Incidence and Clinical Outcome of Acute Kidney Injury in Patients with Sepsis Admitted in Multi-Disciplinary Unit in a Tertiary Care Center

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ABSTRACT

BACKGROUND

A rising trend has been reported in Acute Kidney Injury (AKI) in both developed and developing countries and there is an independent association with increased morbidity and mortality with sepsis being the most common predisposing factor. Sepsis and cardiovascular causes resulted in a high incidence of AKI, and older age was also an important risk factor. Our study aims to determine the incidence, outcome and comorbidities associated with AKI in sepsis patients. Sepsis is a serious medical condition characterized by a whole-body inflammatory state (systemic inflammatory-response syndrome) and the presence of a known or suspected infection that has severe consequences, including multiple organ failure.

METHODS

We did a retrospective observational study in 497 sepsis patients admitted in MDICU. Acute kidney injury in these patients was identified and studied using RIFLE criteria between June 2016 and May 2017.

RESULTS

A total of 497 patients were studied. Mean age was 60 yrs. 59.8% were males and 40.2% were females. 279 have acute kidney injury; so, incidence of AKI in our study is 56.1%. Significant comorbidities associated with AKI are diabetes mellitus 61.6% (p= 0.001), hypertension 76.7% (p= 0.001), CKD 43.3% (p= 0.001), CAD 28.3% (p 0.020). Out of 279 AKI cases, 167 (59.9%) were under RISK, 94 (33.7%) were under kidney injury, 18 (6.5%) under renal failure. 246 (88.1%) received conservative management and 33 (11.9%) received renal replacement therapy. Out of 33 patients receiving RRT, 18 patients (54.5%) expired during the study period (p value 0.011). 14 patients (50%) of those who received early RRT died and 14 patients (50%) survived, whereas in late RRT 4 (80%) died and 1 patient (20%) survived. There is no statistically significant (p= 0.25) association between mortality and early or late initiation of RRT.

CONCLUSIONS

As the incidence of AKI is 56.1% and there is significant association between sepsis patients with AKI and comorbidity, high RIFLE score and mortality, RRT and mortality. So Specific goals for reducing incidence and mortality of acute kidney injury has to be formulated and uniform guidelines regarding initiating RRT should be formed.

KEY WORDS

Sepsis, Acute Kidney Injury, Rifle, AKI Outcome

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BACKGROUND

A rising trend has been reported in Acute Kidney Injury (AKI) in both developed and developing countries and there is an independent association with increased morbidity and mortality in children as well as in adults and subsequent CKD.[1] Incidence of AKI in critically ill patients varied between 15 to 50% in multiple epidemiological investigations.[2] 5.7% of emergency hospital admission is complicated by AKI and it rose 30% in the setting of diarrhoeal illness, infectious diseases like malaria and leptospirosis and natural disasters like earth quakes.[3] In acutely ill sepsis is the most common predisposing factor for AKI.[4] The yearly incidence of AKI in US is estimated to be 500 per 100000 population higher than yearly incidence of stroke.[5] The clinical diagnosis of sepsis requires finding a focus of infection as well as at least two signs of systemic inflammatory-response syndrome that comprise abnormal body temperature (higher than 38°C or less than 36°C), heart rate >90 beats/min, respiration >20 breaths/min or arterial partial pressure of CO2 <32 mmHg, and deranged white blood cell counts (greater than 12 × 103/mm^3, less than 4 × 103/mm^3, or greater than 10% bands).[4]

Only in 2004 AKI has got a uniform definition when the acute dialysis quality initiative (ADQI) proposed the Risk, Injury, Failure, Loss and End stage Kidney disease (RIFLE) criteria.[6] Development of the RIFLE criteria allowed clinicians worldwide to identify and track patients with AKI in a uniform manner. The basic component of RIFLE criteria are variations in serum creatinine and urine output. Increase in severity level increases the specificity of the classification system, with reduction in sensitivity.[7] In 2007 RIFLE criteria was modified by Acute Kidney Injury Network (AKIN) and in 2012 Kidney Disease Improving Global Outcomes (KDIGO) came out with new criteria for AKI. KDIGO reported that there is 17 to 30% incidence of AKI in hospitalized patients.[8-10] 68% of a large cohort of 5443 patients with septic shock developed AKI within 6 hours of presentation and mechanism of development of AKI was individualistic.[11,12] It is yet to understand the potential difference between outcome association and grading of AKI severity in severe sepsis or septic shock.[13]

Individuals with comorbidities have increased risk of developing AKI.[14] Presence of more than one comorbidity result in high severity of result score in AKI.[15] It is shown that comorbidities such as hypertension, diabetes mellitus, heart disease, chronic renal disease predispose a patient to progress with AKI.[16] Increased long term mortality was associated with pre-existing comorbidity than severity of AKI episode.[17] Thus comorbidities play an important role in development, progression of AKI and long term morbidity and mortality.

Among patient admitted to the ICU, mortality rate may exceed 50 %. Even patients surviving an episode of severe AKI, requiring dialysis are at increased risk of later development of ESRD.[5] It was shown that as the severity of AKI increased so did the mortality. Mortality was 5.5% in patients without AKI and it increases to 8.8% in risk group and 26.3% in failure group in RIFLE criteria.[18]In 1996 – 2008, 4.4 community acquired AKI in 1000 admission with a mortality of 10.98% was reported in India.[19] Prolonged intensive care stay, repeated investigations, RRT, cardiac complications and re-admission have increased the health care cost.[20,21] National Confidential Enquiry into Patient Outcomes and Death (NCEPOD) Singapore 2009 reported that among AKI death 50% received suboptimal care and 14% was avoidable AKI.[22] 0 by 25 is an initiative by International Society of Nephrology for eliminating preventable death from AKI by 2025 through improving timely diagnosis and treatment.[23]

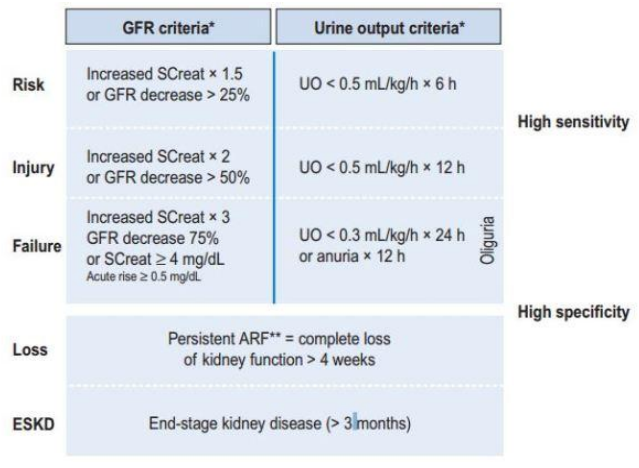
There is less data regarding the incidence and outcome of AKI in critically ill patients from South India, especially in Kerala. In view of this, we have conducted a retrospective study of Patients who have been admitted to the medical ICU in a tertiary care centre in South India.

We wanted to determine the incidence, outcome and comorbidities of AKI in sepsis patient.

METHODS

After obtaining the ethical committee clearance fro the study, patients were included in the study as per inclusion and exclusion criteria, using purposive sampling method till required sample size was achieved. A diagnosis of sepsis was made based on the diagnosis documented at the point of admission by the treating clinician. Patients were assigned to rifle classes at the time of admission.

This is a retrospective observational study in 497 patients with sepsis >18 years admitted in MDICU at Travancore Medical College, Kollam between June -2016 and May-2017. The sample size was taken based on the convenience of the study. We excluded patients with ESRD and those who were lost follow up. Patients filling the inclusion criteria were taken into the study using purposive sampling method till required sample size was achieved. Diagnosis of sepsis was made based on the diagnosis documented at the point of admission by the treating clinician. Patients were assigned to RIFLE class at the time of admission.



AKI Based on the RIFLE Criteria Reference[18]

Source: Internet

Required data collected from the clinical records of patient fitting the criteria. Those patients who received RRT from risk and injury group are defined as early RRT and from failure group as late RRT. Indication for initiating dialysis

include anuria, fluid overload, uraemia, hyperkalaemia, refractory acidosis.

Statistical Analysis

The data collected was entered in Microsoft Excel and analyzed using SPSS V.16. Descriptive analysis was done by calculating frequencies and proportions. Chi square test was used to calculate statistical significance.

RESULTS

Age Group	Frequency (n=497)	Percentage (%)
18-40	85	17.1
40-60	170	34.2
>60	242	48.7
Gender		
Male	297	59.8
Female	200	40.2
AKI		
Present	279	56.1
Absent	218	43.9

Table 1. Demography Distribution

Age Group	AKI	
	Present	Absent
18-40	25(9.0%)	60(27.5%)
40-60	111(39.8%)	59(27.1%)
>60	143(51.3%)	99(45.4%)

Table 1a. AKI Distribution

Comorbidity	AKI		Chi Square Value	p Value
	Yes	No		
Yes	248(65.4%)	131(34.6%)	56.052	0.001*
No	31(26.3%)	87(73.7%)		
Diabetes Mellitus				
Yes	172(67.5%)	83(32.5%)	27.226	0.001*
No	107(44.2%)	135(55.8%)		
Hypertension				
Yes	214(69.5%)	94(30.5%)	58.567	0.001*
No	65(34.4%)	124(65.6%)		
CKD				
Yes	121(91.7%)	11(8.3%)	92.146	0.001*
No	158(43.3%)	207(56.7%)		
CAD				
Yes	79(65.3%)	42(34.7%)	5.441	0.020*
No	200(53.2%)	176(46.8%)		
CVA				
Yes	41(56.2%)	32(43.8%)	0.000	0.996
No	238(56.1%)	186(43.9%)		

Table 2. Comorbidity

*Statistically Significant

RIFLE Score (n=279) Frequency (%)		
Risk	Injury	Failure
167(59.9%)	94(33.7%)	18(6.5%)

Table 3. Rifle Score

Mode of Treatment	RIFLE Score		
	Risk	Injury	Failure
RRT	19(57.6%)	9(27.3%)	5(15.2%)
Conservative	148(60.2%)	85(34.6%)	4(22.2%)

Table 3a. Mode of Treatment

Mortality	Risk	Injury	Failure	Chi Square Value	p
Yes	11(61.1%)	3(16.7%)	4(22.2%)	9.078	0.011*
No	156(59.8%)	91(34.9%)	14(5.4%)		

Table 4. Mortality

RRT	Mortality		Chi Square Value	p Value
	Expired	Surviving		
Yes	18(54.5%)	15(45.5%)	181.410	0.001*
No	7(1.5%)	457(98.5%)		
RRT				
Early RRT	14(50.0%)	14(50.0%)	1.540	0.215
Late RRT	4(80.0%)	1(20.0%)		

Table 4a. Mortality

*Statistically Significant

Clinical Characteristics of Patients

As shown in Table 1, A total of 497 patients studied, 279 have acute kidney injury so incidence of AKI in our study is 56.1%, AKI was found in all age groups (Maximum age was 98 yrs. and Minimum age 18 yrs.) median age 60 yrs. Out of 497 cases studied 297 (59.8%) were males and 200 (40.2%) were females.

As shown in Table 2, Among 497 patients with sepsis, 379 (76.3%) had comorbidities and 118 (23.7%) had no comorbidities. Among 379, 255 (51.3%) had DM, 308 (62.0%) had hypertension, 132 (26.6%) had chronic kidney disease, 121 (24.3%) had Coronary Artery Disease. It was observed that out of 279 patients with AKI, 248 (89.9%) had comorbidities and 31 (11.1%) had no comorbidities. 214 (76.7%) had hypertension, 172 (61.6%) had type 2 DM, 121 (43.4 %) had chronic kidney disease, 79 (28.3%) had coronary artery disease, 41 (14.7%) had cerebrovascular accident. Hypertension was most common co morbidity followed by type 2 DM. It is evident that majority had multiple comorbidities. There is significant association between AKI and co morbidity. Significant comorbidities are diabetes mellitus 67.5% (p= 0.001), Hypertension 69.5% (p value 0.001), CKD 91.5% (p= 0.001), CAD 65.3% (p= 0.020)

As shown in Table 3; Severity of AKI was assessed based on RIFLE criteria. Out of 279 AKI cases; 167(59.9%) were under RISK, 94 (33.7%) were under kidney injury, 18(6.5%) under renal failure. Among 279 AKI patients, 246 (88.1%) received conservative management and 33 (11.9%) received renal replacement therapy.

From Table 4; There is significant association between rifle score and mortality (p value 0.001).Out of 18 patients in failure 4 expired which amounts to 22.2%. It can be concluded that 27.7% of failure required RRT, 9.57% of the injury and 11.3% of risk required RRT. There is significant association between RRT and mortality (p value 0.001). Out of 33 patients who received RRT, 15 (45.5%) patients survived and 18 (54.5%) expired. 14 patients (50%) of those who receive early RRT died and 14 patients (50%)survived whereas in late RRT 4 (80%) died and 1 patient (20%) survived. There is no statistical significance (p value= 0.25) association between mortality and early or late initiation of RRT.

DISCUSSION

Incidence

AKI is a frequently observed clinical syndrome in intensive care unit with overall incidence of 20%-50% associated with the mortality rate over 50%. Incidence of AKI in our study is 56.1%, which is higher than the study done in critically ill patients, where incidence varied between 15% and 50%.[2] In other study, the incidence of community acquired AKI reported in India was 4.14/1000 admissions in 1996 – 2008.[19] This shows that incidence of AKI has increased, so further study regarding factors causing increased AKI incidence is required for proper intervention.

Comorbidities and Acute Kidney Injury

In our study there is significant association between co morbidity and acute kidney injury. Significant co- morbidities

include hypertension (62%), type 2 DM (51.3%), CKD (26.6%), CAD (24.3%). This is in accordance with previous study by of the co-morbidities, hypertension was the commonest (28, 57.1%), with diabetes and ischaemic heart disease present in 27 (55.1%) and 17 (34.7%) respectively.[24] In another study by Tariq Ali, Izhar khan et al, comorbidities associated with AKI CAD (29.5%), hypertension (27.2%), CKD (18.56%), CVA (17.3%), diabetes (15%).[25] Sicker patients were more likely to develop AKI and those with SOFA scores greater than >9 were more likely to develop AKI, and, as expected, had higher mortality. Sepsis and cardiovascular causes resulted in a high incidence of AKI, and older age was also an important risk factor.[25]

With regards to comorbidities, 302 (74.8%) had hypertension, 230 (56.9%) had diabetes mellitus, and 187 (46.3%) had ischemic heart disease in a study of outcomes of acute kidney injury.[26] Study by Ravindra L Mehta et al, comorbidities associated with AKI are CAD (37%), CKD (37%), DM (29%).[27] Pre-existing CKD increases the risk of non-recovery from AKI. In a large community-based study from North California the risk for death or ESRD 30 days after hospital discharge was increased by 30% by an episode of AKI.[28] So, AKI is multi factorial with several different insults affecting the kidney in an additive manner. The combined risk for each patient comprises both acute exposure and insult causing AKI and chronic conditions and patient related factors that define how susceptible each patient is to develop AKI.

Outcome of AKI

Mode of treatment of AKI in our patients was studied. In our study among 279 AKI cases, 246 (88.1%) patients were treated conservatively and 33(11.9%) patients treated with RRT. Hence most patients were treated conservatively. Previous study by Bagshawsm et al, where 67.4% patients were treated conservatively, and 32.6% patient were treated by RRT.[29] In our study among 279 cases; 15 (45.5%) cases with AKI who received RRT survived and 18 (54.5%) expired, whereas out of 279, 246 cases who received conservative management survived. The acute renal failure trial network study found that increasing the intensity of dialysis did not improve clinical outcome.[30]

In another study 22 patients were treated with haemodialysis survived; out of 46 patient who were treated conservatively 17.4% expired.[30] Previous Indian studies by Prakash et al [31] and Singh et al,[32] reported that 34% and 20.58% of the cases respectively required RRT. Renal replacement therapy requirement in recent Indian based study on KDIGO is 29.43%.[33] Delay in initiating dialysis has been shown to contribute to poor outcome with studies even suggesting improved outcome with early initiation of dialysis treatment [34]. The lack of uniform guidelines on when to initiate RRT makes it a complex end point in studies and complicates the assessment of how RRT affects patient outcome.[33]

CONCLUSIONS

In our study the incidence of AKI is high at 56.1%. There is significant association between sepsis patients with AKI and comorbidity, high RIFLE score and mortality, RRT and mortality. We have to consider factors like aetiology, increasing patient age, existence of comorbid condition like diabetes, heart disease, pre-existing renal disease, vascular disease, septic shock, respiratory failure which will increase the rate of mortality. So, further prospective study using KDIGO criteria in small increase in creatinine is needed to identify more precise data regarding incidence and clinical outcome. Specific goals for reducing incidence and mortality of acute kidney injury has to be formulated and uniform guidelines regarding initiating RRT should be formed in order to achieve 0 by 2025 initiative.

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