AETIOLOGY AND OUTCOME OF ACUTE KIDNEY INJURY IN TYPE 2 DIABETES PATIENTS

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ABSTRACT

BACKGROUND

Diabetes is the most important contributor to the growing burden of end stage renal disease, and patients with diabetes are also at a greater risk of requiring hospitalizations and experiencing acute kidney injury. Because of the morbidity and mortality associated with acute kidney injury, it is important for primary care physicians to identify patients who are at a high risk of developing this type of injury and to implement preventive strategies. Though many studies have evaluated the development or progression of chronic kidney disease, only few studies have assessed the risk factors and outcomes of AKI in Type 2 diabetics. Hence, we conducted this study. Early recognition and appropriate management of acute kidney injury in hospitalized patients is one of the ways to curb the growing burden of end stage kidney disease in diabetics.

MATERIALS AND METHODS

We conducted a Cohort study to analyze the causes, recovery of renal function and mortality of AKI in 100 adult diabetic patients admitted in ICU and wards under the Dept. of Medicine and Nephrology in relation to age, sex, mean FBS, PPBS, electrolytes, blood urea and serum creatinine levels.

RESULTS

AKI was predominantly encountered in older males. Most common causes of acute renal failure were found to be infection and urinary tract obstruction. NSAID was most common cause of drug induced renal failure. 69% had a good outcome of which 10% had partial recovery and 59% had full recovery. 31% had poor outcome of which 10% went in for maintenance hemodialysis and 21% expired during the period of study.

CONCLUSION

Most common causes of renal failure in the study were found to be infection and urinary tract obstruction. Acute renal failure recovered in 69%.

KEY WORDS

Acute Kidney Injury; Type 2 Diabetes; Infection.

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BACKGROUND

The incidence of diabetes mellitus in human population has reached epidemic proportions world-wide. It is estimated that ten years down the line, one in every five diabetics will be an Indian.(1) Diabetes mellitus is the single largest contributor to the growing prevalence of chronic kidney disease.(2) Progressive decline in renal function has been well described in patients with Type 2 diabetes mellitus, but few studies have assessed the risk of acute kidney injury in patients with Type 2 diabetes. So this study is planned to find out the aetiology and outcome of acute kidney injury in patients with Type 2 diabetes from a tertiary referral hospital in Kerala.

Acute kidney injury (AKI), formerly called acute renal failure (ARF), is commonly defined as an abrupt decline in renal function resulting in a reversible acute increase in nitrogenous waste products normally cleared by the kidneys.

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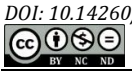

Over the past few years, international guideline groups have attempted to establish consistent definitions and staging systems for AKI. Initially the RIFLE (Risk, Injury, Failure, Loss, End stage kidney disease) system was set up in 2004.(4) This was modified by the AKIN (Acute Kidney Injury Network) and further developed in 2012 by KDIGO (Kidney Disease: Improving Global Outcomes).(5,6,7) They work on levels of creatinine rise-

1. Increase in serum creatinine by > 0.3 mg/dl within 48 hours.
2. Increase in creatinine to >1.5 times baseline, which is known/ presumed to have occurred within the past 7 days.
3. A drop in urine output to 0.5 ml/kg/hour for 6 hours in adults.

The stage of AKI affects both management recommendations and prognosis, hence the importance of defining consistent stages. KDIGO defines stage 1, 2 and 3 through increasing rises in creatinine levels and drop in urinary output-

1. Increase in serum creatinine 1.5–1.9 times baseline or > 0.3 mg/dl increase.
2. Increase in serum creatinine 2.0–2.9 times baseline.
3. Increase in serum creatinine 3.0 times baseline or Increase in serum creatinine to > 4 mg/dl.

Aims and Objectives

1. To study the aetiology of acute kidney injury in patients with type 2 diabetes.
2. To study the outcome of acute kidney injury in type 2 diabetic patients.

MATERIALS AND METHODS

The present study was undertaken to identify the causes and to study the outcome of acute kidney injury in Type 2 diabetic patients.

Study Design

Cohort study.

Study Setting

ICU and wards under the Dept. of Medicine and Nephrology, Govt. Medical College Hospital, Kozhikode

Study Population

Type 2 diabetic patients with acute kidney injury irrespective of age and gender.

Inclusion Criteria

Type 2 diabetic patients 30 years or above, irrespective of gender, diagnosed to have acute kidney injury using KDIGO criteria, admitted to ICU or wards under the Dept of Medicine and Nephrology, Govt. Medical College, Kozhikode.

Exclusion criteria

Patients with preexisting renal disease and those who received renal transplantation.

Study Duration

1 year.

Data Collection

Type 2 diabetic patients admitted in the ICU and wards under Medicine and Nephrology department, Govt. Medical College, Kozhikode were evaluated in detail after taking prior consent. Evaluation includes detailed history taking and physical examination. Acute kidney injury will be assessed on the basis of their serum creatinine and/or urine output fulfilling the KDIGO criteria.

Outcome is assessed by

1. Fully recovered – Creatinine has returned to baseline value.
2. Partial recovery – Less than 50% improvement in creatinine values.
3. Dialysis dependent.
4. Mortality - defined as patients expiring during the hospital stay.

Statistical Analysis

Results were presented as frequency and percentages for Categorical variables and mean+/- SD for continuous variables. Statistical calculations were done using Chi-square tests for categorical data and on independent t-test. For continuous data. $P<0.05$ was considered significant. The calculations were carried out using SPSS (Statistical Package for the Social Sciences).

RESULTS

The study was conducted in a total of 100 diabetic patients who developed acute kidney injury. There were 64 males and 36 females. The aetiology and outcome of acute kidney injury in the above patients were found out. Blood urea, serum creatinine, serum electrolytes, fasting and post-prandial blood sugar, WBC count, platelet count and haemoglobin were included as the baseline parameters.

1. Percentage distribution of age of patients included in the study.

Age group	Percent
<50	21
50 – 59	37
60 – 69	30
>=70	12

Table 1

Most of the patients were in the age group of 50-59 years with 37% incidence

2. Percentage distribution of various drugs leading to the development of acute kidney injury in diabetic patients.

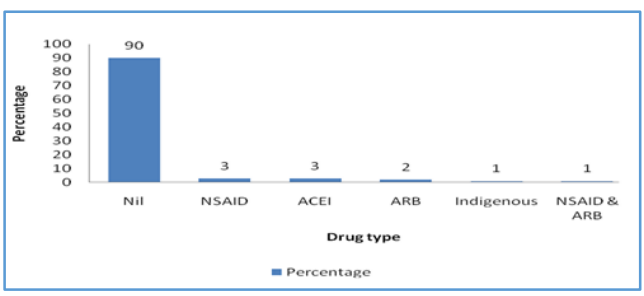

Figure 1

Out of the 10 % of drug induced AKI patients, non-steroidal anti-inflammatory drugs and angiotensin converting enzyme inhibitors and angiotensin receptor blockers were found to cause AKI.

3. Percentage distribution of accelerated hypertension leading to the development of acute kidney injury in diabetic patients.

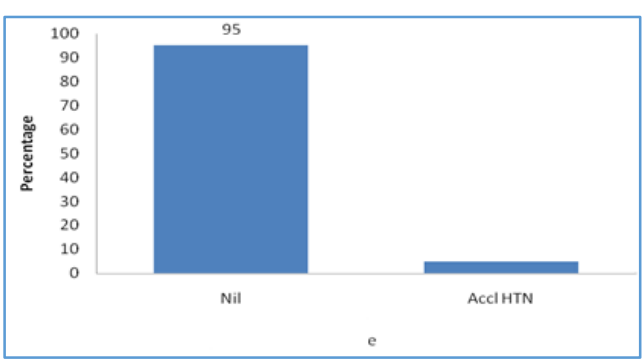

Figure 2

5% of AKI cases in diabetics were due to accelerated hypertension

4. Percentage distribution of CAD/LVD leading to the development of acute kidney injury in diabetic patients.

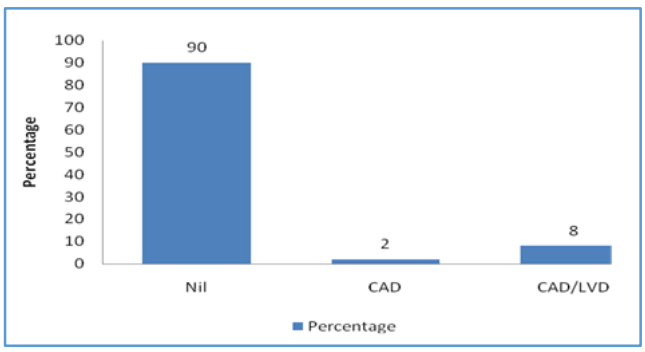

Figure 3

The chance for developing acute kidney injury is increased when CAD is associated with LV dysfunction.

5. Percentage distribution of various infections leading to the development of acute kidney injury in diabetic patients.

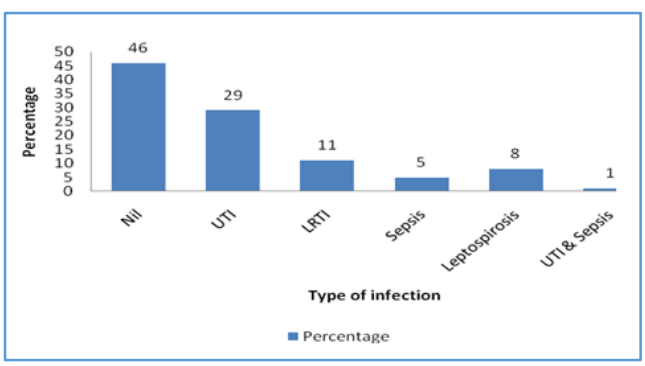

Figure 4

Infections accounted for 54% of AKI in diabetics. Among this, urinary tract infection was found to be the most common cause of AKI in diabetics.

6. Percentage distribution of various forms of obstruction leading to the development of acute kidney injury in diabetic patients

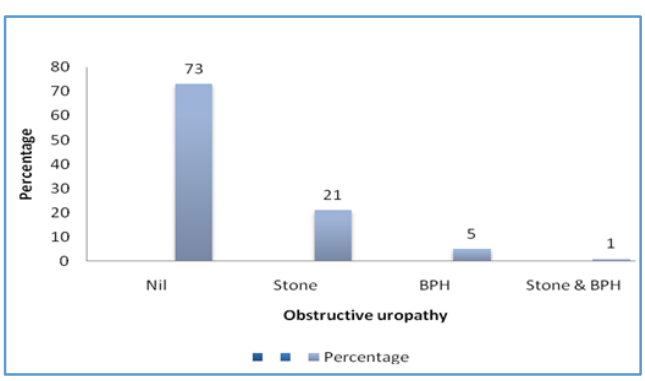

Figure 5

Obstructive uropathy led to the development of AKI in 27% of diabetic patients, of which 21% was due to renal stone.

7. Percentage distribution of aetiology of AKI in diabetic patients

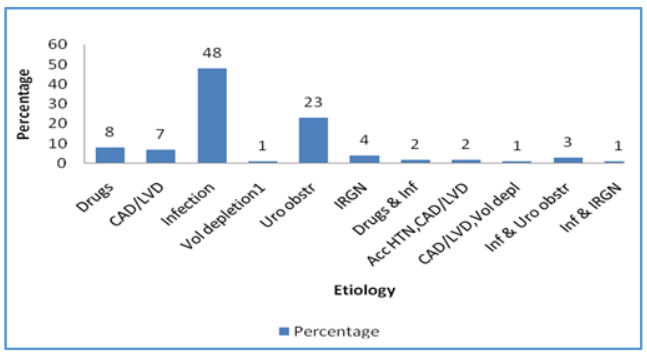

Figure 6

Infections were found to be the most common cause for the development of AKI in diabetic patients. Next was urological obstruction followed by drugs and CAD/LVD.

8. Percentage distribution of outcome of AKI in Type 2 diabetes

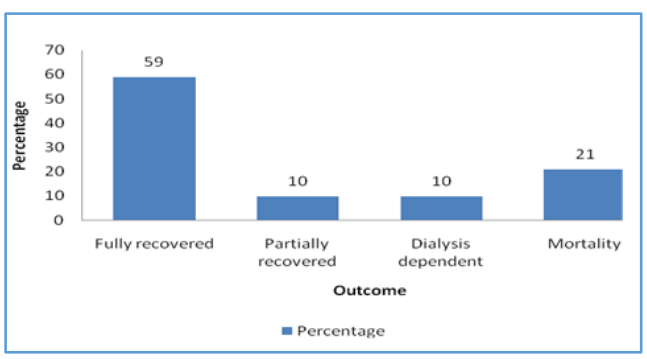

Figure 7

69% of the patients in the study had good outome, of which 59% had full recovery and 10% had partial recovery. 31% had poor outcome of which mortality was found to be 21% and 10% was put on maintenance hemodialysis (Dialysis dependent).

9. Percentage distribution of mortality with age in diabetic AKI patients

Age Group	Mortality		P value
	Yes	No	0.001
< 50	3 (14.35 %)	18 (85.7 %)	
50 – 59	2 (5.4%)	35 (94.6%)	
60 – 69	8 (26.7%)	22 (73.3%)	
>70	7 (58.3%)	5 (41.7%)	

Table 2

Mortality was found to be increasing with age.

10. Mean age of mortality among diabetic AKI patients

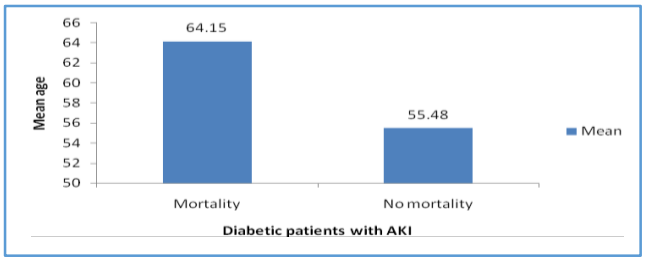

Figure 8

11. Percentage distribution of mortality among male and female diabetic AKI patients

Sex	Mortality		P value
	Yes	No	
Male	16 (25%)	48 (75%)	0.096
Female	4 (11.1%)	32 (88.9%)	
Table 3			

Mortality was found to be more among males with diabetic AKI.

12. Percentage distribution of mortality with various infections in diabetic AKI patients

Infection	Mortality		P value
	Yes	No	
No infection	3 (6.5%)	43 (93.5%)	< 0.001
UTI	7 (24.1%)	22 (75.9%)	
LRTI	0 (.0%)	11 (100%)	
Sepsis	2 (40%)	3 (60%)	
Leptospirosis	7 (87.5%)	1 (12.5%)	
UTI & Sepsis	1 (100%)	0 (.0%)	
Table 4			

Leptospirosis and a combination of sepsis & UTI increased the mortality in diabetic AKI.

13. Percentage distribution of mortality with obstruction in diabetic AKI patients

Obstructive Uropathy	Mortality		P value
	Yes	**No**	
No obstruction	13 (17.8%)	60 (82.2%)	0.591
Stone	5 (23.8%)	16 (76.2%)	
BPH	2 (40%)	3 (60%)	
Stone & BPH	0 (.0%)	1 (100%)	
Table 5			

Among obstructive uropathy, those with BPH had high mortality.

14. Percentage distribution of mortality with aetiology in diabetic AKI patients

Aetiology	Mortality		P value
	Yes	**No**	
Drugs	0 (.0%)	8 (100%)	0.001
CAD/LVD	0 (.0%)	7 (100%)	
Infection	11 (22.9%)	37 (77.1%)	
Volume depletion	0 (.0%)	1 (100%)	
Urological obstruction	3 (13%)	20 (87%)	
IRGN	0 (.0%)	4 (100%)	
Drugs & infection	2 (100%)	0 (.0%)	
Accl HTN & CAD/LVD	0 (.0%)	2(100%)	
CAD/LVD & volume depletion	0 (.0%)	1 (100%)	
Infection & Urological obstruction	3 (100%)	0 (.0%)	
Infection & IRGN	1 (100%)	0 (.0%)	
Table 6			

Mortality in diabetic AKI patients was found to be increased when infections were associated with urological obstruction, drugs or IRGN.

15. Relation of different lab parameters with mortality

	Mortality	No Mortality	P value
Total WBC Count Mean	15060	10985.63	<0.001
SD	3963.969	3690.024	
Platelet Count Mean	1.5955	2.3514	<0.001
SD	0.79759	0.81962	
FBS Mean	220.8	165.29	<0.001
SD	40.963	30.123	
PPBS Mean	390.4	279.09	<0.001
SD	61.711	55.132	
Serum Na Mean	126.4	132.53	<0.001
SD	4.849	4.749	

	Mortality	No mortality	P value
Serum K Mean	5.4	5.003	0.793
SD	0.9712	0.6704	
Blood Urea Base line	88.6316	74.5000	0.028
Admission	196.7000	134.1375	0.000
Discharge	235.0500	94.4000	0.000
Serum Creatinine Baseline	4.5632	3.4513	0.015
Admission	10.8200	11.1338	0.935
Discharge	13.8526	5.8363	0.000
Table 7			

DISCUSSION

Most of the AKI patients in the study were in the age group of 50-59 years with 37% incidence and 60-69 years with 30% incidence (Table 1). Similar age group of 51-60 years with 34.3% incidence was noted in a prospective study of ARF in diabetes mellitus by Vakrani et al.[1] The present study highlights the potential risk of AKI in elderly patients especially above the age of 60 years. The development of AKI in this population could be explained partly as the decline in renal function with age.[6] The increase in mortality with age was found to be statistically significant (p value 0.001).

Infections were found to be the most common cause of AKI in the study. It accounted for 54 % of cases, among which UTI was found in more than half of the cases. In a prospective study by Khan and Ahmed, [7] the most common focus of infection was found to be urinary tract (71.2%).

Sepsis was found to be the most common cause for AKI in several studies.[2,8-11] The lower proportion of sepsis in this study might be attributed to the fact, unlike the above studies, the majority of patients selected for were not critically ill patients from ICU, but from medicine and nephrology wards.

Urinary tract obstruction was the second most common cause in this study that accounted for 23%. Vakrani t al found sepsis (52.9%) and urinary tract obstruction (50%) as the leading causes for renal failure in diabetics.[1] Jha *et al*., and Prakash *et al*., which evaluated AKI had shown that nephrotoxic drugs were the most common cause of AKI.[12, 13]

In the present study, drug induced AKI accounted for only 10 % of the cases, which is lower than the above studies. Similarly, drug induced AKI accounted for only 5.6% of the cases in a study by Eswarappa et al.[2] This might suggest that increasing knowledge of precautions regarding nephrotoxic drugs have helped to reduce the incidence of drug induced AKI. In the present study, NSAIDs were noted to be most common cause of drug induced renal failure with either as unifactorial, or together with other contributory factors as multifactorial (Figure 1). It constituted around 40% of cases of drug induced renal disease which was followed by ACEI and ARBs.

NSAIDs reversibly inhibit the production of renal prostaglandins via their inhibition of COX-1 and COX-2. Renal prostaglandins cause dilatation of the renal afferent arteriole. This mechanism is important for maintaining GFR when renal blood flow is reduced. Therefore, NSAID use is likely to have a greater effect on renal function in patients with increasing age, pre-existing renal disease, chronic hypertension, heart failure, use of ACEI and ARBs etc. Study conducted by Abdul Ghani et al. also concluded that the commonest drugs that induced AKI were non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting-enzyme inhibitors and angiotensin-receptor blockers.[14] In Arrizabalaga study, non-steroidal anti-inflammatory drugs were the most frequent etiology in 44% of cases of drug induced renal disease.[15]

In the study by Prakash et al, 47% patients recovered from renal failure with appropriate institution of treatment.[4] In this study, recovery was found in 64.3%. Our findings are in agreement with a review study by Rodrigo *et al*., which demonstrated a significantly increased risk of AKI in critically ill patients with older age, diabetes, hypertension, higher baseline creatinine, heart failure, sepsis, use of nephrotoxic drugs.[16] The association between higher creatinine levels and risk for AKI was also reported by Charuhas et al.[5]

In this study, 69.0% of the patients recovered normal renal function (Figure 7). Similarly, studies by Eswarappa et al[2] and Vakrani et al[1] showed a recovery rate of 60% and 64.3% respectively. Excluding the patients who passed away, the percentage of complete renal recovery was 75% among the survivors. Complete renal recovery is less commonly reported in the literature, however few studies have previously shown that the majority of patients recover sufficient renal function with one study even showing 68.0% of patients recovered completely.[8, 3] The excellent recovery seen in the present study, might be due to the exclusion of patients with preexisting renal disease. Schiffl, in his study showed that if critically ill patients with normal renal function prior to the renal insults, survive the precipitating cause of ATN, the overwhelming majority will recover sufficient renal function.[17]

Mortality rate in this study was 21% (Figure 7). The crude in-hospital mortality rate reported by Sushrut S. Waikar et al was 25% [18]. The mortality rate in the present study was less compared to that by Eswarappa et al (37.6%), Ali *et al*. (32.7%) and Joaniddis *et al*. (36.5%).[2,8,19] In general AKI in critically ill patients is considered an independent risk factor for an increased morbidity, mortality. The lower mortality rate in our study might be due to the fact that the patients selected for our study did not have preexisting renal disease, better haemodialysis support and better patient care in our institution.

The risk for mortality was found to be increased with increasing age (Table 2), male sex (Table 3), sepsis with UTI (Table 4), BPH (Table 5), increased mean blood urea (Table 7) and serum creatinine levels (Table 7). Similar results were found in studies of Eswarappa et al.[2]

Mortality was also found to be increased in patients with high mean FBS, PPBS, total WBC counts and serum potassium, and low serum sodium and platelet counts. (Table 7)

The increase in awareness of these risk factors will help in the early identification of kidney injury that is critical for treatment or prevention of AKI.

Limitations of the Study

1. Larger sample size could yield more conclusive data and results.
2. The study was conducted among patients admitted to ICU, Medicine and Nephrology wards. Hence the study population does not represent the general population.
3. Diabetic status was assessed based on previous medical history and FBS, PPBS values, so we did not have information on HBA1C levels or exhaustive diabetes complications.
4. AKI was diagnosed according to the KGDIGO guidelines but only based on serum creatinine variations, as urinary output was not available in the database.

CONCLUSION

1. Infection was the most common cause of AKI in Type 2 diabetes patients in our study.
2. Among drug induced renal failure patients, NSAIDS were noted to be most common cause.
3. Age >60 and male gender were prevalent in the majority of AKI patients.
4. About 59% of the total patients recovered to normal renal function, 10% recovered partially, with 10% of the total patients progressed for maintenance hemodialysis.
5. Crude mortality rate among patients with AKI in the study group was 21%.

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