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Precipitants and outcomes of acute exacerbation of chronic kidney disease: A single centre experience.

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Abstract

Background
Chronic kidney Disease (CKD) is a disease of public health importance associated with rising prevalence, exorbitant cost of treatment and high morbidity and mortality. Many patients with CKD are often admitted into the ward with acute deterioration of kidney function from various precipitants. We do not know the pattern of the causes of these deteriorations and its effect on treatment outcomes.
Methods
This is a retrospective study of patients with CKD admitted at the University College Hospital Ibadan between January 2008 and December 2012. The hospital records of all the patients were reviewed to obtain information on demographics, the precipitants of acute deterioration, treatments and outcomes.
Result
A total of 1113 patients with diagnosis of CKD were admitted with a yearly average of 222.6. Out of the 945 with complete data, 882 (93.3%) had acute deterioration of CKD while 63(6.7%) had ESRD. The major precipitants of acute exacerbation of CKD identified were sepsis 426(48.3%) and uncontrolled hypertension 138(15.6%) while no identifiable precipitant in 155(17.6%).The common foci of sepsis were the urinary tract 205(42.7%) and respiratory tract 64(15%). Following treatments 433(49.1%) had partial recovery, 243(27.5%) progressed to ESRD while 206(23.4%) died. Age>60years OR 1.78(1.09–7.35) p<0.02), sepsis OR 1.95(1.45–8.65), p<0.02 and co-morbidity (OR 1.3(1. 16–4.34), p<0.04 were associated with progression to ESRD or death.
Conclusion
Sepsis and uncontrolled hypertension were the common precipitants of acute deterioration of CKD in our patients. In individuals with sepsis as precipitant, urinary tract is the commonest focus of infection. Increasing age, sepsis and co-morbidities were factors independently poor outcomes following episode of acute deterioration of CKD.
Key words: Chronic kidney disease, exacerbation, deterioration, precipitants, Nigeria.

Background

Chronic kidney disease is one of the leading causes of premature morbidity and mortality worldwide, requiring the attention of the global community.[1-3] The burden of the disease is enormous particularly in sub – Saharan Africa (SSA) where the population affected are young people who formed most of the work force of such countries.[4] Adding to this gloomy picture is the fact that a lot of cases are undiagnosed and when they are, it is always at a stage where the disease process can no longer be halted.[5.6] Partly responsible for this are non-functional primary healthcare facilities, inadequate staff to man such facilities and the health seeking behavior of the population. Also, the use of alternative medicine, self-medication and spirituality are common practices among the population.[4,7-9]

Patients with CKD are often admitted for acute deterioration of their kidney function. These episodes of Acute kidney injury (AKI) leads to rapid progression of the kidney disease. Studies have also shown that close to 50% of patients with CKD who suffered episodes of AKI will progress to ESRD.[9,10] Individuals with early stages of CKD are therefore routinely educated on prevention of episodes of AKI in order to prevent and retard CKD progression.

Despite these measures some patients with CKD are admitted regularly for acute deterioration of their kidney function following episodes of AKI and these episodes of AKI lead to progression of the kidney disease. Identifying and eliminating the precipitants of acute deterioration of kidney function among patients with CKD have the potential of preserving the kidney function and retarding its progression. Perhaps adequate knowledge of the precipitants will provide template for secondary prevention among this group of patients. This study aimed to identify common precipitants of acute deterioration of kidney function and its impacts on treatment outcomes, among patients with CKD who were admitted at the University College Hospital, Ibadan, Nigeria.

Methods

This is a retrospective study of patients with CKD that were admitted at the University College Hospital Ibadan with acute deterioration of renal function between January 2008 and December 2012. The hospital records of all the patients with CKD admitted were reviewed, information obtained includes demographics, aetiology of CKD, the precipitants of acute deterioration, treatment offered and outcomes. For the purpose of this study acute deterioration was defined as rise in serum creatinine > 1.5folds above the baseline value during last clinic visit or the value obtained within the last 3 months, prior to admission for individuals with baseline serum creatinine and the need for dialysis in those without baseline serum creatinine. Interventions offered to the patients were conservative therapy which involved treatment of identified precipitants and those who had indications were also offered haemodialysis in addition. The outcome variables include partial recovery of kidney function, end stage renal disease (ESRD) and death. As there is no consensus for the definition of renal recovery yet,[11,12] therefore, for the purpose of this study complete recovery was defined as return of serum creatinine to baseline at discharge or within 6 weeks of episode of AKI. Partial recovery of kidney function was defined as reduction of serum creatinine by 25% or more of the baseline at discharge or within 6 weeks, and for those without baseline serum creatinine, it was defined as absence of the need for maintenance dialysis at discharge or within 6 weeks of the AKI episode. No recovery (progression to ESRD) was defined the need for maintenance dialysis. The death of patients while on admission or within 6 weeks of diagnosis of acute deterioration of kidney function were documented as secondary outcomes.

Data was entered into the Microsoft excel sheet and analyzed using statistical package for social sciences (SPSS) version 20. Continuous variables were expressed as means with standard deviation while categorical variables were expressed as proportions, percentages and ratio. Association between the categorical variables was conducted using chi square. While association between continuous variables was determined using student t –test to compare their means. Multiple logistic regression analysis was used to determine factors that were independently associated with outcomes of acute exacerbation of CKD. Statistical significance was taken when p value is less than 0.05 in all situations.

Results

A total of 1113 patients with diagnosis of CKD were admitted and managed over the period under review. The yearly average was 222.6 and there was a steady rise in cases of CKD admissions over the 5years (January 2008 – December 2012). (see table 1). Only 945 subjects had complete data and were included in the subsequent analysis. (see figure 1) Four

hundred and ninety (51.8%) were males while 455 (47.2%) were females. The mean age of the patients was 43.7±16.1 years. The mean serum creatinine and urea were 6.25±0.8mg/dl and 149.6±14.5mg/dl respectively. Common aetiologies of CKD among the patients included chronic glomerulonephritis (CGN) 276 (29.3%), hypertension 246 (26.1%), diabetes nephropathy 83 (8.8%), human immunodeficiency virus associated nephropathy (HIV) related nephropathy 74 (7.8%), obstructive uropathy 48 (5.1%) and aetiology was unknown in 156 (16.5%) patients. Others causes of CKD identified among the patients include sickle cell nephropathy, lupus nephritis, toxic nephropathy, autosomal dominant polycystic kidney disease (ADPKD), chronic pyelonephritis, analgesic nephropathy, renal tuberculosis, gouty nephropathy and renal artery stenosis, and there were 38(4.0%) in this group. (see Table 1)

Among the 945 patients with CKD included in the analysis, 882 (93.3%) had acute deterioration of an existing CKD while 63

disease (ESRD) and were admitted for various uraemic symptoms. In individuals admitted with acute deterioration of CKD sepsis was the identified precipitant in 426 (48.3%) patients, others were uncontrolled hypertension 138 (15.6%), heart failure 54 (6.1%), isolated urinary tract infection (UTI) 54 (6.1%), herbal consumption 45 (5.1%), nephrotoxic drugs 8 (0.9%), hepatorenal syndrome 2 (0.2%), while no precipitant was identified in 155 (17.6%) subjects. (see figure 2) Among patients with sepsis as precipitant, the common foci of infection were urinary tract 205 (42.7%), respiratory tract 57 (11.9%) and gastrointestinal tract 35 (7.3%) while focus was unidentified in 183 (38.1%) patients. Haemodialysis was required (had indications for dialysis) in 554 (62.8%) of the patients with acute deterioration of CKD, among which only 427 (48.4%) could afford the procedure. While those who had no indication for haemodialysis 327(37.2%) or required but could not afford haemodialysis 127 (14.4%) were managed conservatively. tract 57 (11.9%) and gastrointestinal tract 35 (7.3%) while focus was unidentified in 183 (38.1%) patients. Haemodialysis was required (had indications for dialysis) in 554 (62.8%) of the patients with acute deterioration of CKD, among which only 427 (48.4%) could afford the procedure. While those who had no indication for haemodialysis 327(37.2%) or required but could not afford haemodialysis 127 (14.4%) were managed conservatively.

Table 1: Demographic and clinical characteristics of patients admitted with chronic kidney disease

Parameters	Mean ± SD/ Percentages N = 945
Mean Age (years)	44.2±16.6
Gender	
Female	490 (51.8%)
Male	455 (48.2%)
Number of patients admitted per year	
2008	141 (14.9%)
2009	154 (16.3%)
2010	197 (20.8%)
2011	218 (23.1%)
2012	235 (24.9%)
Biochemical parameters	
Mean serum creatinine (mg/dl)	6.48±0.8
Mean serum urea (mg/dl)	147.2±15.6
Aetiologies of CKD	
Chronic glomerulonephritis	276 (29.3%)
Hypertension	246 (26.1%)
Diabetes mellitus	83 (8.8%)
HIV related nephropathy	75 (8.0%)
Obstructive uropathy	39 (4.1%)
Sickle cell nephropathy	9 (1.0%)
Lupus nephritis	8 (0.9%)
Toxic nephropathy	8 (0.9%)
ADPKD	8 (0.9%)
Chronic pyelonephritis	5 (0.5%)
Analgesic nephropathy	5 (0.5%)
Renal tuberculosis	2 (0.2%)
Gout nephropathy	1 (0.1%)
Renal artery stenosis	1 (0.1%)
CKD of undetermined aetiology	179 (18.9%)
Mode of presentation	
Acute exacerbation of CKD	884 (93.5%)
Established ESRD with ureamia	61 (6.5%)
Outcome	
Partial recovery	433 (49.1%)
Progression to ESRD	243 (27.5%)
Death	206 (23.4%)

ADPKD – Autosomal dominant polycystic kidney disease, CKD – Chronic kidney disease, ESRD – End stage renal failure, HIVAN – Human immunodeficiency virus.

Table 2: Factors associated with outcomes of acute exacerbation of chronic kidney disease

Parameters	Partial recovery N = 433	Progression to ESRD N = 243	Death N = 206	P- value
Mean Age (years)	42.6±14.2	44.9±15.8	46.2±17.5	0.08
Age 60 years and above	157 (36.3%)	98 (40.3%)	120 (58.1%)	0.01*
Female Gender	196 (45.3%)	121 (49.6%)	99 (48.0%)	0.51
Uncontrolled hypertension	49 (11.3%)	36 (14.9%)	30 (14.6%)	0.33
Sepsis	107 (24.7%)	175 (72.1%)	172 (83.5%)	0.01*
Diabetes mellitus	36 (8.3%)	26 (10.8%)	19 (9.3%)	0.56
HIV	30 (7.0%)	23 (9.4%)	22 (10.6%)	0.23
Mean serum creatinine (mg/dl)	5.8±0.6	6.6±0.8	7.1±0.8	0.16
Mean serum urea (mg/dl)	140.0±31.1	151.1±16.6	149.3±15.7	0.08
Presence of co-morbidity	110 (25.4%)	92 (37.8%)	137 (66.3%)	0.03*
Required dialysis	209 (48.3%)	208 (85.6%)	156(75.6%)	0.01*
Had haemodialysis	181 (41.8%)	151 (62.1%)	95 (45.9%)	0.01*

ESRD- End Stage Renal Disease, HIV – Human immunodeficiency virus.

Table 3: Crude and adjusted Odd Ratio of factors associated with progression to ESRD or death.

Factors	Crude Odd Ratio (95% CI)	Adjusted Odd Ratio (95% CI)
Age > 60 years	1.93 (1.12 – 4.23)	1.78 (1.09 – 7.35)
Sepsis	2.4 (1.78 – 8.65)	1.95 (1.45 – 8.65)
Co-morbidity	1.05 (1. 01 – 6.86)	1.34 (1. 16 – 4.34)
Required dialysis	1.25 (1.11 – 7.44)	1.08 (0.98 – 1.86)
Had dialysis	1.69 (1.33 – 3.18)	0.69 (0.46 – 3.18)

(6.7%) had established end stage renal disease (ESRD) and were admitted for various uraemic symptoms. In individuals admitted with acute deterioration of CKD sepsis was the identified precipitant in 426 (48.3%) patients, others were uncontrolled hypertension 138 (15.6%), heart failure 54 (6.1%), isolated urinary tract infection (UTI) 54 (6.1%), herbal consumption 45 (5.1%), nephrotoxic drugs 8 (0.9%), hepatorenal syndrome 2 (0.2%), while no precipitant was identified in 155 (17.6%) subjects. (see figure 2) Among patients with sepsis as precipitant, the common foci of infection were urinary tract 205 (42.7%), respiratory Out of the 882 patients admitted for acute deterioration of CKD following treatments of precipitants, 433 (49.1%) had partial recovery of kidney function and were discharged to the renal clinic for follow up, 243 (27.5%) progressed to ESRD while 206 (23.4%) died while on admission. Factors independently associated with progression to ESRD or death among the patients include age greater than 60 years (OR 1.78, 1.09 – 7.35, $p < 0.02$), sepsis (OR 1.95,

1.45 – 8.65, p < 0.02) and the presence of co-morbidity (OR 1.34, CI – 1. 16 – 4.34, p – 0.04). (see table 3)

Discussion

Our study showed that acute deterioration of chronic kidney disease is a common indication for nephrology admissions in our hospital. And the leading precipitants of this acute deterioration among our patients were sepsis, uncontrolled hypertension, heart failure and urinary tract infection. The high rate of infections among this cohort of patients accounted for most of the episodes of acute deterioration of the kidney function, requiring admission and dialysis. We observed that episodes of acute kidney injury increased the likelihood of progression to ESRD or death and this was similar to findings from previous studies, where it has been demonstrated that acute deterioration of kidney function leads to increased likelihood of hospitalization, progression to ESRD and increased morbidity and mortality.[10-13] Sepsis as the commonest risk factor for acute deterioration of kidney function in this cohort is not surprising, as CKD causes immune suppression, couple with the fact that infectious diseases are more prevalent in the sub-Saharan African region.[14,15] Improved personal hygiene and adequate immunization of patients with CKD against common infections in the tropical environments will go a long way in reducing the likelihood of acute deterioration of CKD and prevent the rapid progression among patients with early stages of CKD. In addition, adequate time should be spent on patients' education on avoidance of precipitants of acute deterioration of kidney and its prevention among patients with CKD, during medical consultations as recommended by several CKD guidelines.[16-18] Uncontrolled hypertension was also identified as precipitant in close to one fifth of the patients, hypertension does not only increased the progression to ESRD but also increases the cardiovascular morbidity and mortality among CKD patients.[19] This buttresses the need to take active steps towards ensuring adequate control of blood pressure control among CKD patients in our busy clinics. In another one fifth of the patients, no precipitant was identified and this posed a challenge in their management as elimination of precipitant is vital to recovery of the kidney function, perhaps most of the patients could not recall some of the agents they might have taken prior to the episode of acute deterioration, as herbal use is a common practice among the general population.[20] The outcomes of episodes of acute deterioration of CKD among our patients were similar to previous reports, kidney function recovery observed in 49.1% of our patients was similar to 51% report by Hsu et al.[9] However the proportion of patients with progression to ESRD in their study was higher 49% compared to 27.5% reported in our study.[9] The difference could be explained by high mortality observed among our cohort 23.4% compared to 4.6% reported in their study. This disparity may be a reflection of standard and affordability of healthcare in Nigeria and the United States. Most patients pay out of pockets for kidney care in Nigeria unlike in the United States where there is adequate insurance healthcare coverage for most patients.[4,9] Increasing age and presence of co-morbidity were among the factors that were independently associated with poor outcomes (progression to ESRD or death). Elderly CKD patients usually present with multiple co-morbidities and have depressed immune status that put them at increased risk of acute deterioration of CKD and rapid progression to ESRD and death[19], it was therefore not surprising that increasing age was associated with poor outcomes. This group of patients will require multidisciplinary approach, where the various co-morbidities will be properly managed in addition to the kidney disease.[21] This study has some limitations which include the fact that being a retrospective study some data such as total number of dialysis

sessions per patient and specific cause of death could not be retrieved in all patients. Also, some of the patients with diagnosis of CKD were presenting for the first time and had no previous baseline serum creatinine, in such patients acute deterioration was defined as the need for dialysis. It was also difficult to appropriately classify patients with full recovery, as some patients had no baseline creatinine and therefore all patients with evidence of recovery were regarded as partial recovery.

Conclusions

The study showed that sepsis was the precipitant of acute deterioration of chronic kidney disease in majority of the patients admitted in this study, contributing to high proportion of patients with non recovery of kidney function and mortality. Factors independently associated with poor treatment outcomes include older age, sepsis and presence of co-morbidity. Strategies towards prevention and early detection and treatment of infections among individuals with CKD should be included in the protocol for their management.

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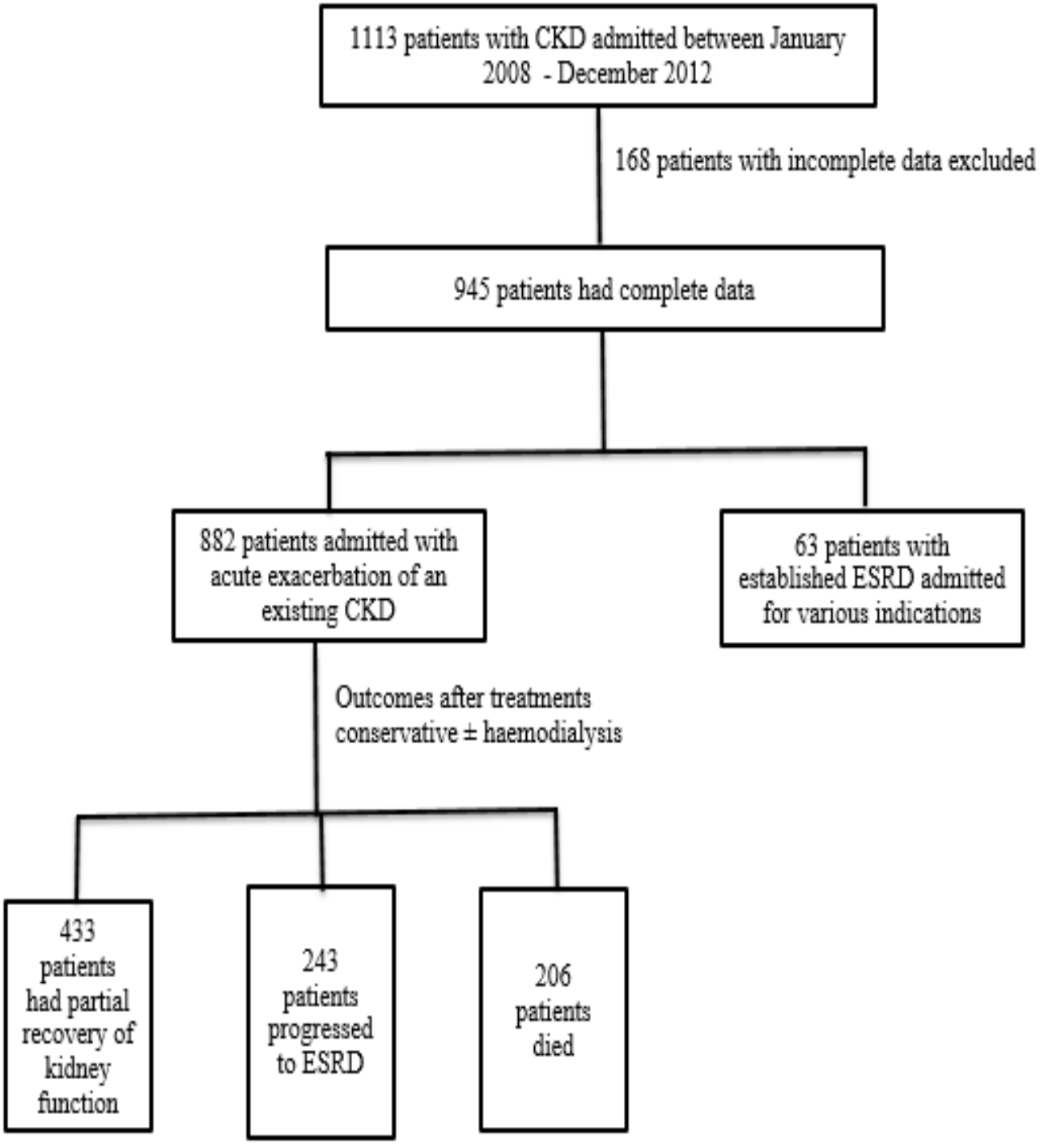

Figure 1: The flow chart of patients with CKD included in the data analysis and their treatment outcomes.

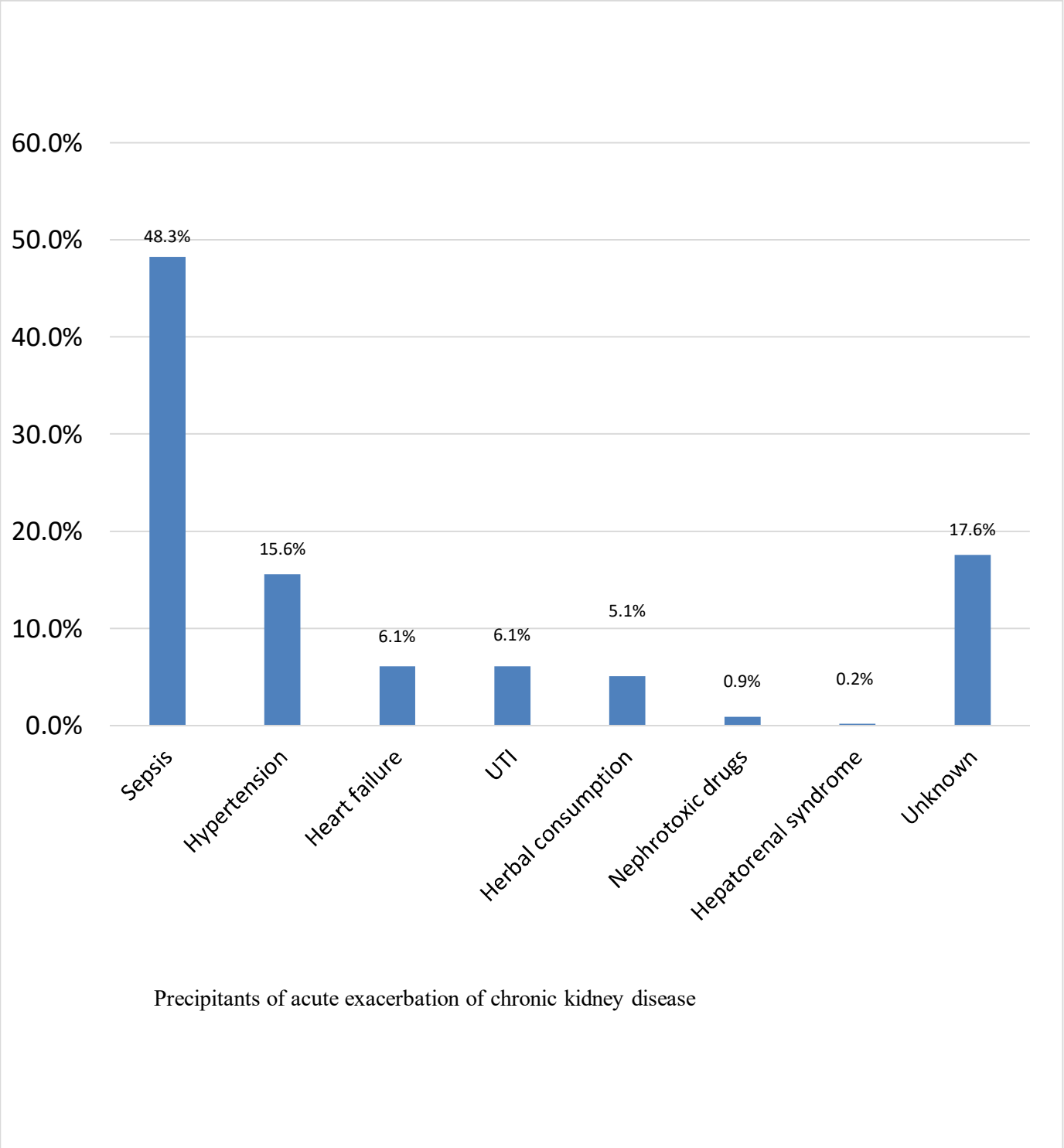

Figure 2: Frequency of precipitants of acute deterioration of chronic kidney disease among the patients.