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OCCURRENCE AND OUTCOME OF PATIENTS ADMITTED WITH HISTORY OF FEVER IN INTENSIVE CARE UNIT: A PROSPECTIVE STUDY

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ABSTRACT **BACKGROUND** Pyrexia is one of the commonest symptoms of various underlying serious diseases, it perplexing to medical professionals due to its varied aetiologies and pathophysiologies. Viruses and bacteria are responsible for different types of infectious diseases. When the duration of fever is more than seven days, etiology can be varied and usually patients are admitted for evaluation. The purpose of our study was to describe the occurrence and outcome of patients admitted with history of fever in intensive care unit. **METHOD** This was a prospective study conducted in tertiary care hospital and attached medical college for a period of 5 months (from July 2021 to November 2021) in 26 bedded medical intensive care unit, in patients of age group (18-80 years). Total 50 patients presenting with acute febrile illness, who tested positive for dengue serology, malaria antigen or slide test, salmonella typhi or para typhi and scrub typhus, pyrexia of unknown origin were included in the study. **RESULT** Out of 50, 31(62%) were males and 19(38%) were females. The commonest etiology was dengue (50%) followed by scrub typhus (22%), typhoid (14%), PUO (12%) malaria (2%). The most common associated comorbidity was DM (10%) followed by HTN (8%), CVA (6%)& AKI (6%),CAD(4%) and TB(2%).Elevated serum creatinine and blood urea levels were observed in 42% and 48% respectively. In liver function test, elevated AST and ALT were observed in 25% and 18%. Out of 25 dengue patients,16% expired during the study period and 18.1% of death in scrub typhus patients **CONCLUSION** Dengue fever patients with associated comorbidities admitted with deranged lab investigations are prone to poor outcome so need ICU care for better outcome of the patients

KEYWORDS : dengue, scrub typhus, malaria, liver function test, serum creatinin, outcome, expired.

INTRODUCTION

Pyrexia is one of the commonest causes of disability, perplexing to medical professionals due to its varied aetiologies and pathophysiologies. It is a potent biologic response modifier with consequences that are profound, but difficult to predict [1].

Viruses and bacteria are responsible for different types of infectious diseases, and while it is of paramount importance to understand the mechanisms of infection, potential effects of fever on this process may have been overlooked [2].

Most febrile illnesses of duration less than a week are due to viral infections which subside without any specific treatment and hospitalization. However, when the duration of fever is more than seven days, etiology can be varied and usually patients are admitted for evaluation. In certain infections like upper respiratory tract infection, lower respiratory tract infection, gastrointestinal tract, infection and skin infection the etiology and site of infection is evident from history and clinical examination itself, but in some cases investigations are required.[3]

Dengue fever is an acute febrile illness (AFI) caused by one or more dengue viruses belonging to genus Flavivirus and transmitted by Aedes aegypti mosquito. Although the majority of infections are self-limiting, a small subset of patients develop severe complications, needing intensive care. These complications including organ failure, occur relatively late in the disease, potentially providing a window of opportunity to identify the group of patients likely to progress to these complications.[4]

In recent years, scrub typhus has rapidly remerged to become the major cause of AFI in many parts of India, especially during the monsoon and postmonsoon seasons. The disease can progress to severe complications like acute respiratory distress syndrome (ARDS), hepatitis, acute kidney injury, myocarditis leading to heart failure, and meningoencephalitis.[5]

Malaria is a parasitic infection transmitted by the Anopheles mosquito that leads to acute life-threatening disease and poses a significant global health threat. The Plasmodium parasite has a multistage lifecycle, which leads to characteristic cyclical fevers. With timely treatment, most people experience rapid resolution of symptoms; however, significant complications may occur, including cerebral malaria, severe malarial anemia, coma, or death.

Only 4 of the over 100 species of plasmodia are infectious to humans. The majority of cases and almost all deaths are caused by Plasmodium falciparum. Plasmodium vivax, Plasmodium ovale and Plasmodium malariae cause less severe disease.

Typhoid fever is one of the major causes of mortality and morbidity in overcrowded and unhygienic areas though comprehensive research and public health interventions have decreased the occurrence. The disease course ranges from early gastrointestinal distress to nonspecific systemic illness but ultimately may lead to multiple complications. Salmonella is said to spread by the 'four Fs" (flies, fingers, faeces, fomites). Fever characteristically comes in a step-wise pattern (i.e., rises and falls alternatively) followed by headache and abdominal pain.

Pyrexia of unknown origin (PUO) is a diagnostic dilemma for physicians worldwide. Defined by Peters Dorf and Beeson1 in 1961 as 'fever higher than 38.31C on several occasions, persisting without diagnosis for at least three weeks in spite of at least one week's investigation in hospital', there have been a number of studies investigating the causes for PUO.

The aim of our study was to describe the occurrence and outcome of patients admitted with history of fever in intensive care unit

METHOD

This prospective observational study was conducted at Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India. In this institute we have 26 bedded medical ICU. After taking approval from Institutional ethical committee, patients who fulfil inclusion criteria were enrolled after taking informed consent from the next of kin. The study period was of five months, ranging from July 2021 to November 2021

Inclusion criteria

Adult patients with age group of 18 to 80, presenting with acute febrile illness, and require ICU admission, who tested positive for dengue serology, malaria antigen or slide test, salmonella typhi or para typhi and scrub typhus were included in the study.

Exclusion criteria

Patients with age less than 18 and 18 to >81 who tested positive for dengue serology, malaria antigen or slide test, salmonella typhi or para typhi and scrub typhus, not require ICU admission were excluded from the study.

All such admitted patients underwent detailed history and examination. Dengue infection was diagnosed using a commercial ELISA NS 1 antigen test and IgM antibody. Only culture proven cases of enteric fever were included in the study. Malaria was confirmed on the basis of positive slide test or positive antigen. Tsutsugamushi in their serum were diagnosed as scrub typhus. Patients suffering from more than one infective etiology were considered as mixed infection. The predefined criteria for diagnosis used were as follows-

Diagnostic criteria for dengue -IgG/ IgM Antibodies to dengue virus by rapid immunochromatographic test Dengue NS1Ag.

Diagnostic criteria for scrub typhus-Eschar or IgM Elisa positive or Weil Felix test positive (OX K titre >80).

Diagnostic criteria for malaria-Peripheral smear showing malarial parasite or pLDH/, HRP2 antigen positive (sure test malarial combo kit).

Diagnostic criteria for enteric fever-Blood culture positive for Salmonella typhi or para typhi or WIDAL positive done by slide agglutination and tube agglutination method more than 1:160 titre.

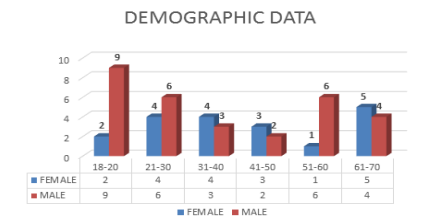
Statical analysis- Demographic data including age, sex was collected. Others parameters such as coexisting co morbidities, laboratory investigations such as LFT, serum electrolytes were recorded. All the collected data were entered in pre-set form and analysed by using SPSS version 23.

RESULT

This prospective observational study of patients with acute undifferentiated febrile illnesses included 50 patients. Out of 50 patients, 31(62%) were males and 19(38%) were females. Most cases presented during the monsoon and post monsoon period. The commonest etiology was dengue (50%) followed by scrub typhus (22%), typhoid (14%), PUO (12%) malaria (2%). Patients presenting with acute febrile illness should not be automatically assumed to have mono infection alone This study has shown that a specific diagnosis could be made in 88% of patients. Preexisting medical conditions were present in 36% of patients. The most common associated comorbidity was DM(10%) followed by HTN(8%),CVA (6%)& AKI (6%),CAD(4%) and TB(2%). Common laboratory abnormalities at presentation were Elevated serum creatinine and blood urea levels were observed in 42% and 48% respectively.In Liver function test,elevated AST and ALT were observed in 25% and 18%.Out of 25 dengue patients,16% expired during the study period and 18.1% of death in scrub typhus patients**.** Occurrence and outcome of patients admitted with history of fever in intensive care unit: A prospective study

DEMOGRAPHIC DATA

AGE	FEMALE	MALE	TOTAL
18-20	2	9	11
21-30	4	6	10
31-40	4	3	7
41-50	3	2	5
51-60	1	6	7
61-70	5	4	9
71-80	-	1	1

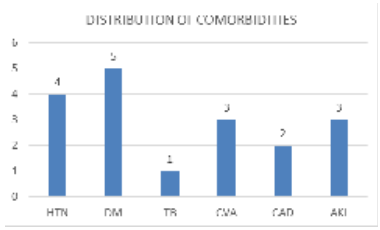


DENGUE NS-1 ANTIGEN	SCRUB TYPHUS	MALARIA	TYPHOID	PYREXIA OF UNKNOWN ORIGIN
25	11	1	7	6

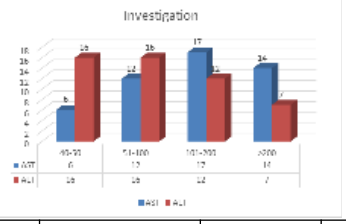
INVESTIGATIONS

DISTRIBUTION OF COMORBIDITIES

HTN	4
DM	5
TB	1
CVA	3
CAD	2
AKI	3

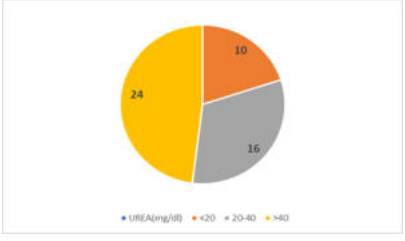


U/L >100	DENGUE	MALARIA	SCRUB TYPHUS	TYPHOID	PUO
AST	8	1	6	2	2
ALT	4	0	4	0	0



mg/dl	<0.5	0.5-1	>1
BILIRUBIN TOTAL	24	12	14

UREA (mg/dl)	<20	20-40	>40
	10	16	24



SERUM CREATININE (mg/dl)	0.5	0.5-1.5	>1.5
	4	25	21

	DISCHARGED	EXPIRED
DENGUE	21	4
SCRUB TYPHUS	9	2
TYPHOID	7	-
PUO	6	-
MALARIA	1	-

DISCUSSION

There are just some Indian studies focussed on mortality predictors in severe dengue patients needing medical care. The mortality reported in our study (50%) is higher than that reported previously in studies done in ICU patients[6,7,8] .This may be explained selection bias because we generally get patients from other hospitals where they're treated for a few days and when complications develop are transferred to us. more modern studies with similar severity indices have shown an increasing trend in mortality.[9,10]

In our study we show the association of pre-existing diseases like diabetes, hypertension or chronic kidney disease with mortality. diabetes has been reported to be a risk factor for dengue severity.[11] Raised ALT levels has been shown to be associated with worse outcomes in several studies.[12] Severe Dengue continues to be a challenge, no vaccine is yet available and also the vector control measures are inadequate.

Despite numerous studies, no adjunctive therapy has been shown yet to confer a survival advantage in malaria. ICU management remains supportive and improved outcomes could even be attributable more to advances in multi-disciplinary team working with mechanical ventilation, careful fluid management, inotropic support, daily assessment of parasitemia, dialysis, and treatment of other infections[13] . just in case of major delay in seeking medical help in patients with severe malaria, patients may soon develop multiorgan failure and even the effective treatment support may not prevent a fatal outcome. But in our study malaria patient survived without sequelae. this might partly be attributed to the particular fact that our patient was young without major co-morbidities.

Scrub typhus is also a potentially fatal infection that affects about one million people every year worldwide.[14]It might be a typical reason behind multi-organ dysfunction and an important reason for admission in ICUs of patients with AFI. Rickettsial infections are documented from various parts of India.[15] There are reports of sporadic outbreaks of scrub typhus mainly within the eastern and southern Indian states with serological evidence of widespread prevalence of spotted fevers and scrub typhus,[16,17] particularly during the monsoon and post-monsoon months.[17-19] Our study also occurred during the identical period.

During our study, 22% of patients with AFI presenting to us had scrub typhus, an observation (24.7%) reasonably just like the study from an adjoining region by Sinha et al.[20]

Age, sex, region and occupation are known to influence the occurrence of scrub thypus. People working outdoors tend to be afflicted more often. Most of our patients were 20–50 years old, an observation rather like Sinha et al.[20]and Madi et al[21]. However, while more women were affected in our series, Rajoor et al.[22] reported more men to be affected.This could probably be because men tend to migrate to cities for work and women look after the agricultural work.

The abnormalities in liver and renal functions in our patients were per those reported in other studies.[18,21]

Complications in scrub typhus develop after the first week of illness. Narvencar et al.[23] found hepatic dysfunction to be the most common followed by ARDS, circulatory collapse and acute renal failure.We found renal dysfunction in over half the patients. The mortality of 18.1%in our study was slightly higher compared to other studies from India by [15]Mahajan et al. (mortality 14.2%),while somewhat low as compared thereto reported by Lai et al. (mortality 15%–30%)[24] and Griffith et al[25].Studies have shown inter-strain variability in virulence [26] and since we didn't do serotyping and genotyping, it's possible that the strain type present in our region was a more virulent one causing higher case fatality. the most strength of our study is that we included confirmed cases of scrub typhus who had IgM antibodies against O. tsutsugamushi.

Typhoid fever is more prevalent in temperate and tropical climates. it's directly associated with sanitation, sewage, and water treatment system. Salmonella typhosa is more common than Salmonella paratyphi. Making a confident clinical diagnosis of enteric fever within the absence of laboratory confirmation is difficult. During our study, all cases were positive for Widal. The mortality within the confirmed typhoid cases in our study was 0 not comparable other studies of hospitalized patients [27–30]. We didn't identify infectious disease caused by S. Para typhi A during this group of patients. it should be that paratyphoid may be a smaller amount severe than typhoid during this setting and fewer likely to guide to hospital admission, although observations across other parts of South Asia suggest that typhoid and paratyphoid is additionally of equal clinical severity.[31] during this study patients admitted to a tertiary care hospital with fever, bacterial infection was the foremost common etiological agent.In general, bacterial sepsis is probably undertreated in tropical countries for several reasons, including unspecific diagnosis of fever, high prevalence of multi-resistant microbes, lack of blood culture facilities, and widespread use of counterfeit drugs. this might explain the high case fatality reported in African patients with fever incorrectly treated as malaria [32]. In India, a retrospective study from Mumbai among 160 patients who died from acute febrile illness reported malaria in 23%, leptospirosis in 22% and communicable disease in 2%, while up to 54% died due to unexplained fever, a proportion of which is perhaps visiting possess been caused by bacterial infections[33] .Infections was the foremost common aetiological diagnoses for PUO. However, in our study, all patients with PUO had negative blood cultures, suggesting that bacteraemia may not are under-diagnosed during this cohort. The study isn't without limitations. Ours being a tertiary centre selection bias is predicted as usually severe cases are being mentioned such centres. The absence of other infections causing fever during this study could even be because the surveillance of febrile patients wasn't conducted throughout t the total year covering all seasons. the insufficient sample size and thus the limited range of diagnostic testing performed. The results of this study should be therefore be considered preliminary and future studies should incorporate a wider panel of diagnostic methods for relevant pathogens and a minimum of a year-long long recruitment period to encompass all potential seasonal variation.

CONCLUSION

Managing a patient with febrile entity entails the understanding of detailed pathophysiology of the disease. Identifying the cause of disease in patients whose condition is deteriorated or alleviated is important. In difficult diseases, multiple repeated invasive examinations are necessary to obtain a diagnosis. A high index of suspicion should be maintained, and an early diagnosis and management is warranted to prevent disease complications.Thus, in north India, an increasing awareness about the disease presentation, clinical features, and laboratory findings will help in reducing the mortality from this infectious disease..

This study showed dengue fever patients with associated comorbidities admitted with deranged lab investigations are prone to poor outcome so need ICU care for better outcome of the patients

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