



Clinical spectrum of fever cases in correlation with hemato-biochemical and radiological parameters- an Experience from a Zonal Hospital in Eastern India

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Abstract

Introduction: The purpose of this study is to study the clinical spectrum of fever cases, outline the hematobiochemical and serological parameters and delineate a syndromic approach to tropical infections in a zonal hospital of eastern India.

Methods: The study included 120 cases of fever admitted to our hospital in ICU and acute medical wards and correlating their clinical manifestations with the lab parameters (hematological, biochemical, serology) and imaging modalities.

Results: Out of 120 cases admitted with fever, 39(32.33%) cases were undifferentiated viral fever, 15(12.5%) were enteric fever, 13(10.8%) were dengue, 8(6.7%) were malaria, 3(2.5%) each of hepatitis A and hepatitis E, 8(6.7%) of varicella, 6(5%) of pneumonia and 5(4.2%) of UTI. 5 cases each of meningoencephalitis and liver abscess were reported along with 2 cases each of scrub typhus, leptospirosis, chikungunya, kala azar and viral interstitial pneumonia.

Conclusion: Our study has focused on the bedside clues which help the physician in solving the diagnostic conundrum of tropical diseases that are encountered commonly in our country and their correlations with hemato-biochemical, serological and diagnostic imaging modalities which will guide us the therapeutic modalities.

Keywords: Tropical infections, dengue fever, mixed infections, enteric fever, meningoencephalitis, leptospirosis.

Introduction

“Humanity has but three enemies: fever, famine and war: of these by far the greatest, by far the most terrible is fever.”-Sir William Osler

In India, fever can have vivid manifestations and can be nightmare for physicians. A syndromic approach to fever will help us in differentiating the diseases and guiding the treatment modality. Fever is defined as an elevation of body temperature above the normal daily variation resulting from an alteration of the hypothalamic set-point by exogenous endogenous cytokines and pyrogens^[1].

A practicing physician in India is likely to encounter many a tropical disease with its protean manifestations in the critical care setting. To this extent, the tropical infections that may present with or get complicated with multi-organ failure include severe falciparum malaria, leptospirosis, dengue fever, scrub typhus, typhoid fever, complicated amoebic liver abscess and occasionally hanta viral infection. The purpose of this study is to delineate a syndromic approach to these diseases, discuss the clinical and bedside clues that help in differentiating these conditions and briefly outline the laboratory parameters (hematological, biochemical, serology) and imaging modalities.

Syndromes

A. Fever and thrombocytopenia.

The diseases that can present with thrombocytopenia and fever are falciparum malaria, Weil's disease, dengue fever and rickettsial infections such as a scrub typhus. However, the most common cause is undifferentiated viral fever.

B. Fever with jaundice

The tropical infections that may be accompanied by jaundice include dengue fever, severe malaria, typhoid hepatitis, amoebic liver abscess, scrub typhus and Weil's disease.

C. Fever with hepatorenal dysfunction

Tropical infections may present with hepatorenal dysfunction as a part of multi-organ failure.

Falciparum malaria, leptospirosis, scrub typhus and dengue enter the deferential diagnosis along with hepatitis A or E associated fulminant hepatic failure.

D. Fever with pulmonary renal syndrome

Tropical diseases that can present with pulmonary renal dysfunction are falciparum malaria, leptospirosis, hanta virus and scrub typhus.

E. Fever with altered sensorium

The important diseases that merit consideration are cerebral malaria, viral encephalitis (HSV and JE), meningitis (pyogenic and tuberculous), and enteric fever besides brain abscess or septic encephalopathy. It is useful to remember that geriatric age group with UTI or pneumonia often present with febrile encephalopathy with few other clinical signs.

F. Fever with acute abdomen

Enteric fever and amoebiasis may present with an acute abdomen secondary to severe abdominal pain from uncomplicated disease or as a result of complications such as bowel perforation in enteric fever or rupture of liver abscess.

Acute pancreatitis has been described in leptospirosis while severe gastroenteritis and abdominal pain are some of the atypical manifestations of malaria.

A good clinical acumen supported by lab parameters will be helpful in differentiating these conditions and guiding the definitive treatment modalities.

Methodology

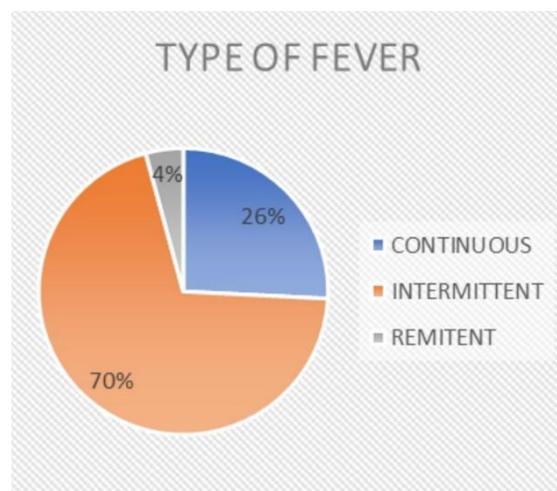
All patients admitted to medical units during the period of study were screened during the period of study from March 2017 to February 2018. 120 patients diagnosed to have fever were evaluated. Patients in age group 12 years and less were excluded from the study.

Data were collected as per the proforma. It included patient particulars, date of admission and ward of admission, clinical parameters and basis of diagnosis of tropical infections. All patients were screened for predisposing factors. Investigations included fever workup (PBS for malaria parasites, NS1Antigen, dengue serology, WIDAL and other specific tests as per clinical suspicion), hematological parameters, biochemical parameters, chest X-ray PA view and other imaging modalities like USG abdomen and KUB if required.

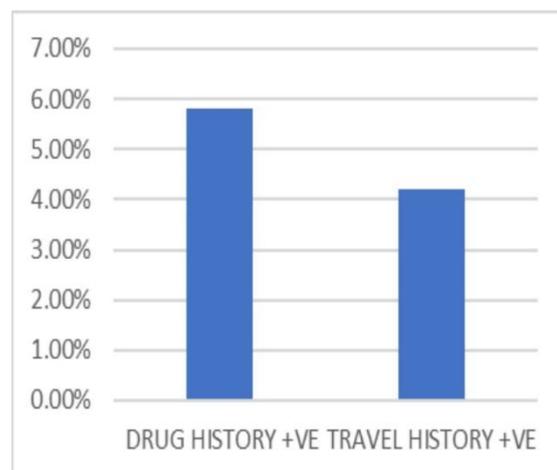
Results

A total of 120 fever cases in acute medical wards and ICU were evaluated. Of these 86(72%) belonged to age group 12-40 years while 28(23%) belonged to 41-60 years and 6(5%) were 61 years and above. 84(70%) of these reported with intermittent fever, 31(25.8%) with continuous while only 5(4.2%) had remittent fever. 14(11.7%) of these cases complained of chills and rigors, 13(10.8%) cases complained of cough with expectoration, 13(10.8%) cases had vomiting with loose stools and 10(8.3%) presented with rashes while the rest had symptoms like malaise, yellowish discoloration of urine, burning micturition and breathlessness. 5(4.2%) cases had history of recent travel while 7(5.8%) cases had history of drug use. On general examination 7 patients had icterus while pallor and pedal edema were present in 1 case each. 17(14.2%) cases were found to have hepatosplenomegaly. Although 108(90%) cases had normal breath sounds, 12(10%) cases had added breath sounds. One case was found to have periumbilical hernia. On further hematological and biochemical workup, 20(6.7%) cases had leukocytosis while 42(35%) cases had leucopenia. 25(20.8%) cases had polymorphic leukocytosis and 42(35%) had lymphocytic leukocytosis. 23(19.2%) cases were found to have elevated bilirubin while deranged SGOT, SGPT and RFT were found in 14(11.7%), 12(12.5%) and 58(48.3%) cases respectively. Diagnostic workup included MP test, Dengue serology, WIDAL and Weil-Felix being positive in 9(7.5%), 14(11.7%), 16(13.3%) and 2(1.7%) cases respectively. One case showed presence of toxic granules and shift to left in peripheral blood smear. Urine culture and Blood culture showed growth in 8 of these cases. Chest X-Ray showed non-homogenous opacities and pleural effusion in 6(5%) cases and 1(0.8%) case respectively. USG abdomen revealed 3 cases had hepatomegaly, 4 cases had splenomegaly and 5 cases had hepatosplenomegaly. The limitation of our study is that it excluded the paediatrics age group or else we could have

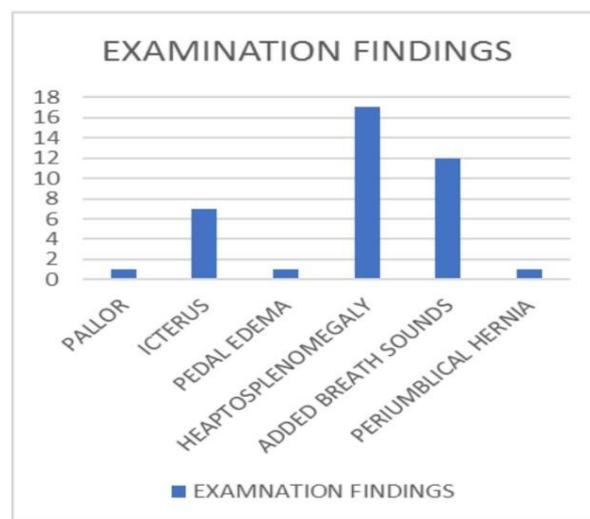
expected to have different fever etiologies due to exposure and immunity. Hence, it is prudent that the pattern of fever etiology found in our study is not representative of general population.



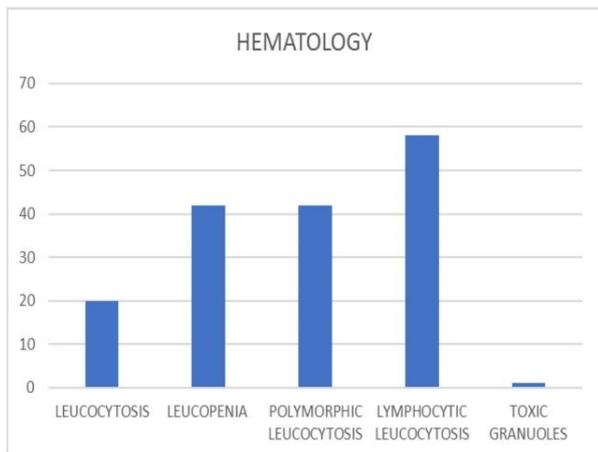
[Fig.1] Various types of fever



[Fig.2] History of recent travel and drug history

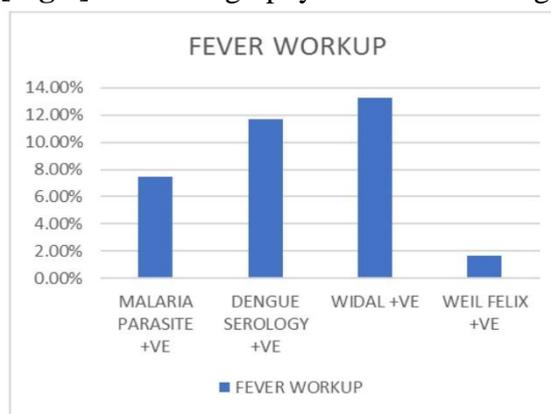


[Fig.3] General and systemic examination findings

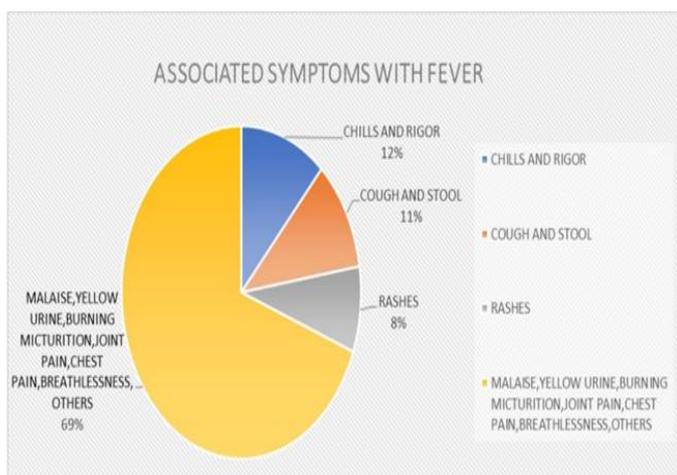


[Fig.4] Hematological Findings

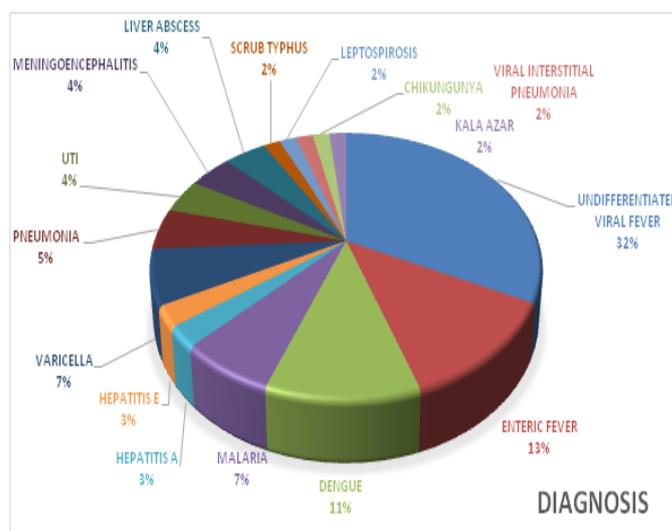
[Fig.7] Ultrasonography Abdomen findings



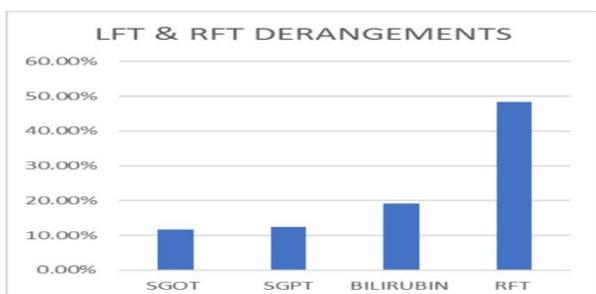
[Fig.8] Percentage of patients positive for PBS for malaria and other serological tests



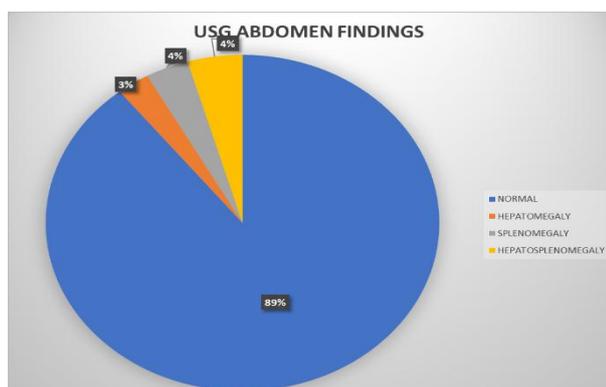
[Fig.5] Common associated symptoms with fever



[Fig.9] Percentage of different tropical infections detected in this study



[Fig.6] Percentage of patients with abnormal LFT and RFT



Discussion

Tropical infections increase the burden of health care and the course and outcome of patients admitted to hospitals. Febrile illness can be accompanied by pernicious manifestations such as altered sensorium, jaundice, renal failure, respiratory distress or combinations thereof. In the critical care setting, apart from the usual diagnosis of sepsis syndrome, in our country it will be prudent to consider the tropical infections. In our study majority of patients had undifferentiated viral fever. Our study showed high incidence of tropical infections such as Clinical Enteric fever, Dengue, Malaria, Varicella, UTI and hepatitis A and E. Few research works in Northern and Southern India also reveal the same [2,3,4].

In a series of 608 cases of severe malaria from Orissa, reported in 2006, Mohapatra et al observed that 53 % of the cases had jaundice. A study from Mumbai reported in 2003, in a series of 301 cases of severe malaria, thrombocytopenia was seen in 38 % cases. In our study, 8(6.7%) cases were diagnosed to have malaria. 4(50%) of malaria cases were mixed infections with deranged liver enzymes and renal parameters. One of the patient with parasitic index of 45% had autoimmune hemolytic anemia who responded well to antimalarials, steroids and supportive therapy. This was a rare case of mixed infections (*Plasmodium vivax*+*Plasmodium falciparum*) with heavy parasitic index who was found to have artesunate induced autoimmune hemolytic anemia.

In our study 13(10.8%) cases were diagnosed as dengue fever. 8 of these cases had transaminitis with serositis (ascites with pleural effusion). A study from SGPGI Lucknow in 2005 looked at liver involvement in 45 cases of proven dengue fever, 15 % of cases had clinical jaundice while transaminases elevation was practically universal (96%). The bedside clues to dengue in a given case of fever with MODS are hemoconcentration, hypoalbuminemia, manifestation of plasma leak, thrombocytopenia and leucopenia^[5,6]. In day to day practice the laboratory diagnosis is centered on serology.

Amoebic liver abscess may be the cause of admission to the acute ward by way of presentation as sepsis syndrome, peritonitis or pleuropulmonary rupture. The clinical clues to the presence of amoebic liver abscess would be an impressive history of abdominal or right hypochondrial pain, tender hepatomegaly or features of peritonism. 5 of our patients had amoebic liver abscess who were positive for amoebic serology.

Five of our cases had fever with altered sensorium. Two of these were diagnosed to have tubercular meningitis while one was diagnosed as a case of pyogenic meningitis. One case each of HSV 1 encephalitis and Japanese encephalitis were diagnosed. The patient with Japanese B encephalitis presented with altered sensorium, seizure and

abnormal posturing. The MRI revealed characteristic lesions involving the thalamus and basal ganglia with EEG showing a generalized slowing.

In our study 15(12.5%) cases were diagnosed to have enteric fever. 9(60%) of these cases were clinical enteric fever. Enteric fever may present with an acute abdomen secondary to severe abdominal pain. As a result of complications of enteric fever, 2 of our cases had bowel perforation while one had developed enteric encephalopathy.

It is useful to remember that geriatric age group with UTI or pneumonia often present with febrile encephalopathy with few other clinical signs. In our study 6(5%) cases had pneumonia (clinico-radiologically proven). Two patients had bilateral pneumonia, one had interstitial pneumonia and two patients had lung abscess. 5(4.2%) of our cases had UTI too.

Two of our cases had scrub typhus which is a rickettsial disease caused by *Orientia tsutsugamushi*, a gram negative coccobacillus that infects vascular endothelium in a multiple organ systems. The disease occurs 7-10 days after the bite of larval form of trombiculid mite and present with fever, relative bradycardia, severe myalgias and a non-pruritic maculopapular rash (10%). Splenomegaly was detected in 44 to 52% of the cases described in the recent outbreaks in the Shimla hills while the characteristic eschar was seen only in a minority of cases (9.5%)^[7,8]. Both of our cases had characteristic eschar formation with splenomegaly and serositis. Clinical jaundice and deranged LFTs have been described in outbreaks of scrub typhus seen in Shimla hills with a reported incidence of jaundice in 10-52% and elevated AST/ALT in 28 to 67 % cases.

Two of our cases had leptospirosis. In the series of 60 cases of leptospirosis, which were encountered in the medical ICU of a teaching hospital in Mumbai in 2002-2003, Jaundice was seen in 63%. Both of our cases had jaundice with deranged renal parameters. One of the cases had AV junctional arrhythmia which is again a rare cardiac finding in case of leptospirosis.

Conclusion

To conclude this study defines the magnitude of tropical infections and reflects on the need to be aware of tropical infection in tertiary health care setup. The clinical picture and presentations of fever are so overlapping that it becomes virtually impossible to diagnose one particular disease with conviction even in the best of the setups. Hence these are clubbed together as 'Tropical fever syndrome'. The incidence of these diseases has increased in recent times possibly because of climate change and global warming.

Accurate assessment plays major role in proper management of the illness. A complete patient profile inclusive of patient history, physical examination and lab findings is a must for this purpose. Patient information such as age, sex, address, occupation, known exposure to illness, and date of disease are the first things to look for. Signs and symptoms along with their origin, precipitating factors, progression, severity and associations also give important clues to reach the diagnosis. History of recent hospitalization, blood transfusion, vaccination, travelling, drugs and exposure to sexually transmitted diseases are all of significant help. Dietary habits, behavior, addictions, bowel bladder activities also form an important personal history segment of patient profile.

The patient examination should start from the vitals viz pulse, blood pressure, temperature and consciousness. Physical examination must assess the skin, mucous membranes, liver, spleen and lymph nodes. Fever ideally acts as the best indicator of many infections. The body temperature has to be taken using the same route consistently and temperature charting along with its pattern and effects of antipyretics need to be documented.

Management of enteric fever continues to pose a challenge because of absence of reliable rapid diagnostic test. The gold standard to confirm the diagnosis still remains the positive growth of *S.typhi* in blood, stool and urine sample of patient suspected having typhoid fever. In case of strong suspicion of typhoid fever clinically (but blood and stool culture are negative) we can go for bone

marrow culture which may reveal organism^[9]. In our study almost half of the patients of typhoid fever had clinical enteric fever diagnosed on the basis of signs and symptoms and response to treatment. Early institution of antibiotics is the mainstay of effective treatment of enteric fever. Therapeutic strategies will have to take into account the local antibiotics sensitivity pattern of *S.typhi* while defining treatment.

Malaria, a protozoan disease, usually starts with nonspecific symptoms though its classical symptoms do persist, sometimes atypical presentations may dominate the pictures. One cannot rule out malaria on the basis of absence of typical intermittent fever or fever with rigors or absence of malarial parasites from peripheral smears. Fever is an important symptom of malaria but the typical periodicity is absent in many cases which was also construed from our study. Therefore, all clinically suspected malaria cases should be investigated by microscopy or rapid diagnostic test^[10]. Various national health programmes targeting its eradication have led to development of many economic and reliable diagnostic tests like blood films and antigen tests. Although the vastness of its symptoms poses a major challenge for the physician but the major advances in its diagnosis and treatment have helped to keep a check on its incidence as compared to 20th century.

In the last decade, dengue has assumed pan India proportions. The spectrum of presentations varies from a mild self-limiting sub-clinical infection to a potentially fatal dengue hemorrhagic fever. The treatment is symptomatic and supportive. A rise in hematocrit value indicates significant plasma loss which was also seen in our patients who were managed with parenteral fluid therapy. We have to either control the dengue vector or an appropriate referral system has to be devised for the unfortunate victims of this easily preventable disease.

There have been spurts of leptospirosis cases during the rainy season which have led to epidemics and thus this disease warrants as much importance as any other tropical infections. The global burden of leptospirosis is hard to quantify because of

difficulties encountered in its clinical diagnosis and lack of efficient confirmatory laboratory testing which limits the public health reporting.

Tropical infections may present with hepatorenal dysfunction as a part of multiorgan failure. Falciparum malaria, mixed infections, dengue, leptospirosis, scrub typhus, entered the differential diagnosis along with hepatitis A or E associated with fulminant hepatic failure.

The approach to a patient with suspected tropical infections start with a good history and physical examination. Our study has focused on the bedside clues which help the physician in solving the diagnostic conundrum of tropical diseases that are encountered commonly in our country and their correlations with hemato-biochemical, serological and diagnostic imaging modalities which will guide us the therapeutic modalities.

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Declaration of Conflicts of Interest

All authors have none to declare.

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