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Original Research Article

A study of incidence and outcome of acute kidney injury in common undifferentiated febrile illnesses

Jacob Cherian, Divya Deodhar*

Department of Internal Medicine, Christian Medical College and Hospital, Ludhiana, Punjab, India

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***Correspondence:**
Dr. Divya Deodhar,
E-mail: divyadeodhar@gmail.com

ABSTRACT

Background: Patients presenting with acute undifferentiated febrile illness may have delay in diagnosis due to nonspecific symptoms and signs. Kidney injury in these patients can cause detrimental effect on their prognosis and hence early diagnosis is warranted.
Methods: This is an observational prospective study conducted in the Department of Medicine at Christian Medical College and Hospital, Ludhiana for a period of one year from 1st November 2014 till 31st October 2015.
Results: Among the 532 patients acute febrile illness included in the study, 437(82.1%) were diagnosed with dengue fever. A total of 190(35.7%) patients were diagnosed to have AKI. The incidence of AKI in specific diseases was found to be the highest in Malaria 8(61.5%) out of 13 patients). In AKI, majority of them were in the risk category with 97(51.0%). A total of 26(13.6%) patients with AKI required Hemodialysis. Among the 190 patients who had AKI 43(22.6%) died.
Conclusions: Dengue was the most common acute febrile illness. Among the patients with acute kidney injury majority were in the risk category with 97(18.2%). 326(61.2%) patients were males with a male to female ratio was found to be 1.5: 1. Dengue with acute kidney injury had the most proportion of patients in the risk and injury category and malaria with acute kidney injury having the highest proportion in failure category. The highest incidence of patients with AKI requiring hemodialysis was seen in scrub typhus. Leptospirosis with AKI had the highest proportion of mortality. The failure category had the highest proportion of mortality.

Keywords: Acute febrile illness, Acute kidney injury, Dengue, Hemodialysis, Leptospirosis, Malaria

INTRODUCTION

Acute undifferentiated Febrile Illness (AFI) is defined as a type of illness characterized by an acute onset of fever above 38oC without a defined cause lasting less than 14 days. Some of the most commonly encountered causes in India include scrub typhus, malaria, dengue fever, leptospirosis and enteric fever (typhoid). Due to limited resources and great diversity in presenting complaints it remains a challenge to diagnose AFI. In a study done by Kashinkunti MD et al, evidence of acute kidney injury was seen in 26%, hepatic dysfunction in 25% patients and 51% of them had multi organ dysfunction.[1]

Acute Kidney Injury (AKI) is commonly defined as an abrupt decline in renal function, clinically manifesting as a reversible acute increase in nitrogen waste products measured by Blood Urea Nitrogen (BUN) and serum creatinine over the course of hours to weeks. In 2002, the Acute Dialysis Quality Initiative (ADQI) created the RIFLE criteria for the treatment and prevention of AKI.[2] RIFLE is an acronym of Risk, Injury, and Failure; and

Loss; and End-stage kidney disease. It categorizes renal failure through changes in serum creatinine or urine output or both with the worse parameter defining the categorization as RIFLE.

Scrub typhus has a multisystemic presentation characterized by rash, fever, localized lymphadenopathy and presence of an eschar. Scrub typhus is known to occur all over India including the hills of North India and can be diagnosed by IgM/ IgG ELISA for scrub typhus.

India is an endemic area for malaria. Southeast Asia contributed to 2.5 million cases to the global burden of malaria. Of this, India alone contributed 76% of the total cases.[3] Malaria can be diagnosed by microscopic parasitic detection in peripheral blood film or Positive Dipstick antigen detection tests (HRP 2 or LDH). Acute renal failure in malaria is seen in 13-17.8% of the cases.[4]

Dengue fever is caused by Aedes aegypti and is hyper endemic in South East Asia. It is diagnosed by detection of dengue IgM/IgG from serum and demonstration of dengue virus antigen. AKI in dengue is due to acute tubular necrosis secondary to hypotension.

Leptospirosis is a zoonosis caused by the spirochetes of the Leptospira species. It is a globally important zoonotic disease most commonly found in the tropical and sub-tropical countries. It can be diagnosed by the detection of IgM Leptospira in serum. AKI is due to a combination of acute tubular necrosis and interstitial nephritis, presenting in 16-40% of patients with severe infection.[5]

Enteric Fever is a systemic infection caused by Salmonella typhi and paratyphi. Diagnosis is by isolation of S. typhi from blood, stool and/ or urine. The annual incidence of typhoid fever (per 100 000 person years) is 493.5 in India. The kidneys are involved as a sequalae of immune complex glomerulitis which is self-resolving on serial renal biopsies.

Moderate to severe AKI accounts for 1.5% of hospital admissions in India. In a study from South India, medical etiology accounted for 87.6% of presentations of in-hospital AKI, of which infective causes including sepsis, leptospirosis and malaria accounted for 9.3, 7.8, 7.5% respectively.[6]

Hence this study is being undertaken to determine the incidence and outcome of AKI among all patients admitted with commonly occurring AFI.

METHODS

This study is a one-year observational prospective study done in the Department of General Medicine at Christian Medical College and Hospital, Ludhiana starting from 1st November 2015 to 31st October 2016. All adult patients admitted with a diagnosis of malaria, scrub typhus, leptospirosis, enteric fever, dengue fever were be included in the study.

Inclusion criteria

- All patients diagnosed with malaria, scrub typhus, leptospirosis, enteric and dengue fever admitted to adult medical wards.
- All patients who consented to the study.

Exclusion criteria

- Patients below the age of 18 years.
- Patients who had an evidence of dual infection.
- Patient who had a prior history of any renal disease.
- Patient who refused to consent.
- Informed consent was taken from patients before enrollment into the study.

A detailed demographic data, history and clinical examination was conducted and recorded in the proforma. Demographic data included name, age and sex. Detailed history included date of fever and presenting complaints like fever, malaise, headache, rash, bleeding and decreased urine output. Clinical examination included recording pulse rate, blood pressure and respiratory rate and temperature. Pallor, icterus, cyanosis, petechiae, ecchymosis, patients in altered sensorium and eschar were looked for. Besides this a detailed systemic examination of the respiratory system, gastrointestinal system, cardiovascular system and central nervous system was done.

Investigations included complete blood count, creatinine levels at the time of admission along with relevant investigations to diagnose scrub typhus, malaria, typhoid fever, leptospirosis and dengue fever. These included Weil- Felix test and scrub typhus spot test (S.D. Bioline) for scrub typhus.

Blood film for malarial parasite, falciparum/ vivax antigen (SureTest malaria PF/PV HRP2/ pLDH Combo) for falciparum and vivax malaria NS1 antigen, IgM/ IgG (Dengue Day 1 test J. Mitra) and IgM ELISA for dengue fever. Blood culture, urine culture, stool culture and WIDAL for salmonella typhi and paratyphi.

RESULTS

Amongst 532 patients in our study 326 (61.2%) patients were males and 206 (38.7%) were females with a male to female ratio was found to be 1.5: 1.

Off the 532 patients included in the study, 437 (82.1%) patients were diagnosed with dengue fever, 46 (8.6%) patients were diagnosed with enteric fever, 22 (4.1%) patients with scrub typhus, 14 (2.6%) patients with leptospirosis and 13 (2.4%) patients with malaria as shown in Figure 1.

The most common presenting feature was fever seen in 166 (87.3%) patients, followed by oliguria seen in 44 (23.1%) patients. Bleeding was the presenting symptom in 42 (22.1%) patients closely followed by rashes observed in 38 (20.0%) patients.

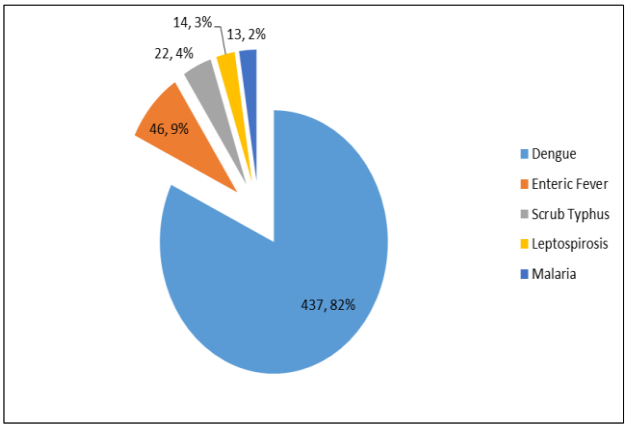

Figure 1: Distribution of acute febrile illnesses.

Tachycardia was seen in 78 (41.0%) out of 190 patients followed by tachypnea seen in 70(36.8%) patients and shock was observed in 67 (35.2%) patients. On examination, icterus was found in 64 (33.6%) patients, followed by pallor seen in 63 (33.1%) patients, petechiae observed in 42 (22.1%) patients and altered sensorium seen in 21(11.0%) patients. Thrombocytopenia was the most commonly seen feature which was present in 112 (58.9%) out of 190 patients with AKI. It was followed by anemia seen in 72 (37.8%) patients, coagulopathy was seen in 43 (22.6%) patients and leukocytosis was found in 17 (8.9%) patients.

Acute kidney injury in AFI

The incidence of acute kidney injury among the study population was 35.7 %. Among 190 patients of AKI, 161 (84.7%) patients had dengue, 3 (1.5%) patients were of enteric fever, 8 (4.2%) patients had malaria. Scrub typhus and leptospirosis was seen in 10 (5.2%) and 8 (4.2%) patients respectively as shown in Table 1.

Table 1: Distribution of acute kidney injury and hemodialysis in each category of fever.

	AKI (n=190)	Hemodialysis (n=26)
Dengue	161	16(9.9%)
Enteric fever	3	1(33.3%)
Malaria	8	3(37.5%)
Scrub typhus	10	4(40.0%)
Leptospirosis	8	2(25.0%)

The incidence of AKI in specific diseases was found to be the highest in Malaria (8(61.5%) out of 13 patients), followed by Leptospirosis (8(57.1%) out of 14 patients), scrub typhus (10(45.4%) out of 22 patients). AKI was seen in 161(36.8%) patients out of 437 patients of dengue and 3(6.5%) out of 46 patients with enteric fever as in Table 1 and Figure 2.

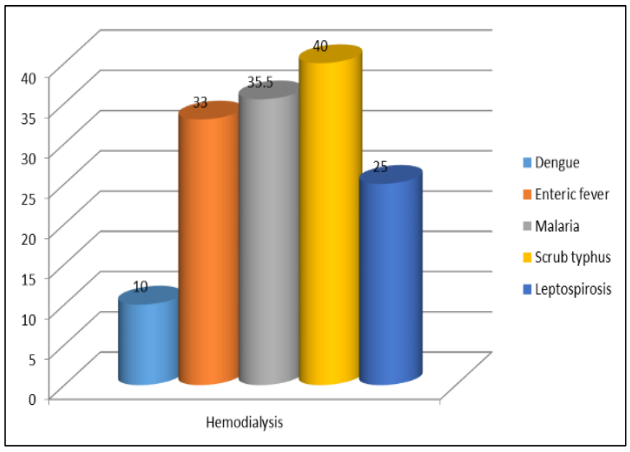

Figure 2: Distribution of hemodialysis in various categories of AFI.

Table 2: Proportion of risk, injury and failure category in various AFI with AKI.

Type of AFI Category of AKI	Dengue (n= 161)	Scrub typhus (n = 10)	Malaria (n=8)	Leptospirosis (n=10)	Enteric fever (n=3)
Risk	86(53.4%)	4(40.0%)	3(37.5%)	3(37.5%)	1(33.3%)
Injury	58(36.0%)	3(30.0%)	1(12.5%)	2(25.0%)	1(33.3%)
Failure	17(10.5%)	3(30.0%)	4(50.0%)	3(37.5%)	1(33.3%)

Proportion of risk, injury and failure category in various AFI with AKI:

All patients with acute kidney injury were divided into 3 categories, risk, injury and failure. The distribution of patients in these above categories according to the type of acute febrile illness were as shown in Table 2. There were 161 patients who were diagnosed with dengue and AKI of which 86(53.4%) patients were in the risk category, 58(36.0%) patients were found to be in the injury category and 17(10.5%) patients were in the failure category. Patients with scrub typhus and AKI had 4(40.0%) out of 10 patients in the risk category, followed by 3(30.0%) patients in the injury category and 3(30.0%) patients were in the failure category.

Amongst 8 patients having Malaria who had developed AKI 3 (37.5%) patients were in the risk category followed by 1 (12.5%) patient in the injury category. As for the failure category, 4 (50.0%) out of the 8 patients were seen in this category.

Leptospirosis with AKI was similarly diagnosed in 8 patients of which 3 (37.5%) patients were in the risk category, 2 (25.0%) out of the 8 patients were found to be in the injury category and 3 (37.5%) patients were characterized in the failure category.

Only 3 patients with enteric fever developed AKI of which 1 (33.3%) patient each was seen in the risk, injury and failure category.

A total of 26 (13.6%) patients with AKI required Hemodialysis. Hemodialysis was done for majority of the patients in the failure category which was 19(67.8%) out of 28 patients. Amongst patients in the injury category 5 (7.6%) out of 65 patients required hemodialysis whereas in the risk category only 2 (1.9%) patients required hemodialysis.

As shown in figure 2 the highest incidence of patients with AKI requiring hemodialysis was seen in scrub typhus which was seen in 4 (40.0%) out of 10 patients, followed by enteric fever in which 1 (33.3%) out of 3 patients required hemodialysis. Amongst patients suffering from malaria and leptospirosis 3 (32.5%) and 2 (25.0%) patients required hemodialysis respectively. In dengue 16 (9.9%) out of 161 patients required hemodialysis.

Mortality in AKI

Among the 190 patients who had AKI 43 (22.6%) died. Patients diagnosed with leptospirosis who had AKI had the highest proportion of mortality with 3 (37.5%) out of 8 patients who died. Patients who had enteric fever with AKI had 1 (33.3%) patient who died out of 3 diagnosed patients. Among patients who had scrub typhus with AKI 3(30.0%) out of 10 patients died. Of the patients diagnosed with dengue having AKI there were 34 (21.1%) deaths out of 161 patients. Finally, patients diagnosed with malaria who suffered AKI has 2 (25.0%) deaths out of 8 patients.

The patients included in the failure category had the highest proportion of mortality with 16 (57.1%) patients followed by patients included in the injury category with 16 (24.6%) deaths. The patients included in the risk category had 6 (6.1%) patients who died.

DISCUSSION

Acute Kidney Injury (AKI) is one of the most common and potentially fatal aspects while treating a patient with Acute Febrile Illness (AFI). Its early diagnosis and prompt management is hence warranted during the course of treatment of any acute febrile illness.

Various criteria were developed to classify the extent of AKI, some of the most common ones being RIFLE and AKIN.[7]

The RIFLE which has been used in this study is a criteria with a multi-level classification system where a wide range of disease spectra was considered from mild (early) to late (severe) intensity of AKI. It has validated for AKI caused by acute febrile illness.[8]

In this study 326 (61.2%) patients were males and 206 (38.7%) were females with a male to female ratio was found to be 1.5: 1. In the study by Gopal Basu et al, there were 60% males of the 367 patients included in the study. 6 A study by Jorge Cerda et al, also concluded that males are more than twice as likely as females to be taken to see medical personnel due to social and financial factors.[8]

Among the 532 patients included in the study, 437 (82.1%) patients were diagnosed with dengue fever, 46 (8.6%) patients were diagnosed with enteric fever, 22 (4.1%) patients with scrub typhus, 14 (2.6%) patients with leptospirosis and 13 (2.4%) patients with malaria as shown in Figure 1. In the study by Gopal Basu et al, the distribution of AFI was scrub typhus (51.2%), falciparum malaria (10.4%), enteric fever (8.7%), dengue (7.6%), mixed malaria (6.5%), leptospirosis (3.3%).[6] In the study by J.J Nair et al, the spectrum of TAFI was vivax malaria (203, 33.8%), leptospirosis (151, 25.2%), dengue fever (85, 14.2%), falciparum malaria (49, 8.2%), mixed malaria (37, 6.2%), enteric fever (7, 1.2%) and scrub typhus (5, 0.8%).[9]

Acute kidney injury in AFI

The incidence of AKI in acute febrile illness in our study was found to be 35.7% and its distribution among various types of AFI was as shown in figure 3. Of this the majority of them were in the risk category with 97(18.2%) patients followed by patients in the injury category which was 65(12.2%) patients and the remaining patients in the failure category which was seen in 28(5.3%). Amongst all the patients with AFI 4.9% patients with AFI required hemodialysis as shown in Table 1. The mortality rate was 6.4% among all the patients with AFI and but it was as high as 22.6% in patients with AKI in AFI. In a study by Gopal Basu et al, the incidence was found to be 41.1% with 17.4%, 9.3% and 14.4% were in the Risk, Injury and Failure classes, respectively. Of the patients, 7.9% required dialysis. 6 In another study by J J Nair et al, the incidence of AKI in Tropical Acute Febrile Illness (TAFI) was found to be 54%. Hemodialysis was required in 10.2% of patients with AKI and TAFI with a mortality of 3% among all the patients included in the study.[9]

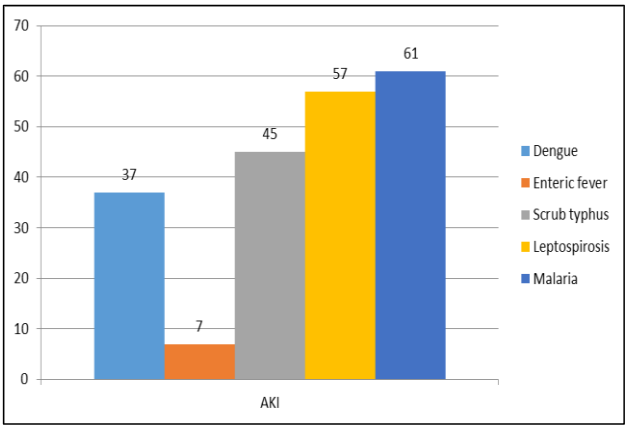

Figure 3: Distribution of AKI in each category of AFI.

The incidence of AKI and its categorization in various AFI are as described below:

Aki in malaria

Acute kidney injury was found in 8 out of 13 patients of malaria (61.5%). There is a wide variation of incidence of AKI in malaria ranging from 0.57% to 60% worldwide. In a study by A K Sharma et al, the incidence of AKI in malaria was reported as 13% in North India, 17.8% in New Delhi and 17.2% in Orissa. 10 Another study by K S Mehta et al, found the incidence of AKI in malaria to be 5.9%.[4] Another study by P B Gupta et al, found the incidence of AKI in malaria to be 10%.[10]

In this study 3(37.5%) out of 8 patients with AKI in malaria required hemodialysis. In a study by P.Wilairatana et al, it was found that 101(90.2%) out of 112 patients with AKI in malaria required hemodialysis.[11] In this study the mortality in patients with AKI in malaria was 2(25%) out of 8 patients. In a study by V B Kute et al, it was observed that there was a mortality of 11.8% in patients with AKI in malaria.[12] The study by P. Wilairatana et al, showed a mortality of 10.7%.[11]

AKI IN dengue

Acute kidney injury was observed in 161(36.9%) out of 437 patients diagnosed with dengue. Laoprasopwattana et al, reported an incidence of 0.9% among children in Thailand, and Lee et al, reported an incidence of 3.3% among adults in Taiwan.[13,14] In a Brazilian intensive care unit for infectious diseases, dengue was the cause of 4% of the cases of AKI diagnosed using the risk, injury, failure, loss of kidney function and end-stage acute kidney disease (RIFLE) criteria.[15] Amongst 161 patients with AKI in dengue 16(9.9%) required hemodialysis. In a study by Mei-ChuanKuo et al, a total of 7(1.3%) patients out of 519 patients with dengue and AKI needed hemodialysis.[16] In this study 34(21.1%) patients out of 161 patients with AKI in dengue died. The study by Mei-ChuanKuo et al, showed a mortality of 28.6% in patients with AKI in dengue.[16] Another study by Muhammad A.M Khalil et al, showed a mortality of 11.3% in patients with AKI in dengue.[17]

Aki in enteric fever

In this study acute kidney injury was diagnosed in 3 (6.6%) out of 46 patients with enteric fever. In a study conducted by S N Khosla et al, 4(16%) patients developed AKI out of 25 patients diagnosed with enteric fever.[18] According to data in this study only 1(33.3%) out of 3 patients having enteric fever with AKI required hemodialysis with an incidence of 2.1%. In the study by Basu et al, none of the 32 patients diagnosed with enteric fever required hemodialysis.[6] This study also showed 1(33.3%) out of 3 patients suffering from enteric fever with AKI died. The study by J J Nair et al, showed a mortality of 1(1.7%) out of 59 patients with enteric fever and AKI.[9]

AKI IN leptospirosis

Amongst 14 patients diagnosed with leptospirosis 8(57.1%) patients had AKI. Amongst these 8 patients, 2(25.0%) required hemodialysis. In the study done by Cetin B.D et al, 8(50.0%) out of 16 patients with leptospirosis were found to have AKI and of those 8 patients, 7(87.5%) required hemodialysis.[19] In this study 3(37.5%) out of 8 patients with leptospirosis having AKI died. According to a study conducted by Daher Ede F et al, the mortality was found to be 22% in patients with leptospirosis having AKI.[20]

Aki in scrub typhus

In this study amongst 22 patients diagnosed with scrub typhus, 10(45.4%) patients developed AKI. Of this 4(40.0%) patients required hemodialysis with a mortality seen in 3(30.0%) out of 10 patients with scrub typhus and AKI. In a study conducted by R P Attur et al, 60(23.2%) out of 259 patients with scrub typhus were diagnosed to have AKI with 6(10.0%) patients requiring hemodialysis and mortality seen in 2(3.3%) out of 60 patients with scrub typhus having AKI.[21]

CONCLUSION

Hence, this study shows the incidence of acute kidney injury in various categories of acute febrile illness and its importance in early recognition and thereby prevention which may lead to increased morbidity and mortality.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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