.2 mg/mg) or negative or trace dipstick on three or more consecutive occasions.
Partial remission	UPr/UCr (based on first morning void or 24 h urine sample) $>$ 0.20 but $<$ 2 and, if available, serum albumin \geq 25g/l or 30 g/l.
Relapse	Recurrence of nephrotic-range proteinuria. In children, relapse is commonly assessed by urine dipstick and is thus defined as dipstick \geq 3+ on 3 consecutive days, or UPCR \geq 200 mg/mmol (2 mg/mg) on a first morning urine sample, with or without reappearance of oedema in a child who had previously achieved partial or complete remission.
CNI-resistant	SRNS Absence of at least partial remission after 6 months of treatment with a CNI at adequate doses and/or levels.
Multi-drug-resistant SRNS:	Absence of complete remission after 12 months of treatment with 2 mechanistically distinct steroid-sparing agents at standard doses (see text).
Secondary steroid resistance	Initial steroid-sensitivity who in subsequent relapses develop SRNS

Definitions are adapted from the 2012 KDIGO guidelines, IPNA guidelines and the Ibadan consensus guideline for management of steroid resistant nephrotic syndrome [5].

Recommendations

2.3.1.1 We recommend dipstick urinalysis and urine microscopy be used as initial screening tests for suspected glomerulonephritis.

Quality of evidence - Very low

Recommendation - Weak

PRACTICE POINT FOR SCREENING AND REFERRAL BY PRIMARY CARE PHYSICIAN

- Primary care physician should triage patients with glomerulonephritis and refer those with both priority and emergent features as shown in table 2.

2.3.1.2 We recommend quantitative analysis of proteinuria with spot urine protein to creatinine ratio (UPr/UCr) for initial evaluation and subsequent monitoring of patients at follow-up (first morning urine is preferred and 24-hour urinary protein excretion may be requested when indicated).

Quality of evidence - High

Recommendation - Strong

2.3.1.2 We recommend measurement of serum electrolytes, urea and creatinine, serum albumin levels, a

lipid profile, and imaging study such as ultrasound renal ultrasound.

Quality of evidence - Low

Recommendation - Weak

2.3.1.3 We recommend assay for C3, C4, anti-double stranded DNA, anti- glomerular basement membrane (GBM), and anti-neutrophil cytoplasmic antibody (ANCA) when there is renal manifestation of a systemic disease.

Quality of evidence - Low

Recommendation - Weak

Table 2: Spectrum of clinical presentation and triage

Glomerulonephritis		Spectrum of clinical presentation					
		Nephritic syndrome		Nephrotic syndrome		Nephritic /Nephrotic syndrome	
Clinical features	Proteinuria	Dipstick UPr/UCr	-	±/+	++	+++	+++
			<0.1 mg/mg	0.1-0.2 mg/mg	0.2-2.0 mg/mg	>2.0 mg/mg	>2.0 mg/mg
	Haematuria		trace	++	+++	-	±/+
	Hypertension		Absent	‡	‡	‡	‡
	Oedema		Absent	‡	‡	‡	‡

UPr/UCr, Urinary protein/urinary creatinine ratio; - = negative; ± = trace; + = positive. ‡ = present or absent. **Note:** the presence and severity of oedema and or hypertension increases the need for urgent referral for specialist care. Repeat urinalysis is advocated for individual with only trace haematuria and further evaluation should be contextualised.

2.3.2 Steroid sensitive nephrotic syndrome (SSNS) in children

Recommendations

2.3.2.1 We recommend oral prednisolone for initial treatment of SSNS for at least 16 weeks.⁷ (IBC)

Quality of evidence - Moderate

Recommendation - Strong

2.3.2.2 We recommend a single morning daily dose of 60 mg/m²/d or 2 mg/kg/d to a maximum of 60 mg/d of prednisolone for initial treatment of SSNS.

Quality of evidence - Moderate

Recommendation - Strong

2.3.2.3 We recommend that the initial episode of NS be treated with oral prednisone at 60mg/m²/day (maximum 60 mg) as single morning daily dose for 6 weeks, followed by 40mg/m² (maximum 40 mg) prednisolone on alternate days for another 6 weeks (figure 1). Prednisolone should thereafter be tapered at the rate of 10 mg/m²/week to 5 mg on alternate days (total cumulative dose of 3595mg/m² for a total of 16 weeks). As the lowest dose available is 5 mg tablets, not suspension, we recommend all doses to be rounded to up to 5 mg accordingly and if at the lowest dose of 5 mg, maintain it until the end of the 16th week.^{5, 7}

Quality of evidence - Low

Recommendation - Strong

2.3.3 Infrequent relapses

2.3.3.1 Recommend a single morning daily dose of prednisolone at 60mg/m² or 2mg/kg (maximum of 60 mg/d) until the child achieves complete remission for at least 3 days. Thereafter, we recommend that a child continue with 40mg/m² or 1.5mg/kg (maximum 40 mg) for one week, then taper by 10 mg/m²/day per week to complete a total of 4 weeks.

Quality of evidence - Low

Recommendation - Weak

2.3.4 Frequent relapses (FR) and steroid dependent (SD)

- 2.3.4.1 We recommend a single daily dose of 60mg/m² or 2mg/kg (maximum of 60 mg/d) of prednisolone be administered to children with FR or SD until complete remission for at least 3 days then switch to alternate day's dose of 40 mg/m²/d for 12weeks (figure 1). Subsequently, the child should be maintained on the lowest tolerable alternate day dose. However, where alternate maintenance dose is not effective, the lowest daily dose is recommended while observing for side effect and toxicity.

Quality of evidence - Low

Recommendation - Weak

- 2.3.4.2 We recommend continuation of alternate day prednisolone in a child with upper respiratory tract infection or other infection to reduce the risk of relapse. Prophylactic dose of prednisolone is not recommended for children with FR or SD who develop malaria.

Quality of evidence - Very low

Recommendation - Weak

- 2.3.4.3 We recommend continuation of alternate day prednisolone in a child with upper respiratory tract infection or other infection to reduce the risk of relapse. Prophylactic dose of prednisolone is not recommended for children with FR or SD who develop malaria

Quality of evidence - Very low

Recommendation - Weak

Steroid-sparing agents for FR and SD nephrotic syndrome

- 2.3.5.1 We recommend levamisole as the first line steroid-sparing agent at 2.5 mg/kg alternate-day (ranges from 1.5 mg/kg to 4 mg/kg) for at least 6 months to determine effectiveness, and use for up to 24 months if effective, allowing for repeated courses.

Quality of evidence - Moderate

Recommendation - Strong

- 2.3.5.2 We recommend monthly monitoring of white blood cell count as mild to moderate reversible neutropenia are not uncommon side effect of medication.

Quality of evidence - Very low

Recommendation - Weak

- 2.3.5.3 We recommend cyclophosphamide as the second line steroid-sparing agents for FR and SD nephrotic syndrome. We recommend either oral cyclophosphamide for a maximum of 12 weeks (total cumulative dose of 168 mg/kg) or intravenous cyclophosphamide 500 mg/m²/dose (maximum dose of 750mg) given monthly for a maximum of 4 - 6 months.

Quality of evidence - Very low

Recommendation - Weak

- 2.3.5.4 We suggest close monitoring, with complete blood counts within 2 weeks of therapy, and every 4 weeks thereafter. For intravenous cyclophosphamide, we recommend complete blood counts within 1- 2 weeks of therapy, and before each infusion.

Quality of evidence - Very low

Recommendation - Weak

- 2.3.5.5 We do not recommend repeated courses of cyclophosphamide.

Quality of evidence - Very low

Recommendation - Weak

- 2.3.5.6 We recommend cyclosporine at a median dose of 3 mg/kg (3-5mg/kg) in two divided doses daily for a minimum of 6 months to assess response but up to 24 months if there is at least partial response Tacrolimus may be a useful alternative to cyclosporine.

Quality of evidence - Moderate

Recommendation - Strong

- 2.3.5.7 We recommend monthly serum creatinine measurements and if possible, cyclosporine 12-hour trough level monitoring targeting 50-100 ng/ml. The peak level could also be utilized.

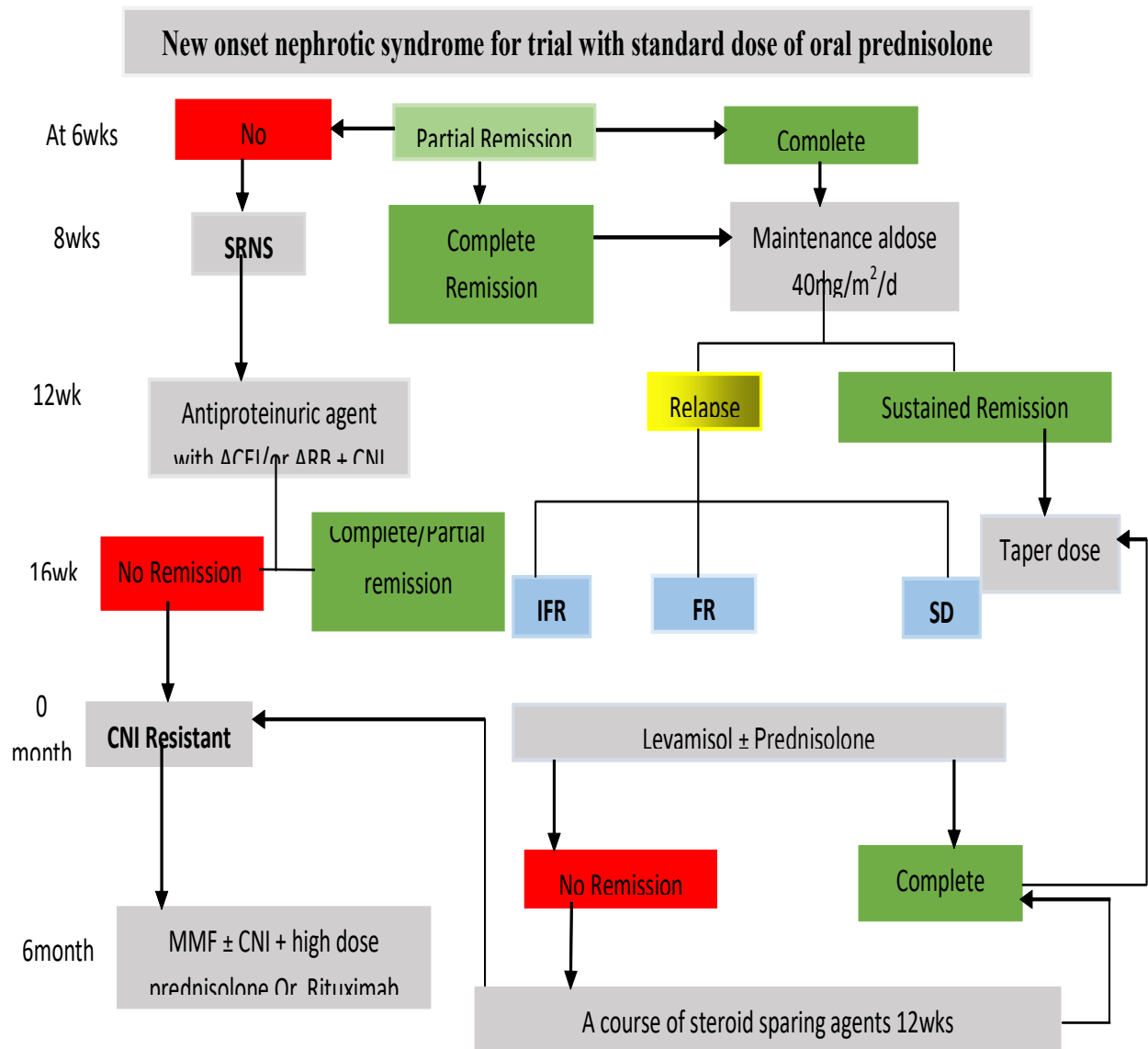
Quality of evidence - Moderate

Recommendation - Strong

2.3.5.8 2.3.7.8 We recommend a kidney biopsy if a child relapses after discontinuation of cyclosporin prior to re-initiating cyclosporine to assess for nephrotoxicity.

Not graded

2.3.5.9 We recommend mycophenolate mofetil (MMF) at a dose of 600 mg/m²/day in two divided doses



with a minimum trial of 6 months to determine responsiveness and continue up to 24 months of therapy when other steroid-sparing agents have failed.

Quality of evidence - Low

Recommendation - Weak

2.3.5.10 We recommend that repeated courses with MMF can be used.

Quality of evidence - Very low

Recommendation - Weak

2.3.5.11 We recommend monthly monitoring of white blood count.

Quality of evidence - Very low

Recommendation - Weak

Figure 1: The schematic diagram above shows a treatment algorithm for the management of new onset nephrotic syndrome. Standard dose refers to 60mg/m²/d for 6weeks while maintenance dose implies 40mg/m² alternate days for 6weeks. SRNS: Steroid resistant nephrotic syndrome, SD; steroid dependent nephrotic syndrome, FR; frequent relapses nephrotic syndrome, IF; infrequent relapses nephrotic syndrome, CNI; calcineurin inhibitors, CP; cyclophosphamide, ACEI; angiotensin converting enzyme, ARB;

angiotensin receptor blockers, MMF; mycophenolate mofetil.

2.3.6 Evaluation of children with steroid resistant nephrotic syndrome

2.3.6.1 We recommend that a child should complete 8 weeks of corticosteroid therapy to establish SRNS except if the corticosteroid is not tolerated (figure 1). However, patients should be evaluated in the confirmatory period (4-8weeks)

Quality of evidence - Very low

Recommendation - Weak

2.3.6.2 We recommend that a child with SRNS should have a diagnostic kidney biopsy, evaluation of kidney function by GFR or eGFR and quantification of urine protein excretion and genetic testing where available.

Quality of evidence - Not graded

Recommendation - Strong

2.3.7 Treatment of children with steroid resistant nephrotic syndrome

2.3.7.1 We recommend treatment with ACEI or ARBs for children with SRNS (preferably those not mainly excreted by the kidney (e.g., ARBs or ramipril)

Quality of evidence - Moderate

Recommendation - Strong

2.3.7.2 We recommend cyclosporine at a median dose of 3 mg/kg (3-5mg/kg) in two divided doses daily for a minimum of 6 months to assess response but up to 24 months if there is at least partial response.

Quality of evidence - Moderate

Recommendation - Strong

2.3.7.3 We recommend that corticosteroid be gradually tapered to 40mg/m² for 4 weeks, then 30mg/m² for 4 weeks, then 20mg/m² for 4 weeks, and finally 10mg/m² for 8 weeks

Quality of evidence - Very low

Recommendation - Weak

2.3.7.4 We recommend monthly serum creatinine measurements and if possible, cyclosporine 12-hour trough level monitoring targeting 50-100 ng/ml.

Quality of evidence - Not graded

Recommendation - Weak

2.3.7.5 We recommend not starting CNI if eGFR is < than 30ml/min/1.73m², AKI is present and uncontrolled hypertension.

Quality of evidence - Not graded

Recommendation - Weak

2.3.7.6 We recommend either oral cyclophosphamide (if CNI is not available) for a maximum of 12 weeks (total cumulative dose of 168 mg/kg) or intravenous cyclophosphamide 500 mg/m²/dose (maximum dose of 750mg) given monthly for a maximum of 4 months.

Quality of evidence - Very low

Recommendation - Weak

2.3.7.7 We recommend a kidney biopsy if a child relapse after discontinuation of cyclosporin prior to re-initiating cyclosporine to assess for nephrotoxicity.

Quality of evidence - Not graded

Recommendation - Weak

2.3.7.8 We recommend mycophenolate mofetil (MMF) at a dose of 600 mg/m²/day in two divided doses with a minimum trial of 6 months to determine responsiveness and continue up to 24 months of therapy when other steroid-sparing agents have failed.

Quality of evidence - Low

Recommendation - Weak

2.3.7.9 We recommend that MMF be used for children with eGFR <30ml/min/1.73m² because it is less nephrotoxic compared with the CNIs.

Quality of evidence - Not graded

Recommendation - Weak

2.3.7.10 We recommend that repeated courses with MMF can be used.

Quality of evidence - Very low

Recommendation - Weak

2.3.7.11 We recommend monthly monitoring of white blood count.

Quality of evidence - Very low

Recommendation - Weak

2.3.7.12 We recommend Rituximab at 375mg/m² (1-2 infusion within 2 weeks) if no partial remission is achieved with CNIs.

Quality of evidence - Not graded

Recommendation - Weak

2.3.7.13 We recommend that mycophenolate mofetil, high-dose corticosteroid or a combination of these agent be considered in children who fail to achieve complete or partial remission with CNIs and corticosteroids.

Quality of evidence - Not graded

Recommendation - Weak

PRACTICE POINT: INDICATION FOR RENAL BIOPSY AND RECOMMENDED IMMUNIZATION IN CHILDREN WITH NEPHROTIC SYNDROME

Indications for renal biopsy in children*

- We recommend renal biopsy when there is resistance to steroid, resistant nephrotic syndrome primary or secondary
- A secondary or genetic cause of nephrotic syndrome
- When there is decreasing kidney function in children receiving CNIs.

Immunization for children with SSNS*

- We recommend that children with SSNS should receive pneumococcal vaccine
- We recommend that children with SSNS defer live vaccine until they are on prednisolone at a dose of 1mg/kg or < 20mg/d.
- We recommend that immunization with live vaccine is contraindicated in children on corticosteroid-sparing agents

**The quality of evidence is not graded but these interventions are strongly recommended*

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2.4 Membranous nephropathy

Background

Idiopathic Membranous Nephropathy(MN) is the most common type of glomerulonephritis (GN) in adults globally representing between 20% and 37% in most series and rising to as high as 40% in adults aged over 60 years.[1,2] It is specifically the most common cause of nephrotic syndrome in white adults.[3] It should however be noted that MN is not commonly seen in children and is reported in 1% - 7% of biopsies.[4]

Spontaneous remission occurs in approximately 30% of affected patients and among patients who continue to have nephrotic syndrome, end-stage renal disease develops in 40% to 50% over a period of 10 years.[5] A total of 70% to 80% of patients with MN have circulating auto-antibodies to the phospholipase A2 receptor (PLA2R), 1% to 3% have circulating antibodies to thrombospondin type-1 domain-containing 7A (THSD7A) while in the remaining patients, the target antigen is unknown.[6,7] In patients with anti-PLA2R antibodies, there is a tight correlation between antibody levels and disease activity suggesting a causal relationship.[6,8-10]

Supporting Evidence

Although renal biopsy remains the gold standard for the diagnosis of renal pathology, the accuracy of the antibodies against the biomarker PLA2R(PLA2Rab) has downplayed the need for biopsy in diagnosing MN in individuals with clinical features suggestive of MN [11].

B-cell's central role in disease pathogenesis, both as precursors of auto-antibody cells and as antigen presenting cells, has provided the rationale for B-cell depleting therapies [12]. Several case reports, cohort studies and randomized trials including GEMRITUX randomized trial and the MENTOR trial (Membranous Nephropathy Trial of Rituximab) have demonstrated the safety and efficacy of rituximab in MN; they report significantly higher complete remission rates at 24 months [13,14]. The results of other randomized trials such as STARMEN (tacrolimus-rituximab vs methylprednisolone-cyclophosphamide) and RI-CYCLO (rituximab vs steroids and cyclophosphamide) are being awaited which may change the mode of treatment of MN. In arriving at our recommendations, the peculiarities and challenges of our practice setting were put into consideration¹⁸. The clinical management of MN in these guidelines are discussed beginning with diagnosis, induction therapy, maintenance therapy, management of relapse and management of resistant disease.

DIAGNOSIS OF MEMBRANOUS NEPHROPATHY IN ADULTS

- A kidney biopsy is ideally required for confirmation of the diagnosis of MN but where serological markers are available, kidney biopsy may not be needed to confirm the diagnosis of MN in patients with compatible clinical and serological presentation**

Table 3: Risk stratification for membranous glomerulonephritis and investigations which should include screening for secondary causes such as HBV, HCV and

Low Risk	Moderate Risk	High Risk*	Very High Risk
<ul style="list-style-type: none"> • Patients should be assessed with clinical and laboratory criteria for risk of progressive loss of kidney function 	<ul style="list-style-type: none"> • Patients should be assessed with clinical and laboratory criteria for risk of progressive loss of kidney function 	<ul style="list-style-type: none"> • Patients should be assessed with clinical and laboratory criteria for risk of progressive loss of kidney function 	<ul style="list-style-type: none"> • Patients should be assessed with clinical and laboratory criteria for risk of progressive loss of kidney function
Normal e-GFR, proteinuria <3.5g/d and/ or serum albumin >30g/L	Normal e-GFR, proteinuria >4g/d and no decrease in kidney function	e-GFR < 60ml/min/1.73m ² Life threatening nephrotic syndrome.	Life threatening nephrotic syndrome.
Quality of evidence: ***	Quality of evidence: **	Quality of evidence: *	Quality of evidence: *
conservative therapy with ACEi/ARB	conservative therapy with ACEi/ARB	conservative therapy with ACEi/ARB	conservative therapy with ACEi/ARB
PLA2Rab <50 RU/ml	PLA2Rab <50 RU/ml	PLA2Rab >150 RU/ml	PLA2Rab >150 RU/ml
Mild low molecular weight proteinuria.	Mild low molecular weight proteinuria.	High low molecular weight proteinuria	High low molecular weight proteinuria
Selectivity index <0.15	Selectivity index <0.15	d Selectivity index >0.20	d Selectivity index >0.20
U IgG <250mg/d	U IgG <250mg/d	U IgG >250mg/d	U IgG >250mg/d

2.4.1 Treatment of membranous nephropathy in adults

Recommendations

2.4.1.1 We recommend that supportive care is indicated in patients with primary MN and proteinuria and this should be mainly antihypertensives and anti-proteinuric therapy.
Quality of evidence - Low Recommendation - Strong

2.4.1.2 We recommend that immunosuppressive therapy should be restricted to patients considered to be at risk for progressive kidney injury.
Quality of evidence - Low Recommendation - Strong

RISK-ASSESSMENT BASED TREATMENT FOR MEMBRANOUS NEPHROPATHY

- Low risk MN: Immunosuppressive therapy not required if proteinuria <3.5g/d and eGFR > 60ml/min/1.73m²).
- Moderate to very high risk: Immunosuppressive therapy (IT) is indicated in patients with MN, Nephrotic syndrome and at least one risk factor for disease progression or patients with serious complications of nephrotic syndrome such as AKI, infections and thromboembolic phenomena.
- Moderate risk: May require no IT; Calcineurin inhibitor (CNI) for 6months. However, CNI monotherapy reportedly less efficient Rituximab
- High risk: CNI Cyclophosphamide or Rituximab (Probably except in patients with disappearance of PLA2Rab)
- Very high risk: Cyclophosphamide
- Overall Treatment Recommendation: It is recommended that patients with MN and at least one risk factor for disease progression use rituximab or cyclophosphamide and steroids for six months, or a tacrolimus-based therapy for at least 6 months, with the choice of treatment based on risk estimate.

The risk assessment-based treatment is based on high quality evidence with strong recommendation

2.4.2 Monitoring of treatment of membranous nephropathy

Recommendations

2.4.2.1 Monitor PLA2Rab at 3 and 6 months after commencement of treatment to evaluate response to and adjustments of treatment. (Reduction of 50-90% of PLA2Rab is considered as a large decrease).
Quality of evidence - Moderate Recommendation - Strong

2.4.2.2 Persistent or increasing high titres after the use of CNI, rituximab and addition of cyclophosphamide may be considered a resistant disease.
Quality of evidence - Moderate Recommendation - Strong

2.4.2.3 Proteinuria and serum Albumin should also be monitored.
Quality of evidence - Moderate Recommendation - Strong

2.4.3 For initial relapse

Definition of Relapse: An increase in proteinuria >3.5g/day in patients who previously achieved a partial or complete remission.

Recommendations

2.4.3.1 Relapse after an initial response to rituximab: repeat rituximab.
Quality of evidence - Moderate Recommendation - Strong

2.4.3.2 Relapse after an initial response to CNI: Rituximab CNI
Quality of evidence - Moderate Recommendation - Strong

2.4.3.3	Relapse after an initial response to cyclophosphamide. Cyclophosphamide, rituximab + CNI	CNI
	Quality of evidence - Moderate	Recommendation - Strong
2.4.3.4	When indicated, Cyclophosphamide therapy can be repeated, but the cumulative dose should not exceed 10g if patient's fertility is to be preserved and to reduce risk of malignancy; cumulative dose should not exceed 25g. In children the maximum dose is 168mg/kg.	
	Quality of evidence - Low	Recommendation - Weak

2.4.4 Management of Resistant Disease

DEFINITION OF RESISTANT DISEASE

- MN is defined as resistant disease if the protein excretion decreased to values between 2 and 3.5 g/day without an increase of serum albumin to normal; the subsequent rise in protein excretion should be considered a resistant disease.
- A patient in clinical remission whose PLA2Rab remains positive is considered to have resistant disease.

Recommendations

2.4.4.1 For initial treatment with Rituximab + stable e-GFR give CNI+ Rituximab if no response after three months give Cyclophosphamide.

Not graded

2.4.4.2 For initial treatment with Rituximab + decreasing e-GFR give Cyclophosphamide.

Not graded

2.4.4.3 For initial treatment with CNI + Stable e-GFR give Rituximab and if no response after 3 months give Cyclophosphamide.

Not graded

2.4.4.4 For initial treatment with CNI + decreasing e-GFR give Cyclophosphamide.

Not graded

2.4.4.5 For initial treatment with Cyclophosphamide + Stable e-GFR give Rituximab and if no response after 3 months repeat Cyclophosphamide.

Not graded

2.4.4.6 For initial treatment with Cyclophosphamide + decreasing e-GFR repeat Cyclophosphamide, if resistant consult a Specialist.

Not graded

2.4.4.7 At Specialist Centres experimental therapies and higher doses of conventional immunosuppressive therapy can be administered.

Not graded

2.4.5 Management of Children with Membranous Nephropathy

Recommendations

2.4.5.1 Perform a kidney biopsy.

Not graded

2.4.5.2 Watchful waiting strategy in children with supportive therapy alone is not usually adopted.

Not graded

2.4.5.3 Children with MN are usually treated with prednisolone for at least 8-12 weeks at same doses used for idiopathic nephrotic syndrome.

Not graded

2.4.5.4 Should exclude secondary forms most frequently chronic HBV, systemic lupus erythematosus, rarely neoplasia.

Not graded

2.4.5.5 If affordable, measure PLA2Rab and THSPD7Aab titers; positive titres can be used to confirm remission and predict relapse.

Not graded

2.4.5.6 Children with MN should be treated in an Expert Centre.

Not graded

2.4.5.7 If serum albumin is >20g/L using Bromocresol purple(BC Purple) or >25g/L using Bromocresol green(BC Green) but the serum albumin is < 30g/L using BC Purple or < 32g/L using BCGreen then no need for Aspirin.

Not graded

2.4.5.8 If serum albumin is <30g/L using BCPurple and <32g/L using BCGreen you should estimate arterial thromboembolic event risk, if low risk no need for aspirin, if high risk give Aspirin.

Not graded

2.4.5.9 If serum albumin is <20g/L using BCPurple and <25g/L using BCGreen note that patient is at high risk of thromboembolic phenomena, assess bleeding risk, if high commence aspirin if low give Warfarin or low molecular weight heparin + aspirin.

Not graded

Table 4: Commonly used treatment regimens for MN with their dosages

Cyclophosphamide (Cyclical)	<ul style="list-style-type: none"> - Methylprednisolone 1gm i.v. for 3 consecutive days at start of month 1,3 and 5 - Prednisolone 0.5 mg/kg/d in months 1,3 and 5 - Cyclophosphamide 2.5 mg/kg/d orally in months 2,4 and 6 	Quality of evidence - High	Recommendation - Strong
Cyclophosphamide (continuous)	<ul style="list-style-type: none"> - Methylprednisolone 1gm i.v. for 3 consecutive days at start of month 1.3 and 5 - Prednisolone 0.5 mg/kg/d every other day in months 1-6, with taper thereafter - Cyclophosphamide 1.5 mg/kg/d orally in months 1-6 		Not graded
Rituximab	<ul style="list-style-type: none"> - Rituximab 1 gm i.v. administered twice within 2 weeks - Rituximab 375 mg/m² given 1-4 times at weekly intervals 	Quality of evidence - High	Recommendation - Strong
Tacrolimus	- Tacrolimus 0.05-0.1 mg/kg/d, target trough level 3-8 µg/ml, duration 12 months		Not graded
Cyclosporine	- Cyclosporine 3.5 mg/kg/d, target trough level 125-225 µg/ml		

Not graded

NOTE: Cyclosporine and tacrolimus are often given in combination with prednisone in a dose of 10 mg/day.

- Intravenous cyclophosphamide might be considered with patients with normal eGFR, in whom the cumulative dose of cyclophosphamide should be used.
- Mycophenolate mofetil is not discussed, the 2012 KDIGO guideline argued against the use of MMF monotherapy in patients with MN.

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2.5 Minimal change disease (MCD) in adults

Background

Minimal change disease (MCD) accounts for 10% to 25% of adult nephrotic syndrome¹⁻³ and could be idiopathic (primary) or secondary. This diagnosis in adults can only be established with a kidney biopsy. Supportive therapy should be given to all while immunosuppressive therapy should be given to patients with primary disease. The mainstay of treatment for adult MCD is oral glucocorticoids and this practice is based on a few randomized controlled trials and extensive observational data in adults⁴. Treatment with corticosteroids results in remission in over 80% of cases and corticosteroid-sensitive MCD is associated with good prognosis.

DEFINITION OF TERMS IN ADULTS WITH NEPHROTIC SYNDROME

- **Complete remission:** Reduction of proteinuria to <0.3 g/day or urine protein: creatinine ratio <300 mg/g (or <30 mg/mmol), stable serum creatinine and serum albumin >3.5 g/dl (or 35 g/l)
- **Partial remission:** Reduction of proteinuria to 0.3-<3.5g/day or urine PCR 300-<3500 mg/g (or 30-<350mg/mmol) and a decrease >50% from peak value
- **Relapse:** Recurrence of nephrotic range proteinuria [>3.5 g/day or urine PCR > 3500 mg/g (or 350 mg/mmol)] after remission has been achieved
- **Corticosteroid-resistant MCD:** Failure to achieve <50% reduction of proteinuria from baseline or persistence of nephrotic range proteinuria in spite of using prednisone at 1mg/kg/day or 2 mg/kg every other day for > 16 weeks.
- **Frequently relapsing MCD:** Having two or more relapses per 6 months (or four or more relapses per 12 months).
- **Corticosteroid-dependent MCD:** Relapse occurring during, or within 2 weeks of completing corticosteroid therapy.

2.5.1 Diagnosis of MCD in adults

2.5.1.1 Kidney biopsy mandatory in making the diagnosis of MCD

Quality of ev New onset minimal change disease in adult

2.5.1.2 Detailed history, thorough physical examination and screening required to rule out secondary causes of MCD

Quality of evidence - Low

Renal biopsy proven minimal change disease n - Strong

TREATMENT

OF ADULT MCD

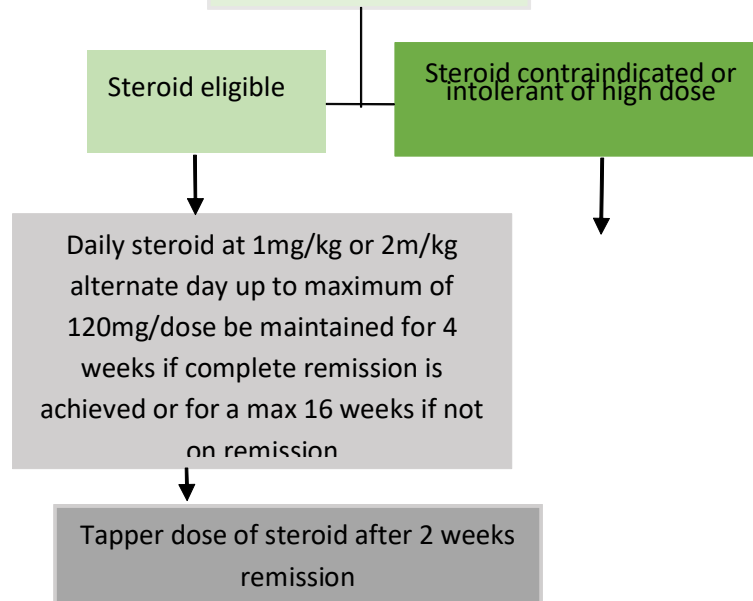


Figure 2. Treatment of initial episode of adult MCD

(In patients who go into remission we suggest that corticosteroids be tapered slowly over a total period of up to 6 months after achieving remission. (2D) Begin tapering of steroids two weeks after remission with reduction of 5mg every 2 weeks or 10 mg every month (KDIGO 2020 & Okpechi and Ameh 2018)

2.5.2 Treatment of relapses and steroid dependence in adults

2.5.2.1 Infrequent Relapses: We suggest using the same dose and duration of corticosteroids for the initial therapy.

Quality of evidence - Low

Recommendation - Weak

2.5.2.2 Frequent Relapses (FR)/Steroid Dependent (SD) MCD: We suggest oral cyclophosphamide 2-2.5 mg/kg/d for 8 weeks for those not previously treated with Cyclophosphamide and those who have

not indicated other preferences.

Quality of evidence -Low

Recommendation - Weak

- 2.5.2.3 Cyclophosphamide can be repeated in adults but the cumulative dose should not exceed 10g if fertility is to be preserved and to reduce risk of malignancy; cumulative dose should not exceed 25g.

Quality of evidence - Low

Recommendation - Weak

- 2.5.2.4 We suggest CNI (cyclosporine) 3-5 mg/kg/d or tacrolimus 0.05-0.1 mg/kg/d in divided doses) for 1-2 years for FR/SD MCD patients who have relapsed despite cyclophosphamide or for people who wish to preserve their fertility.

The CNI therapy should target a trough level of 125-225ng/ml for Cyclosporine and trough levels of 3-8ng/ml for tacrolimus. The peak level may also be used.

Quality of evidence - Low

Recommendation - Weak

- 2.5.2.5 We suggest MMF 500-1000 mg twice daily/ sodium mycophenolate for 1-2 years as alternative for patients who are intolerant of corticosteroids, cyclophosphamide, and CNIs.

Quality of evidence - Low

Recommendation - Weak

- 2.5.2.6 Rituximab is a candidate medication for steroid dependent MCD and could be considered in multiple relapses.

Quality of evidence - Low

Recommendation - Weak

2.5.3 Corticosteroid-resistant MCD

- 2.5.3.1 Re-evaluate patients who are corticosteroid-resistant for other causes of nephrotic syndrome like FSGS.

Not Graded

- 2.5.3.2 Treatment of steroid-resistant MCD should follow same suggestions and recommendations as 4.3.4 subsection (FSGS steroid-resistant)

Not Graded

2.5.4 Supportive therapy

- 2.5.4.1 We suggest that MCD patients who have AKI be treated with renal replacement therapy as indicated, but together with corticosteroids, as for a first episode of MCD.

Quality of evidence - Low

Recommendation - Weak

- 2.5.4.2 We suggest that, for the initial episode of nephrotic syndrome associated with MCD, statins should not be used to treat hyperlipidaemia, and ACE-I or ARBs should not be used in normotensive patients to lower proteinuria.

Quality of evidence - Low

Recommendation - Weak

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2.6 Focal Segmental Glomerular Sclerosis (FSGS)

Background

Focal segmental glomerular sclerosis (FSGS) is the most common primary glomerular histologic lesion associated with ESKD.¹ It accounts for 40% of cases of nephrotic syndrome in adults and 20% in children. It has numerous causes with varied clinical presentations.

Supporting Evidence

Several factors have been shown to predict poor outcome in FSGS these include black race, degree of proteinuria, presence of renal insufficiency, collapsing histologic variant, degree of interstitial fibrosis/tubular atrophy (IFTA), resistance to treatment and male sex. Additionally, patients with primary FSGS are said to fare worse when compared to those with adaptive/secondary causes of FSGS.

2.6.1 Management of primary focal segmental glomerulosclerosis in adults for the initial evaluation of FSGS

2.6.1.1 Kidney biopsy is mandatory for diagnosis of FSGS

Quality of evidence -High

Recommendation - Strong

2.6.1.2 Ensure thorough clinical, laboratory and radiologic evaluation to exclude secondary causes of FSGS which include viral infections, drug-induced disease, systemic disorders and conditions associated with reduced nephron number.

Not Graded

2.6.1.3 Proteinuria and serum albumin should be quantified to enable stratification into FSGS with and FSGS without nephrotic syndrome

Quality of evidence -Low

Recommendation - Strong

2.6.1.4 Where appropriate and possible, consider genetic testing especially in view of drug treatment, kidney transplantation, prognostication and prevention.

Quality of evidence -Low

Recommendation - Strong

2.6.3 Initial treatment of FSGS

Table 6: For the initial treatment of FSGS

	We recommend that corticosteroid and immunosuppressive therapy be given only to patients presenting with primary FSGS and the nephrotic syndrome
	Quality of evidence -Low Recommendation - Strong
Corticosteroid therapy FSGS	We suggest that prednisolone be given at a daily single dose of 1 mg/kg (maximum 80 mg) or alternate-day dose of 2 mg/kg (maximum 120 mg).
	Quality of evidence -Low Recommendation - Weak
	We suggest that the initial high dose of corticosteroids be given for a minimum of 4 (6) weeks; and the high-dose corticosteroids continued for up to a maximum of 16 weeks, as tolerated, or until complete remission has been achieved, whichever is earlier.
	Quality of evidence -Low Recommendation - Weak

Treatment of steroid intolerance or contraindication in adult with FSGS

Recommendations

- 2.6.3.1 We suggest that calcineurin inhibitors (CNIs) be used as first-line therapy for patients with relative contraindications or intolerance to high-dose corticosteroids (e.g. in uncontrolled diabetes mellitus, psychiatric conditions, severe osteoporosis) at doses and target trough levels stated for Steroid resistant FSGS.

Quality of evidence - Low

Recommendation - Strong

2.6.4 Treatment of relapse FSGS

Recommendation

- 2.6.4.1 We suggest that a relapse of nephrotic syndrome is treated in line with the recommendations for relapsing MCD in adults as in 2.3.96.

Quality of evidence - Low

Recommendation - Strong

2.6.5 Treatment of steroid-resistant FSGS

Recommendations

- 2.6.5.1 For steroid-resistant FSGS, we suggest that cyclosporine at 3-5 mg/kg/d in 2 divided doses be given for at least 6 months.

Quality of evidence - High

Recommendation - Strong

- 2.6.5.2 If there is a partial or complete remission, we suggest continuing cyclosporine treatment for at least 12 months, followed by a slow taper. The recommended target trough level for cyclosporine is 100-175ng/ml (2D) The dose of cyclosporine or tacrolimus can be slowly tapered over a course of 6-12 months as tolerated.

Quality of evidence - Low

Recommendation - Strong

- 2.6.5.3 Tacrolimus can be used in place of cyclosporine in steroid resistant FSGS at a dose of 0.05-0.1mg/kg/day in 2 divided doses with a target trough level of 5-10ng/ml.

Quality of evidence - High

Recommendation - Strong

- 2.6.5.4 For the duration of determining CNI efficacy: Cyclosporine should be continued at doses achieving target trough level for at least 6 months, before considering the patient resistant to CNI treatment.

Not Graded

- 2.6.5.5 We suggest that patients with steroid-resistant FSGS, who do not tolerate CNIs, be considered for treatment with a combination of mycophenolate mofetil and high-dose dexamethasone.

Not Graded

- 2.6.5.6 We recommend rituximab for patients who have failed more than one of the recommended initial regimens and management for such patients should be at a Specialist Centre.

Not Graded

2.6.6 Management of FSGS without nephrotic syndrome/secondary FSGS

- 2.6.6.1 We suggest that patients are evaluated for an underlying cause, exclude secondary and genetic forms of FSGS. Immunosuppressives are not needed. Give Supportive therapy. Monitor proteinuria and serum albumin, and if nephrotic syndrome sets in, treat in line with recommendations for FSGS with the Nephrotic syndrome

Quality of evidence - Low

Recommendation - Strong

2.6.7 Supportive therapy for patients with the nephrotic syndrome

Among the general measures used in the management of individuals with nephrotic syndrome are: use of diuretics for oedema, vaccination to prevent infections, and anticoagulation for those at a high risk of venous thrombosis. Some of these have been handled under general management for CKD. Treatment of the specific causes of glomerular disease is important to reduce further damage to the kidneys (e.g., the use of anti-viral agents for hepatitis B and C and HIV infection). One of the challenging aspects of managing an individual with nephrotic syndrome is resistant oedema and the suggested line of management is as shown below:

Management of oedema in the nephrotic syndrome

Recommendations

2.6.7.1 We suggest the use of loop diuretics as first line therapy for the management of oedema in adult nephrotic syndrome. Twice daily dosing is preferred over once daily dosing; daily may be acceptable for reduced GFR and it is advised that dose be increased to cause clinically significant diuresis or until maximally effective dose has been reached.

Not Graded

2.6.7.2 We suggest that treatment be changed from frusemide to torsemide/torsemide or bumetanide if treatment fails or if concerned about oral drug bio-availability.

Not Graded

2.6.7.3 We suggest that dietary sodium intake be restricted to <2.0 g/d (<90 mmol/d).

Not Graded

2.6.7.4 For the treatment of resistant oedema in the nephrotic syndrome, we suggest the use of thiazide-like diuretics and/or mineralocorticoid antagonists in combination with loop diuretics and sodium restriction for their synergistic effect.

Not Graded

2.6.7.5 Monitor for adverse effects of diuretics such as hyponatraemia with thiazide diuretics, hypokalaemia with thiazide and loop diuretics, impaired GFR, volume depletion, especially in paediatric/elderly patients.

Not Graded

2.6.7.6 In diuretic-resistant patients consider the use of the following: amiloride, acetazolamide, intravenous loop diuretics (bolus or infusion) alone or in combination with IV. albumin, intravenous mannitol and intravenous loop diuretics in children, ultrafiltration or haemodialysis.

Not Graded

Identified research areas

1. Genetic testing for in patients with FSGS comparing those with steroid-sensitive and those with steroid-resistant FSGS.
2. Compare efficacy of alternate day steroid therapy with daily treatment after 6-8 weeks of daily high-dose steroid therapy
3. Drug trials for steroid resistant nephrotic syndrome (rituximab vs CNI and low dose steroids)

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2.7 Lupus Nephritis

Management of Lupus Nephritis

Background

Up to 1 in 3 patients with features of systemic lupus erythematosus develop lupus nephritis (LN), the presence of which predicts morbidity and mortality particularly in patients of African descent.⁸⁻¹⁰ In contrast to observations in high-income countries, patients in our settings often present late with multiple complications ~~making both diagnosis and treatment more challenging at the backdrop pre-existing risk for worse outcomes [11, 12]. The aim of this sub-section is to provide guidelines for the management of LN with intended~~ outcomes of complete or partial response through judicious selection of therapeutic options targeting minimal side effect. These guidelines, therefore, summarise the diagnostic steps and adopt the treatment modalities for adults with LN in the context of limited resources. They also provide a guide to the management of paediatric patients with lupus nephritis.

Table 7: Definition of terms for lupus nephritis

Terms	Definition
No kidney response	<ul style="list-style-type: none"> Failure to achieve partial or complete response within 6-12 months of starting therapy
Partial response	<ul style="list-style-type: none"> Reduction in proteinuria by at least 50% or <3g/g measured UPr/UCr in a 24 hour urine sample if there was nephrotic range proteinuria or 0.2-2.0 in a first morning sample Stabilisation or improvement in kidney function within 10-15% of baseline All between 6-12 months of initiating treatment
Complete response	<ul style="list-style-type: none"> Reduction in proteinuria to <0.50 g/g measured UPr/UCr in a 24 hour urine sample or < 0.2 in a spot urine sample Return of kidney function to baseline All between 6-12 months of initiating treatment but may exceed 12 months

Note: Proteinuria remains the most important variable to define clinical response usually assessed at 6-12 months. Early morning UPr/UCr ratio is preferred to spot sample otherwise, estimation from 24 hour urine collection is the gold standard. Baseline (the presenting eGFR).

2.7.1 Diagnosis of SLE and Lupus Nephritis

Recommendations

- 2.7.1.1 We recommend that the American College of Rheumatology diagnostic criteria for SLE be used alongside auto-antibodies strongly associated with lupus nephritis in individuals of African descent (anti-Sm, anti-Ro and anti-ribonucleoprotein antibodies) at presentation.⁸ Following initial screening of SLE for makers of kidney injury at presentation, similar evaluations should be carried at episodes

of flares or yearly in those not previously diagnosed with LN.

Not graded

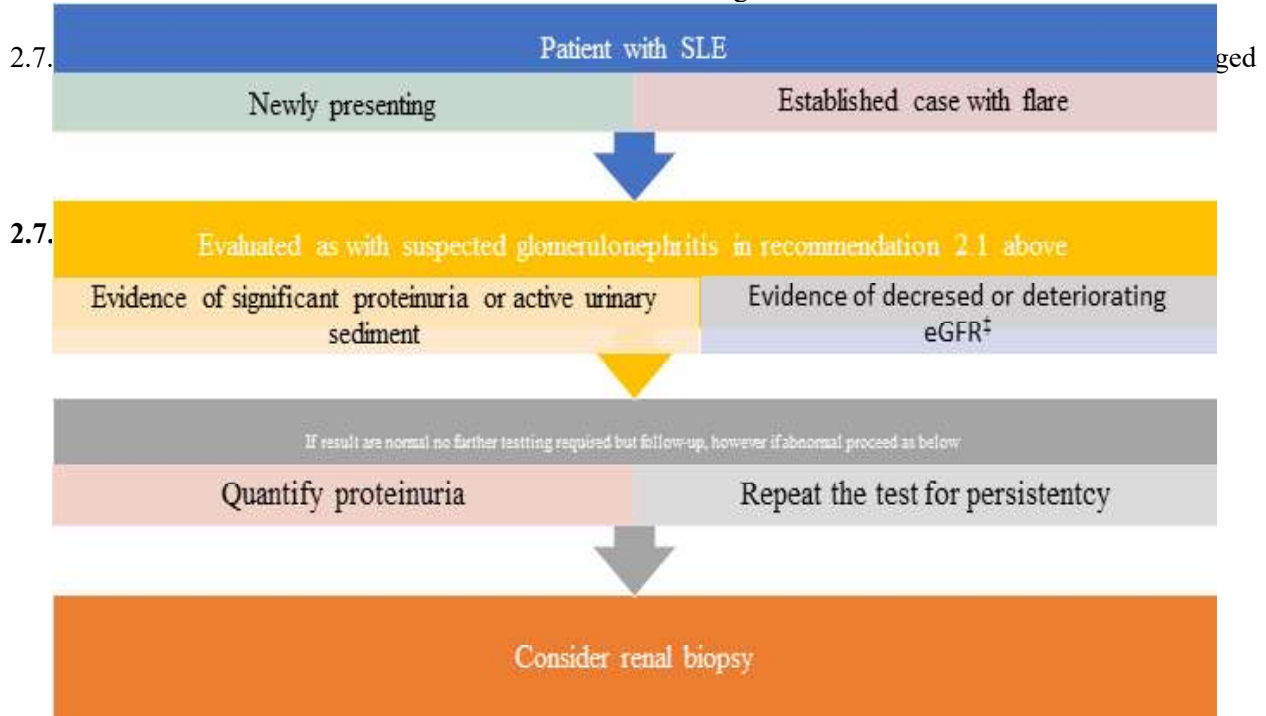


Figure 3: Diagnostic approach to Lupus nephritis

SLE Systemic lupus erythematosus, significant proteinuria: Dipstick proteinuria of $\geq 2+$ irrespective of specific gravity or dilute urine of $\geq 1+$ or UPr/UCr ratio of > 0.5 . Active urinary sediment refers to acanthocytosis of $\geq 5\%$, red or white cell cast. Deteriorating eGFR[‡]: decreased GFR of $< 60 \text{ ml/min/1.73m}^2$ or reduction in GFR of 40% or more from baseline attributable to SLE. First morning urine is preferred for spot urine protein creatinine excretion.*

RECOMMENDATIONS

- In view of the poor correlation that exists between clinical features of LN and the extent of severity of the renal injury on renal biopsy, we suggest that kidney biopsy, the gold standard remains a critical

component for diagnosis, assessing disease activity and chronicity. This is not only useful for prognosticating but also to provide evidence-based information interventions.

- We suggest that the International Society of Nephrology and the Renal Pathology Society classification system and the National Institute of Health (NIH) activity and chronicity scoring indices (Table 3.) be used in reporting the biopsy in LN. Clinicians should pay considerable attention to the subtle acute versus chronic irreversible features in decision making.

Table 8. Lupus Nephritis modified activity and chronicity scoring index

Patterns of injury based on NIH activity scoring Index (0 to 24)	The percentage of glomeruli involvement	Score
Endocapillary hypercellularity		0-3
Neutrophils and/or karyorrhexis	Non=0	0-3
Fibrinoid necrosis	<25% =1	(0-3)x2
Hyaline deposit (wire loop lesions and/or hyaline thrombi)	25%-50% =2 >50% =3	0-3
Cellular/fibrocellular crescents		(0-3)x2
Interstitial leukocytes		0-3

Patterns of injury based on NIH chronic scoring Index (0 to 12)	The percentage of glomeruli involvement	Score
	Non=0	0-3
Total glomerulosclerosis	<25% =1	0-3
Fibrous crescents	25%-50% =2	0-3
Tubular atrophy	>50% =3	0-3
Interstitial fibrosis		0-3

NIH = National Institute of Health

Supportive treatment

- Practice point 2.7.2a We suggest that a glucose-6-phosphate dehydrogenase assay be done for male patients before initiation of hydroxychloroquine. Similarly, baseline retinal examination and annual check be carried out in patients on long term treatment. If the estimated glomerular filtration rate (eGFR) falls below 30ml/min/1.73m², hydroxychloroquine dose should be adjusted to a quarter of the recommended dosage.
- Practice point 2.7.2b All treatment modalities for attenuation of kidney disease progression as outlined in this section apply to patients with LN including the recommendation for cardiovascular risks adjustment such as lifestyle modification, exercise, no smoking, reduction in alcohol intake, lipid-lowering and use of low dose aspirin during pregnancy and bone mineral disease.
- Practice point 2.7.2c We suggest that LN patients be screened for HBV, HCV, HIV and age and sex and specific cancers in view of the side effect of the immunosuppressive.

- Practice point 2.7.2d We suggest that they should be given H. Influenza vaccine, 32-valent pneumococcal vaccine and recombinant zoster vaccine as preventive measures against their susceptibility to these infections as a result of the profound immunosuppressive therapy
- Practice point 2.7.2e Patients with SLE and LN should use broad spectrum sunscreen and limit exposure to UV light
- Practice point 2.7.2f We suggest individualised evaluation and counselling on contraceptives and that pregnancy be well-planned while on treatment.
- Practice point 2.7.2g We suggest that patients be counselled for premature ovarian failure when on the immunosuppressive and appropriate measure be taken e.g. use of GnRH agonist and storage of sperm prior to commencement of therapy where this is feasible.

2.7.3 Specific Treatments

Recommendation

- 2.7.3.1 We recommend that all patients with LN should be treated with hydroxychloroquine at 5mg/kg /day and a maximum of 400mg/day (chloroquine is structurally similar) or its equivalent antimalarial (Quinacrine) when the former is contraindicated.
Quality of evidence - High Recommendation - Strong

Treatment of class I/II Lupus nephritis

Recommendation

- 2.7.3.2 Patients with class I/II LN with sub-nephrotic range proteinuria do not require specific immunosuppressive therapy for their renal disease. They should be treated with anti-proteinuric agents, diuretic where needed and other treatments for non-kidney lupus. However, for those with nephrotic range proteinuria, fig. 4 shows steps for the management of the disease.

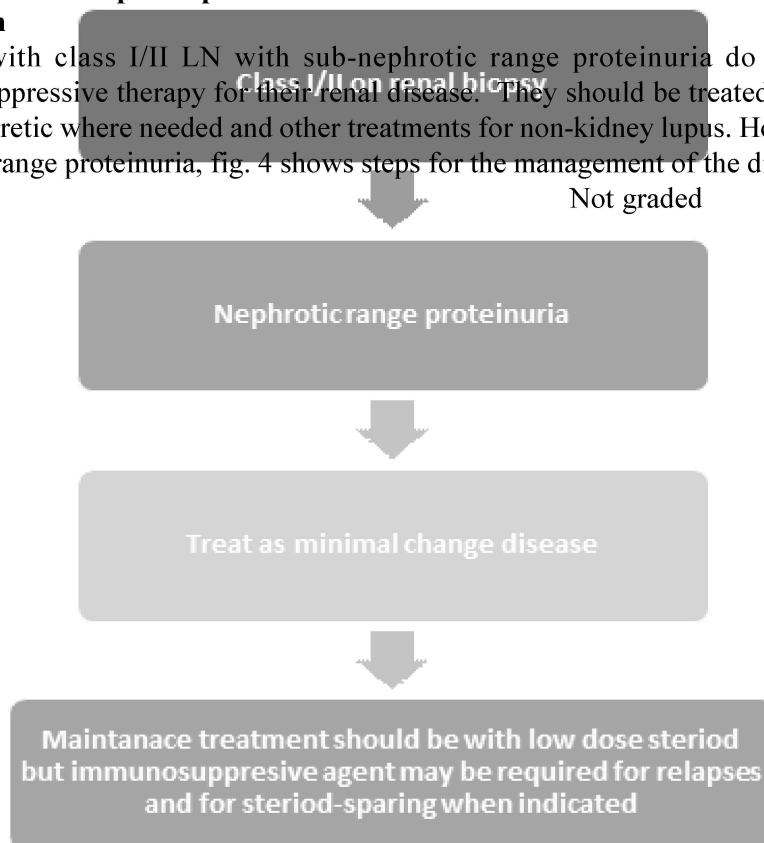


Figure 4. Steps in the treatment of class I/II Lupus nephritis
Class I or class II LN in the presence of sub-nephrotic proteinuria treatment should be guided by the presence of extra-renal manifestations of SLE.

Treatment of LN class III or IV (Induction)

2.7.3.3 We recommend that patients with LN class III or IV pattern of injury should have an initial course of corticosteroid with either low dose cyclophosphamide or mycophenolic acid analogues.

Not graded

Initial course of corticosteroids

Practice point 2.7.3.3a We suggest that the initial pulse dose with methylprednisolone pulses 0.25-0.5 g/day x 3 and subsequent courses of oral prednisolone should not be less than 12 weeks as outlined in figure 2

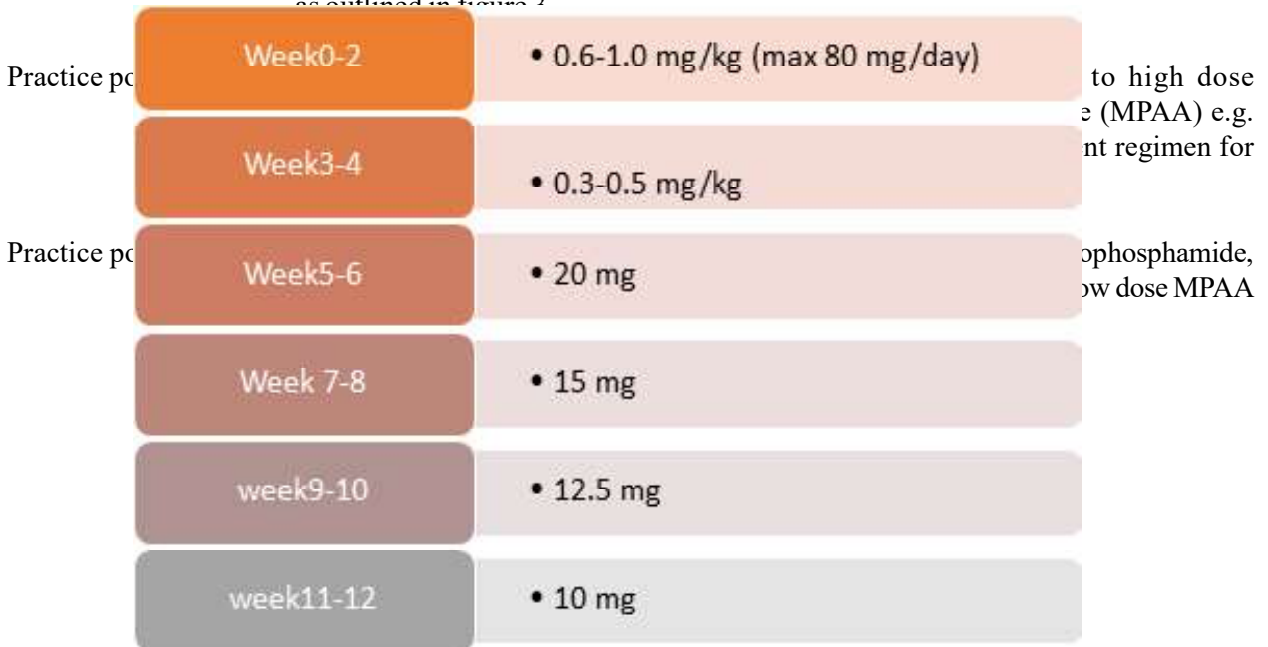


Figure 5: Initial standard-dosage of oral prednisolone for class III or IV lupus nephritis

2.3.7.4 Maintenance therapy for Class III/IV LN

Recommendation

2.7.3.4 We recommend that MPAA-based regimen (e.g., MMF at 1-2g/d) be used as maintenance therapy
 Quality of evidence - High Recommendation - weak

Practice points

- Practice point 2.7.3.4a We suggest azathioprine (1.5-2mg/kg/d) as alternative to maintenance therapy for drug intolerance or inaccessibility to MPAA-based regimen. CNi can be used where azathioprine is also not tolerable.
- Practice point 2.7.3.4b We suggest that the lowest possible dose of steroid should be given for up to 12 months at the maintenance phase and a higher dose may be required temporarily for extra-renal flares.
- Practice point 2.7.3.4c For proliferative LN, a total (initial and maintenance phase) duration 36 months is suggested for complete treatment

2.3.7.5 Treatment

Practice point 2.7.3.4d

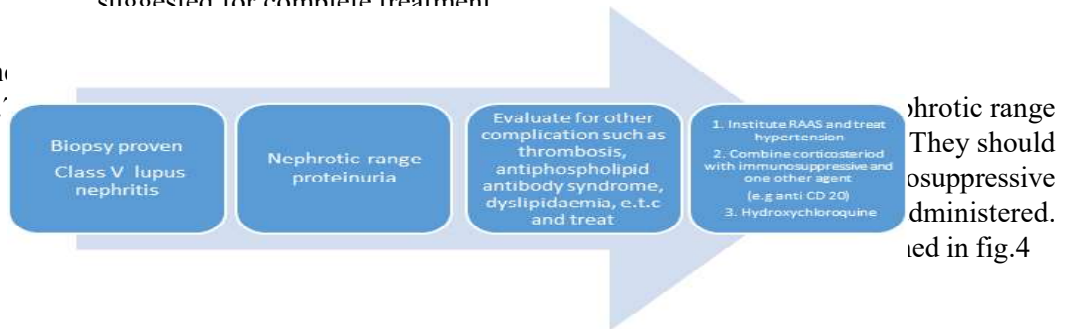


Figure 6. Treatment of Class V lupus nephritis with nephrotic range proteinuria (NAN Guideline revision committee 2020)

Practice point 2.7.3.5b The management of patients with poor treatment response should follow the algorithm shown below

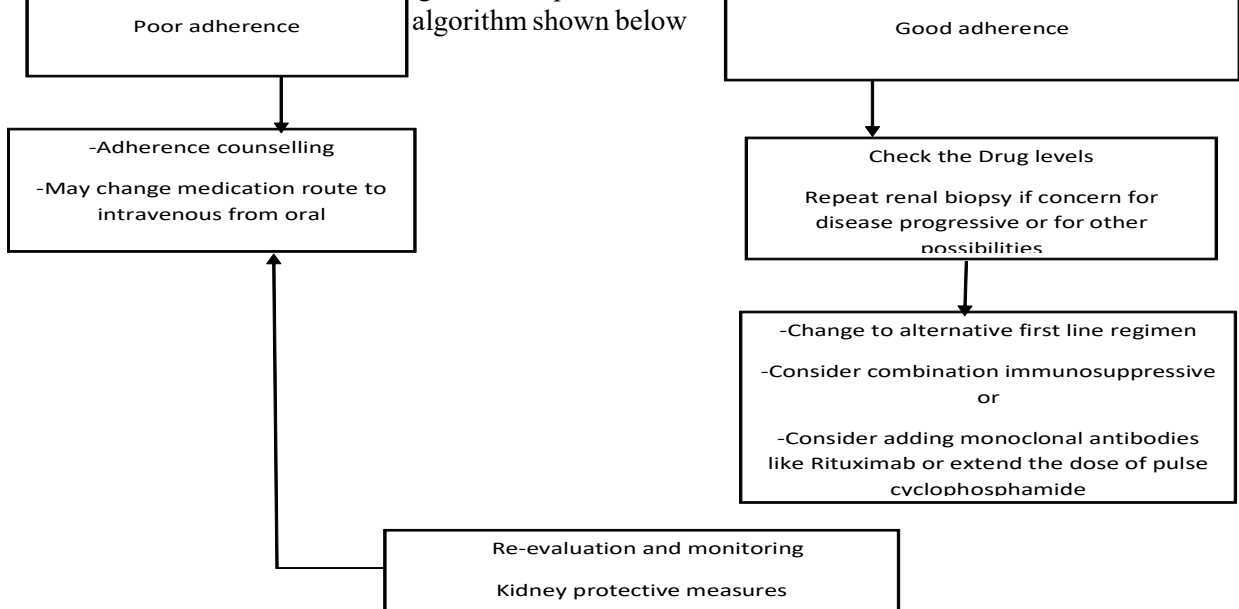


Figure 7: Algorithm for poor treatment response

Patient may require repeat evaluation for proteinuria, renal function and renal biopsy. Kidney protective measures include the use of anti-proteinuric agents such as renin angiotensin aldosterone blockade, angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blockers (ARB), and optimal blood pressure control as done for patients with chronic renal diseases.

2.7.3.6 Treatment of LN in children

Treat paediatric LN patients with immunosuppression similar to regimens used in adults but consider issues relevant to this population, such as dose adjustment, growth, fertility, and psycho-social aspects when designing the therapy plan.

2.7.3.7 Pregnancy and lupus nephritis

Any woman of childbearing age who intends to get pregnant must be in remission for at least 6 months. This is consequent on the deleterious effect of pregnancy state on active lupus nephritis and the disease itself on pregnancy. Such an individual must have been on "pregnancy friendly" medication for at least 3 months to clear the potential mother of possible residual adverse effects of these medications on the conception.

If there are flares, the management of LN in pregnancy can be challenging. Therapeutic options that have been reported to be safe include hydroxychloroquine, azathioprine, IV immunoglobulin, corticosteroid and the CNIs. Hydroxychloroquine has been shown to reduce the frequency of premature birth to 20%, delivery of babies with heart block and significantly reduced disease flares to the barest minimum. A multidisciplinary team is also required to manage these patients.

Kidney biopsy is a safe procedure if performed before 20weeks gestational age.

Conclusion

Management of lupus nephritis is still a challenge not only in resource limited settings but globally despite availability of newer therapeutic molecules and evidence-based treatment protocols generated from randomised control trials.

It is hoped that the development of up-to-date guidelines and their utilisation would provide further evidence for care and shed light on grey areas for further exploration as we await outcomes of other ongoing quality research around the globe.

Identified areas of research

1. We need RCTs among people of African ancestry
2. RCTs using locally sourced molecules

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2.8 MANAGEMENT OF HYPERTENSION IN PRE-DIALYSIS CKD PATIENTS

Background

Hypertension (HTN) is both a cause and effect of CKD and affects the vast majority of patients with CKD.¹ Control of HTN is very important because HTN is a risk factor for CKD progression as well as a major risk factor for CVD [1,2,3]. CVD is a leading cause of death among CKD patients therefore meticulous control of BP is required for slowing down progression of CKD and reducing CVD risk³. Existing guidelines do not offer a consensus on optimal BP targets. Recently, the ACC/AHA hypertension guidelines set a BP of < 130/80mmHg for patients with CKD and those at increased cardiovascular risk [4]. Non-pharmacological measures for treating hypertension are rarely sufficient to control BP. They are usually prescribed in addition to anti-hypertensive medications. Patients with CKD often require combination of anti-hypertensive drugs to achieve target BP.

Supporting Evidence

Adequate control of hypertension among patients with CKD has been shown to retard disease progression and reduce the overall risk of cardiovascular disease [4, 5]. Certain classes of anti-hypertensive drugs provide additional reno-protective and cardio-protective effects beyond lowering BP and must be considered when instituting therapy [5,6]. In addition, direct vasodilators e.g., minoxidil may need to be added to get good BP control.

Recommendations

- 2.8.1 We recommend standardized office BP in preference to routine office BP for the diagnosis and management of high BP in adults.
Quality of evidence - Moderate Recommendation - Strong
- 2.8.2 We suggest that out-of-office BP measurements be used with ambulatory BP monitoring (ABPM) or home BP monitoring (HBPM) to complement standardized office BP readings for the diagnosis and management of high BP
Quality of evidence - Moderate Recommendation - Strong
- 2.8.3 We suggest that adults with CKD and high BP should be treated to a target of SBP < 130mmHg and DBP < 80mmHg using the manual auscultatory devices.
Quality of evidence - Moderate Recommendation - Strong

BLOOD PRESSURE MEASUREMENT

For the management of HTN to be effective, accurate BP essential measurements are required. In practice, the treatment of HTN is based on clinic or office BP readings. There is currently a standardized way of measuring BP taking into consideration proper patient preparation, technique for measurement, measurements and documentation of BP readings. The standardized technique is different from the routine office BP measurements done in most of our clinics. The standardized office BP protocol is consistent with clinical trials and there is moderate quality of evidence that routine office BP is generally higher than standardized office BP regardless of the device used (whether manual or oscillometric).

METHODS OF BLOOD PRESSURE MEASUREMENT

- An oscillometric (automated) BP device may be preferable to a manual BP device for standardized office BP measurement. However, in our environment, due to cost and non-availability of these devices, most centres still use the manual method. We suggest that the standard procedure for BP measurement should be followed even when using these manual devices.
- Automated office BP (AOBP) may be the preferred method of standardized office BP measurement.
- We recommend that only oscillometric devices that have been validated for precision and accuracy against the mercury sphygmomanometer should be used for standardized office BP measurements or home BP monitoring. These devices will require regular recalibration for accuracy

Recommendations

- 2.8.4 We recommend that RAAS blockers (ACEI or ARB) should be used in patients with CKD who have concomitant albuminuria (ACR > 3mg/mmol) and high BP (CKD Stage 1 - 4; Albuminuria A2, A3).
Quality of evidence - Moderate Recommendation - Strong
- 2.8.5 We do not recommend treatment with any combination of ACEI, ARB, and direct renin inhibitor in patients with CKD with or without diabetes.
Quality of evidence - Moderate Recommendation - Strong

BLOOD PRESSURE TARGET

- It is potentially unsafe to apply the recommended SBP target of <120mmHg to BP measurements obtained in a non-standardized way
- Clinicians may consider less intensive BP-lowering therapy to patients with very limited life expectancy or symptomatic postural hypotension due to autonomic neuropathy

USE OF ACE-Is AND ARBs IN CKD

- It is reasonable to use maximally recommended doses of ACEI or ARBs to achieve the benefits described in the clinical trials

- It is advisable to monitor for changes in BP, serum creatinine, and serum potassium within two to four weeks of initiation or increase in the dose of ACEI or ARB
- The dose of ACEI or ARB may be reduced or discontinued if symptomatic hypotension occurs, or there is persistent hyperkalemia despite medical treatment or while preparing for imminent kidney replacement therapy
- Mineralocorticoid receptor antagonists are effective for the treatment of refractory hypertension but they may cause a decline in kidney function and hyperkalemia particularly among patients with low eGFR
- Direct vasodilators e.g. minoxidil is also effective for the treatment of resistant hypertension but ensure patient is on a diuretic and beta blocker as well.

BLOOD PRESSURE MANAGEMENT IN CHILDREN WITH CKD

Recommendation

- 2.8.6 We suggest that in children with CKD, BP should be treated to lower mean 24-mean arterial BP (MAP) by ABPM to less than or equal to the 50th percentile for age, sex, and height.
Quality of evidence - Low Recommendation- Weak

BLOOD PRESSURE TARGET

- It is desirable to monitor BP once a year with ABPM and monitoring every three to six months with standardized auscultatory office BP (**Due to non-availability, ABPM may not be feasible in our environment**)
- Use ACEI or ARB as first-line therapy for high BP in children with CKD. These drugs lower proteinuria and are usually well-tolerated but they carry the risk of hyperkalemia and have adverse fetal risks for pregnant women.

BLOOD PRESSURE MANAGEMENT IN KIDNEY TRANSPLANT RECIPIENTS (CKD G1T - G5T)

Recommendation

- 2.8.7 We recommend that a dihydropyridine calcium channel blocker (CCB) be used as the first-line antihypertensive agent in adult kidney transplant recipients
Quality of evidence - Low Recommendation - Strong

GOALS OF CONSERVATIVE MANAGEMENT OF CKD

Treat adult kidney transplant recipients with high BP to a target BP that is <130 mm Hg systolic and <80 mm Hg diastolic using standardized office BP measurement

Areas that require further research

1. What is the relationship between standardized office BP measurement and routine office BP among CKD patients?
2. What is the relationship between routine office BP measurement and home blood pressure monitoring office BP among CKD patients?
3. What is the correlation between ABPM, standard office BP measurement and home blood pressure measurements in CKD patients
4. Which is the best measurement to use for the monitoring of BP in CKD patients?

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2.9 MANAGEMENT OF CKD MINERAL AND BONE DISORDERS

Background

Mineral and bone disorders are common in CKD and are now collectively referred to as CKD- mineral and bone disorder (MBD). These abnormalities begin to appear even in the early stages of CKD especially from stage 3 1. These alterations are associated with cardiovascular diseases as well as an increase in morbidity and mortality in CKD patients 2.

Definition: A systemic disorder of mineral and bone metabolism due to CKD manifested by either 1 or a combination of the following:

- Abnormalities of calcium, phosphorus, PTH, or vitamin D metabolism
- Abnormalities in bone turnover, mineralization, volume, linear growth, or strength
- Vascular or other soft tissue calcification

Diagnosis: Diagnosis of CKD -MBD should be made by assessing serum levels of calcium, phosphate, PTH, vitamin D and alkaline phosphate

Supporting Evidence

Alterations in the biochemical parameters of CKD-MBD begin in the early stages of CKD. Evidence from large observational studies indicate that mineral abnormalities in CKD-MBD are uncommon in the early stages of CKD stage 1 and 2 and these abnormalities appear in the latter stages [1] . Therefore, it is suggested that the monitoring should commence from stage 3 [3]. In addition, cost of these tests and the logistics of doing these tests especially vitamin D should be taken into consideration.

Justification for inclusion of vitamin D measurements in this guideline includes the fact vitamin D deficiency is common in the CKD population (as a consequence of numerous factors such as reduced sun exposure, reduced skin synthesis, reduced ingestion of foods rich in vitamin D, loss of vitamin D binding protein with proteinuria [1] . Furthermore, vitamin D deficiency may be a cause of early increases in PTH levels⁴. In addition, some observational studies in Nigeria have shown a high prevalence of biochemical abnormalities of CKD-MBD including vitamin deficiency among our CKD patients [5-11].

The measurement of serum calcium, adjusted for albumin concentration, is susceptible to all the problems of inter-assay variation and the use of different formulae for corrected albumin concentration. Calcium should be controlled to avoid symptomatic hypocalcaemia and hypocalcaemia driven stimulation of the parathyroid glands. There is some evidence that, in addition to known associations between hyperphosphataemia and mortality, calcium concentrations have an independent association with relative mortality risk [12,13]. In view of the cardiovascular morbidity associated with CKD-MBD, assessment of calcification of heart valves and blood vessels is therefore reasonable in these patients [3].

These recommendations are made for the management of CKD-MBD in patients with stage 3 - 5D unless otherwise stated

Recommendations

- 2.9.1 We recommend that serum levels of calcium, phosphate, alkaline phosphatase, and PTH, should be assessed beginning in patients with CKD stage 3 and trends in parameters be used rather than a single value
Quality of evidence - Low Recommendation - Strong
-
- 2.9.2 In children, we suggest that such monitoring should begin in CKD stage 2
Quality of evidence - Very low Recommendation - Weak
-
- 2.9.3 The frequency of monitoring of calcium, phosphate and PTH should be based on the CKD stage, rate of CKD progression, the presence and degree of the abnormalities and whether specific treatments have been initiated
Not graded
-

Table 1: Suggested frequency of biochemical testing for CKD-MBD

CKD stage	Calcium	Phosphate	PTH	Alkaline phosphatase	Calcidiol 25(OH)D
3	6 - 12 months	6 - 12 months	Baseline	6 - 12 months	Baseline*
4	3 - 6 months	3 - 6 months	6 - 12 months	3 - 6 months	Baseline*
5 & 5D	1 - 3 months	1 - 3 months	3 - 6 months	1 - 3 months	Baseline*

* Note that the frequencies depicted in the table should be interpreted as tests should be done every 6 -12 months.

CKD-MBD - chronic kidney disease mineral bone disease; CKD - chronic kidney disease; PTH - parathyroid hormone

Recommendations

- 2.9.4 In patients with CKD stage 4 - 5D, alkaline phosphatase activity should be monitored every 12 months, or more frequently in the presence of elevated PTH
Not graded
- 2.9.5 In patients with CKD G3a-G5D, we suggest that 25(OH) D (Calcidiol) levels should be measured and repeat testing is done based on baseline values and treatment interventions
Quality of evidence - Low Recommendation - Weak
- 2.9.6 We suggest that vitamin D deficiency and insufficiency should be corrected using the same treatment strategies for the general population.
Quality of evidence - Low Recommendation - Weak
- 2.9.7 In patients with CKD 3a - 5D, we recommend that treatment decisions should be based on trends in parameters rather than a single laboratory value taking into account all available CKD-MBD assessments.
Recommendation - Strong Quality of evidence - Low

PRACTICE POINTS ON ASSESSMENT AND MONITORING OF LABORATORY PARAMETERS IN CKD-MBD

- Frequency of monitoring may need some modification in this environment because of the high cost of laboratory tests and logistics of carrying out these tests.
- Vitamin D levels should be checked in patients who are not receiving any form of active vitamin D sterol such calcitriol, alfacalcidol, or paricalcitol.

Recommendations

- 2.9.8 In patients with CKD3a - 5D, we suggest that individual values of serum calcium, and phosphate measured at the same time, should be used to guide patients' management rather than the calcium-phosphate product ($\text{Ca} \times \text{PO}_4$).
Quality of evidence - Very low Recommendation - Weak
- 2.9.9 We suggest that PTH or bone-specific alkaline phosphatase measurements can be used to evaluate bone disease as markedly high or low values predict the type of underlying bone turn over.
Quality of evidence - Moderate Recommendation - Weak
- 2.9.10 We recommend that infants with CKD stage 2 - 5D have their length measured every three months, while children in the same CKD stages should be assessed annually for linear growth
Quality of evidence - Moderate Recommendation - Strong
- 2.9.11 For the detection of vascular calcification in patients with CKD G3a - 5D, we suggest that a lateral abdominal X-ray be used, while an echocardiogram be used to detect valvular calcification as reasonable alternatives to CT scan
Quality of evidence - Low Recommendation - Weak
- 2.9.12 In patients with CKD G3a-G5D with evidence of CKD-MBD and/or risk factors for osteoporosis, we suggest BMD testing to assess fracture risk if results will impact treatment decisions
Quality of evidence - Moderate Recommendation - Weak
- 2.9.13 We suggest that patients with CKD G3a-G5D with known vascular or valvular calcification be considered at highest cardiovascular risk
Quality of evidence - High Recommendation - Weak
- 2.9.14 It is rational to use this information to guide the management of CKD-MBD
Not graded

Treatment of CKD-MBD in patients with CKD stage 3a-5d

Calcium and phosphate

Recommendations

- 2.9.15 In patients with CKD G3a-G5D, treatments of CKD-MBD should be based on serial assessments of phosphate, calcium, and PTH levels, considered together (May be challenging in this environment because of the high cost of PTH assay.)
Not Graded
- 2.9.16 We suggest that corrected serum calcium (adjusted for albumin concentration) should be maintained within the normal reference range for the laboratory used.
Quality of evidence - Low Recommendation - Weak
- 2.9.17 We suggest that elevated serum phosphate be treated and maintained within the normal range (0.8 and 1.42 mmol/L).
Quality of evidence - Low Recommendation - Weak
- 2.9.18 We suggest treating hyperphosphatemia by restricting dietary intake of phosphate alone or in combination with phosphate binders

Quality of evidence - Low

Recommendation - Weak

- 2.9.19 In making recommendations on diet, it is reasonable to consider the source of phosphate (Sources of phosphate: Meat, milk, eggs, cheese, yoghurt, cola, chocolate drinks nuts, beans, cereals). It is difficult to balance dietary phosphate restriction and protein intake

Not graded

- 2.9.20 We suggest avoiding hypercalcaemia

Quality of evidence - Low

Recommendation - Weak

- 2.9.21 In children, (CKD:3 - 5) we suggest maintaining serum calcium in the age-appropriate range

Quality of evidence - Low

Recommendation - Weak

- 2.9.22 In children, the serum calcium levels will determine the choice of phosphate binders to be used.

Not graded

- 2.9.23 In patients receiving treatment for hyperphosphatemia, we suggest that the dose of calcium-based phosphate binders be restricted

Quality of evidence - Moderate

Recommendation - Weak

- 2.9.24 We recommend that the use of aluminium-based phosphate binders on a long-term basis should be avoided

Quality of evidence - Low

Recommendation - Strong

- 2.9.25 In patients with CKD G5D, we suggest increasing dialytic phosphate removal in the treatment of persistent hyperphosphatemia

Quality of evidence - Low

Recommendation - Weak

Parathyroid Hormone (PTH)

Recommendations

- 2.9.26 In pre-dialysis CKD patients, the optimal PTH level is unknown, therefore, we suggest that treatment is considered when serum PTH levels are progressively increasing or remain persistently above the upper reference limit for the assay, despite correction of modifiable factors. The modifiable factors that can cause PTH to rise include: hypocalcaemia, hyperphosphatemia, high phosphate intake and vitamin D deficiency.

Quality of evidence - Low

Recommendation - Weak

- 2.9.27 In CKD patients G3a - 5 not on dialysis, we suggest that calcitriol and other vitamin D analogues should not be routinely used

Quality of evidence - Low

Recommendation - Weak

- 2.9.28 It is reasonable to reserve the use of calcitriol and other vitamin D analogues in patients in CKD stage 4 and 5 with severe and progressive hyperparathyroidism.

Not graded

PRACTICE POINTS ON MANAGEMENT OF CKD-MBD

- Above recommendations should be taken seriously given that in most centres CKD patients are routinely commenced on calcitriol without recourse to knowing their PTH levels.
- The same note of caution applies to the use of calcium-based phosphate binders.
- We must ensure that CKD patients get the proper phosphate binders and are not just taking calcium supplements

- 2.9.29 In children, calcitriol and other vitamin D analogues may be considered to maintain the serum calcium levels in the age-appropriate normal range
Not graded
- 2.9.30 In patients with CKD G5D, we suggest maintaining iPTH levels in the range of approximately 2 to 9 times the upper normal limit for the assay
Quality of evidence - Low Recommendation - Weak
- 2.9.31 In patients with CKD G5D requiring PTH-lowering therapy, we suggest calcimimetics, calcitriol, or vitamin D analogues, or a combination of calcimimetics with calcitriol or vitamin D analogy
Quality of evidence - Moderate Recommendation - Weak
- 2.9.32 In patients with CKD G3a-G5D with severe hyperparathyroidism (HPT) who fail to respond to medical or pharmacological therapy, we suggest parathyroidectomy
Quality of evidence - Moderate Recommendation - Weak

Goals of Treatment

Recommendations

- 2.9.33 In patients with CKD stages 3 - 5, we suggest that corrected serum calcium (adjusted for albumin concentration) should be kept maintained within the normal reference range for the laboratory used.
Quality of evidence - Low Recommendation - Weak
- 2.9.34 We suggest that elevated serum phosphate be treated and maintained within the normal range (0.8 and 1.42 mmol/L).
Quality of evidence - Low Recommendation - Weak
- 2.9.35 In patients with CKD G5D, we suggest maintaining iPTH levels in the range of approximately 2 to 9 times the upper normal limit for the assay
Quality of evidence - Low Recommendation - Weak

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2.10 CKD and dyslipidaemia

Background

Chronic kidney disease causes profound dysregulation of lipoprotein metabolism, resulting in major pro-atherogenic lipid abnormalities. Although lipid profile in CKD patients is complex, the most common abnormalities are hypertriglyceridaemia and low HDL-C (high density lipoprotein-C) [1,2]. Dyslipidaemia in CKD patients should be investigated and treated in view of the fact that cardiovascular disease is extremely common in this population.

Supporting Evidence

Specific metabolic alterations of lipoprotein moieties have been associated with CKD [3]. Some observational studies in Nigeria have demonstrated various lipoprotein abnormalities such as elevated triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and total cholesterol (TG) in pre-dialysis CKD patients [4, 5]. Similarly, high prevalence of lipoprotein abnormalities has also been demonstrated in ESKD patients, with worse lipoprotein profile seen among patients on CAPD [6]. Furthermore, available evidence from the Study of Heart and Renal Protection (SHARP) showed that simvastatin plus ezetimibe therapy significantly reduced the risk of major atherosclerotic events including myocardial infarction and acute ischaemic stroke and death in pre-dialysis CKD patients[7]. Other randomized controlled trials comparing statin with placebo among pre-dialysis CKD patients have demonstrated similar benefit [8]. Certain combination therapies such as statin plus fibrate have been shown to increase the risk of rhabdomyolysis [9].

Recommendations

- 2.10.1 Diagnosis of dyslipidaemia should be made in both adults and children by obtaining a lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides). We recommend that evaluation of dyslipidaemia should be made at presentation, or after a change in CKD/nutritional status, or at least annually.
Quality of evidence - Moderate Recommendation - weak
- 2.10.2 Assessment for secondary causes of dyslipidaemia such as medications and co-morbid illnesses should be carefully undertaken and treated appropriately.
Not graded
- 2.10.3 In adults and children with CKD (including pre-dialysis and dialysis patients), we suggest annual follow-up measurement of fasting lipid levels.
Not Graded
- 2.10.4 In CKD patients with high total cholesterol unresponsive to dietary therapy and LDL-C > 100mg/dl, statin therapy should be initiated. Drug dosage should be titrated as required, depending on the severity of dyslipidaemia.
Quality of evidence - Low Recommendation - strong

Pharmacological treatment of dyslipidaemia

Recommendations

- 2.10.5 In children less than 18 years of age with CKD, we suggest that statins or statin/ezetimibe combination not be initiated.
Quality of evidence - Low Recommendation - Weak
- 2.10.6 In adults aged 50 years pre-dialysis and dialysis CKD patients, we recommend treatment with a statin or statin/ezetimibe combination.
Quality of evidence -Low Recommendation - Strong
- 2.10.7 For adults aged 18-49 years pre-dialysis CKD patients, we suggest statin treatment in people with one or more of the following: coronary artery disease, diabetes mellitus, prior ischemic stroke and estimated 10-year incidence of coronary death or non-fatal myocardial infarction 10%.
Quality of evidence - Moderate Recommendation - Weak
- 2.10.8 In adult patients with CKD and hypertriglyceridemia, we suggest therapeutic lifestyle changes towards correction of hypertriglyceridaemia.
Quality of evidence - Very low Recommendation - Weak
- 2.10.9 In pre-dialysis patients with fasting triglycerides 500 mg/dl, we suggest treatment with lifestyle changes and addition of gemfibrozil or niacin.
Quality of evidence - Low Recommendation - Weak

Medication safety and adverse effects

Recommendations

- 2.10.10 Monitoring of creatine kinase and alanine aminotransferase should be done in patients treated with moderate to high doses of statins every 3 - 6 months.
Quality of evidence - Low Recommendation - Weak
- 2.10.11 We recommend that co-administration of statins and fibrates should be avoided in patients with CKD to reduce the risk of rhabdomyolysis.
Quality of evidence - Low Recommendation- Strong

Research areas identified:

1. Long term study of the implications of dyslipidaemia and hyperlipidaemia in Nigerians. (Adults and paediatric patients).
2. Assessment of common cardiovascular risk factors.
3. Dietary management of hyperlipidaemia in low resource settings.

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2.11 End of life care

Background

Palliative, supportive or end of life care are sometimes used interchangeably. World Health Organization (WHO) in 2020 defines palliative care as an approach that improves the health-related quality of life (HRQL) of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual. This type of care is absolutely essential in patients with advanced CKD but this is not readily available and often underutilized in our setting [1,2].

Evidence suggests that chronic kidney disease (CKD) patients in advanced stages have a high burden of morbidity, poor outcomes, and high costs of care [3]. Generally, CKD patients on dialysis have annual mortality rate above 20% and this could exceed 50% in low income countries. Withdrawal from dialysis is a common cause of death for dialysis patients worldwide and usually due to financial constraints in our setting [4].

Supporting Evidence

The high level of disability and symptom burden in some patients with advanced CKD is not necessarily improved by dialysis. To improve the quality of care, it is now recognized that palliative care principles need to be integrated into the routine care of these patients [5]. Care in the last days of life is essential in patients who continue to deteriorate on dialysis, or are moribund in view of coexisting co-morbidities, or cannot afford dialysis for financial and other reasons [6]. End of life care should be carried out with utmost care and empathy for the patients and their family members aiming at good symptomatic relief and provision of psychological, spiritual and culturally support by the managing unit [5,6].

There have been controversies about who should benefit from supportive care and when should such care be instituted especially in resource limited environment like ours. It is important that periodic assessment of HRQL and prognosis in advanced CKD patients is undertaken such as to plan and institute supportive/end of life care. Care in the last days of life is essential in patients who continue to deteriorate on dialysis, or are moribund in view of coexisting co-morbidities, or cannot afford dialysis for financial and other reasons.

Recommendations

- 2.11.1 We recommend that all patients with advanced CKD should be assessed routinely for the need of supportive care with or without KRT.

Not graded

- 2.11.2 We suggest the use of validated Health-related quality of life (HRQL) assessment tools such as Edmonton Symptom Assessment System-revised: Renal (ESAS-r:Renal) and Palliative Care Outcome Scale-Renal. (POS-renal) for global symptoms screening.

Not graded

- 2.11.3 We suggest that symptom management should include first line non-pharmacological interventions and then advancing to more complex therapies including pharmacologic therapy (Second-line treatment).

Not graded

- 2.11.4 We suggest that the prognosis for every patient with CKD should be estimated and communicated to patients and family, balancing biomedical facts with relevant emotional, social, cultural, and spiritual issues.
Not graded
- 2.11.5 We recommend that shared decision making should be undertaken to align treatment with patient and family goals, values and preferences (such as withdrawal from dialysis)
Not graded
- 2.11.6 We recommend that the decision to withdraw dialysis should take into consideration access to appropriate supportive care.
Not graded
- 2.11.7 We recommend a multi-professional team comprising nephrologists /nurses/ social workers / counsellors /psychologist /dieticians and family doctors should deliver the comprehensive supportive and end of life care to patients and their family.
Not graded
- 2.11.8 We recommend in the last days of life; patients and their caregivers should be treated with utmost care and empathy. Therapy should aim at achieving good symptomatic relief. In addition, psychological, spiritual and culturally sensitive care for the dying patient and their family should be provided by the managing unit.
Quality of evidence - Low Recommendation-strong
- 2.11.9 We recommend conservative management for patients with CKD G4 - G5 who cannot afford RRT or willingly opt out of RRT.
Quality of evidence - Low Recommendation- strong

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Appendix

Table 1: Symptoms in CKD and their palliative cares

Uremic pruritus	Associated with decreased HRQL, and contributes to other symptoms such as poor	The highest levels of evidence for efficacy are for topical agents (e.g., capsaicin, emollients if concurrent dry skin), oral medications (e.g.,
Sleep disorders	Associated with fatigue, poor HRQL and	Management involves basic sleep hygiene measures, management of concurrent symptoms, non-pharmacologic interventions including exercise and cognitive behavioral therapy, and pharmacologic
Restless legs syndrome (RLS)	Associated with impaired sleep and HRQL, premature withdrawal from dialysis, and increased cardiovascular morbidity and	Non-pharmacologic measures may include removal of stimulants, good sleep hygiene, changes in the dialysis regime, aerobic exercise, 156-158 pneumatic compression devices, and correction of hyperphosphatemia and iron deficiency. Pharmacologic approaches might include cessation of medications that interfere with the dopamine pathway, or trials of levodopa, nonergot dopamine
Anorexia	Associated with malnutrition, poor HRQL, depression, greater hospitalization rates, and	Management has not been studied systematically in
Nausea	Associated with malnutrition, poor HRQL, depression, greater hospitalization rates, and	Management has not been studied systematically in
Vomiting	Impact has not been assessed systematically in	Management has not been studied systematically in
Constipation	Impact has not been assessed systematically in	Management has not been studied systematically in
Diarrhea	Impact has not been assessed systematically in	Management has not been studied systematically in
Depression	Associated with increased morbidity, hospitalization, and mortality rates [166-169],	A systematic review assessed pharmacologic treatment in CKD stages 3-5, including 28 studies assessing 24 antidepressants [170]. Included were two RCTs of fluoxetine and escitalopram versus placebo in HD patients, both of which did not demonstrate efficacy. However, the 9 non-RCTs all suggested benefit. Side effects were common but mild. Efficacy of non-pharmacologic treatments (e.g., more frequent haemodialysis [171,172],??? cognitive behavioral therapy [173,174],??? and exercise have
Pain	Data consistently show that pain and/or overall symptom burden is associated strongly with substantially lower HRQL and greater psychosocial distress, insomnia, and depressive	Management is determined by both etiology and severity. Non-pharmacological approaches may be appropriate (such as exercise and local heat) for musculoskeletal pain. For pharmacologic management, an adapted World Health Organization (WHO) analgesic ladder that takes into account pharmacokinetic data of analgesics in CKD is recommended [12]. This may include the conservative dosing of opioids for moderate to severe pain that adversely affects physical function and HRQL and that does not respond to non-opioid analgesics. Before commencing opioids, clinicians should assess risk of substance abuse and obtain informed consent following a discussion of goals, expectations, potential risks, and alternatives. Opioid risk mitigation strategies should be used. There are no studies on the long-term use of any analgesics in patients with CKD, and thus careful attention must be paid to issues of efficacy and safety.

SECTION III: CLINICAL PRACTICE GUIDELINES FOR HAEMODIALYSIS

Introduction

Haemodialysis (HD) is the most common form of renal replacement therapy (RRT) worldwide [1]. In Nigeria, haemodialysis still represents the most commonly available modality for renal replacement therapy despite its exorbitant cost [2-5]. Although clinical practice guidelines for haemodialysis developed in countries such as the United States, Canada and the United Kingdom have set clinical standards for best practices in haemodialysis service delivery based on best available evidence [6-8], variations in practice could contextually and appropriately occur when factors such as available resources and practice limitations unique to countries are taken into consideration.

This section on haemodialysis provides an update on the recommendations contained in section III of the NAN 2010 Guidelines for the Detection and Management of Chronic Kidney Disease. Suggestions on the clinical approach to the management of patient populations such as the crashlanders (unplanned dialysis), patients who are dialyzing infrequently (receiving non-standard haemodialysis therapy) and patients who withdraw from dialysis treatment are provided as they constitute a good proportion of patients seen in day-to-day clinical practice in Nigeria.

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3.1 Haemodialysis facilities and equipment

Background

Haemodialysis units provide care that is critical for patients suffering from severe renal function impairment. Renal patients spend an average of 4 hours per session, three times in a week for a standard dialysis treatment in the haemodialysis facility. Therefore, it is imperative that service should be provided within a warm, homelike and comfortable environment. Haemodialysis service could be rendered as an integral part of a hospital, a satellite unit, or as a stand-alone unit.

The spatial design of the facility should take into consideration the requirements for patient and staff areas, support spaces, business and administrative offices, mechanical systems, and any other patient care spaces that are relevant to service delivery in the facility [1-3].

Supporting Evidence

Recommendations for architectural design of haemodialysis facilities, though available in many countries, may not provide the optimal design for facilities in Nigeria given the differences in the climate and environment where such designs are meant to be utilized and what exists locally. Guidelines for construction of dialysis facilities are presently unavailable in Nigeria but building standards and specifications provided in the National building code (NBC2006) could guide architectural designs of dialysis facilities [4].

Recommendations

- 3.1.1 We suggest that in all instances building construction for the facility must adhere strictly to the standards and specifications of the National Building Code (NBC, 2006) and other building regulations applicable to the location in which the facility is intended to be constructed.

Not graded

- 3.1.2 We recommend that each dialysis facility should provide space for the following:

Reception and waiting spaces

- Reception office
- Waiting/refreshment area
- Patient changing area/locker room
- Patients' sanitary facilities

Treatment areas

- Patient-monitoring area
- Dialysis area
- Staff base
- Consulting/examination room
- Treatment/procedures room

Office accommodations

- Technical services manager's office

Support/utility spaces

- Water-treatment plantroom
- Clean/Dirty utility rooms
- Staff rest room
- Pantries: patients and staff
- Staff change/locker room
- Staff sanitary facilities
- Store facilities for equipment, linen storage, and general storage

Technical services, maintenance, and equipment storeroom

Not graded

3.2 Equipment

- 3.2.1 We recommend that all machines for delivery and monitoring of haemodialysis should conform with standard certifications for haemodialysis equipment by relevant authorities and meet safety standards for electrical equipment in clinical use.

Not graded

- 3.2.2 We recommend the use of either a single patient single pass dialysate delivery system or a central delivery system

Not graded

- 3.2.3 We recommend that each dialysis facility should have an emergency electric power supply (back up generating sets or inverters), to power the haemodialysis machines in case of electrical power outage.

Not graded

3.3 Minimum staff composition

Background

With the increasing number of dialysis facilities in the country in recent times, as a result of the increase in prevalence of ESRD in the country, demand for renal care personnel has seen an unprecedented increase. This increase in demand is barely being met by the available training institutions in the country and this has generated a lot of concern as the man power need of the various units is not being met.

Appropriately trained staff is key to patients' safety on dialysis. Therefore, each haemodialysis unit must ensure adequate staffing with appropriately qualified personnel, who have sufficient educational and practical experience to fulfil the responsibilities required of the position occupied in the facility.

Supporting Evidence

Although optimal staffing ratio for dialysis facilities is difficult to specify, as job requirements vary between facilities, inadequate patient to nursing staff ratio has been associated with poor patient outcomes in previous studies, only very few studies have addressed this issue [5-7]. There is a need for more studies on this subject to allow an evidence-based approach to staffing requirements in haemodialysis facilities.

Recommendations

- 3.3.1 We suggest that each facility should have the following minimum staff composition.

Qualified Nephrologist.

Nephrology/dialysis nurses

Dialysis technicians (biomedical technicians)

Counsellors and social workers

Renal dieticians

Secretarial and administrative staff

Domestic staff

Not graded

- 3.3.2 Patient staff ratio:

We suggest:

A maximum patient-to- Nursing staff ratio of 8:1

A machine-to-Dialysis Technician staff ratio of 4:1

Not graded

3.4 Water treatment

Background

During haemodialysis treatment, patients are exposed to more than 300 litres of water per week. This is about 30 times the amount of water exposure non-dialyzed individuals consume in a week. Therefore, appropriate water quality is one of the most important aspects of ensuring safe delivery of haemodialysis. The water treatment is provided by a water pre-treatment system, which may include various components that is determined by the quality of feed water.

Usual components of water treatment systems are: Storage tanks, sediment filters, water softeners, carbon tanks, micro-filters, ultraviolet disinfection units and reverse osmosis (RO) units.

Supporting Evidence

Guidelines for the clinical governance, installation and validation, operation and maintenance and monitoring of the quality of dialysis water for haemodialysis and dialysis fluids are presently not available in the country. In view of the utmost importance of the provision of high quality treated water for dialysis, recommendations for water treatment in haemodialysis published by reputable professional bodies such as The Renal Association and The Association of Renal Technologists in the UK,[8] or the Association for the Advancement of Medical Instrumentation (AAMI) in the US,[9] would be of great help to Renal Units in the country.

Recommendation

- 3.4.1 We recommend that dialysis facilities should utilize recommendations contained in the guidelines on water treatment systems, dialysis water and dialysis fluid quality for haemodialysis published by reputable professional bodies such as The Renal Association and The Association of Renal Technologists in the UK, [8] or the Association for the Advancement of Medical Instrumentation (AAMI) in the US,[8] to guide the installation of water treatment systems for haemodialysis and ensure good quality in the routine production of dialysis water suitable for use for haemodialysis.[10]

Not graded

3.5 Preparation for Haemodialysis

Background

The choice of haemodialysis modality, vascular access and circumstances surrounding the initiation of dialysis have been shown to significantly affect patients' experiences and outcomes. In general, patients who present early to the Nephrologists would have ample follow up management of their CKD progression, CKD complications and co-morbidities with adequate counselling and preparation for haemodialysis treatment. On the other hand, those presenting late to the Nephrologist at the point of requiring immediate or urgent dialysis or within a short time after their presentation usually have multiple comorbidities, CKD related complications and florid uraemic symptoms. In this situation, there is insufficient time for counselling and preparation for haemodialysis treatment is often sub-optimal.

Supporting Evidence

Patients' circumstances at the initiation of dialysis could be categorized as urgent versus non-urgent or planned versus unplanned initiation. In Nigeria, dialysis is most often initiated in urgent and unplanned circumstances.[10] As a result of this, most patients commence dialysis with little understanding of what dialysis treatment requires. Therefore, adequate attention should be paid to patient education, their counselling needs and their support system by the managing team, in order to optimize treatment compliance and improve on patient outcomes.

Recommendations

- 3.5.1 We suggest that the managing team should provide patients with the adequate education and counselling, to ensure patients comprehension of dialysis treatment and the financial implication. An assessment of the patients' support is desirable.

Not graded

- 3.5.1 Patients starting dialysis should have their drugs reviewed and adjusted. For example, the dose of ESA and intravenous iron should be adjusted to RRT dose in accordance with anaemia guideline. In

order not to encourage poor medication compliance, patients should not be routinely advised to omit antihypertensive medications on their dialysis days; should intra-dialytic hypotension be a problem, they should be advised to use their medications in the evening after dialysis.

Not graded

3.6 Vascular access

Background

Reliable vascular access is the cornerstone of HD therapy and timely planning for vascular access is an essential and important part of pre-dialysis management. An Ideal access should enable effective removal of and return of blood from the patient in a safe and effective way. In addition, it should be reliable, practical with minimal risk of injury to the patient.

Autologous arterio-venous fistulas (A-V fistula) and arterio-venous grafts are the preferred vascular access types for haemodialysis. However, they require planning and surgical expertise which may not be readily available in many haemodialysis units in the country. In addition, timely referral for A-V fistula creation in CKD patients is essential to allow sufficient time for maturation of the created access for use at the time of dialysis initiation.

Although usage of venous catheters (tunnel and non-tunnel) offers inferior performance compared with arterio-venous fistulae or grafts, the non-availability of surgical expertise for A-V fistula creation in many units has made their usage common and for many patients, venous catheters remain the only form of available vascular access for haemodialysis.

Supporting Evidence

Meta-analyses of observational studies have shown that creation of AV fistulas early impact positively on the rate of bacteraemia and survival on haemodialysis thus making an early referral for AV fistula desirable for most patients planned for haemodialysis therapy.¹¹ Many guidelines on vascular access for haemodialysis recommend early referral of patients for AV fistula creation given the clear benefit of AV fistulas compared with other forms of vascular access [12-14].

Recommendations

3.6.1 We recommend that CKD patients in stage IV should be referred for assessment and creation of vascular access when eGFR falls between 15- 20mL/min/1.73m².

Not graded

3.6.2 We suggest timely referral for correction or creation of a new vascular access in patients with recurrent vascular access problems.

Not graded

3.6.3 We recommend that placement of venous catheter access should only be done as a last resort, especially in emergency situations. In units where the expertise for creation of fistulae is unavailable, we recognize that venous catheter access may be the only available option.

Quality of evidence - High

Recommendation- Strong

3.6.4 We recommend that vascular access for haemodialysis be monitored and maintained regularly to minimize failure and avoid emergency interventions.

Quality of evidence - Moderate

Recommendation- Strong

3.6.5 We recommend that strict aseptic technique be adhered to at every use of dialysis central venous catheter. The use of 2% chlorhexidine for exit site cleaning is recommended.

Not graded

3.6.6 We recommend that an antimicrobial or antibiotic lock solution be used to reduce catheter related bacteraemia and other infections

Quality of evidence - High

Recommendation- Strong

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3.7 Timing of Haemodialysis Initiation

Background

Haemodialysis (HD) is the predominant renal replacement therapy (RRT) option available to patients in ESRD in Nigeria [Bello 2013, Oluyombo 2014]. The majority of patients often need urgent HD without adequate time for preparation [Ekrikpo 2011, Ashuntantang 2017]. Choosing an initial mode of renal replacement therapy (RRT) is influenced by a range of factors which include financial, medical especially co-morbidities, psycho-social state, availability of RRT modality as well to access to expertise. Nonetheless, the timing of initiation of RRT varies across countries and contextual factors need to be taken into consideration when making this decision. Increasingly, shared decision making in the goals and outcomes of care is becoming more important. Opportunities for this need to be offered in combination with early education on the appropriate timing of initiation of HD.

There is no universal agreement on optimal timing or eGFR for starting dialysis. Therefore, initiating

HD based only on a specific eGFR level cannot be recommended. The main consideration in our patient population would be the clinical state of the patient as well as the cost of the service. Whilst the decision may be easy in wholly insured patients, it is less likely so in the majority who pay out of pocket.

Supporting Evidence

The updated KDOQI guideline recommendations on the timing of HD have been driven by the IDEAL study, a robust multicentre randomized controlled trial in New Zealand and Australia which compared early and late start of HD based on creatinine clearance. The overall difference in mortality, CV, infectious events and complications of HD between the two groups was not significantly different [Cooper 2010]. There are as yet no RCTs in Nigeria or similar contexts to inform our recommendations at this time.

Recommendations

Based on our peculiar patient population and health system considerations, we recommend as follows:

- 3.7.1 If a patient has GFR 30 ml/min per 1.73 m², modality of RRT should be discussed with him/her.
Not graded
- 3.7.2 Dialysis should be instituted whenever GFR is < 15mls/min per 1.73m² in those who can afford it.
Not graded
- 3.7.3 In those who are asymptomatic and unable to afford, HD should be delayed till GFR falls between 6-9ml/min.
Not graded
- 3.7.4 Dialysis should be commenced in patients with higher GFR if there is one or more of the symptoms or signs of uraemia, inability to control BP or fluid overload or a progressive deterioration in nutritional status
Quality of evidence - High Recommendation- Strong

3.8 Haemodialysis dose, frequency, and duration

Background

In the past, recommendations on haemodialysis dose and frequency have relied on several observational and non-randomized experimental studies which suggest that 'more is better' [Suri 2006, Walsh 2005]. More frequent and/or longer duration dialysis reportedly improve patient's quality of life, leads to better control of hyperphosphatemia, greater reduction in high blood pressure and regression of left ventricular hypertrophy (LVH). Consequently, more frequent and longer duration dialysis sessions have become common place. In our setting, many patients are unable to afford even the minimum recommended dialysis dose and frequency ostensibly leading to poorer outcomes.

Supporting Evidence

There are now several RCTs that have compared more frequent or extended dialysis to conventional dialysis [7, 8]. Recommendations have been dominated by those from the National Cooperative Dialysis Study (NCDS) and the HEMO study. The evidence favours adequate dialysis to specific bio-physiological and clinical end-points but there is no significant advantage of extended dialysis compared with conventional dialysis. Nonetheless, HD prescription should be individualised to achieve adequate dialysis. In our context, there are as yet no RCTs studying different haemodialysis frequencies. At the moment, planning such RCTs may be futile unless there is full insurance coverage for the treatment.

Recommendations

- 3.8.1 We recommend the use of eKt/V as the most as a valid measure of dialysis dose, monitoring of dialysis dose on a monthly basis for the majority of centre-based dialysis patients.
Quality of evidence - Moderate Recommendation- Strong

- 3.8.2 Where eKt/V is not possible, Urea Reduction Ratio should be used to assess dialysis adequacy.
Quality of evidence - Moderate Recommendation- Strong
- 3.8.3 We recommend targeting dialysis dose to achieve consistently a minimum eKt/V of for thrice weekly patients, in the absence of a measured contribution from residual function.
Quality of evidence - Moderate Recommendation- Strong
- 3.8.4 We recommend a minimum of 12 hours per week for the majority of patients who dialyse thrice weekly and have minimal residual function.
Quality of evidence - Moderate Recommendation- Strong
- 3.8.5 We recommend augmented HD schedules for those who are not able to achieve adequacy targets or fluid control on a standard thrice weekly(12-15h) schedule.
Not graded

3.9 Management of hypertension in haemodialysis patients

Background

The prevalence of hypertension in patients undergoing haemodialysis is about 90% at the time of initiation of therapy and about 50-60% three months afterwards [Salem 1995]. Several studies in Nigeria suggest wide BP variabilities in the hypertensive haemodialysis population [Okpa 2019, Egbi 2019] underscoring the need for appropriate treatment. An ideal BP in a haemodialysis patient should lead to haemodynamic stability during dialysis, orthostatic tolerance after dialysis, the best cardiovascular survival, and optimal health related quality of life. Optimal blood pressure is defined when pre and post-dialysis BP is $<150/90$ mmHg without therapy or the ambulatory day BP(ABPM) monitoring is $<135/85$ without therapy or the ambulatory night time BP monitoring is $<120/80$ without therapy. Some of these goals can be achieved by fluid status management, dietary and dialysate sodium restriction and use of appropriate antihypertensive medications [Maliara 2007].

Supporting Evidence

Hypertension in haemodialysis patients is diagnosed when pre-dialysis BP is $>140/90$ mmHg or when post-dialysis BP is $>130/80$ mmHg [13]. The diagnosis of hypertension is now known to be unreliable with office or dialysis unit measurements. Blood pressure (BP) recordings obtained before or after haemodialysis display a J- or U-shaped association with cardiovascular events and survival. Consequently, ambulatory BP monitoring is now considered as the gold standard method for BP evaluation [14]. Management of fluid status and adjustment of BP medications in collaboration with other members of the team should be encouraged.

Recommendation

- 3.9.1 We recommend the use of ABPM or home BPM in the diagnosis of hypertension in HD patients.
Quality of evidence - High Recommendation- Weak

Blood Pressure targets

Recommendations

- 3.9.2 We suggest the achievement of individual patient's dry weight as a way of controlling hypertension.
Quality of evidence - Moderate Recommendation- Strong
- 3.9.3 We recommend education and regular counselling by dietitians, low sodium intake (2-3 g/day sodium intake and increased ultrafiltration to help reduce BP in HD patients).
Quality of evidence - Moderate Recommendation- Strong
- 3.9.4 We recommend ACE inhibitors or angiotensin II-receptor blockers, calcium channel blockers and beta blockers for reduction of BP in HD patients.
Quality of evidence - Moderate Recommendation- Strong

3.10 Management of anaemia in haemodialysis patients

Introduction

Anaemia in haemodialysis patients has been studied extensively in Nigeria [15]. The causes extend beyond those reported in higher income countries to include parasite infestation, use of herbal remedies and abuse of NSAIDs. However, its treatment adds to the already very high cost of care and there is a heavy reliance on blood transfusion in our setting.

Supporting Evidence

The evidence for anaemia treatment and targets in HD patients is limited by remarkable heterogeneity of patients entered for HD, the different quality and research designs of the RCTs performed, and differences in definitions of end-points. Much of this is driven by the Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT) [16], Cardiovascular Risk Reduction by Early Anaemia Treatment with Epoetin Beta trial (CREATE) [17] and Correction of Haemoglobin in Outcomes and Renal Insufficiency (CHOIR) trial [18]. However, because the latter two did not have placebo arms, many recommendations rely on the large, placebo controlled TREAT which found no difference between the higher Hb, darbepoetin, group and the lower Hb, placebo, group for the two primary composite outcomes (either death or a cardiovascular event and death or a renal event). Nonetheless, individualization of therapy is reasonable since the Hb at which some patients show improvement in QoL is variable. Presently, there are no studies in Nigeria that have suggested any Hb targets in the haemodialysis population.

Recommendations

- 3.10.1 We recommend that Hb concentration be measured when clinically indicated and at least every 3 months in patients with CKD with no anaemia

Not Graded

- 3.10.2 We recommend that for HD patients with anaemia not being treated with an ESA, Hb concentration be measured when clinically indicated and at least monthly

Not Graded

- 3.10.3 Diagnose anaemia in adults and children >15 years with CKD when the Hb concentration is <13.0 g/dl in males and <12.0 g/dl in females.

Not Graded

- 3.10.4 In patients with CKD and anaemia (regardless of age and CKD stage), we recommend the following tests in initial evaluation of the anaemia

- i. Full blood count (FBC) -Hb concentration, red cell indices, white blood cell count and differential, and platelet count
- ii. Absolute reticulocyte count
- iii. Serum ferritin level
- iv. Serum transferrin saturation (TSAT)
- v. Serum vitamin B12 and folate levels

Not Graded

- 3.10.5 We recommend that in haemodialysis patients, particularly those being prepared for kidney transplantation, blood transfusion should be avoided where possible to reduce allosensitization risk.
Quality of evidence - High Recommendation- Strong

- 3.10.6 For adult haemodialysis patients, we suggest that ESA therapy be started when the haemoglobin is between 9.0-10.0 g/ dl
Quality of evidence - High Recommendation- Strong

- 3.10.7 We recommend that ESAs not be used to intentionally increase the Hb concentration above 13 g/dl
 Quality of evidence - High Recommendation- Strong

3.11 Management of malnutrition in haemodialysis patients

Introduction

Malnutrition in maintenance HD (MHD) patients otherwise known as Protein Energy Wasting (PEW) is prevalent and affects about 28-54% of patients [19]. It is often as a result of institution of a restrictive diet in the pre-dialysis period, reduced appetite and nutrient intake imposed by the uraemic state, loss of nutrients during dialysis as well as an imbalance in protein breakdown and synthesis driven by acidosis, chronic inflammation, insulin resistance and accompanying atherosclerotic disease. A combination of these factors increases mortality risk in HD patients. Other effects include poor functional ability and quality of life as well as heightened infection risk and poor healing. Data on PEW is sparse in Nigeria with a few studies suggesting presence of malnutrition in most pre-dialysis patients [20, 21] and under-dialysis seen in all HD patients who had malnutrition [22].

Supporting Evidence

Many studies including the Dialysis Outcomes and Practice Patterns Study (DOPPS)22 and Haemodialysis (HEMO) study23 have highlighted the presence of malnutrition in haemodialysis patients using several indices such as body mass index (BMI), normalized protein catabolic rate (nPCR), serum albumin levels modified subjective global assessment (mSGA), skin fold thickness, bio-electrical impedance analysis etc. Some are inexpensive and can be applied in low resource settings. Dual-energy x-ray absorptiometry (DXA) is regarded as the gold standard for assessing body composition in HD patients but it is expensive and invasive. No single index can accurately measure malnutrition. A combination of anthropometric and biochemical measurements are often used to assess PEW in individuals and conduct follow up assessment.

Screening and assessment

Recommendations

- 3.11.1 We recommend that patients on maintenance haemodialysis be assessed for PEW at least twice a year (bi-annually)
 Not graded
- 3.11.2 We suggest the use of the following, where, available in the screening of patients at risk of PEW
 (A) Dietary assessment
 (B) Body mass index
 (C) Subjective global assessment (SGA)
 (D) Anthropometry
 (E) nPNA
 (F) Serum albumin and serum prealbumin
 (G) Serum cholesterol
 (H) Technical investigations (bio-impedancemetry, dual X-ray absorptiometry, near infrared reactance)
 Not graded
- 3.11.3 We recommend the involvement of a renal nutritionist in the assessment, management, and monitoring of nutritional status of MHD patients prior to and within three months of initiating HD and annually.
 Not graded

Protein and energy intake

Recommendations

- 3.11.4 We recommend prescription of a dietary protein intake of 1.0 - 1.2 g/kg body weight per day for maintaining acceptable nutritional status in stable individuals who do not have diabetes.

Quality of evidence - Low

Recommendation- Strong

- 3.11.5 We recommend prescription of 1.0 -1.2 g/kg body weight per day of dietary protein for individuals with diabetes. Patients at risk of hyper and/or hypoglycaemia, may need higher levels of dietary protein to ensure good glycaemic control.

Not graded

- 3.11.6 We recommend prescription of total daily energy intake of 25 - 35 kcal/kg body weight taking into consideration several factors such as age, sex, weight goal, stage of CKD, concurrent illness, or degree of inflammation.

Quality of evidence - Low

Recommendation- Weak

- 3.11.7 In general, we do not recommend any particular type of protein source (plant or animal) based on current knowledge of their effects on nutritional status, serum calcium/phosphorus levels or serum lipids. Dietary plans should be individualised and such plans worked on based on patients' preferences and the need to meet their protein and energy needs.

Not graded

Nutritional Supplementation

Recommendations

- 3.11.8 We suggest a trial of oral nutritional supplements for three months in individuals with PEW if dietary counselling fails to improve nutritional state of patients on MHD.

Not graded

- 3.11.9 We suggest trial of enteral feeding if dietary modifications and oral nutritional supplements are not effective.

Not graded

Micronutrient supplementation

Recommendations

- 3.11.10 We suggest micronutrient supplementation in individuals with deficiencies and this should include water soluble vitamins and trace elements

Not graded

- 3.11.11 In MHD individuals those with hyperhomocysteinaemia, we do not recommend routine supplementation with folate and/or B-complex vitamins

Quality of evidence - High

Recommendation- Strong

- 3.11.12 In MHD individuals with clinical signs and symptoms of folate and/or vitamin B12 deficiency, we suggest prescription of either or both vitamins to correct the abnormality.

Quality of evidence - Moderate

Recommendation- Strong

- 3.11.13 In MHD individuals who may be at risk of being deficient in Vitamin C, we suggest supplementation to meet recommended daily intake of 90 mg/day and 75mg/day for men and women respectively.

Not graded

- 3.11.14 We suggest Vitamin D supplementation for MHD individuals who are Vitamin D deficient. This should be prescribed as cholecalciferol or ergocalciferol to correct 25-hydroxyvitamin D (25(OH)D) deficiency or insufficiency.

Not graded

Electrolytes

Recommendations

- 3.11.15 We suggest that in MHD individuals, serum bicarbonate levels be maintained at 24-26 mmol/L
Not graded
- 3.11.16 We suggest that in MHD individuals, calcium intake in any form (dietary calcium, calcium supplements, or calcium-based binders) should be adjusted, bearing in mind use of Vitamin D analogues and calcimimetics. This is to avoid calcium overload.
Not graded
- 3.11.17 In adults on MHD, we recommend adjustment of dietary phosphorus intake to normalise serum phosphate levels.
Quality of evidence - Moderate Recommendation- Strong
- 3.11.18 In adults on MHD, suggest individualising potassium intake based on need and clinicians' judgment.
Quality of evidence - Very low Recommendation- Strong
- 3.11.19 In adults on MHD, we recommend targeting BP reduction and volume control by limiting sodium intake to less than 100 mmol/d (or <2.3 g/ d)
Quality of evidence - Low Recommendation- Strong
- 3.11.20 In adults on MHD, we suggest a combination of dietary sodium reduction and lifestyle modification for volume control and body weight optimisation.
Quality of evidence - Moderate Recommendation- Strong

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3.12 Infection control in haemodialysis units

Background

Haemodialysis is by far the most widely used of all the renal replacement therapies (RRT), worldwide. In Nigeria, it is the predominant form of renal replacement therapy employed for end-stage renal disease (ESRD) [1]. Majority of patients and healthcare workers prefer this option on account of non-availability of peritoneal dialysis fluids and non-affordability of renal transplant by many.

Infection has been ranked as the second most common cause of mortality in ESRD patients on haemodialysis, after cardiovascular diseases and it is the commonest cause of hospital admissions in these group of patients [2].

One of the major factors predisposing to infection in haemodialysis patients is the chronic immunosuppressive state of CKD, increasing their susceptibility to infection, the extracorporeal nature of the treatment [3] and a breach in the infection control practices.

Both the healthcare workers and the patients on haemodialysis are at increased risk of contracting infections as a result of prolonged exposure to potential contaminants and the prolonged duration of the treatment [3].

The major infections are the blood borne viral infections like hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), [4] and the airborne novel coronavirus causing Covid-19.

Infection control is very important in haemodialysis units as it can facilitate patient to patient, or patient to healthcare worker spread of infection, if not strictly adhered to. This has necessitated the establishment of tighter infection prevention and control measures by the Kidney Disease: Improving Global

Outcomes (KDIGO), [5] National Institute for Health and Care Excellence (NICE) and the Renal Association [4].

The aim of section is to establish a common guideline that can be applied to the Nigerian haemodialysis population.

Supporting evidence

The Renal Association clinical practice guidelines on the management of blood-borne viruses published in 2008, was updated in 2019 [4]. The KDIGO guidelines on the prevention, diagnosis, evaluation and treatment of hepatitis C in CKD was also updated in 2018 [5] from the previous guidelines published in 2008. The guideline recommendation of both Renal Association and KDIGO are based on evidence of infection control and systematic reviews of relevant publications [4, 5].

The Nigerian Association of Nephrology developed a clinical practice guideline earlier in the year, for the prevention of Covid-19 in Renal Units and management of Covid-19 positive patients who require RRT [6]. This was adapted from various recommendations, to suit our local environment.

Recommendations

General measures

- 3.12.1 We recommend strict adherence to standard infection control policies, to prevent patient-to-patient and patient to healthcare worker transmission of blood-borne pathogens.
Quality of evidence - High Recommendation- Strong
- 3.12.2 We recommend discarding medicine vials after single use or divided into multiple doses and dispensed from a central area, if it is to be used for multiple patients.
Quality of evidence - Moderate Recommendation- Strong
- 3.12.3 We recommend cleaning of the haemodialysis machine between patients, according to local protocol.
Quality of evidence - Low Recommendation- Strong
- 3.12.4 We suggest inspection of external transducer protectors of blood circuit pressure monitoring lines, by healthcare workers, during and after each session of dialysis. In the case of evidence of breach of blood or saline, the components that have been contaminated should be replaced or decontaminated according to the standard protocol.
Quality of evidence - Low Recommendation- Weak

Viral infections

- 3.12.5 We recommend screening of all patients starting haemodialysis or recommencing haemodialysis following another modality of RRT, for HBsAg, anti-HCV and HIV.
Quality of evidence - High Recommendation--Strong
- 3.12.6 We recommend testing for HBsAg and anti-HCV in all haemodialysis patients with abnormal serum aminotransferases, which cannot be explained by any other cause.
Quality of evidence - Moderate Recommendation--Strong
- 3.12.7 We recommend that in the case of outbreak of a new viral infection in the haemodialysis unit, all exposed patients should have viral DNA or RNA testing.
Quality of evidence - Moderate Recommendation-Strong
- 3.12.8 We recommend that in the case of a new viral infection, expert advice should be sought from a Virologist, to help co-ordinate surveillance of patients and care givers at risk and to treat infected patients.
Quality of evidence - Low Recommendation--Strong

- 3.12.9 We recommend that when there is a new outbreak in the haemodialysis unit, strict infection control measures should be adhered to and there should be a review of disinfection procedures, carried out in the Centre.
Not graded

Hepatitis B virus

- 3.12.10 We recommend using a dedicated dialysis machine for HBV infected patients, preferably, in an isolated room, with dedicated staff. The dialysis machine can be used for HBV negative patients, only after proper decontamination.
Quality of evidence - High Recommendation--Strong
- 3.12.11 We recommend that patients with unknown hepatitis B status should be dialysed separate from other patients and no other patient should use the dialysis machine until the awaited result is known or until the machine is decontaminated.
Quality of evidence - High Recommendation--Strong
- 3.12.12 We recommend 6-12 monthly HBsAg testing of patients who are immune to hepatitis B immunization, while non responders to hepatitis B vaccine should be tested every 3 months.
Quality of evidence - Low Recommendation--Strong
- 3.12.13 We recommend that patients who require haemodialysis should have hepatitis B testing and vaccinated against hepatitis B if indicated.
Quality of evidence - High Recommendation--Strong
- 3.12.14 We suggest that patients with high risk for hepatitis B virus infection should have undetectable levels of anti HBC (hepatitis B core antigen) before commencing the immunization schedule.
Quality of evidence - Moderate Recommendation-- Weak
- 3.12.15 We recommend that all staff in contact with patients should be tested for current hepatitis B infection. Those with evidence of current infection should not be allowed to work in a dialysis unit. Staff who are susceptible to HBV infection should be vaccinated and tested for immunity. Non responders should be tested annually for HBV infection.
Quality of evidence - High Recommendation--Strong
- 3.12.16 We suggest that non immune and non-infective staff to HBV infection should not dialyse HBV infected patients.
Quality of evidence - Moderate Recommendation--Weak
- 3.12.17 We recommend that patients who are likely to require RRT be given hepatitis B vaccination prior to the development of stage 5 CKD.
Quality of evidence - High Recommendation--Strong
- 3.12.18 We suggest that hepatitis B vaccine is not indicated in patients with previous or current hepatitis B infection. Those with only anti-HBc antibodies should not be taken as positive, though they may need vaccination if there is risk of reactivation.
Quality of evidence - Moderate Recommendation--Weak
- 3.12.19 We recommend that the initial hepatitis B immunization schedule should involve high doses, frequent doses or both and the vaccines should preferably be administered intramuscularly or intradermally.
Quality of evidence - High Recommendation--Strong
- 3.12.20 We recommend that adequate responders should be defined as those with anti-HBs antibody titre

>100mIU/ml, 8 weeks after completion of the immunization schedule.

Quality of evidence - Low

Recommendation--Strong

- 3.12.21 We recommend that responders should have anti-HBs titre checked before travelling overseas or before a high-risk procedure. A booster dose should be administered if their anti-HBs antibody titre is <100mIU/ml.

Quality of evidence - Low

Recommendation--Strong

- 3.12.22 We recommend that HBV immunization responders should receive a booster dose of the vaccine if their annual anti-HBs titre is <100mIU/ml.

Quality of evidence - Moderate

Recommendation--Strong

- 3.12.23 We suggest that inadequate responders be defined as those with anti-HBs antibody titre <100mIU/ml, 8 weeks following completion of the immunization schedule.

Quality of evidence - Low

Recommendation--Weak

- 3.12.24 We recommend giving booster doses of the hepatitis B vaccine, if anti-HBs antibody titre is between 10 and 100mIU/ml.

Quality of evidence - Low

Recommendation--Strong

- 3.12.25 We recommend repeating the entire vaccination course, with the high concentration of the vaccine and follow up with anti HBs antibody titre 4 -6 weeks after the last dose, with the recommended titre being > 10mIU/ml. if titres are still < 10mIU/ml after 2 full courses of the vaccination, patient can be labelled a non-responder.

Quality of evidence - Low

Recommendation--Strong

- 3.12.26 We recommend that a non-responder (not immune to HBV), should be counselled on how to avoid exposure to the virus and the recommended actions in case of an accidental exposure.

Quality of evidence - Moderate

Recommendation--Strong

- 3.12.27 We recommend that if a prior unidentified case of HBV is detected, surveillance should be carried out in all patients who are not immune to HBV (anti HBs titre > 100mIU/ml within the previous year), who had been dialysed in the centre since the last negative test of the index patient.

Quality of evidence - Moderate

Recommendation--Strong

- 3.12.28 We recommend that if a prior unidentified case of HBV is detected, patients who have anti-HBs titres between 10-100mIU/ml in the prior 12 months, who have been dialysed in the centre since the last negative test of the index patient, should receive a booster dose of hepatitis B vaccine. Hepatitis B immunoglobulin should be given to previous non-responders to the vaccine (anti-HBs titre <10mIU/ml), provided they were exposed within the last 1 week.

Quality of evidence - Moderate

Recommendation-Strong

- 3.12.29 We recommend that with the identification of a new case of HBV infection, the patient should be referred to an HBV specialist for expert management.

Not graded

- 3.12.30 We recommend that in the detection of a prior unidentified case of HBV infection, there should be enhanced HBV surveillance on patients previously identified to be inadequately immune, who have been dialysed in the centre since the index patient's last negative result.

Quality of evidence - Moderate

Recommendation-Strong

- 3.12.31 We recommend that those with anti-HBs antibody titre between 10 - 100mIU/ml should be given

booster doses of the vaccine. Hepatitis B immunoglobulin should be considered for previous non-responders that have been exposed in the last 7 days.

Not graded

Hepatitis C virus / HIV

- 3.12.32 We recommend screening all patients with no identified risk factor for hepatitis C with nucleic acid test (NAT), provided serological test for HCV is positive. Patients with known risk factors for hepatitis C should have NAT as an initial screening method.

Quality of evidence - High

Recommendation--Strong

- 3.12.33 We recommend that HIV screening prior to commencement of dialysis.

Not graded

- 3.12.34 We recommend a dedicated dialysis machine for both HCV and HIV infected patients. They should be dialysed in a separate area with dedicated staff.

Not graded

- 3.12.35 We recommend 6 monthly anti-HCV testing for patients on regular haemodialysis, those with previous or current risk factors for HCV (like intravenous drug users, homosexuals, commercial sex workers, those infected with other blood-borne viruses), should be screened every 3 months, using NAT.

Quality of evidence - Low

Recommendation--Strong

- 3.12.36 We recommend that if a prior unidentified case of HCV is detected, surveillance should be carried out in all patients who had dialysed at the centre, since the last negative NAT test of the index patient.

Quality of evidence - Low

Recommendation--Strong

Covid-19 (or any other highly contagious viral disease)

Suspected and confirmed Covid-19 cases

- 3.12.37 We recommend that healthcare workers involved in the care of suspected cases should wear full personal protective equipment.

Quality of evidence - High

Recommendation-Strong

- 3.12.38 We recommend that government designated isolation units with facilities for critical care and haemodialysis, be made available for Covid-19 positive patients requiring haemodialysis.

Not graded

- 3.12.39 We recommend the use of an isolated dialysis unit for the management of suspected or confirmed cases of Covid-19. If this is not available, they can be dialyzed in the same Centre as for Covid-19 negative patients, preferably in a negative pressure room, with either a separate route for entering and exiting the centre or they should not enter and exit the centre at the same time as other patients. These group of patients should be dialyzed at the last shift of the day, with dedicated staff wearing full PPE.

Not graded

- 3.12.40 We recommend rapid testing kits for Covid-19 be made available in all dialysis units, for screening suspected patients. Those that test positive should have a confirmatory PCR testing.

Not graded

- 3.12.41 We recommend that all equipment in the haemodialysis unit that patients might have come in contact with should be disinfected according to the standard protocols.

Not graded

- 3.12.42 We recommend that following a suspected or a newly confirmed case in a dialysis centre, there should be immediate disinfection and other patients should not make use of areas in contact with the infected patient until it has been cleared and properly disinfected.

Not graded

- 3.12.43 We recommend that medical wastes from suspected or confirmed cases be considered as highly infectious and disposed of accordingly.

Not graded

Covid-19 positive patients on maintenance haemodialysis

- 3.12.44 We recommend that patients should not change to another dialysis center when confirmed positive; rather they should continue dialysis at their original centre, with dedicated staff wearing full PPE.

Not graded

- 3.12.45 We recommend that any patient who defaults should be screened prior to recommencing dialysis, unless they have a written medical report from the referring physician.

Not graded

- 3.12.46 We recommend screening all patients with fever for Covid-19, and dialyse at the last shift of the day with dedicated staff wearing adequate PPE, till exclusion of the infection.

Not graded

- 3.12.47 We recommend spacing of at least 2 metres between patients in the waiting and treatment areas, with good air conditioning and ventilation.

Not graded

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3.13 Haemodialysis in special population

Haemodialysis in the elderly

Background

Increasing age is a recognized risk factor for developing chronic kidney disease [1, 2] and worldwide, the number of elderly people (≥ 65 years) with ESRD accessing haemodialysis has also increased [3].

Offering haemodialysis to these group of patients is fraught with a lot of uncertainties owing to a higher prevalence of co-morbidities, frailty and functional impairment in them. The risk of mortality in elderly patients on haemodialysis has been shown to be 3-6 times higher when compared to younger population [4].

These challenges are further complicated by lack of clarity from studies done on the benefit of offering dialysis as against conservative management, on outcomes such as improved survival and improvement in quality of life [5].

Hence, the decision on the appropriateness of commencing dialysis or otherwise, difference in dialysis prescription and measures of assessing haemodialysis adequacy is subject to a lot of discrepancies, based on the clinician and care givers choices.

There is no universal consensus as regards haemodialysis in the elderly, and major clinical practice guidelines have not included special sections on haemodialysis in the elderly.

The major emphasis of care in these group of patients is shared decision making between the medical personnel and the patient/caregivers, this cannot be overemphasized.

Supporting Evidence

There are no randomized controlled trials regarding dialysis in the elderly to the best of our knowledge at the time of this write-up. Studies done have been mainly observational studies comparing outcome of renal replacement therapy (RRT) and conservative management (CM). Most studies leaned towards better survival in RRT; however, issue of bias in selection of candidates into RRT and conservative management groups cannot be ruled out.

KDIGO and KDOQI guidelines give no age specific guidance on dialysis in the elderly population.

The European Renal Best Practice guideline6 recommendation in elderly patients with advanced CKD was based on numerous observational studies and expert opinions [7-9].

Recommendations

- 3.13.1 We recommend shared decision making between the clinician and elderly patients and care givers before initiating haemodialysis, with clear option given for conservative management.
Quality of evidence - Moderate Recommendation-Strong
- 3.13.2 We suggest use of the REIN score10 to predict risk of mortality in elderly patient with stage 5 CKD. This will help in counselling during shared decision making.
Not graded
- 3.13.3 We suggest initial conservative dialysis schedules (considering length, number of weekly sessions, ultrafiltration and blood flow rate) in elderly patients especially in the frail with significant co-morbidities. This can be increased periodically as needed
Not graded
- 3.13.4 We suggest that in asymptomatic elderly patients, with no other indication for haemodialysis, initiation of haemodialysis be delayed till eGFR falls between 6-9ml/min/1.73m²
Not graded

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Haemodialysis in pregnancy

Background

Pregnancy, though rare in patients with ESRD, is associated with increased risk of adverse maternal and fetal outcomes when it occurs [1, 2]. CKD has been reported to affect up to 3% of women of reproductive age in high income countries [3]; it is thought to be higher in low and middle income countries, with higher incidence of adverse outcomes [4].

In addition to providing adequate dialysis, the physiologic and metabolic changes in pregnancy and nutritional needs of the growing foetus have to be considered when providing haemodialysis for these patients.

Furthermore, there is lack of clarity on what to offer established dialysis patients who become pregnant, compared to patients who need to be initiated on dialysis after conceiving, considering the latter is expected to have a higher residual renal function.

There is paucity of data on pregnant women on haemodialysis in Nigeria. However, studies done worldwide suggest improved maternal and foetal outcomes with intense haemodialysis sessions [5]. This is however difficult in our setting considering the prohibitive cost of haemodialysis which is borne directly by the patients. Some other studies have demonstrated that maintaining maternal serum urea levels below a certain range is associated with improved outcomes [6].

Supporting evidence

Studies done on pregnant women on haemodialysis are mainly observational studies and we are not aware of any randomized studies on this patient population at the time of writing these recommendations.

The 2015 KDOQI guideline on dialysis in pregnant ESRD patients [7], was based on observational studies and case series, most prominent of which is a Canadian cohort study which reported improved pregnancy outcomes in women who had more frequent and longer dialysis sessions [5] (48+ 5hours /week). This proved to produce significantly better outcomes (in terms of live birth rates, gestational weight at delivery and infant weight) when compared to pregnant patients who had less intense haemodialysis sessions.⁸

The UK Renal Association [9] provides a more robust guideline for management of haemodialysis in pregnancy using similar cohort studies and expert opinions [5,6,8,10-13].

Recommendations

For patients already established on haemodialysis:

3.13.5 We recommend detailed counselling for all women of reproductive age group on the increased risk

of maternal and foetal outcome with pregnancy. They should be counselled on postponing pregnancy till after kidney transplant when possible.

Quality of evidence - Low

Recommendation-Strong

- 3.13.6 We recommend longer and more frequent haemodialysis sessions during pregnancy if affordable by the patient.

Quality of evidence - Low

Recommendation-Strong

- 3.13.7 We recommend weekly assessment of ultrafiltration goals taking into consideration the expected weight gain during pregnancy and clinical state of the patient.

Not graded

- 3.13.8 We recommend regular assessment of maternal nutritional status, serum electrolytes, calcium, magnesium, phosphate levels with a view to supplement when deficient.

Not graded

Initiating Haemodialysis during Pregnancy

- 3.13.9 We recommend a lower threshold for initiating haemodialysis in patients with CKD who conceive before commencing maintenance HD. We suggest considering initiating HD when maternal serum urea concentration exceeds 100mg/dl.

Other considerations, including gestational age, biochemical parameters, fluid balance, rate of renal decline, blood pressure control, and uraemic symptoms should also be considered.

Not graded

- 3.13.10 We recommend initiating HD less intensively and that incremental haemodialysis should be considered based on patient's residual renal function.

Not graded

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Haemodialysis in Children

Timing of dialysis initiation

Background

In Nigeria, haemodialysis is an established form of renal replacement therapy (RRT). It is the predominant form of RRT utilized by adults with end-stage renal disease (Bello 2013). An assessment of paediatric dialysis services available in Nigeria found HD to be the commonest modality available (Esezobor et al 2012).

HD can be utilized in children of all ages although preference is for those older than five years of age. There are several factors that influence the choice of modality of treatment in children and these include patient and parent choice after proper education, finance, social circumstances, co-morbidities, availability of RRT as well as expertise.

Although parent and patient choice are important, guidance from the unit staff is needful as venous access can be difficult to achieve and maintain in children less than 5 years of age as the children tend to be uncooperative especially when needling is required

The decision whether to start RRT or not may be difficult. There is no universal timing to initiate RRT. There is lack of evidence from randomized controlled trials about optimal time to start. The main considerations in our patient population would be the clinical state of the patient as well as the cost of the service. Whilst the decision may be easy in wholly insured patients, it is less likely so in the majority who pay out of pocket.

Supporting evidence

The updated KDOQI guideline recommendations on the timing of HD have been driven by the IDEAL study, a robust multi-centre randomized controlled trial in New Zealand and Australia which compared an early and late start of HD based on creatinine clearance. The overall difference in mortality, Cardiovascular, infectious events and complications of HD between the two groups were not significantly different³. There are no RCTs yet in Nigeria or similar contexts to inform our recommendations at this time.

Recommendations (adapted from ref 4 and 5)

- 3.13.11 We recommend that all children with advanced CKD (GFR < 30ml/min/1.73m²) should be prepared for dialysis, kidney transplant or conservative care before their CKD becomes symptomatic.
Quality of evidence - Low Recommendation-Strong
- 3.13.12 We recommend that for patients who are expected to require dialysis, advance preparation of appropriate access (AV fistula, internal jugular) should be considered while GFR is >15 mL/min/1.73m².
Quality of evidence - Low Recommendation-Strong
- 3.13.13 We recommend that dialysis should be considered in patients with a GFR <15 mL/min/1.73m², when there is one or more of the following: symptoms or signs of uraemia, inability to control hydration status or blood pressure or a progressive deterioration in nutritional status (malnutrition). Majority of patients will be symptomatic and need to start dialysis with GFR in the range 9-6 mL/min/1.73m²
Quality of evidence - High Recommendation-Strong
- 3.13.14 We recommend close monitoring of high-risk patients e.g. diabetics and those whose renal function is deteriorating more rapidly than eGFR 4 mL/min/year. Where close supervision is not feasible and in patients whose uraemic symptoms may be difficult to detect, a planned decision to start dialysis while patient is still asymptomatic may be preferred.

Quality of evidence - Low

Recommendation-Strong

- 3.13.15 We suggest that asymptomatic patients with advanced CKD may benefit from a delay in starting dialysis in order to allow preparation, planning and permanent access creation rather than using temporary access

Quality of evidence - Low

Recommendation-Weak

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3.14 Haemodialysis Dose, Frequency and Duration

Background

In the past, recommendations on haemodialysis dose and frequency have relied on several observational and non-randomized experimental studies which suggest that 'more is better' [1, 2]. Observational and controlled non-randomized studies suggest more frequent and or longer dialysis sessions improve patients' quality of life, controls hyperphosphataemia, reduce hypertension and results in regression of left ventricular hypertrophy. Children have low incidence of dialysis-requiring kidney disease and the import of this is that many treatment decisions are from observational data and studies carried out in adults.

Supporting Evidence

There are now several RCTs that compare more frequent or extended dialysis to conventional dialysis [Culleton 2001, Jardine 2014]. Recommendations have been dominated by two studies namely the National Cooperative Dialysis Study (NCDS) and the HEMO study. The evidence favours adequate dialysis to specific bio-physiological and clinical endpoints but there is no significant advantage of extended dialysis compared with conventional dialysis. Nonetheless, HD prescription should be individualized to achieve adequate dialysis. In our context, there are as yet no RCTs studying different haemodialysis frequencies. At the moment, planning such RCTs may be futile unless there is full insurance coverage for the treatment.

Recommendations (Adapted from ref. 7)

- 3.14.1 In children and adolescents, we recommend assessment of dialysis adequacy which goes beyond biochemical targets, to include clinical goals such as growth, bone health, cardiac function and quality of life.

Quality of evidence - Low

Recommendation-Strong

- 3.14.2 HD should take place at least three times per week in all patients with end-stage chronic renal failure.

Not graded

- 3.14.3 We recommend targeting dialysis dose to achieve a minimum eKt/V of 1.2 (spKt/V of >1.3) for

patients on thrice weekly sessions, or a standardized Kt/V of 2.2 for those on augmented schedules. Alternately a urea reduction rate(URR) above 65% may be acceptable

Quality of evidence - Low

Recommendation-Strong

- 3.14.4 We suggest an augmented schedule for children on predominantly liquid nutrition, and those with ventricular systolic dysfunction.

Not graded

- 3.14.5 We recommend a blood flow rate of 5-7ml/kg/min for the majority of patients, using consumables appropriate to body size, with extracorporeal volume less than 10% of the patient's blood volume.

Quality of evidence - Low

Recommendation-Strong

- 3.14.6 The duration of thrice weekly HD in patients with minimal residual renal function should not be reduced below 4 hours without careful consideration

Not graded

- 3.14.7 Measurement of the "dose" or "adequacy" of HD should be performed monthly in all hospital HD patients.

Not graded

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Haemodialysis Membranes

Background

The balance of evidence supports the use of low flux synthetic and modified cellulose membranes instead of unmodified cellulose membranes because of improved biocompatibility.

The balance of evidence supports the use of high flux synthetic dialyser because of the higher clearance of larger molecules. This is particularly useful in patients who have been on chronic dialysis for several years. Such patients are at risk of developing symptoms of dialysis-related amyloidosis. Treatments with better clearance of middle molecules include haemodialysis with high flux synthetic membranes and haemodiafiltration. Chronic high flux dialysis in the HEMO study did not affect the primary outcome of all-cause mortality or any of the secondary composite outcome measures including the rates of first cardiac hospitalization or all-cause mortality, first infectious hospitalization or all-cause mortality, first 15% decrease in serum albumin or all-cause mortality, or all non-vascular access-related hospitalizations.

Supporting Evidence

Three trials reported primary finding of no survival benefit. Meta-analysis suggested cardiovascular mortality was reduced in high flux membrane, showed significant benefit of high flux dialyzers on all-cause mortality for certain pre-specified conditions (serum albumin less or equal to 4 g/dl, HD for greater than 3.7 years, DM or AV fistulas).

Recommendation

- 3.14.8 We recommend the use of biocompatible, either high or low flux, haemodialysis membranes for intermittent dialysis

Quality of evidence - Moderate

Recommendation-Strong

Fluid in haemodialysis

Fluid control is an essential clinical goal of maintenance HD. In chronic HD, the aim is to end the session with the child at their target or desired weight. The target weight refers to the weight below which the child will become symptomatically hypotensive.

Fluid overload has been attributed to sodium and water retention and extracellular volume expansion. Extracellular volume (ECV) expansion is an important contributor to elevated BP, hence reducing ECV is important and should be considered first line in the treatment. To improve control of the extracellular volume, reduction of dry weight should occur gradually over 4 to 12 weeks. Assessment of target weight in children and adolescents is particularly challenging as it needs frequent adjustment in line with growth or period of illness.

Supporting Evidence

The DRIP study (Dry Weight Reduction Intervention) is the largest RCT demonstrating effect of dry weight reduction on BP control. Safety and tolerability of maintenance HD is dictated by ultrafiltration rate which is determined by the intra-dialytic weight gain and length of each session.

An important way to reduce ultrafiltration rate while achieving optimal control of hypervolemia, is to ensure sodium balance. There is evidence that suggest that high dietary sodium intake and inadequate sodium removal during HD can result in excessive fluid intake and hypertension.

Recommendations

- 3.14.9 We recommend clinical assessment of the fluid status and target weight and dietetic assessment at least monthly.

Quality of evidence - Low

Recommendation-Strong

- 3.14.10 We suggest, where available, supplementing clinical assessment with a validated objective measure of fluid status such as bio-impedance, on a monthly basis or more frequently during periods of rapid growth or illness.

Not graded

- 3.14.11 We recommend regular assessment of ultrafiltration tolerance, using extended times to avoid excessive ultrafiltration rates.

Quality of evidence - Very low

Recommendation-Strong

- 3.14.12 Target weight can be determined by careful, persistent fluid removal to achieve normal BP after dialysis. A safe starting point is 10ml/kg/h. No more than 5% of the child's body weight should be removed in one session or 0.2 ml/kg/min

Not graded

- 3.14.13 We recommend both reducing dietary sodium intake as well as adequate sodium and water removal

with HD to manage hypertension, hypervolemia and left ventricular hypertrophy.

Quality of evidence - Moderate

Recommendation-Strong

Paediatric Dialysate consideration

3.14.14 We recommend that dialysate concentration including potassium, buffer and calcium should be individualised.

Quality of evidence - Low

Recommendation-Strong

3.14.15 We suggest individualised dialysate temperature, between core temperature and 0.5 degrees Celsius below with monitoring of intra-dialytic core temperature for neonate and smaller children.

Not graded

Anticoagulation

3.14.16 We recommend that the patients without increased bleeding risk should be given unfractionated or low molecular weight heparin during dialysis to reduce clotting of the extracorporeal system

Quality of evidence - High

Recommendation-Strong

3.14.17 We recommend systemic anticoagulation should be omitted or minimised in patients with increased bleeding risk.

Quality of evidence - Low

Recommendation-Strong

3.14.18 We recommend that patients with heparin allergies should be prescribed a non-heparin form of anticoagulation.

Quality of evidence - High

Recommendation-Strong

3.15 Withdrawal from haemodialysis

Background

Withdrawal from haemodialysis (HD) can be regarded as any cause of discontinuation from haemodialysis [1]. Reasons for this are diverse; however in Nigeria, financial constraints have been identified as the major cause of withdrawal from haemodialysis with numerous studies showing most patients unable to sustain HD beyond 3 months [2-5]. In contrast, in the developed world HD withdrawal mainly occurs in the context of significant pre-existing co-morbidities usually in the frail elderly patients [6]. Other reasons for withdrawal from HD includes patients preference, reduced life expectancy from other co-morbid diseases, persistent deterioration despite HD.

Some studies have demonstrated a better outcome in terms of survival in patients who started off with conservative management, as against those who started HD then withdrew [7, 8], raising the issue of need to prognosticate survival before initiating HD. Numerous prognostic tools on survival within 6 months of initiating haemodialysis have been developed, and are recommended by guidelines [9, 10, 11], but none have been validated in Nigerian ESRD patients.

Hence, nephrologists are constantly faced with the challenges of caring for patients who need, but can't afford or refuse HD. This brings forth the need for kidney supportive care [12], social support and end of life care for this group of patients.

The kidney supportive care or conservative approach aims to provide all aspects of clinical care, with the exception of dialysis. Main focus of this care is to improve health related quality of life, reduce symptom burden, slow rate of renal function decline where feasible, and plan for end of life.

Supporting Evidence

Available evidence on management of patients withdrawing from haemodialysis are mainly based on observational studies [13-16], expert opinions and consensus statements. Most of these observational studies were conducted in an elderly population in contrast to the relatively younger age of dialysis patients seen in our country.

There is no universally acceptable way of treating these patients and variations in management are

seen within and between countries [17].

The UK Renal Association guidelines on withdrawal from dialysis [18], KDIGO executive summaries on supportive care [12] and the Renal Physician Association [19] were based on similar studies and expert opinions.

Description of what constitutes conservative care is mainly based on expert opinion [20-22].

Recommendations

3.15.1 We recommend a shared decision making between clinicians and patients/care givers in all patients in stage 4 and 5 CKD. This should include discussion on prognosis, capability of the patient/carer to sustain RRT and options for conservative kidney care.

Quality of evidence - Low

Recommendation-Strong

3.15.2 We recommend dialysis withdrawal is appropriate in the following situations;

- Mentally competent patients, who despite adequate counselling, and being well informed, voluntarily decide to discontinue HD. We suggest patients put this decision in writing.
- Patients who lack mental capacity to take decisions but whose legally approved carers decide to discontinue HD despite adequate counselling. We suggest the carers provide legal documentation of their decision (e.g. sworn affidavit) and if necessary, be referred to the legal unit of the hospital.

Not graded

3.15.3 We recommend that in patients who withdraw from haemodialysis a multidisciplinary approach to conservative kidney care should be offered, involving nephrologists, nurses, social workers, dieticians, psychologist and religious personnel.

Quality of evidence - Low

Recommendation-Strong

Role of the Nephrologist

3.15.4 We recommend nephrologists prognosticate every patient with stage 4 and 5 CKD to aid in shared decision making.

Not graded

3.15.5 We recommend the nephrologist determine reasons or condition underlying withdrawal from haemodialysis and address potentially treatable ones e.g. depression, pain, fear of HD. Patient and carers should also be counselled on prognosis and life expectancy following withdrawal of HD.

Not graded

3.15.6 We recommend that an assessment of competence be carried out on all patients who request to withdraw from HD.

Not graded

3.15.7 We recommend regular short clinic appointments for patients who withdraw from haemodialysis, using a patient centred approach.

Goals of clinic follow-up should include;

- i) Regular assessment of symptom burden
- ii) Appropriate management of symptoms using pharmacologic and non-pharmacologic means
- iii) Management of complications associated with renal failure such as: Anaemia, Acidosis, Fluid and electrolyte abnormalities, Hypertension
- iv) Management of co-morbid conditions and intercurrent illness

Not graded

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SECTION IV: PERITONEAL DIALYSIS

4.1 Choosing Modalities of Renal Replacement Therapy

Background

For close to a century, peritoneal dialysis has been considered a key option for renal replacement therapy in patients with end-stage renal disease and acute kidney injury. According to an epidemiological survey published in 2016, the proportion of patients receiving peritoneal dialysis was estimated at 11% with significant disparity between countries [1]. In developed worlds, the choice of modalities for renal replacement therapy varies from intermittent haemodialysis, peritoneal dialysis and continuous RRT. However, the situation is different in sub-Saharan Africa, the choice is largely limited to intermittent HD [2, 3].

NICE clinical guideline published in 2011, recommends that PD should be considered as the initial dialysis option in paediatric patients or in individuals with residual renal function and in adults without significant associated comorbidities [4]. It's a major part of an integrated renal replacement care, and should be considered as a preferred initial dialysis option in children or in patients requiring a swap from HD.

Nigeria association of Nephrology (NAN) has been a strong advocate for the improvement in the use of PD as an important dialysis option, through collaboration with local industries for the local production of consumables. There has also been an awareness campaign among renal care providers and community at large [5].

Acute PD is technically straightforward, affordable, and realistic to deliver, since neither electricity nor complex equipment is needed, this accounts for its advocacy in low-income countries. In AKI patients, despite the introduction of extracorporeal continuous renal replacement therapy (CRRT) in intensive care units (ICUs), there is no evidence in terms of outcomes that CRRT is superior to PD [6, 7, 8].

Supporting evidence

The Renal Association clinical practice guideline published in 2017 recommends that peritoneal dialysis should be used as a component of the integrated dialysis approach is associated with good clinical outcomes and very comparable to haemodialysis [1].

A Cochrane review on peritoneal dialysis for acute kidney injury published in 2017 by Liu et al [9] reported insufficient evidence to show a difference between PD and CRRT in terms of all-cause mortality or kidney function recovery.

The NECOSAD trial is the only randomized study comparing HD to PD as a first treatment, the outcome showed no differences in 2-year quality adjusted life years or 5-year mortality. The number of participants randomized was however insufficient to generalize this observation [10].

The International Society of Nephrology 0 x 25 initiative established the Saving Young Lives (SYL)

program in 2012 with the goal of establishing a sustainable acute PD program in resource limited settings, thus far over 60% of the patients treated recovered their renal function [11].

Recommendations

- 4.1.1 PD should be provided as part of an integrated renal replacement therapy care such that patients would have access to other modalities of care should the need arise.

Not graded

- 4.1.2 CAPD should be presented to all ESRD patients as a viable choice of renal replacement therapy when the necessary equipment(s) and consumables are available and affordable.

Quality of evidence - Low

Recommendation-Strong

- 4.1.3 Acute Peritoneal dialysis should be offered as an efficient method of renal replacement therapy in patients with acute kidney injury particularly in our environment where it may be the only available modality in remote settings.

Quality of evidence - Moderate

Recommendation-Strong

4.2 Peritoneal Dialysis Fluids: Equipment and Resources

Introduction and background

The benefits of biocompatible solutions include preservation of residual renal function and reduction in circulating advanced glycation end-products. These observations have prompted dialysis companies to develop and commercialize biocompatible solutions, with normal pH and/or reduction in glucose degradation products and variable buffering approaches [1, 2].

Commercial solutions are manufactured to high standards with strict asepsis and careful monitoring for bacterial and endotoxin contamination, this is not usual with locally prepared solutions. Recent studies from Africa have shown good outcomes using locally prepared solutions made from commercially available IV fluids [1,3,2,6]. These studies demonstrated a comparable good peritonitis rate and outcomes. In resource limited settings where patients pay out of pocket for care, there is advocacy for more utilization of locally prepared solutions. The purchasing costs, transportation costs, taxes and bureaucratic bottlenecks negatively impact the utilization of commercially prepared solutions in our environment [5].

Tenckhoff catheter can be used for chronic dialysis. They have a bigger diameter lumen and side holes than rigid catheters, resulting in improved dialysate flow rates and reduced obstruction to achieve appropriate clearances. They're also less likely to leak and have fewer cases of peritonitis. The ideal catheter must be sited deep in the pelvis. Nasogastric tubes with side holes cut into them prior to surgical insertion have been reported to be quite successful. Intercostal drainage tubes and haemodialysis catheters are among the other alternatives. Available guidelines do not recommend any of these alternatives as first line [14,15,16].

Supporting Evidence

The International Society of Peritoneal Dialysis (ISPD) has developed a set of recommendations for managing PD catheter insertion in adults and children [17]. Henderson and colleagues [18] reported higher rate of peritonitis in patients with surgically implanted catheters as compared to percutaneous catheters, similar finding was reported by Perakis et al [19]. However, both approaches have comparable rate of leaks and inadequate drainage. Flexible PD catheters can be inserted percutaneously by appropriately trained nephrologists. This reduces the time required from diagnosis of dialysis requiring AKI to initiation of treatment [15].

In chronic and acute PD, a Y-set with a double bag and the disconnect system is associated with lower peritonitis rates than the usual spiking method. Between dwells, disconnection systems allow the fluid infusion set (together with infusion and drainage containers) to be removed from the patient [17].

The reduction in peritonitis rates and transport status stability in the group receiving biocompatible PD fluid were endpoints of the randomized balANZ study [20]. However, a recent systematic review found no effect of biocompatible fluids on peritonitis rates and patient survival. Therefore, further studies need to be done to ascertain the potential benefits of biocompatible fluids. Systematic reviews of existing trials

suggest that biocompatible solutions should be considered for preservation of residual kidney function [21,22,23].

Palmer et al. [24] retrospectively studied patients on acute PD, they found no difference in peritonitis rates between those treated with commercially available solutions and those treated with locally prepared solutions. Similarly, recent studies from Africa have shown comparable good results using locally prepared fluids from commercially available IV fluids [6,13,2].

Recommendation

4.2.1 The PD fluids should satisfy internationally recognized quality standards.

Quality of evidence - Low

Recommendation-Strong

4.3 Peritoneal Dialysis Connectology

Background

Continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD) are two different types of peritoneal dialysis (PD). Continuous ambulatory peritoneal dialysis (CAPD) entails manually PD exchanges, whereas automated peritoneal dialysis (APD) is a wide term that refers to all modalities of PD that use a mechanical device to aid with dialysate delivery and drainage. Continuous cyclical PD (CCPD), intermittent PD (IPD), nocturnal intermittent PD (NIPD), and tidal PD are some of the different types of APD. Every day, the patient or caregiver must perform three to five exchanges in CAPD [8,15].

APD has been proposed as an alternative to CAPD for several medical and psychosocial reasons. APD involves fewer connections and patient independence from dialysis during the daytime. Additional benefits of APD include possibly reduced back pain and body image difficulties due to being free of fluid in the abdomen. The patient's preference should determine whether APD or CAPD is used [12].

When starting PD treatment, the patient's social background, including employment, family, and lifestyle, are all crucial considerations. Automatic PD is the most common modality of PD for paediatric patients. Factors favouring APD include membrane characteristics, relationship with body surface area and psychosocial needs of children attending school. However, lack of data does not allow for a firm recommendation about the type of PD [15,25].

Supporting evidence

Under the auspices of the International Society for Peritoneal Dialysis, guidelines are developed on PD prescription of CAPD or Automated PD [8,12].

A randomized multi-center Danish study by Bjorner JB et al [26] found that APD allows the patient to spend more time with family and provides greater freedom to continue working or schooling, however it is linked to poor sleep quality. A systematic review of RCTs comparing CAPD with all forms of APD was performed by Rabindranath KS et al [8], showed APD to be more beneficial than CAPD in terms of impact on patient's quality of life and peritonitis rates. Several studies have however shown no difference in outcomes, whether CAPD or APD is chosen as initial modality of choice [27,28].

Because of the relatively small paediatric population, few RCTs in CAPD have been conducted; however there have been an increasing number of reports of clinical experience through registries.

In 2005, the International Society for Peritoneal Dialysis (ISPD) established guidelines for small solute clearance and fluid evacuation in peritoneal dialysis, these recommendations were recently updated in 2019. The ADEMEX study enrolled 965 patients on PD in a multicentre prospective, randomized, controlled clinical trial that took place in 24 dialysis centres across Mexico. This study found that while RRF was associated with mortality while peritoneal Kt/V was not [29]. A similar finding was reported by a large observational cohort study in the United States (US) on 1603 people doing PD [30].

Recommendations

4.3.1 The use of disconnect or twin bag systems is generally preferred as standard therapy for acute or chronic treatment.

Quality of evidence - High

Recommendation-Strong

- 4.3.2 Flexible peritoneal catheters are preferred for acute or Chronic PD .
 Quality of evidence - Low Recommendation- Strong

Note: Rigid stylet catheters or other improvised catheters in resource-constrained setting like ours may be lifesaving.

- 4.3.3 The method of catheter insertion should be based on patient factors, equipment available and the skills of the clinician.
 Quality of evidence - Very low Recommendation- Strong
- 4.3.4 In all cases, the catheter should be tunnelled.
 Quality of evidence - Low Recommendation- Strong

4.4 Prescribing Peritoneal Dialysis

Background

Uncorrectable surgical problems (e.g., severe hernias, diaphragmatic hernias, or bladder exstrophy), loss of peritoneal function or many peritoneal adhesions, and physical or mental inability to conduct the method are absolute contraindications to PD [311].

In the presence of abdominal wall cellulitis that may lead to peritonitis, the use of PD is relatively contraindicated. It's also not recommended in patients with severe gastroesophageal reflux disease or adynamic ileus, which can make peritoneal dialysis less effective [32]. Intraperitoneal fluid may increase intra-abdominal pressure, compromising lung function and pulmonary gas exchange in patients with relative respiratory insufficiency. In the treatment of life-threatening hyperkalaemia, acute PD is largely ineffective. In hypercatabolic state, PD is not also the preferred RRT modality [33]. Other relative contraindications include morbid obesity, diverticulitis, ischemic bowel disease, or inflammatory bowel disease [4].

Supporting evidence

NICE Clinical Practice Guidelines (2011) recommends PD as the initial dialysis treatment of choice of chronic kidney disease stage 5 for children, patients with residual renal function, and without major concomitant comorbidities [1].

National Service Framework for Renal Services publication on peritoneal dialysis argues that most patients commencing dialysis are medically eligible to opt for PD, the traditional contraindications to PD are noted to be overstated [34].

Recommendations

- 4.4.1 The prescription of CAPD or Automated PD should follow the ISPD recommended practice points for high-quality goal-directed peritoneal dialysis
 Not graded
- 4.4.2 The choice of PD modality in paediatric patients should be based upon the child's age and size, presence of co-morbidities, family support available, modality contraindications, expertise of the dialysis team and the child's and parents'/caregivers' choice.
 Not graded
- 4.4.3 The desire to optimize fluid management and solute clearance MUST be must be considered within the context of the overall quality of life, ability to attend school, socialize as well as child's and family's expectations.
 Not graded

4.5 Contraindications to Peritoneal Dialysis

Background

Uncorrectable surgical problems (e.g., severe hernias, diaphragmatic hernias, or bladder exstrophy), loss of peritoneal function or many peritoneal adhesions, and physical or mental inability to conduct the method are absolute contraindications to PD [311].

In the presence of abdominal wall cellulitis that may lead to peritonitis, the use of PD is relatively contraindicated. It's also not recommended in patients with severe gastroesophageal reflux disease or adynamic ileus, which can make peritoneal dialysis less effective [32]. Intraperitoneal fluid may increase intra-abdominal pressure, compromising lung function and pulmonary gas exchange in patients with relative respiratory insufficiency. In the treatment of life-threatening hyperkalaemia, acute PD is largely ineffective. In hypercatabolic state, PD is not also the preferred RRT modality [33]. Other relative contraindications include morbid obesity, diverticulitis, ischemic bowel disease, or inflammatory bowel disease [4].

Supporting evidence

NICE Clinical Practice Guidelines (2011) recommends PD as the initial dialysis treatment of choice of chronic kidney disease stage 5 for children, patients with residual renal function, and without major concomitant comorbidities [1].

National Service Framework for Renal Services publication on peritoneal dialysis argues that most patients commencing dialysis are medically eligible to opt for PD, the traditional contraindications to PD are noted to be overstated [34].

Recommendations

4.5.1 PD is unsuitable for some patient populations. We recommend that PD should not be offered to patients with severe obesity, hernias, recent abdominal surgery, active or past history of peritonitis, abdominal aortic aneurysm, absent anterior abdominal wall (Prune Belly syndrome), inflammatory bowel disease, abdominal masses etc except in critical conditions as a lifesaving option.

Quality of evidence - Very low

Recommendation- Strong

4.5.2 The use of peritoneal dialysis is also contraindicated in patients with physical or mental incapacitation or those with uncorrectable mechanical defects in the abdomen, surgically irreparable hernia, omphalocele, gastroschisis, diaphragmatic hernia, and bladder extrophy, as well as those with extensive abdominal adhesions.

Quality of evidence - Very low

Recommendation- Strong

4.5.3 Acute Peritoneal Dialysis should NOT be prescribed for patients with established ESRD except when they develop complications such as inability to secure vascular access, cerebro-vascular disease, cardiovascular instability / severe arrhythmias and other intercurrent illnesses in the absence of any other form of renal replacement therapy.

Quality of evidence - Very low

Recommendation- Strong

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4.6 Commencement of PD after catheter placement

Background

After placement of a catheter, certain complications have been associated with the break-in period (defined as the time between catheter placement and initiation of PD). The most encountered being, peri-catheter leaks, IP bleeds and catheter obstruction, which ultimately lead to catheter dysfunction. A lot of controversies exist between early break-in and delayed break-in, with some authors pointing out that there are no convincing studies proving the superiority of delayed break-in periods. Another thorny issue prior to commencement of PD after catheter placement is post-insertion flushing of the PD catheter. A raft of studies has shown that intraperitoneal flushing following catheter insertion, with 500 to 1000mls of dialysate can be done daily till PD is initiated and this is done to prevent fibrin or clot from blocking the catheter. However, the specific flushing policies for different PD centres vary widely, and some do not even flush at all [1]. Studies have shown that a break-in period of greater than 2 weeks may be necessary to allow healing and identification of any problems prior to initiation of dialysis [1]. Some authors have shown that the dwell volume is directly related to dialysate leaks within the first 2 weeks [1]. Some other concerns centered around patients who needed dialysis urgently within the first 2 weeks post insertion.

Supporting Evidence

A RCT done by Ranganathan et al randomized patients into 3 groups of break-in periods of 1 week, 2 weeks and 4 weeks respectively and found a significant reduction in dialysate leaks as break-in period increased (28.2% vs 9.5% vs 2.4%) [2]. Gadallah et al [3]. in their study showed that intraperitoneal bleed left unflushed predisposed to adhesions, especially when there was evidence of significant bleeding intra or post-operatively [3]. Many small mainly retrospective single-center studies have constantly shown that urgent start on PD with a break-in period of less than 2 weeks may be associated with a minor increased risk of mechanical complications but apparently no detrimental effect on patient survival, peritonitis-free survival, or PD technique survival compared with elective start on PD. In most studies, the apparent increased risk of mechanical complications was managed conservatively without the need to remove the PD catheter. Crabtree et al [4] in their commentary noted that the most important determinant of dialysate leaks was catheter insertion technique, as studies employing long segment rectus sheet embedding techniques recorded very low dialysate leaks even when PD was commenced without delay.

Recommendations

- 4.6.1 We recommend that timing of PD catheter insertion should be well before commencement of CAPD procedure. A break-in period of at least 2 weeks should be allowed for correction of any early catheter-related problems.
Quality of evidence - Moderate Recommendation- Strong
- 4.6.2 We recommend a modified PD prescription using low volume exchanges with the patient in the supine position if urgent start on PD with a break-in period of < 2 weeks is needed.
Quality of evidence - Low Recommendation- Strong
- 4.6.3 We recommend that peri-operative catheter care and catheter complications (leaks, hernias, obstruction) should be managed according to the International Society of Peritoneal Dialysis guidelines.
Not graded

4.7 Viral screening and vaccination

Background

Viral infections have always been associated with CKD, from causation to complication and even in the management of CKD. The main risks from blood-borne viruses are from HBV, HCV and HIV and even though hepatitis G virus (HGV) and hepatitis D virus (HDV) have been identified as being commonly carried by dialysis patients, they are of unknown clinical significance [5]. In many dialysis centres worldwide, differing policies concerning screening for viral agents and handling of patients who test positive to certain viruses exist. In some centers, care is taken to separate patients with HBV, HCV and HIV from other patients by providing different dialysis machines, while some do not even provide haemodialysis services to these patients [6].

Current recommendations (KDIGO and NICE) [5] discourage the use of separate sections/machines for HIV and HCV as the standard machine disinfection processes coupled with standard infection prevention protocols have been noted to be enough to control these two, though a systematic review and meta-analysis done in 2021 showed that the prevalence of BBV is still high in Africa [7]. The worry is usually about protecting other patients and staff from acquiring these infections.

PD seems to offer a solution to these worries as it is an individual-based therapy and can be performed at home with little or no supervision from health care workers, and studies are yet to show any difference in outcomes between PD and HD as a preferred choice of KRT for HIV patients [8]. The study by Lioussfi et al [9] showed that some patients may acquire blood-borne viruses while on treatment, especially those on HD but this may also occur in patients on PD and the major risk is increased length of time on dialysis treatment [9].

The major guidelines, KDIGO, NICE, recommend viral screening prior to commencement, and periodically during dialysis treatment. However, those who decline consent should be treated as if they have blood-borne virus infection, but must not be denied adequate kidney care [10]. Dialysis staff should also be screened for BBV, and HBV negative patients and staff should receive HB vaccine [5,10].

Rational

- To reduce risk of transmission of blood-borne viruses to both patients and staff of the dialysis unit.
- To recognize those that require additional/specialized care.
- For medico-legal reasons.
- To re-enforce the need for standard infection prevention protocols in dialysis units.

Supporting evidence

Early studies documented multiple hepatitis outbreaks in dialysis units and a high prevalence of blood-borne viruses (BBV) even in patients on PD [11,12]. These led to the Rosenheim report that instituted infection prevention protocols that drastically reduced the incidence of BBV infection [10].

Ndlovu et al [13] in South Africa, in 2019, demonstrated significant HIV-1 RNA particles in the peritoneal effluent of HIV positive patients on HAART undergoing PD, and this was noted even in some patients with undetectable plasma viral load. Viral screening is also important in patients who require transplant [14].

The center for disease control and prevention (CDC) recommendations from the Advisory Committee on Immunization Practices (ACIP) suggests routine immunization with preferably, killed vaccines in immunocompromised individuals however states that CKD patients can tolerate live-attenuated vaccines if the killed alternative is unavailable and vaccination is indicated [15]. Pneumococcal vaccine and HBV vaccines are indicated in patients for dialysis and the earlier it is given the better [10,15].

Recommendations

- 4.7.1 We recommend viral screening at initiation of therapy so as to ensure total care for the patient and protect the health personnel. Screening for anti-HCV, HBsAg and anti-HIV antibodies should be performed, however, all necessary pre and post-test counselling must be ensured. It is particularly important as the patient could consider kidney transplant in future.

Quality of evidence - Low

Recommendation- Strong

- 4.7.2 Immunization for Hepatitis B virus is desirable, and influenza(inactivated influenza vaccine) and pneumococcal vaccination could be offered to CAPD patients as well when available.¹⁴

Quality of evidence - Low

Recommendation- Strong

4.8 CAPD prescription

Background

Peritoneal dialysis prescription was traditionally centered on removing small solutes like urea, and a measure of the clearance of this was used to ascertain dialysis adequacy (weekly KT/Vurea ≥ 1.7). Currently, there is a paradigm shift towards a shared decision-making and person-centered PD, being the key to high-quality dialysis care, as many factors are involved in dialysis adequacy. The ISPD proposed a 'goal-directed' PD delivery to 1. Allow the person doing PD to achieve his/her own life goals and 2. Promote the provision of high-quality dialysis care by the dialysis team [16,17].

Supporting evidence

Studies have shown that high-quality goal-directed PD prescription should include appropriate management of fluid status and that hypervolaemia is associated with LVH and markers of inflammation (IL-6, TGF- β_1) in PD patients [18,19]. Blood pressure control is also an important component of volume management.

Many studies including RCTs have shown that icodextrin is superior to glucose based dialysate especially for long dwells and fast transporters in the management of hypervolaemia [20-22]. Loop diuretics, are effective in fluid management and have been shown to preserve residual kidney function (RKF) [23,24]. A RCT done by Medcalf et al showed a clear preservation of RKF, however, this effect was not seen in anuric patients [25].

ACEIs and ARBs have been shown in two RCTs to preserve RKF, independent of their antihypertensive effects [26,27] [26,27].

Peritoneal equilibration test (PET) is an important part of PD that elucidates the peritoneal membrane characteristics of patients on PD. These characteristics can change following commencement of PD and should be evaluated periodically to optimize patient care [28-31]. The ISPD recommends that the peritoneal solute transfer rate (PSTR) of patients be determined using a 4-hr PET early in the course of PD treatment, i.e., between 6 to 12 weeks [32]. Some literature suggests within 6 weeks of commencement of PD [28,29,33].

Recommendations

- 4.8.1 We recommend that the Prescription of CAPD or APD should follow the ISPD recommended practice points for high-quality goal-directed peritoneal dialysis listed below.

- i. The initial PD prescription should be based on the amount of residual renal function and targeted at achieving good quality of life, euolemia and biochemical well-being of the patients at the lowest cost, through the use of incremental PD with fewer bags and PD free days.
- ii. Efforts should be made to preserve residual kidney function and peritoneal membrane function, and in so doing, maintain PD ultrafiltration for an extended period without the need to intensify PD prescription.
- iii. Low-cost adjunctive management modalities such as dietary and life-style modification should be used to reduce the need to intensify the PD prescription prematurely.
- iv. PET and weekly Kt/V should be encouraged if the cost of these tests does not compromise the affordability of PD treatment. Where facility-performed PET or Kt/V is unavailable or unaffordable, quality and adequacy of PD should be assessed based on clinical, biochemical parameters and clinical well-being of patients.

Not graded

- 4.8.2 We recommend a regular assessment of fluid status, with history-taking and clinical examination

including blood pressure.

Not graded

4.8.3 For CAPD patients with hypervolaemia;

- Daily dietary sodium intake should not be more than 90 mmol (2000mg)

Not graded

- Loop diuretics can be used in patients with residual kidney function (RKF) such as Frusemide with or without metolazone.

Quality of evidence - Low

Recommendation- Strong

- Hypertonic 4.25% dextrose solution may be used to achieve euvolaemia; however, sustained use of such solution is not desirable

Quality of evidence - Low

Recommendation- Weak

- Icodextrin solution is preferred over glucose-based dialysate for long-duration (>8-hour) dwells.

Quality of evidence - High

Recommendation- Strong

4.8.4 Peritoneal equilibration test (PET)

In addition, strategies that retard progression of CKD or preserve residual kidney function should be encouraged. These include control of anaemia, blood pressure (using ACEI and ARBs), calcium-phosphate homeostasis, dyslipidaemia, avoidance of nephrotoxins (including NSAIDs), hydration and malnutrition. (Refer to appropriate section of this guideline on CKD)

Quality of evidence - Low

Recommendation- Strong

4.8.5 Peritoneal membrane function should be monitored using Peritoneal Equilibration Test (PET) at least 6 weeks after commencing CAPD or automated PD to determine the peritoneal solute transfer rate (PSTR) and subsequently repeated if there are unexplained or unexpected changes in volume status or UF.

Quality of evidence - High

Recommendation- Strong

4.9 Assessment of PD adequacy

Background and supporting evidence:

There is currently a paradigm shift in the assessment of PD adequacy from assessing only small solute clearance to evaluating and maintaining RKF and also the Health-related quality of life (HRQOL), blood pressure, fluid status, nutritional status and other clinical parameters [16]. The Canada-USA peritoneal dialysis study group (CANUSA study) suggested that RKF was an important predictor of mortality and should be considered in PD prescription [34,35].

Recommendation

4.9.1 Both residual endogenous creatinine clearance and peritoneal dialysis clearance are important in CAPD and should be monitored every 6 months except otherwise clinically indicated. The minimal treatment doses mentioned above should be maintained.

Quality of evidence - Moderate

Recommendation- Strong

4.10 Medical management of PD patient

Recommendations

4.10.1 • Hypertension:

Hypertension should be managed according to recommendations on Section 2 subsection D. The use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) should be given preference as appropriate, However, comorbid conditions should be

taken into account when prescribing antihypertensives.

Quality of evidence -Moderate

Recommendation- Strong

- **Malnutrition (Refer Section 2)**

Nutritional status should be regularly assessed and monitored to maintain a normal nutrition status with restriction of sodium, phosphorus and potassium. (Refer to appropriate section of this guideline)

- Anaemia (Refer Section 2)
- Bone Disease (Refer Section 2)
- Dyslipidaemia (Refer Section 2)

4.11 Achievement of treatment targets

- 4.11.1 Local experience is very limited on achievability of treatment targets in CAPD. However, in patients with inadequate dialysis and low clearance of less than 1.7 there may be a need to increase dwell volume and addition of extra exchanges in CAPD patients while in Automated PD patients an addition of a day dwell may be instituted to improve the clearance status.[16]

Not Graded

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4.12 PD Peritonitis and care of PD catheter/exit site

Background

Peritonitis is a common complication of peritoneal dialysis accounting for 0.75 (0.56-2.20) episodes per patient-year in Africa [1]. Although peritoneal dialysis has been advocated for low income communities, lack of availability of PD consumables has been responsible for the low utilization of PD in Africa [2]. The pathogenesis of peritonitis in PD patients is related to the presence of the PD catheter which provides a portal of entry of microorganisms to the otherwise sterile peritoneum. Several microorganisms have been found to cause peritonitis. A systematic review showed that Gram positive organisms account for 37.0 to 85.3% of infections in Africa [1]. Despite the rates of culture positive peritonitis in Africa, some studies have shown that up to 50% of cases were culture negative [3]. Factors that have been found to be associated with peritonitis include low socioeconomic status, poor housing, exit site and catheter-tunnel infections.

Supporting evidence

PD associated peritonitis is the direct or major contributing cause of death in >15% of patients on PD [4]. In a bid to reduce this untidy trend the International Society for Peritoneal dialysis (ISPD) has published guidelines for the definition, treatment and prevention of PD associated peritonitis and encouraged the adoption of uniform definition of terms for easy comparison of infection rates and outcomes between centres [5]. The peculiarities in the conduct of peritoneal dialysis and management of its complication in Nigeria will be taken into account in these guidelines.

Definitions of term

Background

Standardization of the definitions of complications of peritoneal dialysis is important in enabling comparisons between centers. It can also facilitate benchmarking of performance to improve and address practice variations. A meta-analysis by Sahlawi MA et al [6] [PD2] showed that 29% of studies on PD peritonitis did not specify how peritonitis was defined. And among studies that provided definition for PD associated peritonitis; only one of the three components in the definition were reported: effluent cell count (54%), clinical features consistent with peritonitis (45%), and positive culture (25%). The international society for peritoneal dialysis (ISPD) has encouraged the adoption of uniform definition of complications of peritoneal dialysis.

Supporting evidence

Several centers and researchers have defined infectious complications of peritoneal dialysis differently. This has made it impossible for comparison of outcomes within centers and across centers. It has also made it difficult to determine the outcomes of interventions in various peritoneal dialysis units. Manera KE et al [7] in a meta-analysis of 59 clinical trials showed that there were 383 different outcome measures. This problem has made it necessary that a uniform definition of terms be adopted to facilitate comparison of outcomes between various centers.

Definition of terms [4].

Term	Definition
Peritonitis	can be diagnosed if the patient presents with two of the following criteria <ul style="list-style-type: none">• Cloudy effluent or abdominal pain• Elevated effluent WBC count (>100 cells/mm³) or Neutrophil count (>50 cells/mm³)• Positive culture of PD effluent NB: PD patients presenting with cloudy effluent be presumed to have peritonitis and treated as such until the diagnosis can be confirmed or excluded.

	the catheter-epidermal surface
Catheter-tunnel infection	The presence of clinical inflammation or ultra-sonographic evidence of collection along the catheter tunnel
Relapsing peritonitis	An episode of peritonitis that occurs within 4 weeks of completion of a prior episode with the same organism
Refractory peritonitis	Failure to respond to appropriate antibiotics within 5 days
Recurrent peritonitis	An episode of peritonitis that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism

WBC- white blood cells; mm³- millimeter cube; PD - peritoneal dialysis

Treatment

Background

Treatment of peritoneal dialysis-associated infections should be commenced once diagnosis has been confirmed to achieve rapid resolution of inflammation, reduction of pain and preservation of peritoneal membrane. Prompt commencement of antibiotics therapy is associated with better outcomes of peritonitis treatment. In a prospective conducted by Muthucumarana et al [8], showed that the contact-to-treatment time is independently associated with treatment failure. Several antibiotics have been used to treat peritonitis; however no antibiotic regimen has been proven to be superior to others. The antibiotic regimen should cover for both gram positive and negative organisms.

Supporting evidence

Peritoneal dialysis-associated peritonitis is associated with substantial morbidity, contributing to death in 8.6% of patients [8,9]. Peritonitis increases treatment cost and is a major reason for transition to haemodialysis. Despite attempt by the International society for peritoneal dialysis to provide guidelines for treatment of peritonitis; there exist a wide variation in the diagnosis and treatment of PD-associated peritonitis across centers. This may have contributed to the high rates of peritonitis treatment failure. The ISPD recommends the initiation of empirical antibiotics through the intra-peritoneal route (IP) in patients without systemic features of sepsis. Bennet-Jones et al [10] observed that there was a higher rate of treatment failure among patients who were treated with intravenous than IP antibiotics. Intra-peritoneal administration of antibiotics provides higher concentrations of the drugs at the site where it is most needed, avoids intravenous access and the possibility of home administration of the drugs is enhanced.

Recommendations

- 4.12.1 We recommend that Exit-site or catheter tunnel infection should be treated to reduce subsequent peritonitis risk.
Quality of evidence - High Recommendation- Strong
- 4.12.2 We recommend that Initial treatment regimens for peritonitis should cover for both Gram positive and Gram-negative bacteria pending microbiology results.
 - i. Empirical antibiotic therapy should be initiated as soon as possible after appropriate microbiological specimens have been obtained
Quality of evidence - Low Recommendation- Strong
 - ii. Empirical antibiotic regimens should be center-specific and cover both Gram-positive and Gram-negative organisms.
Quality of evidence - Low Recommendation- Strong
 - iii. Gram-positive organisms should be covered by a first-generation cephalosporin and gram-negative organisms by an aminoglycoside.
Quality of evidence - Moderate Recommendation- Strong

culture and sensitivity test results.

Quality of evidence - Low

Recommendation- Strong

- 4.12.3 We recommend that intra-peritoneal antibiotic treatment should be instituted unless the patient has features of systemic sepsis.

Quality of evidence - Moderate

Recommendation- Strong

- 4.12. 4 We recommend that catheter should be removed if there is relapsing peritonitis, refractory peritonitis, refractory tunnel infection and fungal peritonitis.

Quality of evidence - Moderate

Recommendation- Strong

- 4.12. 5 We recommend that systemic antibiotic therapy should be given in cases of sepsis but particular attention must be paid to dose adjustments relative to the kidney function of the patients on CAPD.

Quality of evidence - High

Recommendation- Strong

4.13 Prevention strategies

Background

Preventive strategies of catheter-associated infections are key to success of this modality of renal replacement therapy. Catheter-related infection in peritoneal dialysis patients is associated with increased morbidity and mortality among PD patients. Infections are commonly acquired from patients, their relations or caregivers who are nasal carriers of pathogenic staphylococcus aureus [1,10].

Supporting evidence

Catheter-related infections occur due to contamination of the catheter during catheter placement or PD fluid exchanges. Hagen et al [6] in a systematic review showed that catheter type has no influence on the rate of infection. Marshall et al [7] showed that there is progressive decrement of the rate of peritonitis in the world from 1992 to 2019. This underscores the impact of establishing and maintaining prevention strategies in PD units.

Recommendations

- 4.13.1 We recommend that PD units should observe universal precautions on sterility and cleanliness. Hand washing with antiseptic soap MUST be ensured before and after performing procedures both by the patients and the hospital personnel.

Quality of evidence - High

Recommendation- Strong

- 4.13.2 We recommend that units should undertake regular audit of their infection rates, and identify causative organism(s) and treatment outcomes. Local treatment and prevention protocols need to be developed.

Quality of evidence - Moderate

Recommendation- Strong

- 4.13.3 We recommend that disconnect systems with a "flush before fill" design be used for CAPD patients.

Quality of evidence - High

Recommendation- Strong

- 4.13.4 We recommend that PD patients should receive regular training to be conducted by healthcare staff with the appropriate qualifications and experience.

Quality of evidence - Moderate

Recommendation- Strong

- 4.13.5 We recommend that systemic prophylactic antibiotics be administered prior to catheter insertion.

Quality of evidence - High

Recommendation- Strong

Note: Antibiotic prophylaxis is encouraged and Clavulanate potentiated Amoxicillin, quinolones, ceftriazone or ceftazidime have been used in various units in Nigeria with success.

- 4.13.6 We recommend that topical antibiotic administration could be used to reduce the frequency of exit-site infection and peritonitis.

Quality of evidence - Moderate

Recommendation- Strong

Research areas identified:

- Wider multicenter prospective study on applicability and usefulness of CAPD in Nigeria.
- Peritoneal membrane characteristics and its impact on mortality in Nigerians.
- Cost containment measures in CAPD management.
- Pattern of peritonitis and modalities of controlling and reducing it.
- Health related QOL in CAPD patients in Nigeria.

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SECTION V: KIDNEY TRANSPLANTATION

KIDNEY TRANSPLANTATION

Introduction

Kidney transplantation has been available in Nigeria since the year 2000. It remains the best option for long term management of patients with established End Stage Kidney Disease (ESKD) in whom there is no contraindication regardless of the age of the patient and the aetiology of chronic kidney disease (CKD) [1]. It offers the best possible Quality of Life, Mortality risk reduction and considerable and significant cost savings when compared with other modalities of management in ESRD [1].

Studies have also consistently established that the earlier a successful transplant is carried out, the better the short term and long-term outcomes for the patient, post renal transplant [2,3]. A successful kidney transplant however requires considerable preoperative evaluation of both the donor and recipient and stabilization of the potential recipient prior to actual transplant itself. It also requires relatively strict adherence to established protocols and guidelines in the management of the patient through the transplant process itself and long-term management following. Several factors have been identified as positive prognostic factors in determining the likelihood of a positive outcome following a kidney transplant anywhere that this is performed and strict compliance to these protocols have been established as strong determinants of the success of any transplant program [4,5].

Given the current state of development of the healthcare services in the country in general, the rather low health expenditure as a fraction of the GDP (less than 5%), and the poor penetration of participation in the National Health insurance scheme (less than 5%), over 92% of individuals still rely on out-of-pocket payment for health services. This deficiency is further compounded by renal units that are few, limited to urban areas and a paucity of adequately trained and motivated staff to run these units. It is not surprising, therefore, that kidney transplantation numbers and centres with the capacity to carry out transplants successfully remain inadequate to cater for the numbers of our patients with ESRD requiring Kidney Transplantation [6].

These guidelines, specific for the evaluation and management of kidney transplant recipients and donors, aims to guide practitioners in the identification, preparation and management of the potential transplant recipients and donors bearing in mind the peculiar circumstances under which most transplants are performed in the country. It bears in mind relevant aspects of the 2014 Nigerian National Health Act and the Declaration of Istanbul both of which specify the necessity for the Ethical conduct of all practitioners in the process of Kidney Transplantation [7,8]. It also bears in mind that other international guidelines are in existence and would focus on aspects that are peculiar to our environment and those that require particular emphasis. It is an update of the earlier guidelines published 10 years ago.

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5.1 Pre-transplant assessment of recipient

Who to consider for kidney transplantation

Background

In view of the progressive nature of CKD, all patients in stage G4 and G5 must be counselled about preparation for kidney replacement therapy (KRT) including kidney transplantation. In our setting, where most patients pay out of pocket for health services, economic status and cultural beliefs about organ donation may limit accessibility to kidney transplantation but should not deprive the patient from being adequately informed about kidney transplantation.

Supporting Evidence

A large observational study that compared the mortality rate reduction, quality of life and cost effectiveness showed a superior benefit from kidney transplantation compared to dialysis among ESKD patients [1]. Similarly, other observational studies have demonstrated advantage in both short and long term outcomes among KTRs who had early kidney transplantation compared to late [2].

Recommendations

- 5.1.1 We recommend that patients with CKD G4 and G5, regardless of religious belief, gender or social status, must be provided with adequate information / counselling about kidney transplantation. The emphasis of such counselling must include, but not limited to, availability of viable kidney transplantation programmes within the country, with outcome comparable to that obtainable abroad, advantages over dialysis therapies, financial implication and need for maintenance immunosuppressives and its attendant side-effects and contraindications to kidney transplantation. however, the decision on where to access kidney transplantation lies with the patient.
Not graded
- 5.1.2 We recommend that CKD (G4 and G5) patients on conservative care must be reviewed by a nephrologist at least 6 months before the projected first dialysis session.
Not graded
- 5.1.3 We recommend kidney transplantation for all ESKD patients with eGFR 15ml/min/1.73m² for at least 3 months, who have been on maintenance dialysis.

Quality of evidence - Moderate

Recommendation- Strong

- 5.1.4 We recommend pre-emptive kidney transplantation for ESKD patients in terminal CKD stage 4 and stage 5, for at least 3 months, who are yet to be initiated on dialysis.

Quality of evidence - Moderate

Recommendation- Strong

Conditions where kidney transplantation should be delayed

Successful kidney transplantation may be difficult to achieve if the prospective KTR is not properly evaluated before kidney transplantation procedure. Certain conditions that can adversely impact the post-transplant period justify the need to delay kidney transplantation until acceptable clinical resolution is achieved.

Box 1

Conditions where kidney transplantation should be delayed

1. Active infection
2. Unresolved psychiatric disorders and substance abuse that affects patient's judgement
3. Active malignancy
4. Any medical or surgical condition that reduces life expectancy to < 2 years
5. Advanced cardiovascular disease including coronary artery disease and CCF with significantly depressed ejection fraction < 30%
6. Positive T-cell on complement-dependent cytotoxicity (CDC) crossmatch
7. Decompensated liver cirrhosis
8. Endoscopically diagnosed peptic ulcer disease

Relative contraindications to kidney transplantation

1. Previous history of non-compliance with medications
2. Malnutrition
3. Obesity
4. Elderly

5.2 Active Infection

Background

The survival rate of patients after kidney transplantation has improved significantly with newer immunosuppressive protocols [9]. However, mortality related to infections is still high.

Supporting Evidence

Some observational studies have shown that infection is a common non-cardiovascular cause of death in kidney transplant recipients (KTRs), responsible for an estimated 20% of deaths [10,11]. Reactivation of latent infection such as tuberculosis and viral infections following commencement of immunosuppressive medications have also been reported [12,13]. Therefore, infection remains a major contributor to morbidity and mortality in KTRs; the presence of active infection before kidney transplantation will require proper evaluation and treatment before the procedure.

Recommendations

- 5.2.1 We recommend treating all forms of active infections before kidney transplantation.

Quality of evidence - High

Recommendation- Strong

- 5.2.2 We recommend that positive HIV test should not be a contra-indication to kidney transplantation.

Not graded

- 5.2.3 For HIV seropositive recipient, we recommend that documented evidence of viral suppression on anti-retroviral therapy (ART) including CD4 count >200 and HIV viral load at undetectable levels and absence of AIDS-defining disease before kidney transplantation).

Not graded

- 5.2.4 HBsAg positivity should not be a contra-indication to kidney transplantation.
Quality of evidence - Low Recommendation- Strong
- 5.2.5 We recommend that all HBsAg positive patients should do HBV DNA for viral load quantification and hepatitis B viral markers.
Quality of evidence - Low Recommendation- Strong
- 5.2.6 For HBsAg positive patients, we recommend that kidney transplantation can be done if the patient has been reviewed by a hepatologist and is stable on antiviral agents with documented evidence of viral suppression, including HBV viral load at undetectable levels and evidence of negative screening for hepatocellular cancer (using liver ultrasound and α -fetoprotein).
Quality of evidence - High Recommendation- Strong
- 5.2.7 Anti-HCV positivity should not be a contra-indication to kidney transplantation.
Not graded
- 5.2.8 HCV screening should be done using immunoassay. Prospective recipients who test positive should be subjected to nucleic acid testing (NAT).
Quality of evidence - Low Recommendation- Strong
- 5.2.9 We recommend that prospective recipients who are HCV positive with compensated cirrhosis may be transplanted in the absence of portal hypertension.
Quality of evidence - High Recommendation- Strong
- 5.2.10 We recommend COVID-19 screening (PCR) for all prospective KTRs. It is desirable to screen other relevant prevailing infectious diseases.
Not graded

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5.3 Unresolved psychiatric disorders and substance abuse that affects patient's judgement

Background

Available evidence from observational studies reveal that psychiatric disorders are common in ESKD patients with a wide range of psychiatric disorders including depression, anxiety, adjustment disorders and harmful use of medications reported in previous studies [14,15]. Similarly, the prevalence of depression after kidney transplant has been shown to be high, 22% was found in an observational study; depression was also identified as an independent predictor of mortality among kidney transplant recipients [16].

Supporting Evidence

Several observational studies have shown the high prevalence of psychiatric disorders among ESKD patients; similar findings have been reported in KTRs [14-16].

Recommendations

- 5.3.1 We recommend that all prospective KTRs who have psychiatric disorders should be referred to a psychiatrist and clinical psychologist for proper evaluation and management. The process of kidney transplantation should be halted until an acceptable clinical improvement and a 'fitness to proceed' document is signed by the psychiatrist.

Quality of evidence - Low

Recommendation- Strong

- 5.3.2 We recommend that patients who are being managed for substance abuse should be excluded from kidney transplantation, until acceptable clinical resolution and 'fitness to proceed' document signed by psychiatrist.

Not graded

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5.4 Active malignancy and other medical/surgical condition that reduces the life expectancy to <2 years

Background

A previous study demonstrated increased risk of cancer among ESKD patients [17]. Use of immunosuppressives may further worsen the risk of cancer in this group of patients after kidney transplantation.

Supporting Evidence

A case-control study compared elderly patients on maintenance haemodialysis with elderly controls and found increased risk of specific cancers [including lung, cervical, liver, colorectal, stomach, multiple myeloma and chronic myeloid leukaemia(CML)] in the ESKD patients [17]. A scheduled waiting time (0-5 years) has been proposed for prospective KTRs who were found to have curable cancer [18]. In addition, cancer incidence after kidney transplant was found to be significantly increased compared to cancer incidence among ESKD patients before and after initiation of dialysis [19].

Recommendations

- 5.4.1 We suggest curative treatment followed by strict adherence to the stipulated waiting time in prospective kidney transplant recipients who have active malignancy.

Quality of evidence - Very low

Recommendation- Weak

- 5.4.2 We recommend that all patients who have risk factors for common cancers seen in ESKD patients (such as prostate cancer, liver cancer, cervical cancer, lung cancer, breast cancer, colorectal cancer, thyroid cancer, multiple myeloma and CML) should be screened to exclude presence of malignancy.

Not graded

- 5.4.3 We suggest that ESKD patients who have any medical or surgical illness that reduces life expectancy to < 2 years (other than renal failure) should be excluded from kidney transplantation.

Not graded

- 5.4.4 We recommend that ESKD patients who have any medical or surgical illness (other than renal failure) that reduces life expectancy to < 2 years should be allowed to continue dialysis.

Not graded

- 5.4.5 We recommend that all female prospective KTRs (40 years) should have mammogram ± USS (when indicated) while those younger than 40 years should have breast USS.

Not graded

- 5.4.6 We recommend that all female prospective recipients who are sexually active should do PAP smear.

Not graded

- 5.4.7 We recommend that PSA levels should be assessed in all males (age 40 years).

Not graded

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5.5 Advanced cardiovascular disease, including congestive cardiac failure (CCF) with significantly depressed left ventricular ejection fraction (LVEF) < 30%.

Background

Chronic kidney disease patients have a 10-20-fold risk of developing cardiovascular disease (CVD) compared to the general population [20].

Supporting Evidence

CVD is responsible for 50% of deaths among ESKD patients [21]. Report from an observational study showed that atherosclerotic vascular disease (AsVD) was more prevalent among ESKD patients, especially peritoneal dialysis (PD) patients compared to healthy controls and CKD G3 [22]. Several observational studies have shown that left ventricular dysfunction is a strong predictor of mortality in general population and KTRs [23,24]. The risk of cardiovascular death among haemodialysis patients with LVEF <30% was nine times more than those with LVEF >60% [25].

Recommendations

- 5.5.1 We recommend that all prospective KTRs must have cardiovascular evaluation with history, physical examination, chest X-ray, electrocardiogram (ECG) and Echocardiogram to ascertain the presence and severity of pre-existing CVD.

Not graded

- 5.5.2 We recommend that all prospective KTRs who have symptoms and signs of cardiovascular disease such as heart failure, Arrhythmia, valvular heart disease, ischaemic heart disease, pericardial effusion (moderately severe) or cardiomyopathy should be referred to a cardiologist for review and management based on current local guideline prior to kidney transplant.

Not graded

- 5.5.3 We suggest that all prospective KTRs who have 3 or more of the following coronary artery disease

(CAD) risk factors (older age, smoking, renal failure, diabetes mellitus, previous CAD or CVD, duration on dialysis >1year, hypertension, dyslipidaemia) should have non-invasive stress test regardless of functional capacity.

Quality of evidence - Very low

Recommendation - Weak

- 5.5.4 We recommend that coronary angiography should be done if any of the following is present, recurrent typical chest pain despite normal ECG and ECHO, ECG and/or ECHO evidence of CAD, diabetes mellitus in prospective KTRs older than 50 years.

Quality of evidence - Low

Recommendation - Strong

- 5.5.5 We recommend evaluating for vascular patency in patients with evidence of significant peripheral arterial disease, previous kidney transplantation, previous use of femoral vascular access for dialysis with or without presence of femoral bruit, deep venous thrombosis or pelvic surgery.

Quality of evidence - Low

Recommendation - Strong

- 5.5.6 We suggest that prospective KTR who are asymptomatic but have advance triple vessel CAD be excluded from kidney transplantation until successful coronary reperfusion therapy.

Quality of evidence - Very low

Recommendation - Strong

- 5.5.7 We recommend that prospective KTRs who have symptomatic, uncorrectable advanced cardiovascular disease, such as CCF (NYHA III or IV) with significantly reduced EF < 30% and severe valvular disease, regardless of aetiology of the heart failure, should be excluded from kidney transplantation. Such patient should be referred for cardiologist review, then planned for combined heart/kidney transplantation.

Quality of evidence - Very low

Recommendation - Weak

References

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5.6 Positive T-cell on Complement-Dependent Cytotoxicity (CDC) crossmatch

Background

Compatibility screening such as CDC crossmatch is an essential component of pre-transplant assessment and its relevance includes predicting risk of acute rejection and allograft survival [26].

Supporting Evidence

The earlier study on the significance of crossmatch in kidney transplantation found a significantly higher number of allografts that failed to function immediately among patients that were crossmatch positive

compared to those that were crossmatch negative [26-28].

Recommendations

- 5.6.1 We recommend that prospective KTRs who are T-cell positive on CDC crossmatch should be excluded from kidney transplantation. Such prospective recipient may be reconsidered for kidney transplantation following successful desensitization or provision a new donor or via kidney-paired donor exchange.

Quality of Evidence - Moderate

Recommendation - Strong

References

26. Mulley WR, Kanellis J. Understanding crossmatch testing in organ transplantation: A centre-based guide for the general nephrologist. *Nephrology* 2011; 16:125-133
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28. Susal C, Opelz G. Current role of human leukocyte antigen in kidney transplantation. *Curr Opin organ Transplant*. 2013;18(4):438-444

5.7 Decompensated liver cirrhosis

Background

Among the well documented causes of liver cirrhosis and hepatocellular carcinoma in our environment are the hepatotropic viruses (hepatitis B and C) [29,30]. Both hepatitis B and C have been associated with specific forms of CKD [31]. It is therefore conceivable that a patient with hepatitis B-associated liver cirrhosis may have a co-existing HBV-associated kidney disease, which commonly progresses to ESKD in 30-50% of cases [32].

Supporting Evidence

Available evidence shows that most prospective KTR without decompensated liver cirrhosis or severe portal hypertension can undergo successful isolated kidney transplantation [33].

Recommendations

- 5.7.1 All prospective KTR should be screened with liver function test and international normalized ratio (INR).

Not graded

- 5.7.2 We suggest that kidney transplantation should be delayed in acute hepatitis, regardless of the aetiology, until acceptable clinical resolution.

Not graded

- 5.7.3 We recommend that prospective KTR with decompensated liver cirrhosis should be co-managed with the Gastroenterologist and planned for combined liver and kidney transplantation.

Quality of Evidence - Moderate

Recommendation - Strong

- 5.7.4 We recommend that prospective KTR who have compensated liver cirrhosis after review by a gastroenterologist can have an isolated kidney transplantation.

Quality of Evidence - Moderate

Recommendation - Strong

References

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33. Eason JD, Gonwa TA, Davis CL, et al. Proceedings of consensus conference on simultaneous liver kidney transplantation. *Am J Transplant.* 2008; 8: 2243-2251

5.8 Endoscopically-diagnosed symptomatic peptic ulcer disease

Background

The most common post-transplant gastrointestinal complication is peptic ulcer disease [34, 35]. The prevalence of endoscopically-diagnosed peptic ulcer disease among KTR was found to be 16.9% which was 1.7-fold rise compared to the general gastroenterology patients.

Supporting Evidence

The recommendations were based on the finding of increased frequency of early post-transplant severe peptic ulcer disease and associated surgical complications [36, 37].

Recommendations

- 5.8.1 We recommend screening all prospective KTR who have symptomatic peptic ulcer disease with upper gastrointestinal endoscopy and *Helicobacter pylori* tests prior to kidney transplantation.
Quality of evidence - Low Recommendation - Strong
- 5.8.2 We suggest that kidney transplantation be delayed in KTR who have endoscopically-diagnosed, symptomatic peptic ulcer disease.
Not graded
- 5.8.3 We recommend that prospective KTR who have history of peptic ulcer disease should not be excluded from kidney transplantation.
Quality of evidence - Very low Recommendation - Strong

References

34. Sarkio S, Halme L, Kyllonen L, et al. Severe gastrointestinal complications after 1515 adult kidney transplantations. *Transpl Int.* 2004; 17: 505-510.
35. Telkes G, Peter A, Tulassay Z, et al. High frequency of ulcers, not associated with *helicobacter pylori*, in the stomach in the first year after kidney transplantation. *Nephrol Dial Transplant.* 2011; 26:727-732.
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on eligibility for kidney transplantation. CMAJ 2005; 173: S1-25

The pre-transplant assessment of the prospective kidney transplant recipient requires a well-designed approach aimed at identifying a recipient, devoid of unamenable contraindications to kidney transplantation, with acceptable ABO and immunologic match with the donor. Ultimately, the end result of recipient pre-transplant assessment is to identify a recipient that is fit enough to make an acceptable donor-recipient pair.

It is desirable to ensure a flow of the necessary investigations from the relatively less expensive but important, to more expensive investigations. The stages of investigations suggested below should serve as a guide for prospective KTR evaluation.

Stage	Focus	Investigations
1	Blood group and kidney function	ABO blood grouping Haemoglobin genotype Serum E, U, Cr Creatinine clearance Abdominopelvic ultrasound scan with emphasis on kidneys, bladder and prostate
2	Viral screening	HIV, HBsAg, Anti-HCV, VDRL, EBV (IgG & IgM), CMV (IgG & IgM), COVID-19
3	Baseline tests	Blood - calcium, phosphorus, parathyroid hormone (PTH), uric acid, liver function test (LFT), fasting blood glucose (FBG), 2-Hr post-prandial, glycated haemoglobin (HbA1c), fasting lipid profile (FLP), full blood count (FBC), Erythrocyte sedimentation rate (ESR), Haemoglobin electrophoresis (only in sickle cell disease and trait), prothrombin time (PT), partial thromboplastin time (PTTk), international normalised ratio (INR), tumour markers (if indicated) Urine - Urinalysis, Urine microscopy, culture & sensitivity (M/C/S)
4	Gender-specific tests	Females - Mammogram \pm breast USS (if ≥ 40 years), PAP smear Males - prostate specific antigen (PSA) definitive (if ≥ 40 years)
5	Cardiovascular evaluation	Chest X-ray (PA view), 12-lead ECG + long rhythm strip, ECHO, Coronary angiography (if indicated), Venous and Arterial Doppler USS (if indicated)
6	Imaging and endoscopy	Abdominopelvic CT (if indicated), upper GI Endoscopy (if indicated), Colonoscopy (if indicated)
7	Genetic testing	ApoL1 genotyping (when possible)
8	Immunologic screen	Complement-dependent cytotoxicity (CDC) Crossmatch, panel reactive antibodies (PRA), Human leucocyte antigens (HLA), HLA screening antibodies, donor-specific antibodies (DSA)

5.9 Pre-transplant assessment of donor

Background

The objectives of live donor evaluation are to ensure that the donor has two normal kidneys, to exclude diseases transmissible to the recipient, to identify risk factors for future kidney disease, assess medical, surgical and anaesthetic fitness for surgery and to ascertain the donor candidate willingness to donate a kidney voluntarily without undue pressure.

Legal and ethics framework

Kidney donation process should be in accordance with international best practices and principles as contained in the declaration of Istanbul and the Nigerian Health Act [7,38].

Donor candidates should be counseled about the risks associated with living donation. The donor should give an informed consent to donate (verbal and written) and the decision to withdraw at any stage of the evaluation process should be respected and supported in a manner that protects confidentiality.

The donation process should be stopped if there is any identified medical condition that can put the donor at an increased risk of having a chronic kidney disease or places them at an unacceptable surgical or psychosocial risk [39].

A transplant coordinator different from those of the recipient and an ethical committee are required in evaluation of donors. The constitution of the ethical committee should reflect the clinical and socio-cultural conditions associated with Kidney donation e.g., clergy, retired judge, a physician that is not part of the transplant process, traditional ruler etc.

It is also important to get the consent of the donor candidate before evaluation for a kidney transplant. Strategies for sharing the results should be formulated and agreed upon between the donor and the transplant team.

As much as possible, donor candidates should be family related up to third degree relatives. Emotionally-related and altruistic donor can be considered for kidney donation but these would need to be approved by the Ethics committee. Where feasible a paired organ donation process/program can also be considered.

References

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39. Kher A, Mandelbrot DA. The living kidney donor evaluation: focus on renal issues. *Clinical Journal of the American Society of Nephrology : Cli J Am Soc Nephrol*. 2012;7:366-371.

History and Physical examination

Physical examination should be thoroughly done. Blood pressure and Body Mass Index should be correctly measured.

Laboratory evaluations

Laboratory tests for live kidney donor evaluation is as shown in appendix 1. Laboratory tests for each stage can vary from one centre to another

Recommendations

Live Kidney Donor Age [40,41]

5.9.1 WE recommend that Age of the donor must be from 18 years and above.

Not graded

- 5.9.2 We recommend that donors above 65 years may be accepted but given that they are at a heightened risk of peri-operative complications this risk needs to be communicated to the donor.
Quality of Evidence - Moderate Recommendation - Strong

Reference

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Kidney function

- 5.9.3 Kidney function should be expressed as glomerular filtration rate (GFR) and not as serum creatinine concentration and expressed in mL/min per 1.73 m² rather than mL/min [42]
Not graded
- 5.9.4 Accurate methods of assessing GFR such as use of 51Cr-EDTA or use of iohexol clearance technique should be used when and where available. Alternative methods of measuring GFR such as 24-hr creatinine clearance is preferred over estimates from serum creatinine concentration (eGFR) [43].
Not graded
- 5.9.5 Acceptable level of kidney function to donate is GFR greater than 80 mL/min/1.73m² [44].
Not graded
- 5.9.6 For donors with GFR 60 to 79 mL/min/1.73m², the decision to donate should be individualized in the local transplant program based on acceptable risk threshold.
Not graded

References

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ABO blood group

- 5.9.7 It is preferable to have ABO compatible donor-recipient pair (Strong Recommendation, High Quality)
Quality of Evidence - High Recommendation - Strong
- 5.9.8 ABO incompatible kidney transplantation can be considered in Nigeria when and where facilities and requisite expertise are available for the procedure.
Not graded

Albuminuria

- 5.9.8 Donor proteinuria should be quantified and preferably measured as albuminuria.
Quality of Evidence - Moderate Recommendation - Strong

- 5.9.8 Evaluation of donor albuminuria should be performed using urine albumin-to-creatinine ratio (ACR) in a spot urine specimen voided on waking (Strong Recommendation, High Quality) Alternative methods of urine protein excretion such as 24hr urine protein and protein creatinine ratio are equally acceptable
Quality of evidence - High Recommendation - Strong
- 5.9.9 Donors with urine ACR more than 30 mg/mmol, 24 hr urine protein more than 300mg/day or Protein creatinine ratio more than 50mg/mmol should not proceed with the kidney donation
Quality of Evidence - Moderate Recommendation - Strong

Haematuria

- 5.9.10 Donor candidates should be assessed for non-visible haematuria using reagent strips on two separate occasions
Quality of evidence - Moderate Recommendation - Strong
- 5.9.11 Donor candidates in Nigeria with persistent non visible haematuria of glomerular origin should not donate the kidneys
Not graded

Kidney stones

- 5.9.12 Donor candidates should be interviewed about previous kidney stones and associated medical records should be reviewed, if available.
Not graded
- 5.9.13 The imaging performed to assess anatomy before donor nephrectomy (eg, renal ultrasound scan, computed tomography angiogram) should be reviewed for the presence of kidney stones
Not graded
- 5.9.14 Donor candidates with history of previous small calculi, or a current small renal calculus on imaging, in the absence of metabolic abnormality predisposing to stone formation, may still be considered as potential kidney donors
Quality of evidence - Low Recommendation - Weak

Pre donation Blood pressure

- 5.9.15 Blood pressure (BP) of the donor should be within normal limit at the time of kidney donation. It is desirable to adhere strictly to optimal BP measurement protocols, including strategies for management of white coat hypertension and mild hypertension [45,46]
Not graded
- 5.9.16 Office blood pressure measurement on, at least, 2 occasions by clinical staff trained in accurate measurement technique, using equipment calibrated for accuracy is usually sufficient
Quality of Evidence - Moderate Recommendation - Strong
- 5.9.17 For donor candidates SBP<140mmHg or DBP<90mmHg is acceptable for kidney donation
Quality of Evidence - Moderate Recommendation - Strong
- 5.9.18 Donors with white coat hypertension should have 24-hrs ambulatory blood pressure monitoring (ABPM). Using ABPM, hypertension will be defined as 24 hr mean blood pressure more than 125/80mmHg.
Not graded
- 5.9.19 Donor candidates with hypertension and TOD or requiring more than 1 antihypertensives medication

for optimal control of blood pressure should not proceed with kidney donation.

Not graded

References

45. Williams B, Poulter NR, Brown MJ, Davis M, Mcinnes GT, Potter JF, et al. British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. *BMJ* 2004;328(7440):634-640.
46. European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension (2003). *J Hypertens* 2003;21:1011-1053.

Glucose Intolerance and Diabetes Mellitus

- 5.9.20 History of prior diagnosis of diabetes mellitus, gestational diabetes, and family history of diabetes should be documented.

Not graded

- 5.9.21 Glycemia should be assessed by fasting venous plasma glucose and/or glycated haemoglobin (HbA1c) before donation

Not graded

- 5.9.22 Donor candidates with elevated fasting plasma glucose, history of gestational diabetes, or family history of diabetes in a first-degree relative should undergo a 2-hour glucose tolerance or HbA1c testing. The results should be used to classify diabetes or prediabetes status accordingly.

Not graded

- 5.9.23 Donor candidates with pre-diabetes, type 1 or type 2 diabetes mellitus should not donate

Not graded

Obesity

- 5.9.24 Body mass index (BMI) should be calculated based on weight and height measured before donation, and classified according to World Health Organization (WHO) criteria.

Not graded

- 5.9.25 Donor candidates with BMI greater than 35kg/m³ should not donate the kidneys

Quality of Evidence - Low

Recommendation - Weak

Cardiovascular risk assessment

- 5.9.26 As part of overall cardiovascular assessment, fasting lipid profile (including total cholesterol, LDL-C, HDL-C and triglycerides) should be evaluated in all donor candidates.

Not graded

- 5.9.27 Donor candidates with dyslipidaemia should be evaluated further and decision to donate should be individualized based on health profile of the patients.

Not graded

- 5.9.28 Electrocardiography assessment is necessary as it may show presence of ischaemic heart disease or cardiomyopathy; the latter is a common cause of death in otherwise healthy individuals.

Not graded

- 5.9.29 Other investigations such as chest x-ray and echocardiography will be important in the overall assessment of cardiovascular health as well as assessment of functional status as directed by the cardiologist

Not graded

Tobacco Use

- 5.9.30 The use of tobacco products should be assessed before donation.
Not graded

- 5.9.31 Donor candidates who use tobacco products should be counselled on the risks of peri-operative complications, cancer, cardio-pulmonary disease and kidney failure and should be advised to abstain from use of tobacco products. They should be referred to a tobacco cessation support program if possible; before proceeding with the transplantation
Not graded

Prevention of infection

- 5.9.32 It is very important to screen for evidence of recent or past infections in the donor candidate so as to assess the risk of transmission of infection to the recipient
Quality of Evidence - Moderate Recommendation - Strong
- 5.9.33 Donor candidates should complete a urinalysis and culture and testing for HIV, HBV, HCV, cytomegalovirus (CMV), Epstein Barr virus (EBV), Treponema pallidum (syphilis), HHV-8, COVID 19 and other prevailing viral infections. The risk of transmission of infection should be as minimal as possible.
Not graded
- 5.9.34 The presence of HIV infection in the donor candidate precludes kidney donation
Quality of Evidence - Moderate Recommendation - Strong
- 5.9.35 The risk of transmission and development of diseases associated with CMV and EBV should be assessed and the donor and recipient counselled accordingly
Quality of Evidence - Moderate Recommendation - Strong

Cancer screening

- 5.9.36 Donor candidates should undergo cancer screening consistent with clinical practice guidelines for Nigeria. Transplant programs should ensure that screening is current according to guideline criteria at the time of donation.
Not graded
- 5.9.37 Donor candidates with active malignancy should be excluded from donation.
Not graded

Evaluation of Genetic kidney disease

- 5.9.38 Family history of kidney disease should be obtained from the donor candidates. When present, the type of disease, time of onset, and other manifestations associated with the disease should be documented.
Not graded
- 5.9.39 Donor candidates found to have a genetic kidney disease that can cause kidney failure should not donate
Not graded
- 5.9.40 Donor candidates with Autosomal Dominant Polycystic Kidney Disease (ADPKD) should not donate
Not graded

5.9.41 Donor candidates with a family history of ADPKD in a first-degree relative may be acceptable for donation if they meet age-specific imaging or genetic testing criteria that reliably exclude ADPKD
Not graded

5.9.42 Apolipoprotein L1 (APOL1) genotyping may be offered to donor candidates. Donor candidates should be informed that having two APOL1 risk alleles increases the lifetime risk of kidney failure but that the precise kidney failure risk for an affected individual after donation cannot currently be quantified.
Not graded

Pregnancy

5.9.43 Women should not donate while pregnant.
Not graded

5.9.44 Women should not be excluded from donation solely because they desire to conceive children after donation.
Not graded

Psychosocial evaluation

5.9.45 The psychosocial evaluation of the donor candidate should be performed by health professionals not involved in the care of the intended recipient.
Not graded

5.9.46 Transplant programs should follow protocols for assessing the donor candidate's psychosocial suitability, available support, preparation and concerns for donation.
Not graded

Haematological abnormalities

5.9.47 Donor anaemia (Hb <13g/dL for men and <12g/dL for women) need to be investigated and treated prior to donation.
Not graded

5.9.48 Patients with Sickle Cell Anaemia should not donate
Not graded

Stages of donor evaluation

Stage 1

ABO Blood group x2
Urine albumin-creatinine ratio
Kidney function test (24 hr creatinine clearance)
HBsAg
AntiHCV
HIV
FBS
Rapid plasma Reagin test
Abdominal ultrasound scan
LFT

Stage 2

HLA tissue typing I & II
T & B lymphocyte crossmatch
Donor Specific antibody
CMV IgG
EBV

TB Quantiferon

Stage 3

CXR
Electrocardiography

Echocardiography
CT renal angiography
Stage 4
Complete Blood Count
Fasting Lipid profile
Albumin
Calcium
Phosphorus
Clotting profile
Urine M/c/s

5.10 Induction and maintenance immunosuppressives

Background

A very important clinical problem following kidney transplantation is allograft dysfunction. In this, immunosuppression has a major role to play. Significant advances have been made in immunosuppression strategies over the past three decades to reduce the incidence of allograft rejection, limit side effects of the drugs and improve graft survival [47]. The immunosuppressive regimen used can be divided into induction, maintenance and rescue therapies.

The induction phase of immunosuppression is the intense phase designed to inhibit immune responsiveness prophylactically at the time of transplantation. Maintenance therapy begins immediately after renal transplantation and continues for life. The choice of agent is often protocol driven but usually adapted to each recipient's risk profile. High immunologic risk patients are usually treated with more intense immunosuppression and this includes those with high levels of preformed antibodies [48].

Evidence

The need for induction immunosuppression is supported by strong evidence showing intense immunologic response to the renal allograft in the immediate post-transplant period [49, 50]. The point of induction therapy is to limit the risk of rejection during this period when oral drugs would not be effective.

There is good evidence that IL2-RAs reduce the risk of early rejection compared to placebo and this may lead to improved graft survival. This comes from dialysis and transplant registry data in Australia and New Zealand [51]. Additionally, there is moderate evidence that T-cell depleting agents reduce the risk of acute rejection in high immunologic risk recipients [52,53]. Available RCTs comparing ATG to IL2RAs in high immunologic risk recipients show lower incidence of acute rejection with ATG but no significant difference in 5 year [52] or 10 year outcomes [53]. This is also embodied in the British Transplant Society Guidelines [54]. There are as yet no RCTs in Nigeria or similar contexts to inform a differing recommendation at this time.

Maintenance immunosuppression requires a careful and considered balance between the risk of rejection, complications associated with reduced immunity and side effects of the drugs. A large RCT has shown that maintenance therapy with tacrolimus, mycophenolate mofetil (MMF) and corticosteroids was superior at 12 months in terms of graft function, graft survival and acute rejection rate to either standard or low dose ciclosporin in low immunological risk KTRs [55,56]. However, tacrolimus may cause severe side effects in some patients including posterior reversible encephalopathy syndrome, haemolytic uraemic syndrome, alopecia and gastrointestinal disturbance. In such cases, a second line agent like ciclosporin, m-TORi or belatacept may be considered. High, medium and low trough (C0) levels for tacrolimus are >10, 5-10 and <5 ng/ml respectively.

There is increased interest in steroid withdrawal and avoidance regimes, however, clinical experience indicates that outcomes are poor without steroids. A more detailed discussion of steroid withdrawal is presented in the British Transplant Society Guidelines [54].

Recommendations

Induction therapy

5.10.1 We recommend that immunosuppressive drugs should be started before or at the time of renal transplantation

Quality of evidence - High Recommendation - Strong

- 5.10.2 We suggest that induction therapy with a biological agent be administered to all kidney transplant recipients (KTRs)

Quality of evidence - High Recommendation - Strong

- 5.10.3 We recommend that the first line should be an interleukin-2 receptor antagonist (IL2-RA) in patients with low immunologic risk

Quality of evidence - Moderate Recommendation - Weak

- 5.10.4 We recommend that in those with high immunologic risk, a T-cell lymphocyte depleting agent (TDA) should be used

Quality of evidence - Moderate Recommendation - Strong

- 5.10.5 We suggest that induction with a TDA may be useful in a case of low immunologic risk with the intention to avoid steroids or calcineurin inhibitors (CNIs)

Quality of evidence - Low Recommendation - Strong

- 5.10.6 We suggest starting CNIs at the time of transplant and not delaying until graft function is established.

Quality of evidence - Low Recommendation - Weak

Maintenance therapy

- 5.10.7 We recommend that in low and medium immunologic risk, maintenance immunosuppression should consist of a CNI and an anti-proliferative agent, with or without steroids

Quality of evidence - Low Recommendation - Strong

- 5.10.8 We recommend that low to medium dose tacrolimus (trough 4-8 ng/ml) should be the first line choice in low and medium immunologic risk patients who are taking steroids and who are not at high risk of developing post-transplant diabetes mellitus (PTDM)

Quality of evidence - Low Recommendation - Strong

- 5.10.9 We suggest using mycophenolic acid based drugs as the first line antiproliferative agent over azathioprine, except in the case of child bearing age transplant recipients who are unwilling to use reliable contraception

Quality of evidence - Moderate Recommendation - Weak

- 5.10.10 We suggest using slow release tacrolimus as a second line agent in patients who have intolerable adverse effects related to peak dose toxicity

Quality of evidence - Low Recommendation - Weak

- 5.10.11 We recommend that in kidney transplant recipients who cannot tolerate tacrolimus, second line agents like cyclosporin, sirolimus, everolimus, or belatacept should be considered for use

Quality of evidence - Moderate Recommendation - Strong

- 5.10.12 We suggest that steroids should be continued as low dose after 4-6 weeks [44] with specific regimen determined by unit protocol

Quality of evidence - Low Recommendation - Weak

- 5.10.13 We suggest aiming for minimum target levels for CNIs by 3 months after transplantation, if there are no complications

Quality of evidence - Low Recommendation - Weak

5.10.14 We suggest that CNIs should not be withdrawn except when they are not tolerated	
Quality of evidence - Moderate	Recommendation - Weak

References

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5.11 Immediate post-transplant care (including management of acute rejection)

Background

Important aspects of immediate post-transplant care focus on optimizing graft function, preventing acute rejection and minimizing the risk of opportunistic infections. The risk of acute rejection and opportunistic infections represent a delicate balance where under- or over- immunosuppression can tilt the balance to the former or latter. Acute rejection results from an immune response of the host to destroy the graft, and is characterized by a decline in kidney function accompanied by well-established diagnostic features on kidney allograft biopsy. There are several causes of impaired graft function, and these have to be distinguished from acute rejection by a renal allograft biopsy [57]. Acute rejection can be T-cell mediated or anti-body mediated. Majority of patients with acute cellular rejection respond to corticosteroid therapy [57,58]. However, in milder grades of cellular rejection (Banff category 4 type I), treatment with anti-T-cell antibodies may be more effective in restoring kidney function and preventing graft loss than treatment with corticosteroids [59]. In the case of antibody mediated rejection, there is limited evidence that treatment modalities like corticosteroids, plasmapheresis, immunoadsorption, intravenous immunoglobulin or monoclonal antibodies may be beneficial [57,60,61].

Supporting Evidence

Several management options have been considered with the aim of improving graft function. Inadequate fluid management is an important factor that may lead to dehydration (which causes DGF) or fluid overload. The usefulness of central venous pressure (CVP) as a guide for fluid management and its impact on graft function is unclear. However, evidence from a small prospective randomized open trial in 40-living donor kidney transplant recipients showed that monitoring of fluid with CVP target >15 mmHg was associated with better early graft function [62]. There is no evidence of a difference in outcomes between using normal saline versus lactated Ringer's solution [63]. 'Renal dose dopamine' has also been proposed as a way of improving graft function. However, evidence supporting its effectiveness is poor [64-66].

The diagnosis of acute rejection is best established by a percutaneous biopsy since it differentiates rejection clearly from other causes of graft dysfunction. C4d and SV40 staining on biopsy samples to rule out other causes of graft dysfunction is recommended in line with BTS guidelines and those of The Transplantation Society [64,65].

In terms of treatment, majority of acute cellular rejection episodes respond to corticosteroids [67]. The optimal regime for steroid administration has not been determined and usually depends on unit protocol. If antibody mediated rejection is diagnosed, there is limited evidence that treatment with alternative modalities including plasmapheresis, immunoadsorption, intravenous immunoglobulin or monoclonal antibodies may be beneficial [57]. Trial evidence is conflicting and of low quality. Therefore, the risk and benefit of using different agents should be considered on a patient by patient basis.

Recommendations

Immediate post-transplant care

- 5.11.1 We suggest that CVP be measured and also corrected in the immediate post-transplant period to prevent hypovolaemia and delayed graft function
Not graded
- 5.11.2 We suggest considering a target CVP of > 15mmHg
Quality of evidence - Very low Recommendation - Weak
- 5.11.3 We recommend that kidney transplant recipients be monitored for metabolic acidosis when normal saline is used as the only intravenous fluid in the post-transplant period
Quality of evidence - Moderate Recommendation - Strong
- 5.11.4 There is no evidence supporting the use of one type of fluid over another (i.e. normal saline versus ringers) as the preferred choice in intravenous volume management of kidney transplant recipients
Not graded
- 5.11.5 Renal doses of dopaminergic agents is not recommended as a means of improving early graft function in the immediate post-transplant period
Quality of evidence - Moderate Recommendation - Strong
- 5.11.6 We suggest that urine volume be measured hourly for the first week after transplantation
Quality of evidence - Very low Recommendation - Weak
- 5.11.7 We suggest that the urinary catheter be removed as soon as possible after kidney transplantation while taking into consideration the risk of urine leak against the risk of urinary tract infection
Quality of evidence - Very low Recommendation - Weak
- 5.11.8 We suggest that urine protein excretion be measured at least once in the first month after

transplantation

Quality of evidence - Very low

Recommendation - Weak

- 5.11.9 We recommend that serum electrolytes, urea and creatinine should be measured 12 hourly for the first 72 hours and daily thereafter up until the patient is discharged

Quality of evidence - Low

Recommendation - Strong

- 5.11.10 We suggest that kidney allograft Doppler ultrasound be done when assessing for kidney allograft dysfunction

Quality of evidence - Low

Recommendation - Weak

Acute rejection: Assessment

- 5.11.11 We recommend carrying out a transplant renal biopsy before starting treatment for acute rejection, except in situations where a biopsy would present a significant risk to the patient (for example haemorrhage) or would lead to considerable delays in treatment

Quality of evidence - Low

Recommendation - Strong

- 5.11.12 We recommend that a transplant renal biopsy be done if clinically indicated, and indications include delayed graft function, acute rejection episodes and rising urea or creatinine values

Quality of evidence - Low

Recommendation - Strong

- 5.11.13 We recommend that conducting a protocol biopsy should be considered by individual transplant programs

Quality of evidence - Low

Recommendation - Strong

- 5.11.14 We recommend performing routine C4d and SV40 staining on biopsy samples to rule out other causes of graft dysfunction

Quality of evidence - Low

Recommendation - Weak

- 5.11.15 We suggest testing for human leucocyte antigen (HLA)-specific antibodies (serum sample) at the time of biopsy, where available

Quality of evidence - Low

Recommendation - Weak

Acute rejection: Treatment

- 5.11.16 We suggest treating borderline and subclinical acute rejection

Quality of evidence - Very low

Recommendation - Weak

- 5.11.17 We recommend intravenous high dose corticosteroids as the first line therapy for acute cellular rejection

Quality of evidence - Very low

Recommendation - Strong

- 5.11.18 We suggest considering lymphocyte depleting antibodies to treat cases that do not respond to corticosteroids

Quality of evidence - Low

Recommendation - Weak

- 5.11.19 We suggest considering lymphocyte depleting agent for aggressive vascular cellular rejection (i.e. Banff category 4 Type II and III)

Quality of evidence - Low

Recommendation - Weak

- 5.11.20 We suggest treating antibody mediated rejection (ABMR) with one or a combination of the following:

- Steroids
- Plasma exchange

- Intravenous immunoglobulins
- Anti-CD20 antibody (rituximab)
- Lymphocyte depleting antibody
- Bortezomib

Quality of evidence - Low

Recommendation - Weak

- 5.11.21 We suggest replacing azathioprine with mycophenolate in patients who have a rejection episode or adding mycophenolate or maximizing the dose

Quality of evidence - Very low

Recommendation - Weak

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5.12 Special considerations concerning paediatric kidney transplantation

General Overview

Children in ESKD undergo pre-emptive kidney transplantation more frequently than adults. In the allocation of kidneys from deceased donors, children are prioritized to receive the more compatible kidneys as they are more likely to live long enough to need a second transplant [68,69]. On the other hand children are susceptible to growth and developmental delay a side-effect of immunosuppressant treatment with corticosteroids. Medication non-adherence which may be associated with graft loss also occurs commonly in the paediatric age group especially among adolescents and young adults [68,69]. This period also tends to coincide with period of transition to adult care. Medication non-adherence in the paediatric age group may be related in part to side-effects of medications such as cosmetic side-effects of cyclosporine, and growth delay and changes in body image side-effects of corticosteroids [70].

Kidney transplantation in the setting of congenital anomalies of the kidneys and urinary tract (CAKUT)

is seen more frequently in the paediatric age group compared to adults. Some of the children with background CAKUT or obstructive uropathy may need evaluation such as micturating cystourethrogram to assess the lower urinary tract and urodynamic studies to assess bladder function. Some patients with CAKUT or obstructive uropathy may have lesions that need to be corrected prior to kidney transplantation. For instance, a few children with bladder dysfunction may need bladder augmentation procedure before kidney transplantation [68,69].

The procedure of kidney transplantation can be carried out in children who weigh above 6.5 -10kg. Surgically, children who weigh 30 kg and above can be managed similarly to adults. Younger children can be transplanted with kidneys from adults, but may be at a greater risk for thrombosis to the renal vessels because of the small size of their blood vessels. For children who weigh less than 10 kg the graft kidney may be placed in the peritoneal cavity and the vessels anastomosed to the aorta and the inferior vena cava. For children weighing between 10 and 30 kg, the location of the graft can be individualized based on the child's anatomy between the intraperitoneal or the usual extraperitoneal location [69]. Fluid management post up should take into consideration the fluids that may be required to perfuse the adult graft kidney.

Infectious complications of kidney transplantation are common in paediatric kidney recipients. Urinary tract infections are the most common post-transplant infections in the paediatric age group, and the predisposing factors include bladder dysfunction and the immature immune system. Viral infections are also common complications in paediatric kidney transplantations because children are more immunologically naïve than adults [69]. Appropriate vaccination protocols, and monitoring of antibody levels are very important in the paediatric kidney transplant setting.

Graft survival has improved in paediatric kidney recipients in developed countries over the last several decades and 1, 5 and 10 year graft survival is about 97, 78 and 60% respectively [71]. Patient survival in paediatric kidney transplants is better than in adults [72].

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Induction Immunosuppressive therapy in children

Background

The choice of immunosuppressive therapy for the induction phase in children is largely based on studies in adults, the limited studies available in children and the peculiarities of the childhood population such as the side -effects of short-stature in children. Induction therapy in children usually involves the combination of antibody agents directed against T-cell antigens and conventional agents i.e., calcineurin inhibitors (Tacrolimus or Cyclosporine), anti-metabolites (Mycophenolate Mofetil more often than Azathioprine) and corticosteroids. Practice varies from centre to centre and may depend on the patient -risk for acute rejection and graft failure, and the potential side-effects of treatment such as growth failure. Factors that affect kidney allograft

survival in children include the following, improved immunosuppressive regimen, source of donor kidney, preemptive transplant, human leukocyte antigen (HLA) compatibility, age of the donor and recipient, presence of preformed anti-HLA antibodies (sensitization), prolonged cold ischemia time, ethnicity of the recipient [73], delayed allograft function, acute rejection episodes, infections, adherence, repeat transplant, and underlying primary disease [70,72,74].

Supporting Evidence

The benefit of antibodies to T-lymphocyte antigens or Interleukin-2 (IL-2) receptor antibodies as induction agents in paediatric kidney transplant recipients has not been verified in controlled trials. The choice of the use of antibody induction agents in children is based on the outcome of studies in adults and observational studies from the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) which show that antibody induction agents in combination with conventional immunosuppressive agents are superior to conventional agents alone in reducing acute rejection and kidney allograft failure [75-77].

Large trials in children do not show that there is advantage of IL-2 receptor antibodies over conventional immunosuppressive medications in reducing acute rejection, and graft survival in the medium risk patient [78,79]. Studies in adults show advantage of Anti-lymphocyte antibodies over IL2 Receptors in preventing acute rejection in high-risk adults [76]. Single centre studies in children show that Antilymphocyte antibodies induction therapy in combination with steroid minimization protocols were comparable to historic steroid based immunosuppressive protocols in terms of frequency of acute rejection and graft loss and patient survival, and no increased risk of infections, and may minimize the risk of steroid toxicity [80-82]. The potential long term risk of Post-Transplant Lymphoproliferative (PTLD) in patients who received Anti-lymphocyte or IL-2 Receptor antibodies is yet to be determined.

Non-biologic medications i.e., conventional medications i.e., intravenous methyl prednisolone, calcineurin inhibitors, and antimetabolites have been used for induction before both in paediatrics and in the adult age groups [83,84]. Usually the medications are given at higher doses when they are used for induction without the anti-lymphocyte antibodies. The most common nonbiologic agent for induction therapy is i.v. methyl prednisone given at a starting dose of 10mg/kg up to a maximum of 1 g [70].

However, most centres in developed countries will use a combination of anti-lymphocyte antibodies, and conventional agents based on a risk stratification approach and whether patient is planned for a steroid minimization protocol or not [70]. For example, high risk patients that will be on steroid minimization protocol will receive induction with thymoglobulin. Moderate risk patients will however, receive induction with IL2-receptor antibody (Basliximab) followed by conventional agents

Recommendations

- | | | |
|--------|---|-------------------------|
| 5.12.1 | We recommend starting a combination of immunosuppressive medications before or at the time of kidney transplantation. | |
| | Quality of evidence - High | Recommendation - Strong |
| 5.12.2 | We recommend using a biologic agent for induction therapy. In addition with other conventional medications in kidney transplant recipients. | |
| | Quality of evidence - Moderate | Recommendation - Strong |
| 5.12.3 | We suggest using a lymphocyte-depleting agent, rather than an IL2-RA, for kidney transplant recipients at high immunologic risk. | |
| | Quality of evidence - Moderate | Recommendation - Weak |
| 5.12.4 | We recommend starting a combination of immunosuppressive medications before or at kidney transplantation. | |
| | Quality of evidence - High | Recommendation - Strong |
| 5.12.5 | We recommend using a biologic agent for induction therapy. In addition with other conventional | |

medications in kidney transplant recipients.

Quality of evidence - Moderate

Recommendation - Weak

- 5.12.6 We suggest using a lymphocyte-depleting agent, rather than an IL2-RA, for kidney transplant recipients at high immunologic risk.

Quality of evidence - Moderate

Recommendation - Weak

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5.13 Maintenance immunosuppression

Background

The goals of maintenance immunosuppression therapy are to prevent acute graft rejection and graft failure and to minimize drug toxicity. It usually consists of a combination of medications which act through different pathways. Examples of combinations that are utilized are calcineurin inhibitors (tacrolimus more frequently than cyclosporine), antimetabolites (mycophenolate mofetil more frequently than azathioprine) and corticosteroids. Other categories of drugs include the mechanistic target of rapamycin (mTOR) inhibitors such as sirolimus and everolimus [70].

Evidence

Corticosteroids: The immunosuppressive ability of corticosteroids are based on their ability to inhibit the activity and proliferation of T Lymphocytes [70]. They inhibit the transcription of genes that code for several cytokines [85,86]. They also reduce the activity of monocytes and neutrophils, but have little effect on antibody [70]. Side-effects include growth failure, susceptibility to infections, cushingoid appearance, acne,

hypertension, cataracts, aseptic bone diseases, and delayed wound healing. The side-effect of corticosteroids on appearance may contribute to poor adherence to therapy in adolescents.

Corticosteroids dosage is usually switched from daily to alternate day regimen from the 6-12th month post-transplant to minimize the growth inhibiting effect of corticosteroids [70,87,88]. Alternate day regimen is the most common method used to minimize the side-effects of corticosteroids [70,87,88].

Several steroid minimization or withdrawal protocols have been found to improve growth, without increasing the rate of acute rejection or compromising graft and patient survival [70,89]. These protocols are based on anti-lymphocyte antibody (rATG-Thymoglobulin) or IL-2 receptor antibody induction and modified maintenance immunotherapy regimens. The maintenance immunotherapy for instance may be based on tacrolimus and MMF only. Steroid avoidance or minimization maintenance immunotherapy methods being investigated include a combination of antimetabolic agents e.g MMF, calcineurin inhibitor e.g cyclosporine, and a mechanistic target of Rapamycin (mTor) inhibitor. Steroid withdrawal protocol was not associated with increased risk of recurrent disease [90].

Calcineurin Inhibitors: The calcineurin inhibitors likely account for the continuing improvement in allograft survival and have been the backbone of maintenance immunosuppressive therapy in kidney transplantation in the last ten years [70,91-93]. The two calcineurin inhibitors used in paediatric kidney transplantation are Cyclosporine and Tacrolimus. The preferred choice is Tacrolimus because it has lower frequency of cosmetic side effects and a lower rate of acute rejection than cyclosporine, but less frequently choice may reflect centre preference [70].

Trials in adults indicate that tacrolimus and cyclosporine have similar allograft survival but tacrolimus has reduced rate of acute rejection and less requirements for intensive immunosuppression compared to cyclosporine [94]. Data comparing cyclosporine and Tacrolimus in children are however limited: one retrospective study of 986 children showed no difference in 1 and 2 year allograft survival [95]. On the other hand, an open label trial of 192 paediatric patients showed similar patient survival but better graft survival with tacrolimus [96].

Anti-Metabolites: In Children, MMF appears to be beneficial and safe [70]. One and five year allograft survival rates of MMF were better than those of historical controls who had azathioprine [97,98]. MMF was also associated with a lower rate of acute rejection when compared with historical controls who had azathioprine [97]. In a study that reviewed patients with MMF, CSA, and corticosteroids, among those who received induction therapy, the 3 year acute rejection rate was 26% with Induction therapy and 41% without induction therapy [99].

Mycophenolate sodium (MMS) was developed to decrease gastric side-effects of MMF [70]. Mycophenolate sodium was associated with significant improvement in gastrointestinal symptoms in a small cross over study [100]. MMS was associated with resolution of gastrointestinal symptoms in a small case series of patients who were switched from MMF to MMS [101]. However, MMS cannot be crushed or made into suspension, so that it can only be used only in patients that can swallow pills whole.

Mechanistic target of rapamycin (mTOR) inhibitors: Target of Rapamycin (mTOR) inhibitors block the proliferative response of lymphocytes to IL 2/7. They include Sirolimus and Everolimus. Protocols will use either sirolimus or everolimus, they are not used in combination. mTOR inhibitors are effective when used in combination with calcineurin inhibitors and steroids [102]. They increase the risk of nephrotoxicity of CNIs and therefore it is recommended that dosage of CNIs is reduced when it is used in combination with an mTOR inhibitor [103]. Sirolimus has been associated with delayed wound healing therefore mTOR inhibitors are not usually used shortly after kidney transplantation [102].

Use of Basiliximab in combination with protocols including sirolimus, although associated with decreased rate of acute rejection, may increase the risk of post-transplant lymphoproliferative disorder (PTLD). It appears the combination causes excessive immunosuppression [104,105]. Everolimus has been used in CNI minimization and steroid withdrawal protocols with good graft and patient survival rates, with comparable rates of acute rejection leading to medication discontinuation [106-108]. Variable success is reported in the studies which utilized sirolimus in CNI avoidance, or minimization protocols [109,110].

The best maintenance immunotherapy protocol for kidney transplant recipients, has not been described. The most widely used are combinations of CNI, MMF and corticosteroids. Efforts are ongoing to describe medications that will avoid the chronic nephrotoxicity secondary to calcineurin inhibitors or the side-effects of steroid therapy such as growth failure.

Recommendations

- 5.13.1 We recommend the use of maintenance immunosuppressive medications in all paediatric renal transplant recipients.
Quality of evidence - High Recommendation - Strong
- 5.13.2 The most commonly used agents are corticosteroids (Prednisolone or prednisone), calcineurin inhibitors (Tacrolimus or cyclosporine) and antimetabolites (mycophenolate mofetil or azathioprine).
Quality of evidence - Moderate Recommendation - Strong

Starting dosages and monitoring drug levels

Starting dose of cyclosporine for children aged < 6 years is 500mg/m²/day p.o 8 hourly. For children older than 6 years and in combination with steroids or purine synthesis inhibitors the dose is between 12-15 mg/kg/day 12 hourly. The dose is adjusted to maintain a trough whole blood level of 150-300 mcg/L for the first 3-6 months post-transplant. The dose is reduced to about 4-6mg/kg thereafter with targeted trough levels of about 75-125 mcg/L. Target trough levels can be reduced at the end of 1 year in patients who are rejection free to 3 and 5mcg/L

The typical dose of tacrolimus is 0.2-0.3mg/kg/day p.o in two divided doses. Target trough whole blood levels are 10 to 15 ng/mL during the first month, and 5 to 10 ng/mL thereafter.

Mycophenolate mofetil is typically given at a dose of 1200mg/m²/day p.o in two divided doses, while azathioprine is given at a dose of 1-2 mg/kg p.o once a day when used in conjunction with a triple regimen of corticosteroids and calcineurin inhibitors.

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5.14 Management of Acute Rejection

Background

Acute rejection can be defined as an acute deterioration in graft function associated with specific pathologic changes in the graft [70]. Acute rejection is common and may occur after several days to months after transplantation. Acute rejection accounts for graft failure or death in 5% of children with kidneys from living donors and 8% of those with kidneys from deceased donors [72,111]. The estimated half-life of the kidney allograft is shorter in those who have had acute rejection compared to those who have not [112,113]. In addition, acute rejection episodes also increase the risk of chronic rejection and affect the long term survival of the graft [72,114].

The beneficial effects of optimal HLA typing and immunosuppressive management are in part due to the reduction in the number of acute rejection episodes [72].

The rate of acute rejection in children has reduced over the last thirty years, and this appears to be based on the use of newer immunosuppressive medications [111,115]. The classic signs of acute rejection such as fever and graft tenderness are seen less frequently with the new immunosuppressive regimens, and now acute rejection commonly manifests as elevated serum creatinine [115,116]. Differential diagnosis for elevated serum creatinine post-renal transplant are as follows urinary tract obstruction, calcineurin inhibitor nephrotoxicity, cytomegalovirus and BK virus infection, renal artery stenosis and pyelonephritis [115].

Recommendation for the timing of serum creatinine estimation in stable allograft recipients is available [117].

The two major forms of acute rejection are

- i. T - cell mediated acute rejection
- ii. Antibody mediated acute rejection

Supporting Evidence:

There has been no controlled trial for the treatment of acute rejection in children. In general, T-cell mediated acute rejection in children is treated with intravenous methyl prednisolone, followed by oral prednisolone. Children with steroid resistant acute rejection may receive treatment with antilymphocyte antibodies. Other considerations in children who have had acute rejection include medication adherence, and change in the immunosuppressive medication especially if the patient has been adherent with medications. Such changes include from cyclosporine and azathioprine to Tacrolimus and MMF, or from cyclosporine and MMF to Tacrolimus and Sirolimus [70].

Antibody mediated rejection is less common and may be managed by plasma exchange, high dose intravenous immunoglobulin (IVIG), and/or Rituximab [70,118].

Recommendations

- 5.14.1 Biopsy is recommended in patients with suspected rejection after exclusion of obstructive uropathy
Quality of evidence - High Recommendation - Strong

T cell mediated Acute rejection

- 5.14.2 We recommend that T cell mediated acute rejection be treated with pulse i.v methyl prednisolone given at a dose of 10-30mg/kg daily for 3 days
Quality of evidence - Low Recommendation - Strong
- 5.14.3 We recommend that i.v pulse methyl prednisolone be followed by daily oral prednisolone starting at 1-2 mg/kg and thereafter slow tapering to pre-rejection prednisolone dosage
Quality of evidence - Low Recommendation - Strong
- 5.14.4 We recommend that a rejection episode be considered steroid resistant if after 7-10 days of steroid therapy, no improvement is seen in serum creatinine levels
Quality of evidence - Low Recommendation - Strong
- 5.14.5 We recommend that steroid resistant T cell mediated acute rejection be managed with lymphocyte depleting antibodies.

Quality of evidence - Low

Recommendation - Strong

- 5.14.6 We recommend that for patients who have been adherent to medications and have rejection, alternative maintenance immune-suppressive be considered

Quality of evidence - Low

Recommendation - Strong

B -cell mediated acute rejection

- 5.14.7 We suggest that management of antibody mediated acute rejection be with plasma exchange, high dose IVIG, and anti CD20 therapy

Quality of evidence - Low

Recommendation - Weak

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5.15 Growth and Development

A unique feature of chronic kidney disease in children is impaired growth and development. Management of impaired growth in children with chronic kidney disease includes early commencement of optimal nutrition. Other modalities include management of metabolic acidosis with oral bicarbonate, management of renal osteodystrophy with phosphate restriction, calcium supplementation and vitamin D, replacement of excessive renal fluid and electrolyte losses, and correction of anaemia with erythropoietin [119]. However, when the children develop ESRD growth rate deteriorates [119].

The best form of renal replacement therapy for the achievement of growth and improved quality of life is kidney transplantation, however the growth response following kidney transplantation may be variable [119-121]. The use of daily steroids in patients who have received kidney transplantation may cause impaired growth [121]. Other factors that may influence growth and/or final height include the degree of allograft dysfunction, the height at the time of kidney transplantation and the age of the patient [119-121]. Kidney transplant immunosuppressive medication protocols that minimize or avoid steroid therapy may enhance

growth post-kidney transplantation [87,88,119,122,123]. Administration of exogenous growth hormone in pharmacologic doses to patients with CKD including those with persisting growth retardation post-kidney transplantation may enhance growth [124-129].

Supporting Evidence

Successful kidney transplantation usually allows the optimal effect of the normal endogenous growth hormone [130]. Impaired growth in this setting is usually due to reduced graft function and daily glucocorticoid therapy. Growth hormone therapy is recommended in post kidney transplantation patients with diminished graft function, (GFR below 50 mL/min per 1.73 m²) who need to be on daily corticosteroids and who are unlikely to have adequate spontaneous catch up growth [128,129].

Spontaneous growth needs to be monitored for the first year post kidney transplantation, so growth hormone therapy is usually started second year post kidney transplantation.

Clinical trials show clearly that growth hormone induces catch up growth in kidney transplant recipients [131-134]. However, the effect may become limited with time [132]. A large registry retrospective study also showed that growth was better in kidney transplant recipients who received growth hormone compared with controls but growth was better in participants who were younger than 10 years old [135]. Studies have also showed increased mean height in short pubertal transplant children who receive recombinant growth hormone compared with historical controls [134,136]. Recombinant growth hormone has not been associated with increased risk of acute rejection in kidney allograft [131,133,135,137].

Recombinant growth hormone at 28IU /week/m² which corresponds to 4IU/day/m² (about 0.5mg/kg/day) resulted in a higher growth velocity than placebo or growth hormone at 14IU/week/m² [133, 137].

Recommendations

- 5.15.1 We recommend the measurement of growth and development in children
Quality of evidence - Moderate Recommendation - Strong
- 5.15.2 At least every 3 months if <3 years old (including head circumference) and every 6 months in children ≥3 years until final adult height.
Not graded
- 5.15.3 We recommend the use of recombinant human growth hormone 28 IU/m²/week (or 0.05 mg/kg/day) in children with persisting growth failure after kidney transplantation.
Quality of evidence - Moderate Recommendation - Strong
- 5.15.4 We recommend minimizing the use of corticosteroids in children who still have growth potential.
Quality of evidence - High Recommendation - Strong

References

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5.16 Medication non adherence

Background

Medication non-adherence is an important contributor to both acute and chronic rejection in paediatric kidney transplant recipients. Greater adherence has been associated with improved allograft survival [138]. Rate of medication non-adherence among children in a review of literature ranged from 5-70% [139]. Factors that were associated with medication non-adherence included poor socioeconomic status, family stress and conflicts, lack of parental supervision, patient depression, cosmetic side effects of medications, large number of medications, size of tablets and difficulty swallowing tablets, taste of medication, poor patient knowledge, striving for increased autonomy and independence [139]. Other factors that may contribute to low medication adherence in some developing countries are the cost and availability of the medications, and absence of health insurance.

Supporting Evidence

Medication non-adherence is a risk factor for graft non-function [139-142]. Discontinuation of medication was the cause of graft loss in about 5% of patients in the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) 2010 transplant report. A review of data from the Organ Procurement and Transplantation Network (OPTN) indicated that medication non-adherence contributed to 3.5% of graft loss among African-Americans and 1.5% among other races. Patients who were aged less than 10 years had significant lower rates of medication adherence (0.9%), compared to patients aged 10-14 years (2.2%) and those aged 15-20 years (2.0%) [142].

Although it is clear that improving adherence will lead to better outcomes in kidney transplant recipients, data is limited on outcomes of interventions to improve medication non-adherence. A study among adults that utilized patient, education phone calls and home visits over a period of 3 months and 6 month follow up, noted a significant improvement in adherence in the intervention group within 3 months, but the change was not significant in both groups after 6 months and at 9 months [143]. The sample size was however small.

Recommendations

- 5.16.1 We suggest providing patients who have received kidney transplant and their family members with education on the prevention and treatment measures to minimize nonadherence to therapy.

Not graded

- 5.16.2 We suggest that kidney transplant recipients at increased risk for nonadherence Be monitored with increased levels of screening for nonadherence.

Not graded

- 5.16.3 We suggest that phone reminders such as text messages sent to care givers and patients where applicable to minimize non-adherence.

Not graded

References

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Areas for Future Research

Research into the role of steroid and CNI sparing medications in our environment--

5.17 Recurrence of primary disease in the post-transplant period

Many glomerulonephritis can recur following kidney transplantation. Recurrence of native kidney disease accounts for the third leading cause of graft failure [144-146].

Supporting Evidence

The Kidney disease improving global outcomes (KDIGO), bases its recommendation on some 20% of glomerular diseases recurring in allograft. At this time in Nigeria, no large scale published data can be found [144].

Recommendations

- 5.17.1 We recommend that kidney biopsy should be offered to every patient whose aetiology of CKD is glomerulonephritis, especially early stages -- I, II and III. This will help to establish the cause of kidney disease in such patients and help to plan their care
Quality of evidence - High Recommendation - Strong
- 5.17.2 We recommend that kidney transplantation should not be withheld from patients whose aetiology of CKD could recur. These include: Focal segmental glomerulosclerosis, membranous nephropathy, membranoproliferative glomerulonephritis, lupus nephritis, sickle cell nephropathy and Immunoglobulin A nephropathy. Recurrence of these diseases after transplant and outcomes should be discussed with recipients and family
Quality of evidence - Moderate Recommendation - Strong

References

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Recurrent Focal segmental glomerulosclerosis (FSGS)

Background

Focal segmental glomerulosclerosis (FSGS) is the commonest glomerular pattern of injury among African Americans and some studies in Nigeria has confirmed the same [147-149]. Primary FSGS can recur in 30 - 50% following first kidney transplant and in second transplant, up to 80% recurrence rates has been reported [150-152]. Factors that may lead to recurrent FSGS following kidney transplant include: nephrotic range proteinuria, younger recipient age < 20 years, rapid progression of FSGS to ESKD, bilateral nephrectomy pre-transplant, mesangial proliferative lesion in native kidneys, living donation, and prior allograft failure from FSGS [153-158].

Recommendations

- 5.17.3 An allograft loss due to recurrent FSGS puts the recipient at greater risk of allograft failure in subsequent transplants
Not graded
- 5.17.4 We suggest performing genetic testing for children and young adults suspected to have genetic forms of FSGS. Where available tests done could include APOL 1, nephrin and podocin genetic screening. This will help prognosticate chance of recurrence
Quality of evidence - Low Recommendation - Weak

- 5.17.5 We suggest that pre-transplant treatment with rituximab and plasmapheresis should not be done as it has not been shown to influence risk of recurrent FSGS
Quality of evidence - Very low Recommendation - Weak

References

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Recurrent membranous nephropathy (MN)

Background

The risk of membranous nephropathy (MN) recurring following kidney transplantation is between 10 - 50% [159]. About 70% of patients who have idiopathic MN have antibodies to phospholipase A2 receptor (PLA2R) [160,161].

Recommendations

- 5.17.6 We suggest, where available measuring the serum level of antibodies to PLA2R prior to transplant as high levels may predict recurrent MN
Quality of evidence - Low Recommendation - Weak
- 5.17.7 We suggest that rituximab or alkylating agents should not be used routinely for prevention of recurrent MN, as pre-transplant use has not reduced recurrence rates
Quality of evidence - Very low Recommendation - Weak

References

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Recurrent Membrano-proliferative glomerulonephritis (MPGN).

Background

The rate of recurrence of MPGN varies from 41% for immune complex disease (IgG), to 70% in Complement 3 glomerulopathy (C3G) and up to 100% in patients who have dense deposit disease (DDD) [162-164].

Recommendations

- 5.17.8 We recommend evaluating transplant recipients for autoimmune diseases, paraproteinemia and infections, as the cause of immune complex MPGN
Quality of evidence - Low Recommendation - Strong
- 5.17.9 We suggest that if the cause of MPGN is detected, treatment should precede kidney transplantation
Quality of evidence - Low Recommendation - Weak
- 5.17.10 We suggest that when C3G is known to be the cause of ESKD, genetic screening where available for complement disorders be done to help plan future care after transplantation
Quality of evidence - Low Recommendation - Weak

References

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Recurrent Lupus nephritis (LN)

Background

Systemic lupus erythematosus (SLE) is a connective tissue disorder, the risk of recurrence in the allograft ranges from 2.5 to 54% [165]. Some risk factors for recurrence include younger age, female gender and Black race. Antiphospholipid syndrome (APS) may accompany LN, which can present as thrombotic microangiopathy [166,167].

Recommendations

- 5.17.11 Prior to kidney transplantation, LN patient should be in remission or need minimal immunosuppression for control of the disease
Quality of evidence - Very Low Recommendation - Strong
- 5.17.12 Screening for APS should be done for LN patients before kidney transplantation
Quality of evidence - Low Recommendation - Strong

References

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Recurrence of Sickle cell nephropathy (SCN)

Background

Although sickle cell nephropathy can recur following transplantation, the rates are not known [168,169].

Recommendations

- 5.17.13 We suggest that where available, a bone marrow transplant can be considered before or after the kidney transplant

Not graded

References

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5.18 New onset diabetes after transplantation (NODAT)

Background

New onset diabetes after transplantation is when recipient develop diabetes mellitus following transplantation. The frequency is 10 - 40% among KTR [170,171]. The risk factors include family history of diabetes, obesity, advancing age, impaired glucose tolerance and hepatitis C positive. The steps taken to reduce the risk of NODAT includes use of cyclosporine instead of tacrolimus, minimization of steroids and early use of insulin post-transplant [172,173]. Diagnosis of NODAT is based on abnormal oral glucose tolerance test, as fasting blood glucose and glycated hemoglobin are not reliable in ESKD [174,175].

Recommendation

- 5.18.1 We suggest that recipients undergo oral glucose tolerance test and fasting blood glucose as a screening for NODAT

Quality of evidence - low

Recommendation - Strong

- Can be done monthly for first 3 months post-transplant

Quality of evidence - Very low

Recommendation - Weak

- Done every 3 months till end of first year post-transplant

Quality of evidence - Very low

Recommendation - Weak

- Every year after the first-year post-transplant

Quality of evidence - Very low

Recommendation - Weak

References

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5.19 Chronic Allograft Injury (CAI)

Background

The decline in allograft function over time is now termed chronic allograft injury as opposed to the previous terminologies of chronic allograft nephropathy or chronic rejection [176]. Interstitial fibrosis and tubular atrophy (IF/TA) are the major findings on allograft biopsy [176]. The aetiology includes: chronic antibody-mediated rejection, calcineurin inhibitor toxicity, hypertension, viral infections and others [177,178].

Recommendations

- 5.19.1 We recommend that when there is declining allograft function in kidney transplant recipient, an allograft biopsy is needed to diagnose treatable cause of CAI
 Quality of evidence - Low Recommendation - Strong
- 5.19.2 We suggest reducing dose of calcineurin inhibitors (CNI) or stopping it when histology of CAI is due to CNI toxicity
 Quality of evidence - Low Recommendation - Weak
- 5.19.3 We suggest replacing CNI with m TOR inhibitors when e GFR is > 40 ml/min/1.73 m² and urinary protein-creatinine ratio is < 500 mg/g
 Quality of evidence - Very low Recommendation - Weak

References

176. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. *American Journal of Transplantation* 2009; 9(Suppl 3): S1-S157.
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178. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. *American Journal of Transplantation* 2009; 9(Suppl 3): S1-S157.

5.20 BK Polyoma Virus

Background

BK virus (BKV) belongs to the Polyoma virus family. It is a recognized cause of allograft nephropathy and CAI in KTR [179,180].

Recommendations

- 5.20.1 We suggest that where available, KTR should undergo plasma nucleic acid test for BKV
 Quality of evidence - Very low Recommendation - Weak
- Every month for 3 - 6 months post-transplantation
 Quality of evidence - Very low Recommendation - Weak

- Every 3 months for 6 - 12 months post-transplantation
Quality of evidence - Very low Recommendation - Weak
 - Any rise in serum creatinine post-transplantation
Quality of evidence - Very low Recommendation - Weak
 - Following treatment for acute rejection episodes
Quality of evidence - Very low Recommendation - Weak
- 5.20.2 We suggest that when plasma nucleic acid test levels of BKV exceeds 10,000 copies/mL the dose of immunosuppression should be reduced
Quality of evidence - Very low Recommendation - Weak
- 5.20.3 We suggest that KTR with suspected BK virus nephropathy should undergo an allograft biopsy
Not graded

5.21 Epstein-Barr Virus and Post-Transplant Lymphoproliferative Disease

Background

Epstein-Barr Virus (EBV) is human herpesvirus 4, part of the herpes virus family. It has been linked to post-transplant lymphoproliferative disease (PTLD) in about 80% of cases [181,182].

Recommendations

- 5.21.1 We suggest that where available, KTR who are seronegative for EBV and donor is seropositive for EBV; should have plasma nucleic acid test for EBV
Quality of evidence - Low Recommendation - Weak
- Done once in first week post-transplant
Quality of evidence - Very Low Recommendation - Weak
 - Done monthly for 3 - 6 months post-transplant
Quality evidence - Very Low Recommendation - Weak
 - Done every 3 months for 6 - 12 months post-transplant
Quality evidence - Very Low Recommendation - Weak
 - Done following treatment for acute rejection
Quality evidence - Very Low Recommendation - Weak
- 5.21.2 We suggest reducing dose of immunosuppression in EBV-seronegative KTR when level of plasma nucleic acid test is on the rise
Quality evidence - Very Low Recommendation - Weak
- 5.21.3 We recommend dose reduction or complete discontinuation of immunosuppression medications in severe EBV disease as well as KTR developing PTLD
Quality evidence - Low Recommendation - Strong

References

179. Epstein-Barr virus and lymphoproliferative disorders after transplantation. Am J Transplant 2004;

4: 59-65.

180. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. American Journal of Transplantation 2009; 9(Suppl 3): S1-S157.

5.22 cardiovascular diseases in Kidney Transplant Recipient

Hypertension

Recommendations

- 5.22.1 We recommend that at each clinic visit by KTR, the blood pressure should be measured
Quality evidence - Low Recommendation - Strong
- 5.22.2 We suggest that target blood pressure should be < 140 mmHg systolic and < 90 mmHg diastolic
Quality evidence - Low Recommendation - Weak
- 5.22.3 For the treatment of hypertension
 - any appropriate class of anti-hypertensive medication,
 - adverse side effects should be monitored, as well as drug interactions with immunosuppressives,
 - use of ACEI or ARB when urinary excretion of protein 1 gram/day or in paediatrics when 600 mg/m²/day.Not graded
- 5.22.4 We suggest for KTR with atherosclerotic cardiovascular disease receive aspirin, except there is contraindication for its use
Quality evidence - Moderate Recommendation - Weak

Dyslipidaemias

Recommendations

- 5.22.5 Check lipid profile for KTR every 3 months during first year post-transplant; after the first year it can be done annually. This applies to KTR with no prior dyslipidaemia
Not graded

Obesity

Recommendations

- 5.22.6 During each visit after kidney transplantation, assess for obesity using:
 - Height and weight should be measured and BMI calculated
 - Waist and hip circumference should be measuredNot graded
- 5.22.7 For obese KTR, offer a diet that will help with weight reduction
Not graded

References

181. Kidney Disease: Improving Global Outcomes (KDIGO) Kidney Transplant Candidate Work Group. KDIGO Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation. Transplantation. 2020;104: S1-S103.
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5.23 Post-transplant malignancies

Kaposi Sarcoma (KS)

Background

This is the commonest malignancy reported among KTR in Nigeria [184,185]. The skin lesion affects the lower limbs more often than other parts of the body. Human herpes virus 8 (HHV 8) has been linked with KS.

Recommendations

- 5.23.1 We suggest screening potential KTR for HHV 8
Quality of evidence - Very Low Recommendation - Weak
- 5.23.2 We suggest substitution of CNI with m TOR inhibitor for KTR who develop KS
Quality of evidence - Low Recommendation - Strong
- 5.23.3 We suggest reduction in dose of immunosuppression with possible commencement of chemotherapy
Quality of evidence - Low Recommendation - Strong

Skin and Lip Cancers

Recommendations

- 5.23.4 We recommend screening KTR living in climates with high sun exposure or occupations that expose KTR to intense sunlight for skin and lip cancers
Quality of evidence - Low Recommendation - Strong
- 5.23.5 We recommend that KTR exposure to sunlight be minimized by using ultraviolet light blocking agents (sun screening agent) or wide brimmed hats
Quality of evidence - Low Recommendation - Strong
- 5.23.6 We suggest annual visit to a Dermatologist with experience in skin cancer care
Quality of evidence - Very Low Recommendation - Weak
- 5.23.7 We suggest appropriate follow-up for KTR with previous skin cancer by a Dermatologist
Quality of evidence - Very Low Recommendation - Weak

Reference

184. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. American Journal of Transplantation 2009; 9(Suppl 3): S1-S157.

Non-Skin Malignancy

Recommendations

- 5.23.8 A personalized plan for each KTR, this will take into cognizance history of tobacco use, family history of malignancy and other factors
Not graded
- 5.23.9 Follow local guidelines in screening for these cancers
• Women: breast, cervical and colon cancers
• Men: colon and prostate cancers
Not graded
- 5.23.10 Perform annual hepatic ultrasound scan and alpha feto-protein for KTR with liver cirrhosis
Not graded

Reference

185. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. American Journal of Transplantation 2009; 9(Suppl 3): S1-S157.

5.24 Special considerations**Desensitization protocols in Kidney transplantation.****Background**

Many potential candidates for Kidney transplantation in Nigeria are found during evaluation towards a possible kidney transplantation to have become sensitized. This is often because of previous multiple blood transfusions on account of poorly managed anaemia pretransplant, multiple pregnancies in women and increasingly these days previous failed transplants.

Evidence

Sensitization to HLAs is a significant obstacle to kidney transplantation and a risk factor for antibody-mediated rejection [27]. Recently developed desensitization protocols comprising plasmapheresis, IVIG, rituximab and bortezomib can decrease antibody (Ab) levels against allogeneic HLAs in some highly HLA-sensitized patients with end-stage renal disease, resulting in successful kidney transplantation [188-191].

Recommendations

- 5.24.1 We recommend that blood transfusions should be avoided as much as possible in patients with CKD to avoid the risk of sensitization.
Quality of Evidence - Moderate Recommendation - Strong
- 5.24.2 We recommend that a detailed history of all potentially sensitizing events should be taken during the evaluation period. Inclusive of numbers of blood transfusions, previous pregnancies whether carried to term or not and any previous transplants should be taken.
Quality of Evidence - Moderate Recommendation - Strong
- 5.24.3 We recommend that all potential recipients should be evaluated for HLA antibodies and for Donor specific antibodies during their evaluation.
Quality of Evidence - Moderate Recommendation - Strong
- 5.24.4 We recommend offering such sensitized patients access to antibody avoidance protocols such as access to a larger deceased donor pool and kidney exchange programs ahead of desensitization where these are available.
Quality of Evidence - Moderate Recommendation - Strong
- 5.24.5 We recommend the use of one or multiple options for desensitization when these are available and experience with their use and cost are acceptable.
Quality of Evidence - Moderate Recommendation - Strong

References

186. Glotz D, Antoine C, Julia P, et al. Desensitization and subsequent kidney transplantation of patients using intravenous immunoglobulins (IVIg). *Am J Transplant*. 2002;2:758-760
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188. Vieira CA, Agarwal A, Book BK, et al. Rituximab for reduction of anti-HLA antibodies in patients awaiting renal transplantation: Safety, pharmacodynamics, and pharmacokinetics. *Transplantation*. 2004;77:542-548
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5.25 Kidney Paired Exchange Programs

Background

Kidney transplantation remains the best treatment option for ESKD patients. However, significant shortage in donor kidney has reduced the number of ESKD patients that are able to access kidney transplantation [1]. The main contraindications to kidney transplantation include ABO incompatibility and presence of donor specific antibodies in recipients; more than 57% of otherwise compatible donor-recipient pairs have been disqualified because of these factors [192].

Supporting Evidence

Kidney Paired exchange (KPE) has been shown as an acceptable modality of increasing donor kidney availability, hence, increasing kidney transplant rate [193]. A ten-year retrospective study on KPE program in three centres evaluated 332 kidney transplants done over 12 years and found that the KPE program increased the donor pool for difficult to match pairs [194].

Recommendations

- 5.25.1 We recommend that transplant programs should offer this as an option for sensitized patients.
Quality of evidence - Moderate Recommendation - Strong
- 5.25.2 We recommend that this should be offered ahead of desensitization protocols if available pairs can be identified.
Quality of evidence - Moderate Recommendation - Strong
- 5.25.3 We recommend this as an option for ABO incompatible donor/recipient pairs ahead of desensitization protocols
Quality of evidence - Moderate Recommendation - Strong

References

190. Maggiore U, Oberbauer R, Pascual J, Viklicky O, Dudley C, Budde K, et al. Strategies to increase the donor pool and access to kidney transplantation: an international perspective. *Nephrol Dial Transplant* 2015;30(2):217 - 222
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192. Basu A, Prieto M, Kosberg C, Mai M, Khamash HA, Jadlowiec CC, et al. Ten years of kidney paired donation at Mayo Clinic: The benefits of incorporating ABO/HLA compatible pairs. *Transplantation* 2020; 104(6):1229 - 1238

5.26 Immunization and kidney transplantation

Background

There is general decline in the immunogenicity of vaccine among CKD patients and kidney transplant recipients.

Evidence

Existing guidelines have suggested that live-attenuated vaccines should be given 4 weeks before kidney transplantation to allow enough time to clear viraemia, while inactivated vaccines can be administered before or after kidney transplantation [195,196].

Recommendations

- 5.26.1 We recommend that vaccination series be completed before kidney transplantation.
Quality of Evidence - Low Recommendation - Strong

- 5.26.2 We recommend that kidney transplantation must be delayed for 4 weeks after the administration of live vaccine such as measles-mumps-rubella (MMR), live oral polio, varicella, yellow fever, live oral typhoid (Ty21), Bacillus Calmette-Guerin (BCG) and influenza vaccine.
Quality of Evidence - Low Recommendation - Strong
- 5.26.3 We recommend that sickle cell disease patient should receive pre-transplant pneumococcal, haemophilus and meningococcal vaccination.
Quality of Evidence - Low Recommendation - Strong

References

193. Chadban SJ, Ahn C, Axelrod DA, Foster BJ, Kasiske BL, Kher V, et al. KDIGO Clinical Practice Guideline on the evaluation and management of candidates for kidney transplantation. Transplantation. 2020; 104(4 Suppl1):S11 - S103
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5.27 Contraception and Pregnancy in the Kidney Transplant recipient.

Background

Most female transplant recipients become sexually active, and ovulation and menstruation usually resume shortly after transplant surgery [197,198]. To reduce the risks of unintended pregnancy and to address the unmet need for contraception, contraception must be incorporated into the protocols of female transplant recipients.

Evidence

Among female prospective kidney transplant patients of child bearing age group, it is important to ensure optimal contraception to avoid peri transplant pregnancy [199]. The American Society of Transplantation Consensus Conference report recommends that post-transplant patients be counselled on contraception using barrier and intrauterine devices although this may not be optimal because of the need for intact immune system for maximum efficacy [200,201]. The optimal time for pregnancy is two years post-transplant period or when the allograft function is stable evidenced by serum creatinine <1.5mg/dl, <500mg protein excretion in 24 hours, no concurrent use of teratogenic or fetotoxic medications and stable levels of immunosuppressives [200]. Hypertension is common among kidney transplant recipients and this is associated with increased risk of preeclampsia, intrauterine growth retardation and preterm delivery [202].

Complications are higher and outcomes are worse for post-transplant women with serum creatinine levels over 115 µmol/L. Up to 10-15% of women have a temporary or permanent decline in kidney function following an attempted pregnancy [203].

Recommendations

- 5.27.1 We recommend a pregnancy test should be done at the time of assessment of the female recipient for a kidney transplant.
Quality of Evidence - Low Recommendation - Strong
- 5.27.2 We recommend all female transplant recipients must be counselled on available contraception options prior to the transplant.
Quality of Evidence - Low Recommendation - Weak
- 5.27.3 We recommend female transplant recipients avoid pregnancies within the first-year post-transplant.
Quality of Evidence - Moderate Recommendation - Strong

- 5.27.4 We recommend that women with uncomplicated kidney transplants may initiate any method of contraception.
Quality of Evidence - Moderate Recommendation - Weak
- 5.27.5 We recommend that Women with complicated kidney transplants, defined as acute or chronic graft failure or rejection, may continue to use IUDs that are already in place.
Quality of Evidence - Low Recommendation - Weak
- 5.27.6 For complicated transplant patients, inserting a new IUD is not advisable.
Quality of Evidence - Low Recommendation - Weak
- 5.27.7 We suggest that intended pregnancies should be planned between the 2nd and 5th years post-transplant.
Quality of Evidence - Moderate Recommendation - Strong
- 5.27.8 We recommend that pregnancies be approved when planned only if the graft function remains optimal.
Quality of Evidence - Moderate Recommendation - Strong
- 5.27.9 We recommend that the patient must be counselled on the risks to the baby (prematurity, IUGR and IUFD) and mother (heightened risk of preeclampsia and graft failure).
Quality of Evidence - Low Recommendation - Weak
- 5.27.10 We recommend that prior to becoming pregnant the immunosuppression must be changed from Mycophenolate regimen as this has been proven to be teratogenic.
Quality of Evidence - High Recommendation - Strong
- 5.27.11 We recommend that sexually active male transplant recipients exposed to Mycophenolate should use condoms during treatment and for 90 days after discontinuation.
Quality of Evidence - Low Recommendation - Strong
- 5.27.12 We recommend that Female partners of male transplant recipients treated with mycophenolate mofetil or mycophenolic acid should use highly effective contraception during treatment and for 90 days after the last dose.
Quality of Evidence - Low Recommendation - Strong

References

195. Josephson MA, McKay DB. Women and Transplantation: fertility, sexuality, pregnancy, contraception. *Adv. Chronic Kidney Dis.* 2013;20(5):433-440. doi:10.1053/jackd.2013.06.005
196. Watnick S, Rueda J. Reproduction and contraception after kidney transplantation. *Curr Opin Obstet Gynecol.* 2008;20(3):308-312.
197. Kenny LC, Baker PN, Venning M, Parrott N. Successful renal transplant during the first trimester of pregnancy. *Transpl Int.* 2007;20:390 - 391
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200. Sibanda N, Briggs JD, Davison JM, Johnson RJ, Rudge CJ. Pregnancy after organ transplantation. A report from the UK Transplant Pregnancy Registry. *Transplantation* 2007;83(10):1301 - 1307
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5.28 Kidney Transplants in the Elderly Background

Age on its own is not a barrier to kidney transplants and many patients have had successful kidney transplants even in their seventies. There are however several considerations that are peculiar to patients within this age bracket that must be met in order to ensure an uneventful transplant.

Supporting Evidence

Several studies have consistently revealed that elderly patients following a transplant do consistently better than matched controls that remain on dialysis offering better survival and quality of life [199,200].

Comorbidity burden, disability, frailty, cardiovascular disease, risk of infection, and malignancy are all associated with poor outcomes in elderly transplantation patients and should be carefully evaluated during the pre-transplantation screening process [200].

Recommendations

5.28.1 We suggest that age on its own should not be seen as a barrier to consideration for a successful transplant.

Not graded

5.28.2 We suggest that patients within the age range of 65-75 years may still be considered for a kidney transplant if there are no mitigating contraindicating comorbidities.

Not graded

5.28.3 We recommend a "Frailty" test be performed prior to consideration for a kidney transplant in the elderly.

Not graded

5.28.4 We recommend extensive evaluation to exclude common malignancies in the elderly, including but not limited to; Prostate in men, cervical cancer and breast in women, colon, Multiple myeloma, pancreas. Liver and gallbladder cancers in both and lung cancer in smokers.

Not graded

5.28.5 We recommend all elderly candidate transplant recipients must have extensive cardiovascular assessment inclusive of stress echocardiography and plus or minus a coronary angiography if preliminary tests are suggestive of ischaemic heart disease. Strong Recommendation Good evidence

Not graded

5.28.6 We recommend a neurology/psychiatric assessment for the presence and severity of dementia prior to consideration for a kidney transplant. Strong Recommendation.

Not graded

References

202. Bunnapradist S, Danovitch GM. Kidney Transplants for the Elderly: Hope or Hype? *Clin J Am Soc Nephrol.* 2010;5(11):1910-1911
203. Rao PS, Merion RM, Ashby VB, Port FK, Wolfe RA, Kayler LK; Renal transplantation in elderly patients older than 70 years of age: Results from the Scientific Registry of Transplant Recipients. *Transplantation* 2007;83:1069-1074.

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