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Original Research Article

Spectrum of acute kidney injury in patients of tropical acute febrile illness in a tertiary hospital

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ABSTRACT

Background: Tropical acute febrile illnesses (TAFI) such as malaria, typhoid, leptospirosis, dengue are major causes of AKI in the tropics. The spectrum of AKI due to TAFI in developing countries like India is still underestimated. Hence, we conducted a study to know the spectrum of AKI in patients of TAFI.
Methods: The prospective study was conducted in Yashoda hospital, Secunderabad a tertiary care hospital in India from April 2019 to March 2020. AKI was defined as per KDIGO. The clinical history, physical examination and laboratory investigations were recorded in a standard proforma.
Results: Hundred patients suffering from TAFI were admitted during the study period. Mean age of the study population was 43.12±14.33 years. Twenty-six (60.5%) were males. Most common presenting feature was fever (100%), chills (81.4%) and vomiting (67.4%). The most common cause of TAFI was dengue (n=49, 49%), leptospirosis (n=20, 20%), followed by malaria (n=10, 10%), scrub typhus (n=10, 10%) and undifferentiated fever (n=6, 6%). 43 patients (43%) had AKI as per KDIGO definition. 23 patients (53.5%) had stage 1, 11 (25.6%) had stage 2 and 9 (20.9%) had stage 3 AKI. RRT was required in 16.3% of patients. Dengue and leptospirosis were the most common causes for requirement of RRT. SLED was the most common modality of dialysis. Mortality was observed in 6.98% patients and Dengue was the most common cause of mortality.
Conclusions: AKI is common in tropical acute febrile illness. However, RRT was required only in 16.3% and mortality was observed in 6.98% patients.

Keywords: Acute kidney injury, Tropical acute febrile illness, Dengue, Malaria, Leptospirosis

INTRODUCTION

Acute kidney injury (AKI) has now replaced the term acute renal failure and a universal definition and staging system has been proposed to allow earlier detection and management of AKI. The new terminology enables healthcare professionals to consider the disease as a spectrum of injury.[1] Worldwide incidence of acute kidney injury (AKI) is variable and even more among the developed and the developing countries. Tropical acute febrile illnesses such as malaria, typhoid, leptospirosis, dengue and others are a major cause of AKI in the tropics. Incidence of AKI with these infections has been unclear due to varying definitions of AKI and overestimation due to referral bias in tertiary care centre reports.[2] Several definitions of AKI have been proposed in order to provide a uniform definition of AKI. These definitions are based on the serum creatinine and urine output. The Kidney Disease: Improving Global Outcomes (KDIGO) definition and staging system is the most recent and preferred definition. Other criteria include the RIFLE criteria (risk, injury, failure, loss of kidney function, and

end-stage kidney disease) and a subsequent modification proposed by the acute kidney injury network (AKIN).[3] tropical acute febrile illness is defined as all acute febrile syndromes with oral temperature over 37.5°C within the last 24 hours and less than two weeks, in tropical and sub-tropical developing countries with non-specific symptoms.[4] These infections present mostly with fever as cardinal sign. Clinical profile of AKI in tropics is modified by a number of factors such as severe systemic infection, severe toxemia, shock, dehydration, disseminated intravascular coagulation, hepatocellular injury, pulmonary injury, or central nervous system involvement. AKI, in these infections is a result of direct invasion of renal parenchyma by microbial agents, tubular necrosis due to hemodynamic disturbances, renal inflammation due to immune response, or iatrogenic renal injury associated with treatment. It is assumed that these illnesses contribute to more than two-thirds of AKI in tropics.[5] Mechanisms of renal involvement in tropical infections include direct invasion of the tubules leading to tubulointerstitial inflammation with leptospirosis and scrub typhus. Plasmodium falciparum has been shown to affect the glomerular endothelium through cytoadherence of infected red blood cells in circulation. Hemolysis occurring in infections like malaria, scrub typhus or viral infections can lead to hemoglobinuria associated acute tubular necrosis. Also, antibiotics especially penicillins, cephalosporins and fluoroquinolones used to treat various infections in tropical regions can lead to drug induced allergic tubulointerstitial nephritis. Though infections have been typically considered as a cause of AKI, there is increasing realization that residual damage, which may be subclinical, leads to CKD at least in some of these patients with infection related AKI.[6]

METHODS

The study was conducted in Yashoda Hospitals, Secunderabad a tertiary care hospital in India. It was a Prospective observational study and the study period was one year from April 2019 to March 2020. All the adult patients with age more than 18 years who fulfill acute kidney injury definition admitted with tropical fever in wards, stepdown units and ICCU were included in the study. The patients who were excluded with age <18 years, Patients with obvious focus of infections like Urinary tract infection or respiratory tract infections, Tuberculosis, non-infectious causes of fever like Systemic lupus erythematous, lymphoma, drug induced fever, Patients who are immunocompromised like HIV or on immunosuppressive drugs and Patients who had evidence of proteinuria before admission. The incidence of AKI in tropical fever is between 40-50% worldwide. We took an average prevalence of AKI to be 45% and estimated a reasonable sample size, a total of 100 patients were included in this study. Informed consent of all the patients was taken. A detailed clinical history, physical examination and laboratory investigations like Complete blood picture (Hemoglobin, total leucocyte count, Platelets), Blood urea, serum sodium, serum potassium was done. Serum creatinine was measured at admission and after 48 hrs and on day 7. Liver function test (bilirubin direct and indirect, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), albumin and total protein). complete urine examination, peripheral blood smears for malaria, chest radiograph, abdominal ultrasonogram, blood and urine cultures, widal test and cultures for enteric fever, leptospiral IgM ELISA, dengue IgM ELISA, scrub typhus ELISA. The values provided by manufacturers were used for test interpretation. KDIGO guidelines were used for AKI diagnosis and classification. Management was based on standard guidelines. Indicated patients were initiated on renal replacement therapy (RRT) in form of Intermittent Hemodialysis (IHD), sustained low efficiency dialysis (SLED) and continuous renal replacement theparyt (CRRT) based on the hemodynamic instability. All patients were monitored till the end of hospital stay. Mortality and need of renal replacement therapy was the primary outcome. The data collected was analyzed using descriptive statistical tools at the end of the study. Data entry was done using M.S. Excel and it was statistically analyzed using Statistical package for social sciences (SPSS Version 20) for M.S. Windows. All results were also presented in tabular form and are also shown graphically using bar diagram or pie diagram as appropriate. The difference in the two groups were tested for statistical significance using Parametric tests such as t-test, Pearson correlation, and categorical variables were tested by chi square test. P-value less than 0.05 was considered to be statistically significant.

RESULTS

In our study population of 100 patients of tropical acute febrile illness, the incidence of AKI was (n=43, 43%). The mean age group of patients developing AKI in our study was 43.12 years. Majority of study population developing AKI was ±14.33 between 30-50 years. Majority of the patients involved were males 26 (60.5%) as compared to females 17 (39.5%). Hypertension (30.2%) was the most common comorbid condition observed in our study. The most common presenting feature in our study was fever (100%) followed by chills (81.4%) and vomiting (67.4%). In our study population 100 patients of tropical acute febrile illness, patients who had AGE were 5 (5%), dengue 49 (49%), leptospirosis 20 (20%), malaria 10 (10%), scrub typhus 10 (10%) and undifferentiated were 6 (6%). 43 patients had AKI. In this, patients who had AGE were 2(4.7%), dengue 17 (39.5%), leptospirosis 12 (27.9%), malaria 8 (18.6%), scrub typhus 2 (4.7%) and undifferentiated fever in 2 (4.7%). The most common cause of tropical acute febrile illness in our study was dengue (49%), also the most common etiology of AKI due to tropical fever was dengue (39.5%) followed by leptospirosis (27.9%) (Table 1). Out of 43 patients who had AKI, patients in stage 1 were 23 (53.5%), stage 2 were 11 (25.6%) and stage 3 were 9 (20.9%) (Figure 1). Factors like systolic blood pressure, decrease urine output and encephalopathy all

are significantly associated with RRT whereas age and gender were not associated (Table 2). In our study renal replacement therapy was required in 7 (16.3%) patients (Figure 2). 3 patients RRT of dengue and leptospirosis each and 1 patient of malaria required RRT. Sustained low efficient dialysis (SLED) was done in 6 patients and 1 patient required Continuous renal replacement therapy (CRRT). The most common mode for RRT in our study was Sustained low efficiency dialysis (SLED). 43 patients with AKI, patients out of who died were 3 (6.98%) (Figure 3). 2 had dengue and 1 patient had leptospirosis. Factors which were significantly associated with mortality are systolic blood pressure, severity of AKI (stage 3), decrease urine output, encephalopathy and RRT whereas hyperbilirubinemia was not significantly associated (Table 3). Dengue was the most common cause of mortality in our study.

Table 1: Characteristics of study population with TAFI.

Characteristics n=100 (%)	AKI N=43 (%)	Non-AKI N=57 (%)
Age (years) Mean±SD	43.12±14.50	39.53±16.38
Sex n (%)	M=26 (60.5) F =17 (39.5)	M=36 (63.2) F=21(36.8)
HTN n (%)	13 (30.2)	13 (22.8)
DM n (%)	10 (23.3)	9 (15.8)
Asthama n (%)	1 (2.3)	1 (1.8)
CAD n (%)	5 (11.6)	5 (8.8)
CLD n (%)	1 (2.3)	0 (0.0)
Hb (g/dl) Mean±SD	11.72±2.33	13.07±2.35
TLC Mean±SD	9307.30±5234.79	5615.86±3079.59
PLT (10^3/mm^3) Mean±SD	1.8 0±1.16	1.7482±1.16
Urea (mg/dl) Mean±SD	66.12±50.71	25.91±13.69
Creat at 0 hrs (mg/dl) Mean±SD	2.63±1.34	0.98±0.35
Creatinine at 48 hrs (mg/dl) Mean±SD	2.42±1.41	1.00±0.26
Creat at day 7 (mg/dl), Mean±SD	1.66±1.58	0.97±0.42
Na (meq/l) Mean±SD	138.67±6.23	138.30±4.5
K (meq/l) Mean±SD	4.51±0.73	4.09 ±0.60
S. Bil (mg/dl) Mean±SD	1.28±1.29	0.86±0.81
SGOT (u/l) Mean±SD	322.33±1259.34	65.02±120.85
SGPT (u/l) Mean±SD	503.53±2032.00	101.86±224.31
S. albumin (gm/dl) Mean±SD	3.53±0.63	3.67±0.47
Temp Mean±SD	100.63±1.29	100.33±1.41
Pulse Mean±SD	93.81±13.45	89.00±17.52
SBP Mean±SD	109.53±13.96	110.35±13.08
RR Mean±SD	18.72±2.74	17.74±2.06
Dengue n (%)	17 (39.5)	49 (49)
Leptospirosis n (%)	12 (27.9)	20 (20)
Scrub typhus n (%)	2 (4.7)	10 (10)
Malaria n (%)	8 (18.6)	10 (10)
Acute GE n (%)	2 (4.7)	5 (5)
Undiff. fever n (%)	2 (4.7)	6 (6)

Table 2: Characteristics of study population with AKI and RRT.

Characteristics n=43 (%)	RRT n=7 (%)	No RRT n=36 (%)	P value
Age>50 (years)	4 (30.8)	9 (62.2)	0.13
Male	4 (15.4)	22 (84.6)	0.84
Female	3 (17.6)	14 (82.4)	0.84
AKI 3	7 (100)	2 (5.6)	<0.01
DUO	6 (85.7)	2 (5.6)	<0.01
Encephalopathy	4 (57.1)	0 (0)	<0.01
Recovery <7 days	0 (0)	30(83.34)	0.03
Recovery >7 days	4 (57.14)	6 (16.66)	0.02
Mortality	3 (42.9)	0 (0)	<0.01

Table 3: Characteristics of study population with AKI and RRT.

Characteristics n=43 (%)	Mortality n=3 (%)	No mortality n=40 (%)	P value
Age > 50	3 (23.1)	10 (76.9)	0.02
Male	2 (7.7)	24 (92.3)	0.82
Female	1 (5.9)	16 (94.1)	0.82
AKI 3	3 (100)	6 (15)	<0.01
DUO	3 (3.7)	5 (62.5)	<0.01
Encephalopathy	3 (75)	1 (25)	<0.01
RRT	3 (42.3)	4 (57.1)	<0.01

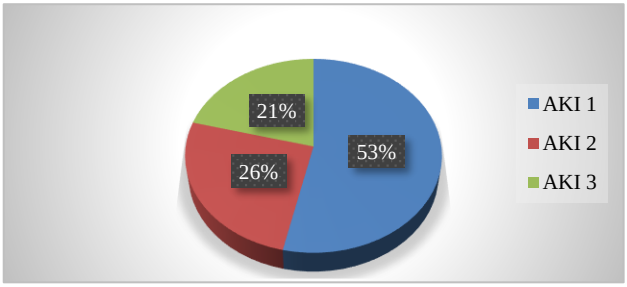

Figure 1: Severity of AKI.

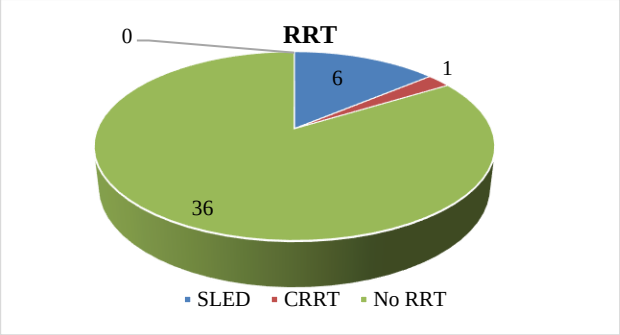

Figure 2: RRT.

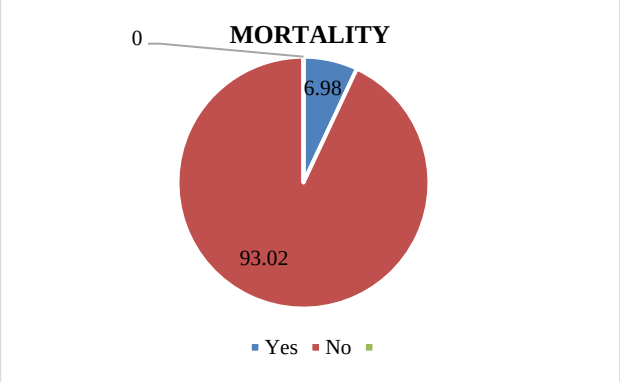

Figure 3: Mortality.

DISCUSSION

In this study we have highlighted the occurrence of AKI in various tropical infections like dengue, scrub typhus, malaria, leptospirosis and undifferentiated fever in southern part of India. The incidence of AKI in tropical acute febrile illness in our study population was 43% which is similar to other studies from Indian subcontinent where they found incidence of AKI in tropical fever between 37.7 to 54%. However, this was much higher as compared to tropical regions of south America where the incidence of AKI due to infectious etiology was low.[2,4,7] This shows wide variations of the incidence of AKI in different geographical regions of the world. The reason for this high proportion of AKI in our study could be because we use KDIGO classification for AKI which has greater sensitivity as compared to RIFLE and AKIN classification. Males are affected more than females; this could be because of outdoor work-related activities in which men are more involved than women.

In our study for simplification, we have considered all cases of dengue fever, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) in a single category as dengue. Similarly, we have considered vivax malaria and falciparum malaria in a single category as malaria. The most common cause of tropical acute febrile illness in our study was dengue followed by leptospirosis. This was similar to other studies from southeast Asia where they found dengue as the most common cause of acute tropical fever followed by leptospirosis.[8,9] Like all TAFI patients, the most common disease for acute kidney injury due to tropical fever in our study population was also dengue followed by leptospirosis and malaria. This is in contrast to other studies from Asia where they found low incidence of AKI due to dengue fever.[10-12] So, the most common cause of acute AKI amongst tropical febrile illness in our study was dengue, the reason for this could be related to the epidemic of dengue fever in the city where the study was conducted in the study period. This also shows us that the spectrum of AKI due to various tropical infections is variable if the study was conducted during periods of epidemic and pandemic.

In this study we found 43% patients had AKI, patients in stage 1 23(53.5%), Stage 2 11(25.6%) and stage 3 was 9(20.9%) which was similar to other Indian studies. However, this was in contrast from a Chinese study where maximum number of patients were seen in stage 3.[4,13] So in our study the most common Stage of AKI was Stage 1 followed by stage 2 and 3. Most common etiology for stage 1 and stage 2 AKI was dengue. Whereas, dengue and leptospirosis were seen in equal proportion in stage 3.

Renal replacement therapy (RRT) in the form of dialysis was required in 7 (16.3%) of patients. 3 patients of dengue and leptospirosis each and 1 patient of malaria required dialysis. Total number of sessions of SLED and CRRT done was 15 and 1 respectively. None of the patients required IHD and acute peritoneal dialysis. In this study, mortality was observed in 3 (6.98%) patients. Mortality was seen in 42.85% of patients who required RRT. The association between mortality and RRT was significant. The mortality rate and requirement of RRT was comparable with similar studies from Asia. However, it differs from a study conducted by Czempil P et al.[2,4,5,14] The most common cause of mortality in our study was dengue followed by leptospirosis. This is also found in a study by Lizarraga et al where they observed that the development of AKI in patients with Dengue infection is associated with increased mortality.[15]

In this study, factors like systolic blood pressure, severity of AKI, decrease urine output, encephalopathy and RRT all were significantly associated with mortality ($p<0.05$) whereas etiology and hyperbilirubinemia were not associated. This is similar to other studies from tropical regions of other parts of the world.[16]

Limitations

The study was conducted in a single tertiary care center in an urban area hence it may not reflect the true frequency of AKI in TAFI within the community. Sample size was also small (100) in our study.AKI in TAFI patients may be missed because of asymptomatic disease, non-referral, delay in treatment initiation before presentation, death before admission. There was no baseline serum creatinine values prior to admission so the

possibility of acute on chronic kidney disease cannot be excluded.

CONCLUSION

This study found that tropical acute febrile illness like Dengue, leptospirosis, scrub typhus and malaria are important causes of acute kidney injury in tropical countries like India. So, it is important for the early identification of potential risk factors, their prevention and timely therapeutic interventions when required, to reduce long hospital stay, morbidity and mortality as the single most lifesaving and cost-effective measure.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Bhadade R, De'Souza R, Harde MJ, Mehta KS, Bhargava P. A prospective study of acute kidney injury according to KDIGO definition and its mortality predictors. J Assoc Physicians India. 2016;64:22-8.
2. Basu G, Chrispal A, Boorugu H, Gopinath KG, Chandy S, Prakash JAJ, et al. Acute kidney injury in tropical acute febrile illness in a tertiary care centreRIFLE criteria validation. Nephrol Dial Transplant. 2011;26(2):524-31.
3. It F, Graded N, Graded N, Graded N, Ckd W. Section 2: AKI Definition Chapter 2. 1: Definition and classification of AKI. 2012;19-36.
4. Nair JJ. A Clinical Study of Acute Kidney Injury in Tropical Acute Febrile Illness. J Clin DiagnosticRes.2016;10(8):1-5.
5. Mehta K, Pajai A, Bhurke S, Shirkande A, Bhadade R, D'Souza R. Acute Kidney Injury of Infectious Etiology in Monsoon Season: A Prospective Study Using Acute Kidney Injury Network Criteria. Indian J Nephrol. 2018;28(2):143-52.
6. Kumar V, Kohli HS. Renal involvement in tropical infections. In: Bhalla A, eds. Association of Physicians of India Indian College of Physicians Update on Tropical Fever. Maharasthra; 2015: 50-9.
7. Daher EE, Marques CN, Lima RSA, Silva GB, Barbosa AS, Barbosa ES, et al. Acute kidney injury in an infectious disease intensive care unit - An assessment of prognostic factors. Swiss Med Wkly. 2008;138(9-10):128-33.
8. Wangdi K, Kasturiaratchi K, Nery SV, Lau CL, Gray DJ, Clements ACA. Diversity of infectious aetiologies of acute undifferentiated febrile illnesses in south and Southeast Asia: A systematic review. BMC Infect Dis. 2019;19(1):1-17.
9. Andrews MA, Ittyachen AM. Aetiology of acute febrile illness: a multicentre study from the province of Kerala in southern India. Trop Doct. 2018;48(4):322-5.
10. Sarriff A, Jummaat F, Khan AH, Mallhi TH, Khan YH, Adnan AS. Incidence, Characteristics and Risk Factors of Acute Kidney Injury among Dengue Patients: A Retrospective Analysis. PLoS One. 2015;10(9):e0138465.
11. Mbbs NM, Frcp GA. Short Report Acute kidney injury in dengue fever using Acute factors. 2012;12(July):160-2.
12. Lee IK, Liu JW, Yang KD. Clinical characteristics, risk factors, and outcomes in adults experiencing dengue hemorrhagic fever complicated with acute renal failure. Am J Trop Med Hyg. 2009;80(4):651-5.
13. Yang F, Zhang L, Wu H, Zou H, Du Y. Clinical analysis of cause, treatment and prognosis in acute kidney injury patients. PLoS One. 2014;9(2).
14. Czempik P, Cieśla D, Knapik P, Krzych Ł. Mortality of patients with acute kidney injury requiring renal replacement therapy. Adv Clin Exp Med. 2018;27(3):327-33
15. Lizarraga KJ, Nayer A. Dengue-associated kidney disease. J Nephropathol. 2014;3(2):57-62.
16. da Silva GB, De Francesco Daher E, Salani Mota RM, Menezes FA. Risk factors for death among critically ill patients with acute renal failure. Sao Paulo Med J. 2006;124(5):257-63.

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