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A Critical Analysis of Acute Kidney Injury in the Setting of Type 2 Diabetes Mellitus

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Abstract

Introduction: One of the commonest yet underrated complications of the hospitalized patients is acute kidney injury (AKI), the incidence of which has been steadily on the rise. Of late it has been observed that Diabetes Mellitus plays an important role not only in the causation but also in influencing the outcome of AKI. However, this burning problem has not been properly highlighted in the literature. As such, it was decided to evaluate the causes and outcome of AKI in type 2 Diabetes Mellitus.

Methods: This single-centric prospective study was conducted at the Medicine department, Silchar Medical College for a period of 1 year i.e. from January 2017 to December 2017. All adult type 2 diabetic patients presenting with AKI were included in the study. The classification of AKI was based on the principles of Kidney Disease Improving Global Outcomes criteria. The treatment options were conservative and dialysis. The selected cases were followed for 4 weeks for evaluation of outcome which could be one of the three viz. recovery, dialysis dependency or death.

Results: The selected cases comprised of 105 type 2 diabetic patients with AKI all of whom were subjected to detailed evaluation. The most common cause of AKI was found to be sepsis (52.4%) and the commonest source being urinary tract infection (65.5%). Only 30.5% patients required dialysis, while 69.5% of the patients were managed conservatively. Eventually 78.1% of the patients recovered, 11.4% had dialysis dependency and the rest comprising 10.5% died. Sepsis was related to all deaths and hemodialysis was performed in all of them.

Conclusion: In the background of type 2 Diabetes Mellitus, sepsis, whose commonest nidus was urinary tract, was the hallmark of the present study. Recovery rate was 78.1% and outcome was favorable in those who did not require dialysis.

Keywords: AKI; Diabetes Mellitus; Infection; Dialysis

Introduction

An important development in the recent years is the observation that relative small elevation of serum creatinine has been associated with worsening of outcome in various diseases [1]. Acute kidney injury is recognized as a contributor to unfavorable outcome in different clinical settings and should be considered as a risk factor for mortality in a host of clinical entities [2,3]. AKI is observed in 7% of patients requiring hospitalisation and in 36% to 67% of critically ill patients depending on the definition used [2,4]. Diabetic population are at risk of developing AKI either resulting from fluid loss associated with diabetic ketoacidosis and non ketotic hyperosmoar coma or due to other adversaries like hypotension, infection or exposure to nephrotoxic substances. Astonishingly, not only the individual but also the epidemiological and economic consequences of both disorders i.e. DM and AKI, have been an unflavored topic for the researchers and very few studies have addressed the topic of "AKI in diabetes mellitus." As such, this study was aimed to find out the factors leading to AKI in the setting of type 2 Diabetes Mellitus and to observe its fatal outcome.

Materials and Methods

This single centric prospective study was conducted at the department of Medicine, Silchar Medical College for a period of 1 year i.e. from January 2017 to December 2017 upon approval by the Institutional Ethics Committee of the Silchar Medical College and Hospital.

Inclusion and exclusion criteria

Patients selected for the present study were above 18 years, had a confirmed diagnosis of type 2 Diabetes Mellitus, and had not undergone renal replacement therapy (renal transplantation or dialysis) before admission. Patients with pre-existing renal disease and those who did not give consent were excluded from the study.

Definition of AKI

The diagnosis and staging of AKI was based on the principles of KDIGO criteria. The lowest creatinine level between the dates of hospital admission and discharge was considered as the reference creatinine value. The comparison of the highest creatinine value observed during hospitalization to the reference serum creatinine value was considered to facilitate the staging [5] (Table 1).

All the cases underwent a rigorous protocol of detailed history taking, including history regarding type 2 Diabetes Mellitus, its duration and therapy, history of Hypertension, coronary or cerebrovascular artery diseases and subsequent intervention if any, history of intake of drugs like ACEI/ARB, NSAIDS, antibiotics and diuretics and a detailed physical examination. Informed consent as per the protocol was obtained from the selected cases. The baseline serum creatinine if available and serum creatinine on admission were documented. All the cases were subjected to urine culture, Blood culture, and ultrasound examination of the Kidney-Urinary Bladder system with emphasis on echo-texture, cortico-medulary differentiation, pelvicalyceal system dilatation or constriction and presence or absence of calculi in the Kidney-Urinary bladder region. The therapy included conservative and or hemodialysis and the duration in weeks of hemodialysis of each cases were recorded. The selected cases were followed up for 4 weeks.

Clinical Outcomes

The clinical outcome of the cases was categorized under three headings:

1. Recovery: Renal functions resuming to normal status or baseline with/without dialysis OR >50% reduction in serum creatinine from the admission value OR dialysis-dependent patients becoming dialysis-independent.
2. Dialysis dependency.
3. Mortality.

The documentation done in the pre-designed proforma and the Statistical evaluation of the results was analysed using the statistical package SPSS21. The value $p<0.05$ was considered significant in terms of statistical evaluation

Results and observations

Type 2 diabetic patients numbering 105 (67 males and 38 females) with AKI were enrolled in the study. Baseline characteristics of the selected cases are depicted in Table 2. Majority of cases with AKI belonged to the age group of 61-70 years with the median age being 57.3 ± 8.6 years.

Etiology

Among the patients (n=105) enrolled in our study, most common cause of AKI was sepsis. Urinary tract infections were the most common source of sepsis, followed by respiratory infections. Gastroenteritis was observed as the second common cause of AKI in the present study. Malaria, dengue, leptospirosis, drug induced AKI were the other causes of AKI, although less common. *Klebsiella* [15 (41.7%)] was the most common microorganism detected in the urine culture in patients admitted with sepsis, followed by *Escherichia coli* [14(38.9%)] and *pseudomonas* [5(13.9%)]. The observations regarding the etiology of AKI in our study are summarized in Table 3.

Clinical characteristics

Hypotension was the most commonly associated clinical finding, prevalent in 53.3% (n=56) of the patients. (Figure 1) 71.4% (n=75) of the patients were oliguric and 28.6% of the patients non-oliguric. Non-oliguric patients had faster renal recovery. Fever, tachycardia, hypovolemia, edema were seen in 46.7% (n=49), 51.4% (n=54), 21.9% (n=23) and 15.2% (n=16) of the patients respectively. The other commonly associated findings were pallor (31.4%, n=33), icterus (9.5%, n=10), cyanosis (10.5%, n=11).

Outcome

Based on the therapeutic regimen, the cases were subdivided into two groups:

i) Those requiring dialysis and

ii) Those on conservative regimen and not requiring dialysis. The detailed description of the outcome is depicted in the table below (Table 4) (Figure 2).

Discussion

Age and gender distribution

The mean age of the study population was 57.3 ± 8.6 years and majority of the cases were in the age group of 51-60 years

Table 1: AKI was defined as any of the following: Increase in baseline serum creatinine level to ≥ 50% or ≥ 0.3 mg/dl (≥ 26.5mmol/L) versus the reference serum creatinine level or a urine volume < 0.5 ml/kg/h for 6 hours. AKI was further classified by stage [5].

Stage	Serum creatinine	Urine output
1	1.5-1.9 times baseline value OR ≥ 0.3 mg/dl (≥ 26.5 mmol/l) increase	<0.5 ml/kg/h for 6-12 hours
2	2.0-2.9 times baseline value	<0.5 ml/kg/h for ≥ 12 hours
3	3.0 times baseline value OR Increase in serum creatinine to ≥ 4.0 mg/dl (≥ 353.6 mmol/l) OR Initiation of renal replacement therapy	<0.3 ml/kg/h for ≥ 24 hours OR Anuria for ≥ 12 hours

Table 2: Baseline characteristics of patients

Characteristics	N (%)
Mean age (in years)	57.3 ± 8.6
Male	67 (63.8%)
Female	38 (36.2%)
Mean duration of type 2 Diabetes Mellitus (in years)	9.96 ± 4.6
History of hypertension	83 (79.04%)
History of consumption of antihypertensive medications	63 (75.9%)
ACEI/ARB	28 (44.4%)
Others	35 (55.6%)
IHD	32 (30.5%)
Smokers	55 (52.4%)

Table 3: Etiology of AKI in present study

Etiology		Number of patients
Sepsis	Total	55 (52.4%)
	Urinary tract infection	36 (65.5%)
	Respiratory tract infection	11 (20%)
	Skin infection	8 (14.5%)
Acute gastroenteritis		17 (16.2%)
Cardiac causes		8 (7.6%)
Hepatic causes		5 (4.8%)
Malaria, Dengue, leptospirosis		6 (5.7%)
Drug induced		8 (7.6%)
Others		6 (5.7%)
Total		105 (100%)

Table 4: Outcome of the patients in the study

Outcome	N (%)
Dialysed	32 (30.5%)
Non-dialysed	73 (69.5%)
Recovered	82 (78.1%)
Dialysis dependent	12 (11.4%)
Death	11 (10.5%)

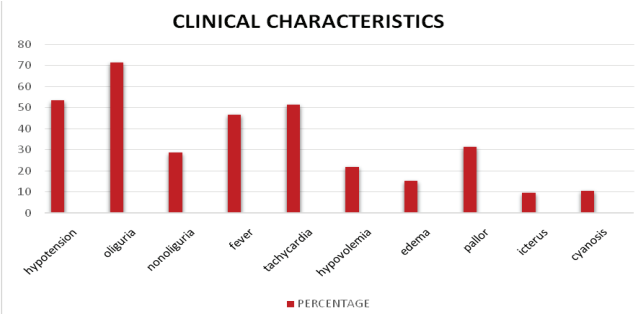

Figure 1: clinical characteristics of the patients in the present study

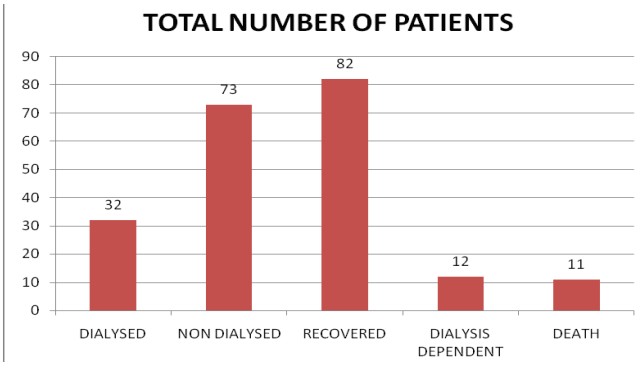

Figure 2: Outcome of the patients in the study

and the male to female ratio was 1.76:1. In the study by Vakrani, et al. [6], the mean age observed was 57.57 ± 11.29 years and majority of the cases were in the age group of 51-60 years whereas Prakash, et al. [7] observed the age range between 35-72 with a mean of 54.15 years.

Aetiology

Sepsis was the leading cause of AKI in the present study. Diabetic populations are increasingly susceptible to a wide range of infections. Diabetic population either type 1 or type 2 are susceptible to risk of infection the commonest source being respiratory tract, urinary tract and skin and mucous membrane in comparison to controlled hypertensive as per Muller, et al. [8]. Hyperglycemic environment in combination with malfunctioning of the immune system, angiopathies involving micro and macro vasculature, neuropathies especially the autonomic neuropathies either alone or in combination lead to depletion of antimicrobial activities of urinary and gastrointestinal system and contribute to urinary tract dysmotility and increase in medical interventions in these subset of patient population [9]. The role of sepsis in AKI has been well documented in western literature, causing nearly 50% of the AKI cases in few studies [10]. Jha, et al., and Prakash, et al., in their study evaluated AKI irrespective of ICU setting. They had shown that nephrotoxic drugs were the most common cause of AKI [11,12]. However, Kaul, et al. in their study reported acute diarrhoea as the most common cause [13] The commonest cause of sepsis in the present study was urinary tract infection (UTI) [36 (65.5%)] followed by respiratory tract infection [11(20%)] and skin/ soft tissue infection [8 (14.5%)]. It is seen that diabetic patients have a higher incidence of UTI than their non-diabetic counterparts [14]. The increased frequency of UTI in diabetic patients might be due to neuropathy affecting the ability of the bladder to sense the presence of urine and thus allowing urine to stay for a relatively longer duration in the bladder and thereby, increasing infection probability [15,16]. Another explanation is that high glucose levels in urine enhance the chances of the bacterial proliferation in the urine [12,17].

In our study, the drug induced AKI accounted for only 7.6% of the cases, which is lower than the previous studies. This might suggest that precautions regarding nephrotoxic drugs and appropriate choice of antibiotics have helped to reduce the incidence of drug induced AKI. Malaria, dengue and leptospirosis accounted for 5.7% of the cases of AKI. These represent a unique etiological spectrum of AKI in our country in comparison with the western literature.

Outcome

RRT was required in 30.5% (n=32) of the patients in our study. Studies undertaken in the country by other researchers like Prakash et al., and Singh et al. reported that 34% (n=28) and 20.58% (n=7) of the cases respectively, required RRT [18]. Intermittent hemodialysis was the most commonly used modalities of RRT in our hospital. These modes are associated with lower cost, lesser adverse effects when compared to the other RRT modes.

No mortality was observed in 73 (69.5%) patients treated conservatively, whereas, on the other hand 11 (10.5%) of the cases expired among 32 (30.5%) of patients requiring dialysis and an overall, 82 (78.1%) of the cases achieved recovery. Tariq, et al. demonstrated that 8% of cases with AKI received RRT of which 51% underwent hemodialysis and the remaining 49%

received hemofiltration as the first mode of RRT. The mortality of 57% of those who received RRT was documented [10].

Conclusion

Even though, AKI in Type 2 DM is an important determinant of final outcome and is a significant prognostic predictor, this has been a less traversed field for most of the researchers in India as well as abroad. As such, this humble effort was undertaken by us to highlight the fact that AKI like other established renal complications in Type 2 Diabetes Mellitus play a major role to determine the eventual outcome of the diabetics.

Limitation of the study

This was a single centered observational and analytical study conducted over a small sample size within a limited time frame. More studies over a larger sample size for an extended duration in different centers will illuminate on this very important subject.

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