ejpmr, 2021,8(4), 19-36

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

A CLINICOEPIDEMOLOGICAL STUDY OF ACUTE KIDNEY INJURY AMONG PATIENTS ADMITTED WITH SHORT DURATION FEVER

[1]Dr. Debajyoti Majumdar, [2*]Dr. Arindam Naskar, [3]Dr. Manab Kumar Ghosh, [4]Dr. Sudeshna Mallik and [5]Prof. (Dr.) Bibhuti Saha

[1]MBBS, MD, Clinical Tutor, School of Tropical Medicine, 108, C. R. Avenue, Kolkata, Pin- 700073.
[2]MBBS, MD, MRCP(UK), Assistant Professor, School of Tropical Medicine, 108, C. R. Avenue, Kolkata, Pin- 700073.
[3]MBBS, MD, Assistant Professor, School of Tropical Medicine, 108, C. R. Avenue, Kolkata, Pin- 700073.
[4]Associate Professor, School of Tropical Medicine, 108, C. R. Avenue, Kolkata, Pin- 700073.
[5]Head of the Department, School of Tropical Medicine, 108, C. R. Avenue, Kolkata, Pin- 700073.

***Corresponding Author: Dr. Arindam Naskar**

MBBS, MD, MRCP(UK), Assistant Professor, School of Tropical Medicine, 108, C. R. Avenue, Kolkata, Pin- 700073.

Article Received on 28/01/2021 **Article Revised on 18/02/2021** **Article Accepted on 08/03/2021**

ABSTRACT

Acute kidney injury associated with fever in tropics is predominantly community acquired and affects young, previously healthy persons.

In this prospective study from a tertiary care centre in Eastern India, the common acute febrile illnesses among hospitalized patients included dengue, malaria, typhoid, lower respiratory tract infections, scrub typhus, urinary tract infection, leptospirosis, mixed infections and others. Overall incidence of AKI was 18.54%. AKI was present in 100%in patient with leptospirosis, 50% in LRTI, 12.8% in Dengue and 11.8% in P. Vivax. Despite the use of a standard battery of tests for acute febrile illness, the aetiology of fever could not be ascertained in 6.7% of the patients, who had 20% of AKI without any mortality. The study showed significantly higher incidence of AKI in elderly, male, known diabetic and hypertensive patients.

It is now possible to identify patients at an early stage of AKI using KDIGO criteria and effective therapeutic or preventive measures that can contain and prevent AKI reducing morbidity and mortality thus saving money and lives.

KEYWORDS

1. AKI- Acute Kidney Injury
2. KDIGO- Kidney Disease: Improving Global Outcomes
3. Short duration fever.

INTRODUCTION

Humanity has but three great enemies: fever, famine, and war; of these by far the greatest, by far the most terrible, is fever.

William Osler

Fever is not by itself an illness. It's usually a symptom of an underlying condition, most often an infection. Many experts believe that fever is a natural bodily defence against infection. There are also many non-infectious causes of fever. Fever in tropical and subtropical areas has unique characteristics and mostly infectious in origin. Some of these occur throughout the year and some especially in rainy and post-rainy season.

Geographically, the tropical region is limited to an area till 23° 26' 16'' on either side of equator and characterized by direct overhead presence of sun at least once in a year. This definition encompasses almost one third of earth's landmass, which is home to majority of the world population along with animal and plant biodiversity. Generally, tropics are characterized by a hot climate, usually throughout the year. The level of rainfall varies from as low as 2 cm/year in dry arid deserts to almost 9 m/year in tropical rainforests. Hot and humid climate that is conducive to support life in its various forms is hallmark of tropical ecosystem. Persistence of microorganisms, their reservoirs and vectors is greatly facilitated by this tropical ecology. The great biodiversity adds to complex interactions between them and adds to evolution with changing circumstances. Human contact with this ecosystem in almost unavoidable in most of the poor tropical countries because of prevailing poor social and economic circumstances translating into increased

susceptibility to infections and poor access to health care services.

Renal diseases in the tropics aptly reflect the uniqueness of tropical diseases. Acute kidney injury (AKI) in tropics is predominantly community acquired and affects young, previously healthy and economically productive age group. Infections like malaria, leptospirosis, dengue, scrub typhus and acute gastroenteritis especially in children or over the counter drugs are the main causes for community acquired AKI in these regions.

Acute kidney injury is the new consensus term for acute kidney insult. It refers to a clinical syndrome characterised by a rapid (hours to days) decrease in renal excretory function, with the accumulation of products of nitrogen metabolism such as creatinine and urea and other clinically unmeasured waste products. Other common clinical and laboratory manifestations include decreased urine output (not always present), accumulation of metabolic acids, and increased potassium and phosphate concentrations. The term acute kidney injury has replaced acute renal failure to emphasize that a continuum of kidney injury exists that begins long before sufficient loss of excretory kidney function can be measured with standard laboratory tests.

Clinically AKI is characterised by a rapid reduction in kidney function resulting in a failure to maintain fluid, electrolyte and acid-base homoeostasis. There have previously been many different definitions of AKI used in the literature which has made it difficult to determine the epidemiology and outcomes of AKI. To address the lack of a universal definition for AKI a collaborative network of international experts representing nephrology and intensive care societies established the Acute Dialysis Quality Initiative (ADQI) and devised the RIFLE definition and staging system for AKI. Shortly after this many of the original members of the ADQI group collaborated to form the Acute Kidney Injury Network (AKIN). The AKIN group modified the RIFLE staging system to reflect the clinical significance of relatively small rises in serum creatinine. Most recently the international guideline group, Kidney Disease: Improving Global Outcomes (KDIGO) has brought together international experts from many different specialties to produce a definition and staging system that harmonises the previous definitions and staging systems proposed by both ADQI and AKIN. It is anticipated that this definition and staging system will be adopted globally. This will enable future comparisons of the incidence, outcomes and efficacy of therapeutic interventions for AKI.[1] To date there is a paucity of data on the incidence of AKI whether community or hospital-acquired.

Acute kidney injury is no longer considered to be an innocent bystander merely reflecting co-existent pathologies. It has been demonstrated to be an independent risk factor for mortality.[2-4] The cause of this is unclear but is possibly associated with an increased risk of “non-renal” complications such as bleeding and sepsis. An alternative explanation may lie in experimental work that has demonstrated the "distant effects" of ischaemic AKI on the other organs. In these experimental models isolated ischaemic AKI upregulates inflammatory mediators in other organs including the brain, lungs and heart.

In a recent study from a large tertiary care hospital in South India, AKI was seen in 41.1% of patients with tropical acute febrile illness with the most common causes being scrub typhus, malaria, salmonellosis, dengue and leptospirosis.[5] This is in contrast to developed countries (mostly located in cold temperate zones) where AKI is most often seen in older individuals who have co-morbidities and are admitted in hospitals for various reasons. It is important to note that with fast economic development, increasing life expectancy and high incidence of hypertension and diabetes, this form of hospital acquired AKI is also becoming important in tropical regions. Nevertheless, the burden of AKI especially infection related remains huge. Similarly, chronic kidney disease (CKD) in tropics also affects young, is diagnosed late and etiology remains unclear in 16% patients.[6]

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.[7] Moreover, some infections like malaria schistosomiasis, filariasis etc. have been associated with immunologic glomerular injury, which is often resistant to therapy and progresses overtime. Therefore, epidemiology of renal disease in tropics is greatly influenced by infections.

At times, it is diagnosed either incidentally or when patients develop CKD. Usually, multiple mechanisms are at play in an individual patient and it is difficult to distinguish between different types of infection only on the basis of clinical or biochemical manifestations.

A recent metaanalysis has showed 1 in 5 adults and 1 in 3 children worldwide experience AKI during a hospital episode of care.[8] In India, the incidence of hospital acquired renal failure varies from 4.9–7.2% and it is due to increasing use of nephrotoxic drugs, invasive procedures, intravascular catheters, major surgical procedure and sepsis. Mortality varies from 19–59%.[9] It is recognized that the epidemiology of AKI in developing countries differs from that of the developed world in many important ways. Whereas in developed regions elderly patients predominate, in developing countries, AKI is a disease of the young and children, in whom volume-responsive “prerenal” mechanisms are common. Although overall mortality seems to be lower than in developed countries, this finding is not true across all age groups: In these regions, AKI affects predominantly the young and children and mortality is

high.[10] During the monsoon season in Southeast Asia, the incidence of AKI may increase by 18 to 24% as a result of the increase in new cases of malaria, leptospirosis, acute gastroenteritis, and dysentery.[11]

Malaria represents an especially important problem. There is an upsurge in worldwide malarial incidence. In India, for example, the overall yearly incidence is 13 to 17.8% of malarial cases. Incidence is increasing in Africa, India, Thailand, and New Guinea. As its worldwide incidence increases, so are the complications of severe falciparum malaria, including AKI. Each year, 300 million people contract the disease, which will be responsible for more than 1 million yearly deaths in Africa alone. It is estimated that in 1% of cases (3000,000/yr), a combination of parasite and host factors will lead to severe malaria, jaundice, and AKI, a complication associated with 45% mortality; in areas of endemic malaria, the incidence of AKI may be >4% of malarial cases. Worldwide, the incidence of AKI as a result of malaria varies between 0.6 and 60% of malarial cases, depending on the region.[10]

Dengue Viral Infection imperils an estimated 2.5 billion people living in tropical and subtropical regions. The incidence of AKI is high at 14.2% among dengue patients, and those with AKI portended significant morbidity, mortality, longer hospital stay and poor renal outcomes.[12]

Leptospirosis is estimated to affect 0.1 to 1 per 100 000 people living in temperate climates are affected each year, with the number increasing to 10 or more per 100 000 people living in tropical climates. If there is an epidemic, the incidence can soar to 100 or more per 100000 people. The disease is underreported for many reasons, including difficulty in distinguishing clinical signs from those of other endemic diseases and a lack of appropriate diagnostic laboratory services. The incidence of AKI varies from 10% to 60%, depending on the severity of the disease, age, and definition of AKI.[13]

There are many more infectious causes which can produce short duration febrile illness with acute kidney injury…

MATERIALS AND METHODS

Study area

The study will be conducted in the inpatient department of Tropical Medicine in Calcutta School of Tropical Medicine.

Study population

Any febrile patient admitted in the department of tropical medicine in Calcutta School of Tropical Medicine during August 2015 to July 2016 fulfilling the inclusion criteria.

Study design

This will be a cross-sectional, observational, descriptive study.

Study duration

Total duration one year from August 2015 to July2016

Operational definitions

Acute kidney injury will be defined as **(KDIGO criteria)**

- Serum creatinine rises by ≥ 26.4µmol/L or ≥0.3mg/dl from the baseline value within 48 hours
  or
- Serum creatinine rises ≥ 1.5 fold from the baseline value which is known or presumed to have occurred within one week
  or
- Urine output is < 0.5ml/kg/hr for >6 consecutive hours

If the patient does not have a baseline serum creatinine value within one week of their admission or presentation it is acceptable to use a reference serum creatinine value within 3 months (acceptable up to one year)

1. If a reference serum creatinine value is not available within 3 months (acceptable up to one year) and AKI is suspected
   - repeat serum creatinine within 24 hours
   - a reference serum creatinine value can be estimated from the nadir serum creatinine value if patient recovers from AKI

Inclusion criteria

1. Those who are willing to participate in the study
2. Those who had a history of fever of less or equal to14 days.

Exclusion criteria

1. Those who are not willing to participate in the study
2. Those with established chronic kidney disease

Sample size

All the patients admitted in Calcutta School of Tropical Medicine fulfilling the inclusion criteria within the study period will be included in the study sample. At least 100 subjects will be included in the study population.

Study technique

We will screen all the patients admitted in the Carmichael hospital for tropical diseases with a history of fever of less than fourteen days. Those who found to have an established AKI as per operational definition will be evaluated further for aetiology of fever (they will be provided appropriate therapy for fever) and outcome analysis of AKI will be done by doing a repeat creatinine value on seventh day, if value does not return back to baseline we will repeat it again on fourteenth day and twenty eighth day and after ninety days of fever or may be in between if necessary. All biochemical parameters will be estimated in the same laboratory.

Tools of study

1. Predesigned and pretested schedule

2. Past prescriptions/ OPD tickets/ investigation reports
3. History and clinical examinations
4. Thermometer
5. Urometer

Laboratory specimens

1. Serum creatinine value on date of admission, after 48hrs, on day seven and if necessary on day fourteenth, twenty eighth and after ninety days or in between.
2. Other blood investigations listed below to find out the cause of fever

- Complete haemogram
- Liver function test
- Routine microscopic examination of urine and culture sensitivity test if necessary
- Chest X-ray PA view
- Ultrasonography of whole abdomen
- Blood culture and sensitivity
- Blood for malaria parasites
- Blood for dengue NS_1 /IgM antibody
- Other tests to evaluate the cause of fever which are clinically justified

Statistical analysis

Data collected will be compiled and analysed using appropriate statistical methods

RESULT & ANALYSIS

A total of 151 patients reporting during the study period who fulfilled inclusion and exclusion criteria were included. All of them were admitted in different wards or CCU.

1. Age of the Population

The mean age of the study population was 32.97years with minimum age of 8 yrs to maximum age of 78yrs.

Table 1: Distribution Of Patient According To Different Age Groups.

AGE GROUPS	NUMBER OF PATIENTS
0-10	5
11-20	39
21-30	33
31-40	29
41-50	21
51-60	17
>60	7

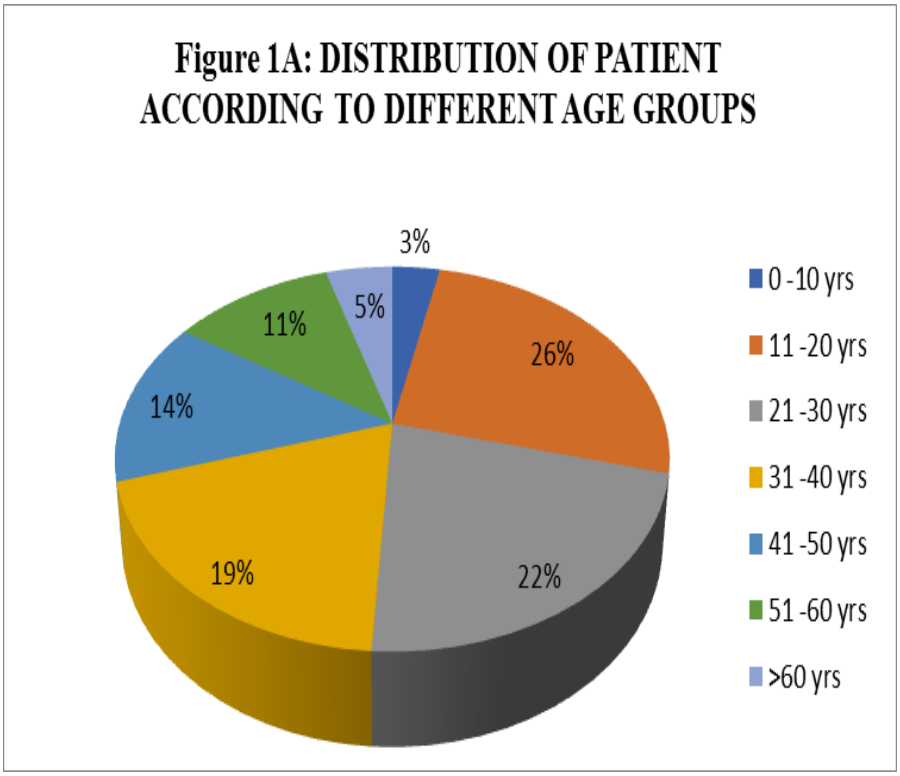
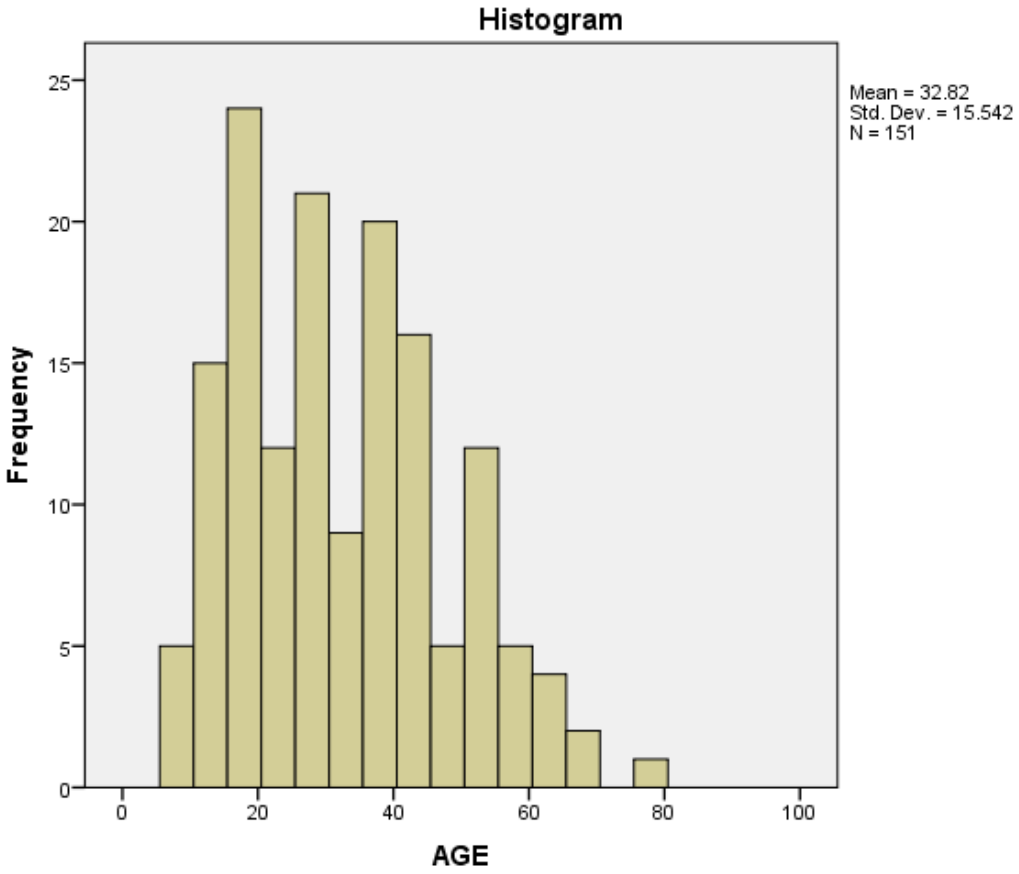


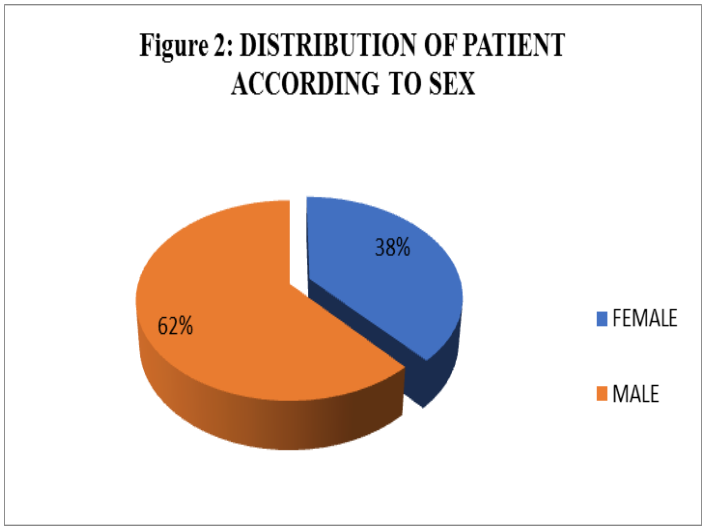
Figure 1B: Histogram And Normal Distribution Curve Showing Normally Distributed Age Of The Sample Population.



3. Distribution of study population according to gender

Table 2: Distribution Of Patients According To Sex.

	Frequency	Percent
FEMALE	**58**	**38.4**
MALE	**93**	**61.6**
Total	**151**	**100.0**



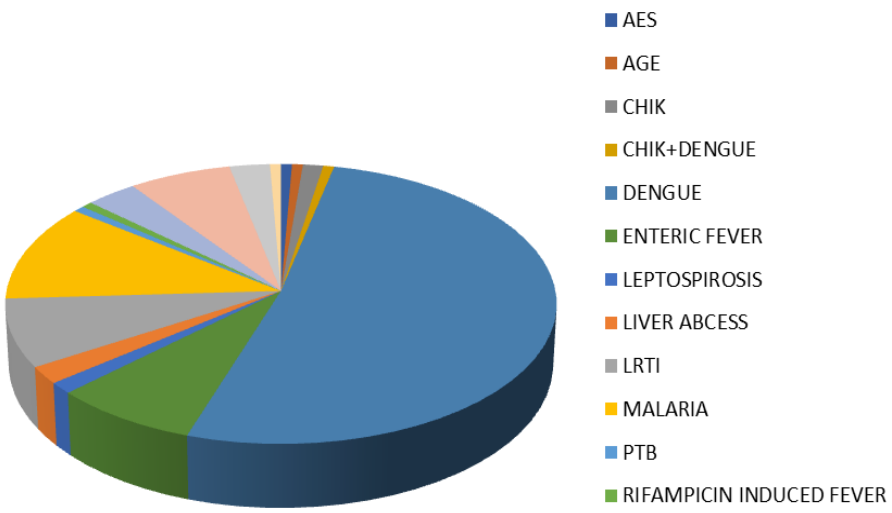
4. Distribution of study population according to etiology of fever

Among 151 patients, etiology was identified in 141 patients while 10 remained undiagnosed, although fever subsided in them with treatment.

Table 3: Distribution Of Diseases Among Study Population.

DIAGNOSIS	Frequency	Percent
AES	1	0.7
AGE	1	0.7
CHIK	2	1.3
CHIK+DENGUE	1	0.7
DENGUE	78	51.7
ENTERIC FEVER	12	7.9
LEPTOSPIROSIS	2	1.3
LIVER ABCESS	3	2.0
LRTI	12	7.9
MALARIA	17	11.3
PTB	1	0.7
RIFAMPICIN INDUCED FEVER	1	0.7
SCRUB	5	3.3
UNDIFFERENTIATED	10	6.6
UTI	4	2.6
UTI+ DENGUE	1	0.7
Total	151	100.0

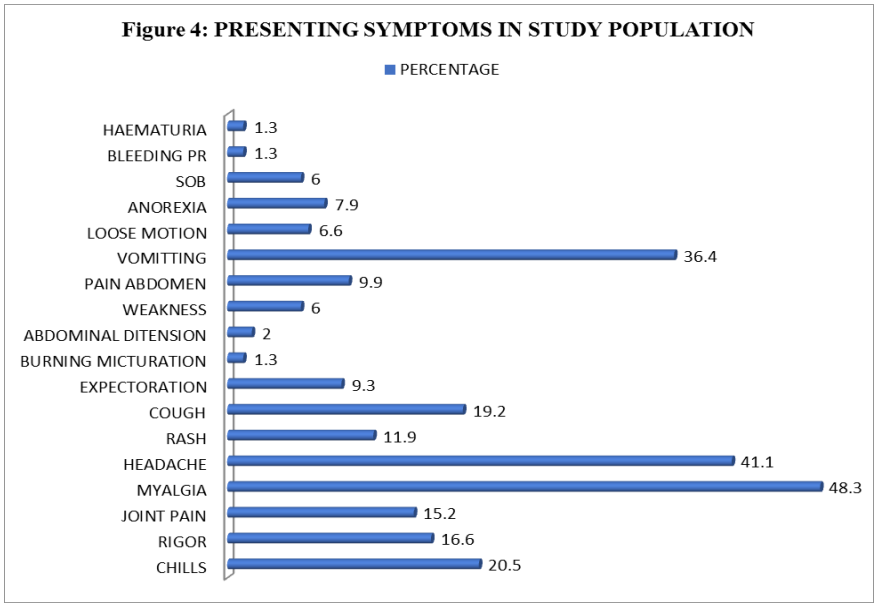
Figure 3: DISTRIBUTION OF DISEASES AMONG STUDY POPULATION



In the study population (n=151) most common cause of short duration fever was found to be dengue (51.7%) followed by malaria (11.3%). The other causes were enteric fever (7.9%), lower respiratory tract infection (7.9%), scrub typhus (3.3%), They were followed by urinary tract infection (n=4), liver abscess (n=3), multiple co infection (n=2), chikunguniya (n=2), leptospirosis (n=2), acute gastroenteritis (n=1), pulmonary tuberculosis (n=1), rifampicin induced fever (n=1). In 10 cases (6.6%) etiology could not be identified and they were labelled as undifferentiated fever.

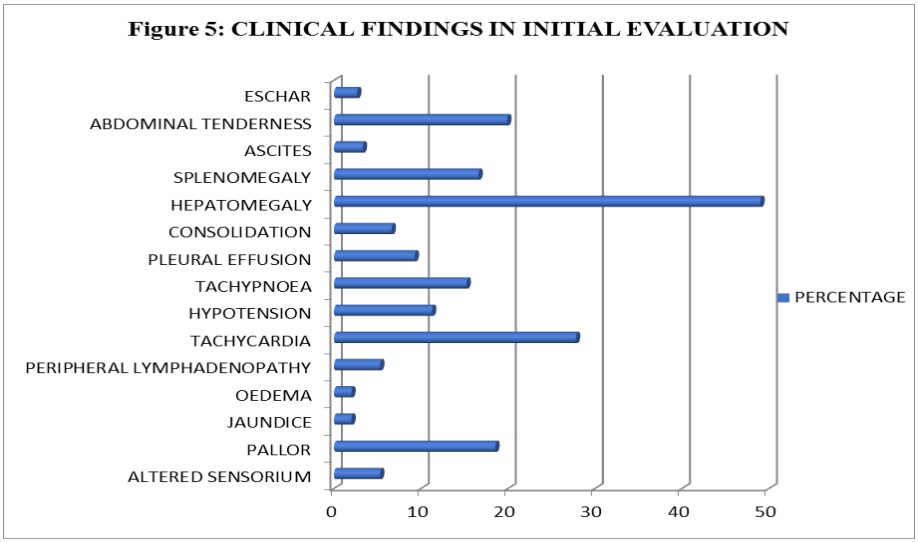
4. Common presenting symptoms in study population

Myalgia (48.3%) was the commonest presenting complaintfollowed by headache (41.1%), vomiting (36.4%), chills (19.2%), cough (19.2%), rigor (16.6%), joint pain (15.2%), rash (11.9%), pain abdomen (9.9%), expectoration (9.3%), loose motion (6.6%), shortness of breath(6%). 2 patients presented with haematuria and 2 patients presented with melaena.



5. Clinical findings in initial evaluation among study population

Commonest clinical finding in the study population was hepatomegaly (49%) followed by splenomegaly (16.6%). Tachycardia was present at the time of admission in 27.8% cases and hypotension in 11.26% of cases. Other important findings were pallor (18.54%), upper abdominal tenderness (19.9%), pleural effusion (9.27%), consolidation (6.62%). 8 patients (5.3%) had altered sensorium and 4 patients had definite eschar in the body.

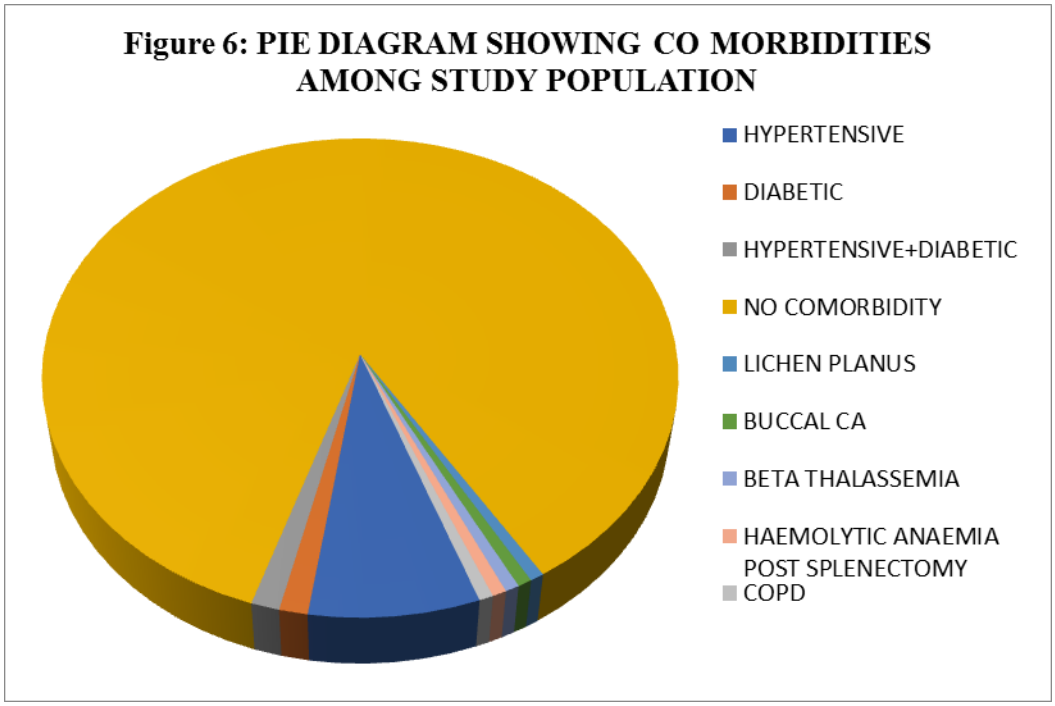


6. Co morbidities among study population

Most of the study patients (86.1%) did not have any associated illness or co morbidities. 12 patients (7.94%) had hypertension and 2 had diabetes. 2 patients had both diabetes and hypertension. Others are described in the chart below.

Table 6: Co Morbidities Among Study Population.

CO MORBIDITIES	NO OF PATIENTS
HYPERTENSIVE	12
DIABETIC	2
HYPERTENSIVE+DIABETIC	2
NO COMORBIDITY	130
LICHEN PLANUS	1
BUCCAL CA	1
BETA THALASSEMIA	1
HAEMOLYTIC ANAEMIA POST SPLENECTOMY	1
COPD	1



6. Duration of illness at the time of admission

The mean duration of illness at the time of admission was 6.41 days with a standard deviation of 3.293. The minimum duration was 1 day to a maximum of 14 days.

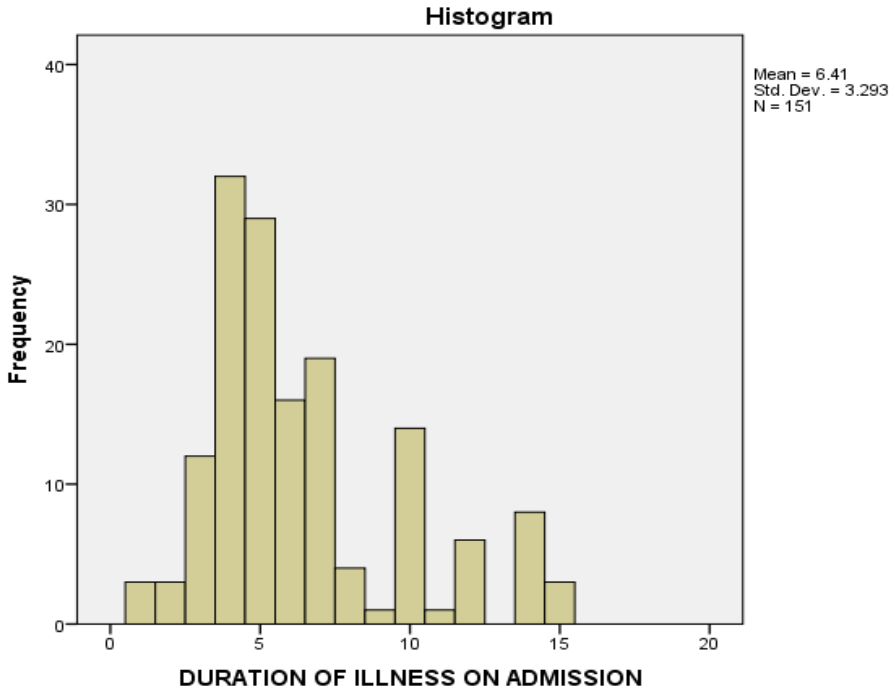


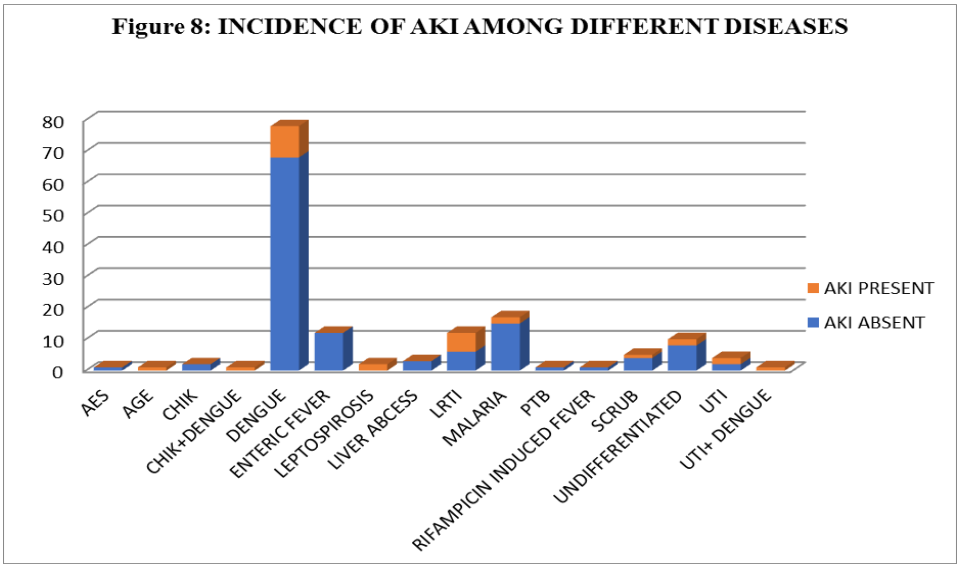
Figure 7: Histogram Showing Duration Of Illness On Admission.

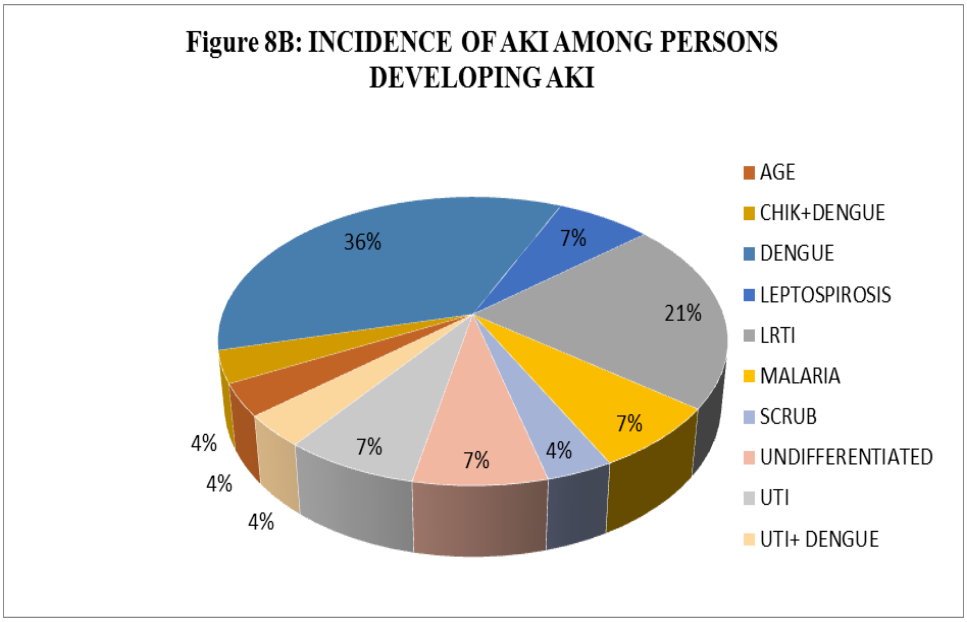
8. Incidence of acute kidney injury in different diseases among study population.

Out of the 151 patients 28 (18.54%) were diagnosed to have acute kidney injury. Dengue was found to be the most common etiology (n=10) of AKI although it was also the commonest illness in study population. Lower respiratory tract infection was the second contributing factor (n=6), followed by mixed infections (n=3), leptospirosis (n=2), urinary tract infection (n=2), undifferentiated fever (n=2). Others were malaria (n=2), scrub typhus (n=1), acute gastroenteritis (n=1).

Table 8: Incidence Of Aki In Different Diseases.

DIAGNOSIS	AKI ABSENT	AKI PRESENT	TOTAL
AES	1	0	1
AGE	0	1	1
CHIK	2	0	2
CHIK+DENGUE	0	1	1
DENGUE	68	10	78
ENTERIC FEVER	12	0	12
LEPTOSPIROSIS	0	2	2
LIVER ABCESS	3	0	3
LRTI	6	6	12
MALARIA	15	2	17
PTB	1	0	1
RIFAMPICIN INDUCED FEVER	1	0	1
SCRUB	4	1	5
UNDIFFERENTIATED	8	2	10
UTI	2	2	4
UTI+ DENGUE	0	1	1
TOTAL	123	28	151



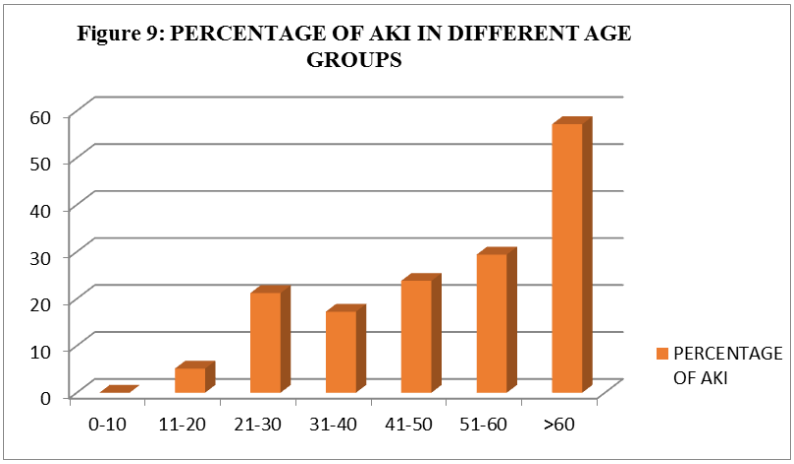


9. Incidence of acute kidney injury in different age groups

Acute kidney injury was found to be present in all age groups above 20 years in similar frequency except in persons aged more than 60 yrs.

Table 9: Aki In Different Age Groups.

AGE	NUMBER OF PATIENTS	NUMBER OF PATIENTS WITH AKI	PERCENTAGE OF AKI
0-10	5	0	0
11-20	39	2	5.13
21-30	33	7	21.2
31-40	29	5	17.24
41-50	21	5	23.8
51-60	17	5	29.4
>60	7	4	57.14

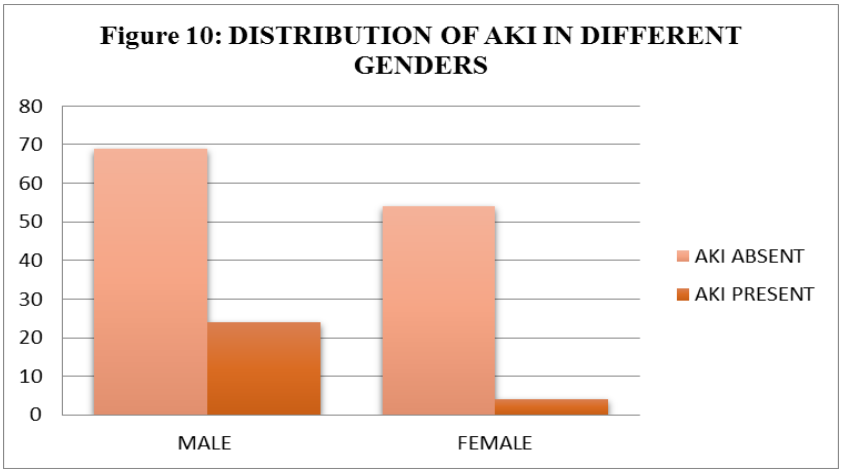


Out of 144 patients aged less or equal to 60 years 24 patients developed acute kidney injury. But out of 7 patients aged more or equal to 60 years 4 patients developed AKI, with an incidence rate of 57.14%. The correlation is also found to be significant by Fisher exact two tailed test (p= 0.0226).

10. Distribution of AKI in different gender of study population

25.8% male patients in this study population had AKI compared to only 6.9% involvement in female group. The findings of male preponderance also found to be statiscally significant (The two-tailed P value equals 0.0045).

	AKI PRESENT	AKI ABSENT	% OF POSITIVITY
MALE	24	69	25.8
FEMALE	4	54	6.9

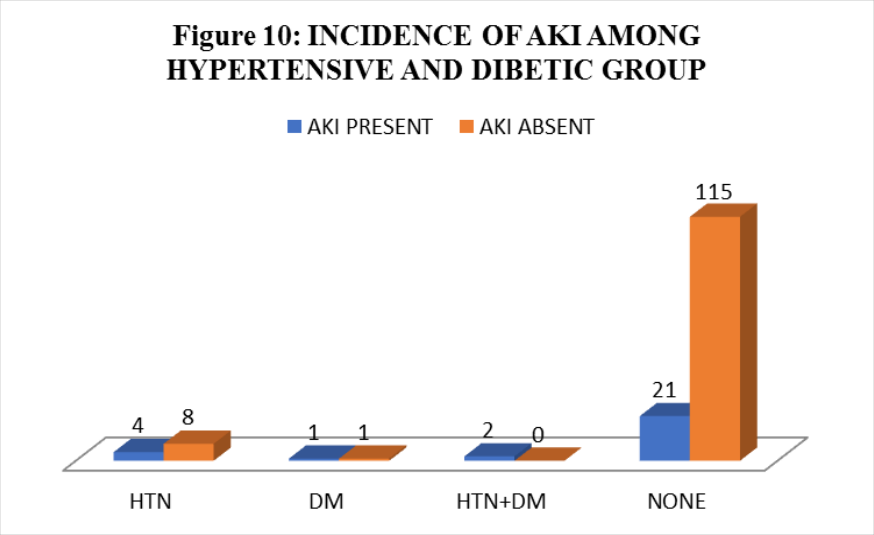


10. Association of major pre existing co morbidities and acute kidney injury

Among the study population 12 patients had hypertension, 2 patients had diabetes mellitus and 2 patients had both diabetes and hypertension. 4 out of those 12 hypertensive cases and one of the 2 diabetics developed acute kidney injury. Those 2 patients with both diabetes and hypertension developed AKI. The correlation was also found to be statistically insignificant by logistic regression method.

Table 10: Incidence of diabetes and hypertension in study population and also in AKI.

	AKI PRESENT	AKI ABSENT
HYPERTENSIVE	4	8
DIABETIC	1	1
HYPERTENSIVE+DIABETIC	2	0
NONHYPERTENSIVE+NONDIABETIC	21	115



12. Duration of hospital stay in study population

Mean duration of hospital stay in patient with acute kidney injury is higher than patient without AKI. The correlation was also found to be statistically significant [The two-tailed P value is less than 0.0001].

Table 12: Duration of hospital stay in AKI and non AKI group.

GROUP	HOSPITAL STAY IN AKI	HOSPITAL STAY IN NON AKI
MEAN	8.63	4.59
SD	4.76	2.22
SEM	0.92	0.20
N	27	123

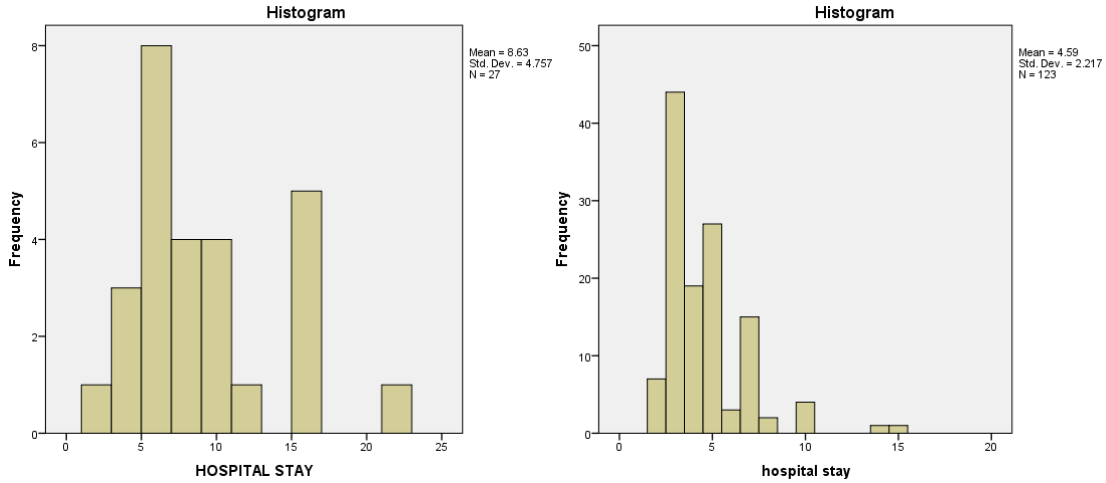


Figure 12: Histogram showing distribution of duration of hospital stay among AKI and non AKI group.

13. Association of hypotension as clinical finding and acute kidney injury

Out of the 151 patients, 17 presented with hypotension. 9 of them were managed by fluid replacement. Rest required additional ionotropic support. Out of those 17 cases 8 developed acute kidney injury. The correlation was also found to be significant by Fisher's exact two tail test (P value is 0.0040)

Table 13: Association hypotension as clinical finding and occurrence of AKI.

		AKI		Total
		N	Y	
HYPOTENSION	N	114	20	134
	Y	9	8	17
Total		123	28	151

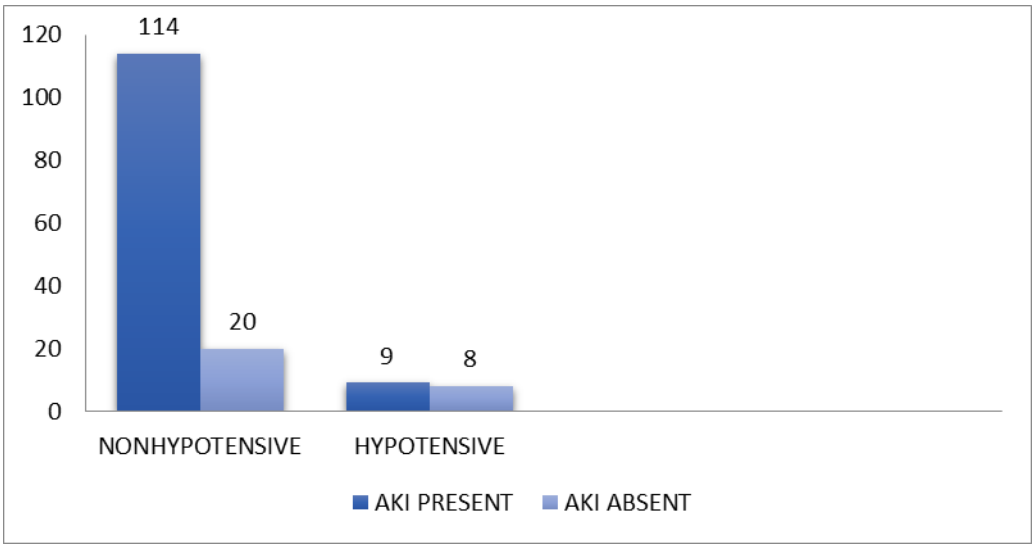


Figure 13: Correlation of Hypotension on presentation and occurrence of AKI.

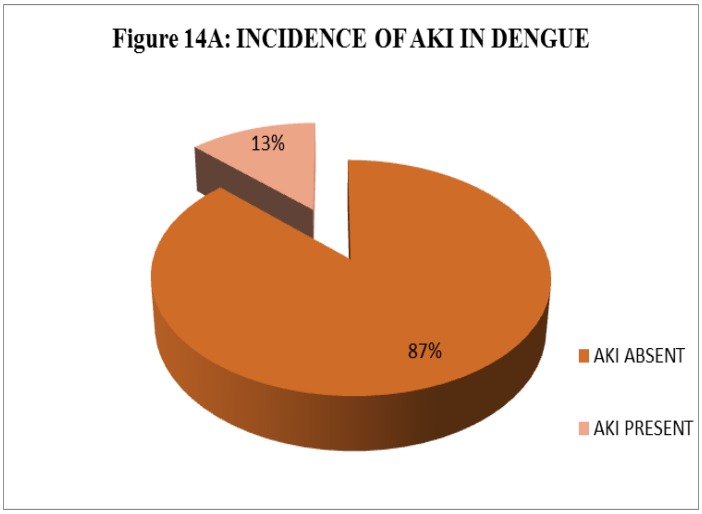
14. Incidence of acute kidney injury in different diseases

A. Dengue

The major etiology of fever in the study group is dengue (51.3%). This huge burden of dengue was due to the epidemic of dengue which was going on during the study period. 12% of cases (out of 77) developed acute kidney injury. The only dengue patient who died had AKI.

Table 14A: Incidence of AKI in Dengue.

AKI	Frequency	Percent
N	68	87.2
Y	10	12.8
Total	78	100.0

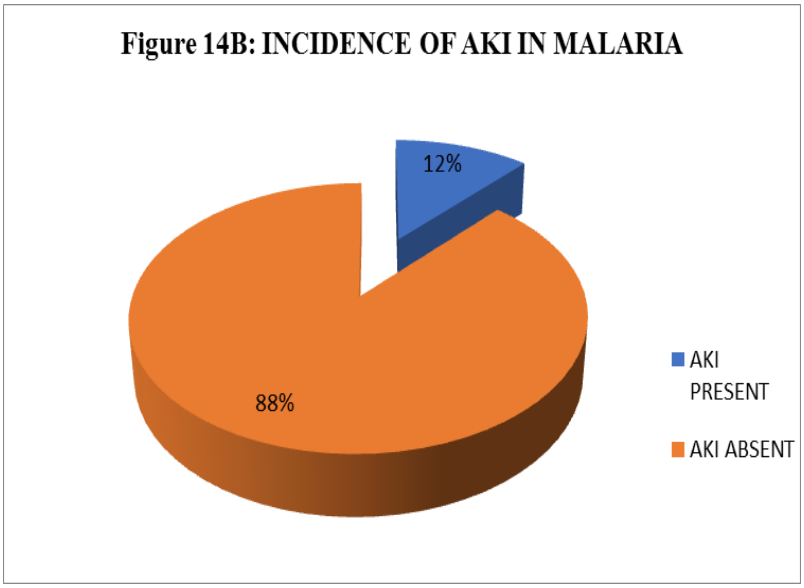


B. Malaria

Malaria was found in 17 patients, of which 15 were due to P. vivax infection and one due to P. falciparum. Out of these 16 patients, 2 patients with P.vivax malaria developed AKI .

Table 14B: Incidence of AKI in Malaria.

AKI	Frequency	Percentage
Y	2	11.8
N	15	88.2
Total	17	100

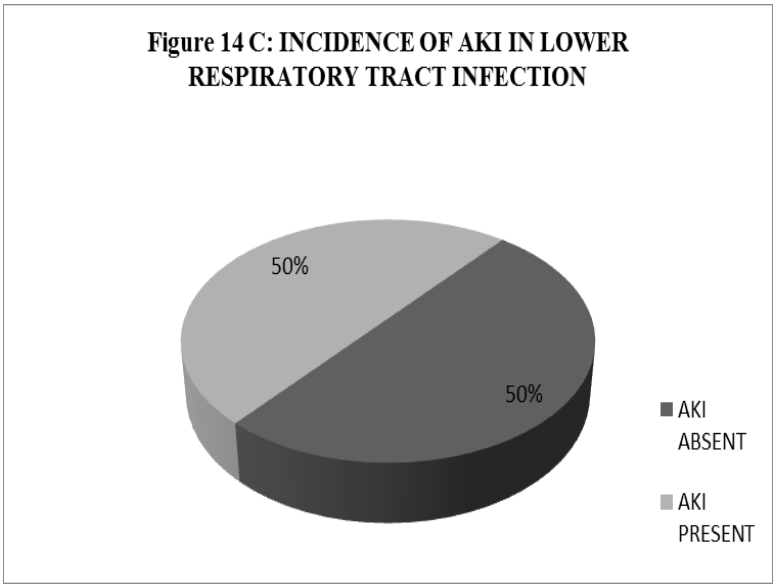


C. Lower respiratory tract infection

In the study population 12 patients were found to be suffering from lower respiratory tract infection. Of them 50% was developed acute kidney injury. The only patient who died in this group had AKI.

Table 14C: Incidence of AKI in LRTI.

AKI	Frequency	Percent
N	6	50.0
Y	6	50.0
Total	12	100.0

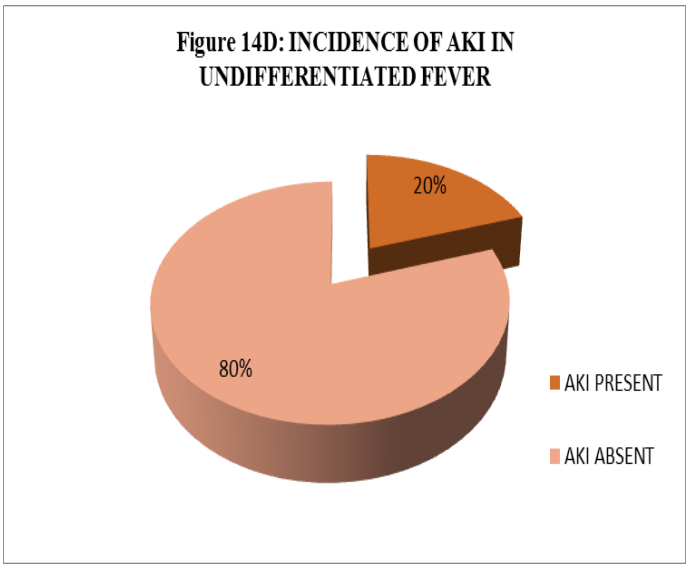


D. Undifferentiated fever

10 cases remain undiagnosed in the study group. In this group 20% patients were found to have AKI.

Table 14D: Incidence of AKI in Undifferentiated fever.

AKI	Frequency	Percent
N	8	80.0
Y	2	20.0
Total	10	100.0

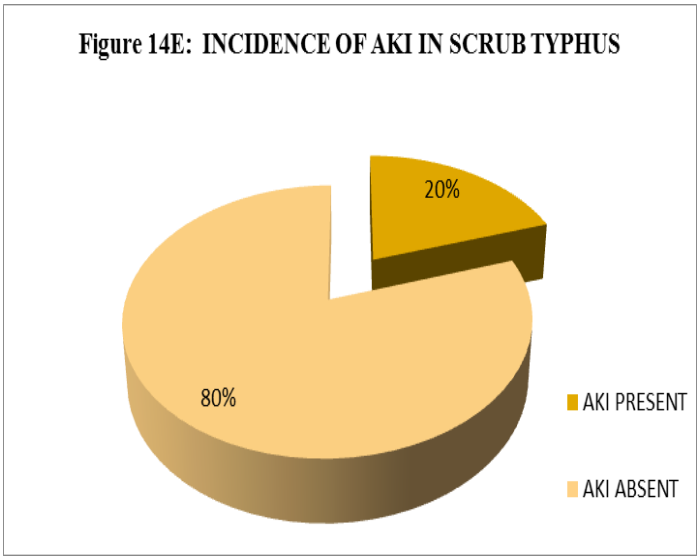


E. Scrub typhus

Five patients were diagnosed as scrub typhus. Of them 1 patient had AKI.

Table 14E: Incidence of AKI in Scrub typhus.

AKI	Frequency	Percent
N	4	80.0
Y	1	20.0
Total	5	100.0



F. Leptospirosis

2 patients of leptospirosis developed AKI (incidence 100%) and resolved conservatively without renal replacement therapy.

G. Others

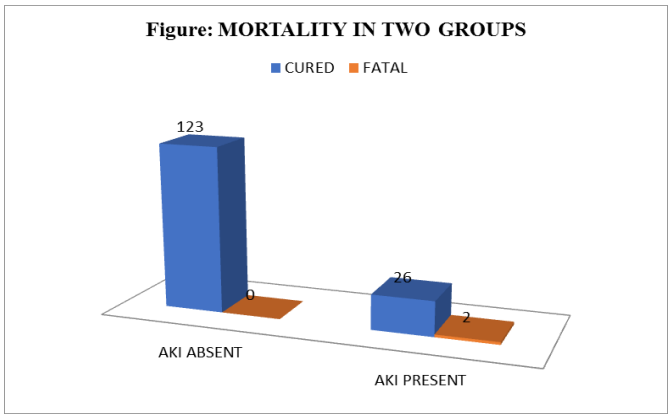
50% of patients with urinary tract infection (n=4) had AKI. Those 2 patients with mixed infections (dengue & chikunguniya, dengue & urinary tract infection) developed AKI. The single patient in study population with acute gastroenteritis had AKI.

15. Correlation of acute kidney injury and mortality

2 out of 28 patients with acute kidney injury died. But there was no death in patients without acute kidney injury. There was significant correlation between acute kidney injury and mortality by Fisher's exact two tail test (p= 0.0374).

Table 15: Association Of Aki With Mortality.

		FATAL		Total
		N	Y	
AKI	N	123	0	123
	Y	26	2	28
Total		149	2	151



16. Time required for correction of AKI in the affected group:

Out of the 28 patients with AKI one died before reverting to normal renal function. Rest of the patients reverted to normal renal function within the period of hospital stay. The mean duration was 4.15 days with minimum being 1 day to maximum of 11 days. No one needed renal replacement therapy during the course of illness.

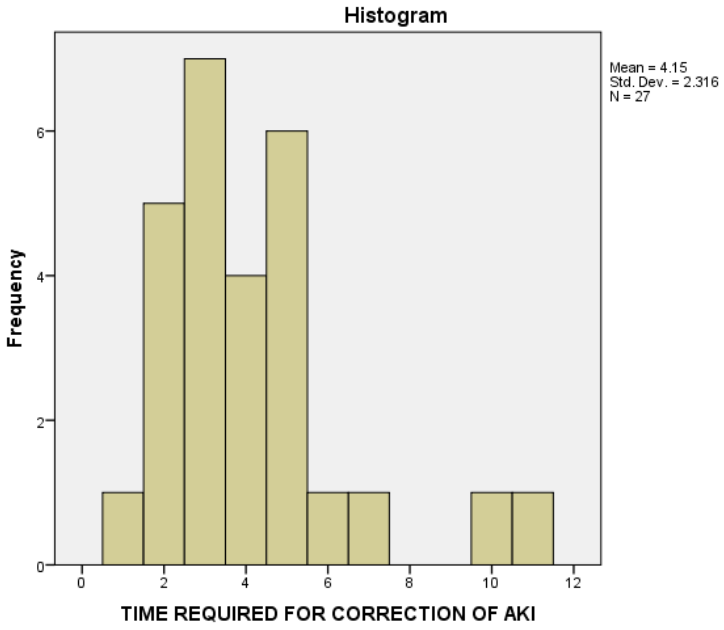


Figure 16: Histogram Showing Time Required For Crrection Of Aki.

17. Correlation of drugs with development of AKI

It is not possible to derive conclusions regarding other predisposing factors such as drug exposure. Most of the patients were not exposed to any kind of drugs (except Paracetamol) prior to hospital admission. And rest of the patients are exposed to mostly nonnephrotoxic drugs.

DISCUSSION

Acute febrile illnesses are a common cause of AKI in the developing countries. In this prospective study from a tertiary care centre in eastern India, the common acute febrile illnesses among hospitalized patients included dengue, malaria, typhoid, lower respiratory tract infection, scrub typhus, urinary tract infection, leptospirosis, mixed infections and others. Dengue accounted for the majority of acute febrile illnesses in our study. The incidence of dengue in the study population was much higher, because an epidemic was going on during the study period in the locality harboring medical access through the institution.

The incidence of AKI was 18.54% in this study group. The rate was much higher than the study by Kaul et al in SGPGI, which showed only 2.5% incidence of community acquired AKI.[14] One of the reason for such low incidence in that study was that, it included all the admission in that hospital including obstetric and surgical cases, which has a comparatively low incidence of AKI than medical admission. The incidence in present study was much less than the reported incidences from a South Indian study by Basu et al. which showed an incidence of 41.1%.[15] One of the reasons for lesser incidence in present study is lack emergency admission in our hospital and restricted pediatric admission.

The predominant population in the study was from the rural and the suburban regions, people having to travel long distances to reach our hospital. Patients usually do not have health insurance coverage or check-up, and hospital visits are usually for major illnesses. Therefore, most patients do not have a pre-admission baseline serum creatinine. Patients with AKI had a significantly higher Cr on admission, as all patients developed AKI prior to admission. Therefore, Cr on admission could not be used as a marker of baseline renal function.

The patient population is predominantly young (mean age of 32.97 ±15.5 years) with a minority being elderly (4.63%). Few are suffering from diabetes (2.67%) or hypertension (9.33%). 61.3% patients in study population are male. These characteristics are almost similar to the study conducted by Basu et al.[15]

AKI was associated with higher age group, the elderly and patients with a severe illness, presenting with shock, tachycardia, tachypnoea, breathlessness, oliguria and icterus. 17 patients presented with hypotension. 52.9% patient out of them had AKI which is statistically significant (p=0.0040). This observation is also supported by Li Wei et al.[16] Diabetics and hypertensives had a relatively higher incidence of AKI, though not statistically significant because of small numbers. These associations would help in selecting patients for initiating effective therapeutic/preventive strategies against AKI at the primary care level. This finding is also similar to the study by Basu et al.

Dengue disease has emerged globally as the most frequent and medically relevant viral infection transmitted by a mosquito bite (Aedes aegypti). It is diagnosed by Dengue NS1 (by ELISA method) or by Dengue IgM reactivity. 25.83% of patients affected with dengue have a platelet count less than 50000/cmm during hospital admission. Out of them 3 patients had a platelet count of less or equal to 10000/cmm. 4 patients presented with bleeding manifestation. 12.8% patient had AKI. One of the patients in this group died who had a established AKI. This finding is almost similar to the findings published in PLOS journal by Malhi et al, which had a 14.2% incidence of AKI by AKIN criteria.[17] Khalil et al also showed similar incidence (13.3%) of AKI among dengue infection.[18] A study from Madras Mission hospital showed little less incidence of AKI (10.8%) among study population.[19] All the patients in this group have a transaminase abnormality with 24.7% patient having a SGOT level more than 200 IU/L (max=2320IU/L). 84.4% patients had a higher SGOT than SGPT level. These findings are similar to a study published in American Journal of the Medical Sciences by C D Salgado et al.[20] Two other patients had co infection with dengue i.e. Chikungunya and UTI in one each. Both of them had AKI and responded to treatment.

Malaria is the next most common cause of acute febrile illness in our study group. 16 out of the 17 cases were due to P. vivax malaria and rest due to P. falciparum. In contrast to commonly reported association of acute kidney injury and multi organ failure with P. falciparum malaria present study observed a significant percentage of vivax malaria having multi organ involvement. 17.64% patient with P. vivax had multi organ dysfunction in the study population. 87.5% patient had thrombocytopenia (platelet count<150000/cmm) with 56.2% patient had a platelet count of less than 100000/cmm. This finding is corroborated with the findings by Patil et al who showed 89.2% haematological abnormality in severe vivax malaria.[21] 11.8% patient with P. vivax infection had an established diagnosis of AKI. There was a similar finding in the study from Sardar Patel Medical College, Bikaner, by P. Ratan et al, which showed 10.4% incidence of AKI in P. vivax infection.[22]

Lower respiratory tract infection is found to be the third most common etiology in the study group. 50% patients developed AKI in this group. Etiological agent of LRTI could not be identified in 59% of cases. The most common etiological agent identified was Streptococcus pyogenes. All patients in this group who had AKI were aged more than 60 years. One of them died, rest reverted

to normal kidney function and discharged in a haemodynamically stable condition. The incidence rate in this group is much higher than the percentage documented in the literature. One of the reasons may be that all the patients in this group are more than 60 years which itself has a high incidence of AKI. Another cause may be most of the patients were suffering from sepsis which is an independent predictor of AKI.

In our study, AKI was observed in 20% of patients with scrub typhus. It is similar to the findings of the study done in Republic of Korea, which had an incidence of 21.1% among study population. Another study by Attur et al also showed similar incidence rate (23.2%).[23]

The incidence of Leptospirosis in this study was only 1.3% (n=2). This incidence rate was much lower than that observed in centres with humid, marshy environment and higher rainfall. Another cause may be lack of investigations in our resource poor settings. All the patients suffered AKI, though none of them died or required RRT. AKI is predominantly a non-oliguric type.

Urinary tract infection was documented in 2.6% of patients. Out of them 50% developed AKI. As previously explained, one patient with UTI and dengue had AKI.

Only one patient had a diagnosis of acute gastroenteritis and he had AKI. The admission rate of these diseases is markedly low probably due to absence of emergency admission in our institute.
Despite the use of a standard battery of tests for acute febrile illness, the aetiology of fever could not be ascertained in 6.7% of the patients, who had higher percentage (20%) of AKI without any mortality.

Out of the 28 patients with AKI one patient died before reverting to normal renal function. Rest of the patients reverted to normal renal function within the period of hospital stay. The mean duration was 4.19 days with a SD of 2.35 days. No one needed renal replacement therapy during the course of illness.

The study showed significantly higher incidence of AKI in older age group (age>=60yrs) (p=0.0226). It also observed a significant correlation of AKI with mortality (p=0.0374). AKI increased hospital stay (p<0.0001), thus increasing the morbidity also. These findings also supported by the study of Basu et al.

The study also indicated higher incidence of AKI among male gender (p=0.0040). This finding was supported by the study of Iwagami et al.

Considering there is a high incidence of AKI, a significant risk factor for death among the large number of patients admitted with acute febrile illness in a tertiary hospital, validation of KDIGO criteria assumes great importance. Apart from increased mortality, longer duration of hospital stay and the requirement of renal replacement therapy, the loss of the young workforce adds to the economic burden. It is now possible to identify patients at an early stage of AKI using these criteria and study effective therapeutic or preventive measures that can contain and prevent AKI reducing morbidity and mortality thus saving money and lives.

This tertiary hospital data, with its inherent referral bias arising from more ill patients reaching a tertiary care centre, presence of dengue epidemic and absence of emergency admission, may overestimate or underestimate the incidence of AKI. Though patients who are ill get referred to larger centers, 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. Health administrators should think of strategies to train primary care physicians on early diagnosis of AKI for identifying these patients and refer them to appropriate levels of care to reduce morbidity and mortality. In addition, as this relatively young population is studied only at hospitalization (without any background information on pre-existing renal status) and the renal dysfunction is thought to be acute, the possibility of a small proportion having an acute on chronic renal failure cannot be excluded.

CONCLUSION

- In this study we found dengue is the most common etiology of fever, followed by malaria, respiratory tract infection, enteric fever, scrub typhus, urinary tract infection and others. 6.6% patient remain undiagnosed despite battery of tests which ever possible in our resource poor setting.
- 18.54% patient of the study population developed acute kidney injury with dengue being the most common contributing disease.
- 17.64% of patient infected with P.vivax developed multiorgan dysfunction syndrome with an incidence rate of AKI of 11.8%.
- The incidences of AKI in different disease conditions in this study found to be similar as found in other literature.
- Acute kidney injury was most common among older age group.
- AKI is common among male gender.
- AKI has a strong correlation with hypotension at presentation.
- Two patients with AKI died during the course of the study. Rest reverted to normal without any requirement of renal replacement therapy.

- Acute kidney injury is a significant risk factor for mortality and it is also associated with increased hospital stay.

- KDIGO criteria is valid and applicable in AKI related to acute febrile illnesses in tropical countries showing both an incremental risk of in hospital mortality and increased duration of hospital stay.

- Although the incidence of AKI in diabetic and hypertensive group is higher but it is not statistically significant in this study and also other related studies due to low sample size. So it remains an open area for research in near future.

BIBLIOGRAPHY

1. *CLINICAL PRACTICE GUIDELINES ACUTE KIDNEY INJURY UK Renal Association 5th Edition, 2010. www.renal.org/guidelines*
2. *Chertow GM, Levy EM, Hammermeister KE et al. Independent association between acute renal failure and mortality following cardiac surgery. Am J Med, 1998; 104: 343-348.*
3. *Levy EM, Viscoli CM, Horwitz RI. The effect of acute renal failure on mortality: a cohort analysis. JAMA, 1996; 275: 1489-1494*
4. *Uchino S, Bellomo R, Goldsmith D et al. An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. Crit Care Med, 2006; 34: 1913-1917.*
5. *Acute kidney injury in tropical acute febrile illness in a tertiary care centre—RIFLE criteria validation Nephrol. Dial. Transplant, 2011; 26(2): 524531. doi: 10.1093/ndt/gfq477 First published online: August 11, 2010*
6. *Rajapurkar MM, John GT, Kirpalani AL, et al. What do we know about chronic kidney disease in India: firstreport of the Indian CKD registry. BMC nephrology, 2012; 13: 10.*
7. *Leung KC, Tonelli M, James MT. Chronic kidney disease following acute kidney injury-risk and outcomes. Nature reviews Nephrology, 2013; 9: 77-85.*
8. *Clin J Am Soc Nephrol, 2013; 8(9): 148293. doi: 10.2215/CJN.00710113. Epub*
9. *Biradar V, Urmila A, Renuka S, et al. Clinical spectrum of hospital acquired renal failure: a study from tertiary care hospital. Indian J Nephrol, 2004; 14: 93-6.*
10. *Clin J Am Soc Nephrol, 2008; 3: 881-886. doi: 10.2215/CJN.04961107*
11. *Chitalia VC, Almeida AF, Rai H, Bapat M, Chitalia KV, Acharya VN, Khanna R: Is peritoneal dialysis adequate for hypercatabolic acute renal failure in developing countries? Kidney Int, 2002; 61: 747–757.*
12. *Incidence, Characteristics and Risk Factors of Acute Kidney Injury among Dengue Patients: A Retrospective Analysis Published, 2015; 30. http://dx.doi.org/10.1371/journal.pone.0138465*
13. *WHO | Leptospirosis Burden Epidemiology Reference Group (LERG), 2016.*
14. *Spectrum of community acquired acute kidney injury in India: a retrospective study.Kaul A , Sharma RK, Tripathi R, Suresh KJ, Bhatt S, Prasad N. Saudi J Kidney Dis Transpl. 2012; 23(3): 61928.*
15. *Basu G, Chrispal A, Boorugu H, et al. Acute kidney injury in tropical acute febrile illness in a tertiary care centre–RIFLE criteria validation. Nephrol Dial Transplant, 2011; 26: 524–531. [PubMed]*
16. *Hypotension as a Risk Factor for Acute Kidney Injury in ICU Patients Li-wei Lehman1, Mohammed Saeed1,2, George Moody1, and Roger Mark11 Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA, USA Comput Cardiol, 2010; 1095–1098.*
17. *Incidence, Characteristics and Risk Factors of Acute Kidney Injury among Dengue Patients:A Retrospective Analysis Tauqeer Hussain Mallhi1,2*, Amer Hayat Khan1,2, Azreen Syazril Adnan2, Azmi Sarriff1,Yusra Habib Khan1,2, Fauziah Jummaat.3*
18. *Acute kidney injury in dengue virus infection Muhammad A.M. Khalil, Sarfaraz Sarwar, Muhammad A. Chaudry, Baila Maqbool, Zarghoona Khalil, Jackson Tan, Sonia Yaqub and Syed A. Hussain, Clin Kidney J, 2012; 5: 390–394. doi: 10.1093/ckj/sfs117*
19. *Acute kidney injury in dengue fever using Acute Kidney Injury Network criteria: incidence and risk factorsNikita Mehra, Amish Patel, Georgi Abraham, Yogesh N V Reddy, Yuvaram N V Reddy, doi: 10.1258/td.2012.120023 Trop Doct, 2012; 42.*
20. *Dengue Fever Presenting with Hepatitis Seth Bowman, MD, Cassandra Salgado, MD and Deborah J. DeWaay, MD Am J Med Sci, 2012; 344(4): 335–336.*
21. *Multiorgan Dysfunction in Plasmodium vivax Malaria: A Prospective Study Dilip R Patil1 , S D Nikumbh2 , Akhil Parulekar2 , Kedar Roplekar2 International Journal of Scientific Study, 2015; 3; 5.*
22. *Clinical Profile of Multiorgan Involvement in Malaria P Ratan, KC Nayak, S Kumar, V Singh, BK Gupta, M Sisodiya, V Tundwal, V Kulkarni, A Vyas Indian Journal of Clinical Practice, 2013; 24; 3.*
23. *Clinical profile and improving mortality trend of scrub typhus in South India George M. Varghese Press enter key for correspondence information Press enter key to Email the author Paul Trowbridge Jeshina Janardhanan Kurien Thomas John V. Peter Prasad Mathews Ooriapadickal C. Abraham M.L. Kavitha*