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INCIDENCE OF ACUTE KIDNEY INJURY IN PATIENTS WITH TROPICAL FEVER

KEY WORDS: Tropical fever, acute kidney injury, malaria, scrub typhus

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ABSTRACT

Acute febrile illnesses are a common cause of Acute Kidney Injury (AKI) in the tropics. Tropical fever is an infection common in tropics and subtropics. Some diseases occur throughout the year and some specially in rainy and post-rainy season.These infections eg.Malaria, Scrub typhus, can cause life threatening organ dysfunction . Most patients present with features like fever, breathlessness, rashes etc. Many patients may present with multiorgan dysfunction. In addition to specific anti infective therapy, management of organ dysfunction might require the use of mechanical ventilation, vasopressor drugs, dialysis and blood products.

INTRODUCTION

Worldwide incidence of renal failure is variable[1,2] and even more in the developed and the developing countries[3].Tropical illnesses such as Malaria, Scrub typhus, Dengue etc are a major cause of acute renal failure in the tropics[4,5].These diseases have caught the world's eye with their emergence in the developed nations & non tropical regions[6,7] due to global warming[8,9] and increased travel to tropics[10,11].Incidence of AKI with these illnesses has been unclear due to varying definitions of AKI[12,13] .The Risk, Injury, Failure, Loss of function and End stage (RIFLE) criteria has helped in unifying the definition of AKI[14]. RIFLE criteria was originally validated for ischemic AKI[15] and is commonly used in ICU setting. We evaluated the incidence of acute kidney injury and validity of RIFLE classification in tropical acute febrile illnesses.

MATERIAL AND METHODS

The study was a retrospective study. Patients admitted to medical ICU with sepsis were included in the study . Surviving sepsis guidelines 2017 criteria was used to define sepsis. Patients with chronic illnesses such as chronic liver disease, chronic kidney disease , CVA, malignancies, autoimmune diseases, chronic lung diseases were excluded.

All patients had a detailed clinical history and examination. A standard set of investigations including complete blood counts, liver function tests, serum creatinine, urea, electrolytes, chest radiograph, peripheral blood smear for malaria, urinalysis, blood cultures were done. Serological investigations including Leptospiral IgM ELISA, Scrub typhus IgM ELISA, MPQbc, Dengue IgM-IgG ELISA, Dengue NS1 antigen, Typhidot ELISA were also done. Patients with non-contributory preliminary tests were subjected to convalescent serological tests. Patients were monitored till the end of their hospital stay.

Serum creatinine was measured using the modified Jaffe's kinetic alkaline picrate method (colorimetry) without deproteinization using an automated chemistry analyzer Olympus AV 2700 (Japan).AKI was classified based on RIFLE classification. When baseline creatinine was not available,it was derived using the four-variable MDRD equation by assuming a baseline glomerular filtration rate (GFR) of 90ml/min/1.73 m2.The RIFLE class was determined based on the worst of either the serum creatinine or GFR criteria or urine output criteria. RRT (intermittent haemodialysis and slow low efficiency haemodialysis) was initiated for standard indications. The primary outcomes studied were in hospital mortality and requirement of RRT. Statistical analysis was performed using SPSS software version 11.0.The statistical significance of the associations between AKI based on RIFLE classification and mortality or dialysis requirement was assessed by Chi Square test or Fisher's Exact test. Patients were retrospectively studied for the incidence and severity of renal failure based on RIFLE classification and its association with mortality and dialysis requirement. The aim of the study was to identify the incidence of acute kidney injury in patients suffering from tropical fever admitted to our ICU.

RESULTS

Of the 79 patients (mean age 46.33yr);54.43%were males and 45.56% were females The most common causes of acute febrile illness were scrub typhus(25.31%),malaria(12.65%), dengue(13.9%),enteric fever, and the overall mortality rate was 26.58%.The incidence of renal SOFA score

0 was 40.5%
1 was 20.25%
2 was 17.72%
3 was 10.12%
4 was 11.39%

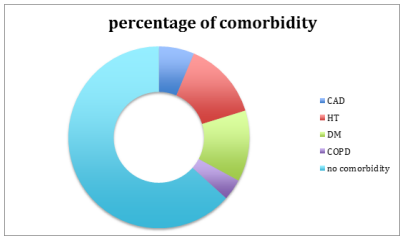
Of the patients 18.98% patients suffering from AKI dialysis and the average duration to be of dialysis was 3.2 days. Patients had fever for a mean duration of 10+_5 days prior to admission.

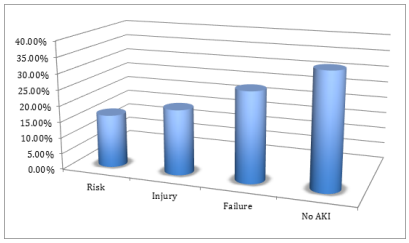
The overall incidence of AKI among the tropical acute febrile illnesses was 64.56% of which 16.4%,20.2% and 27.8% were in Risk, Injury and Failure classes respectively. RRT in the form of intermittent haemodialysis or slow low efficiency dialysis was initiated in 18.98% patients with AKI for medically unresponsive severe metabolic acidosis, hyperkalemia, pulmonary oedema. The overall mortality rate was 26.58%.Among the 17.72% elderly patients (age >=65 years),incidence of AKI was 35.71%.

Diabetes Mellitus was present in 12.65% patients. Though the incidence of AKI was higher among diabetic patients but mortality was not. Apart from the elderly age group, presence of icterus, oliguria, breathlessness, tachycardia, tachypnea and shock at presentation predicted the occurrence of AKI and mortality. The mean serum creatinine at admission was significantly higher among the patients who had AKI across all the three classes of RIFLE classification compared with the non AKI patient. A GFR at admission of <60ml/min/1.73m2 was predictive of both AKI and in hospital mortality.

The most common cause of febrile illness in this study was scrub typhus (25.31%) followed by malaria, dengue. In 16.45% patients, the aetiology could not be ascertained. Most patients with AKI were those with scrub typhus. AKI was observed at an average rate of 25.31% in scrub typhus patients. In general 16.4% belonged to the Risk class,20.2% to the Injury class and 27.8% to the failure class.

30.30% patients with AKI Non Invasive Ventilation/Pressure support and 18.98% patients required intubation and Mechanical Ventilation. Mortality rate among the patients with AKI was 26.58%.





Graph depicting percentage of patients with Risk, Injury, Failure and no AKI

DISCUSSION

Tropical acute febrile illnesses are a common cause of AKI .In this retrospective study from a tertiary care centre in southern Rajasthan in India the common tropical acute febrile illness among hospitalized patients included malaria, typhoid, scrub typhus, dengue fever. Scrub typhus accounted for the majority of tropical acute febrile illnesses .

The incidence of AKI in this study is 18.98%. We have used an estimated baseline creatinine derived by back calculating a normalized eGFR of 90 ml/min/1.73m 2 using the four-variable MDRD equation. The predominant population was from the rural and the suburban regions of Udaipur. Patients usually do not have health insurance coverage or check-up, and hospital visits are usually for major illnesses. Therefore, most patients did not have a pre-admission baseline serum creatinine. Patients with AKI had a significantly higher Cr adm ,as most patients developed AKI prior to admission. Therefore ,Cr adm could not be used as a uniform marker of baseline renal function, being valid only for a small group of patients. Measures to prevent AKI are best initiated at the community and primary healthcare level . The mean GFR value of a young healthy Indian adult is 80-100 ml/min/1.73 m 2 BSA, which is significantly different from the normal value of 109-125 ml/min derived from a western population[16]. RIFLE classification based on an estimated baseline creatinine is unlikely to misclassify the Injury and Failure groups but may increase the number included in the Risk group.[17]. An advantage of availability of pre-calculated baseline serum creatinine and cut-off values for the RIFLE classes for a patient sensitizes the doctor for timely diagnosis and institution of appropriate preventive/therapeutic measures to avoid progression of AKI in hospital.

The patient population is predominantly young (mean age of 46.33 Years) with a minority being elderly(17.72%),suffering from diabetes(12.65%). AKI was more common in the elderly and patients with a severe illness characterized by shorter duration of fever, presenting with shock, tachycardia, tachypnea, breathlessness, oliguria and icterus. Diabetics had a higher incidence of AKI. These associations would help in selecting patients for initiating effective therapeutic/preventive strategies against AKI at the primary care level.

Scrub typhus, a rickettsial infection caused by Orientia tsutsugamushi, is transmitted by trombiculid mites , found in semi-arid regions . Its distribution includes Japan, eastern Australia, eastern Russia, India, China and the Far East.[18].This infection often presents with fever, maculopapular rash with an eschar at mite-bite site, myalgia, hepatosplenomegaly and in severe cases with multi-organ dysfunction [19]. The case fatality rate ranges from 3% to 50%[20].It is diagnosed by a scrub typhus ELISA [21] and treated with Doxycycline . It is grossly under-reported and under-diagnosed, due to lack of awareness, non-availability of the diagnostic test at peripheral centres and widespread use of empirical broad-spectrum antibiotics for acute febrile illnesses. In our study AKI was observed in 25.31% of patients with scrub typhus. The disease was observed across the rural-urban divisions. The mechanisms involved in evolution of AKI in this infection include pre-renal failure[22], septic shock[23], rhabdomyolysis[24], direct renal invasion of O. tsutsugamushi [25], acute interstitial nephritis secondary to empirical use of antibiotics (eg. Ciprofloxacin).

Falciparum malaria, the next common tropical infection, is caused by P.falciparum and transmitted by Anopheles mosquito. It manifests with fever, haemolysis, and systemic inflammatory response with microvascular plugging due to aggregation of infected as well as uninfected erythrocytes[26].AKI in malaria is due to renal ischaemia(microvascular plugging), tubular toxicity(haemolysis), and widespread inflammation secondary to sepsis syndrome. Probably due to early diagnosis and effective treatment, the mortality is much lower compared with the other acute febrile illnesses.

Dengue is caused by various strains of Dengue flavivirus, transmitted by a mosquito (Aedes aegypti). Exposure to another viral strain can cause dengue haemorrhagic fever. AKI is predominantly due to reduced renal blood flow as in dengue shock syndrome[27],sepsis syndrome[28], rhabdomyolysis[29], empirical use of NSAIDs for analgesic-antipyretic effects, and other rare causes[30].

Considering a high incidence of AKI and its recognition as a significant risk factor for death among the large number of patients admitted with acute febrile illness in tropical region, validation of RIFLE criteria assumes great importance. Apart from increased mortality, longer duration of hospital stay and the requirement of renal replacement therapy adds to the economic burden. It is possible to identify patients at an early stage of AKI using these criteria and employ therapeutic or preventive measures to contain and prevent AKI .

Though patients who are ill get referred to larger centres, a large but undefined number of patients with AKI in febrile illnesses in tropics have no access to medical attention or reside far away from large hospitals and will succumb to complications, making this a major public health concern.

CONCLUSION

Current results suggest that the presence of underlying CKD, older age, and time to hospital presentation after symptom onset were risk factors to determine the occurrence of AKI. Scrub typhus, malaria, dengue ,typhoid fever were the most common tropical acute febrile illnesses in our study. RIFLE criteria is applicable in AKI related to tropical acute febrile illness with a risk of in-hospital mortality and RRT requirement.

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Conflicts of interest

There are no conflicts of interest.

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