

Typhus Fever - A Diagnosis Often Missed as A Cause of Fever

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Abstract:

Background: In tropical countries epidemic and endemic typhus are sometimes misdiagnosed as typhoid fever. Typhus infection is emerging in the subcontinent and clinically presents as nonspecific febrile illness. So high index of clinical suspicion is essential and the objective of the study was to detect typhus infection as a cause of febrile illness.

Materials & Method: This is a prospective observational study done from January to December 2019. A total 50 patients of different age groups were taken randomly who were suffering from fever for more than 7 days. All relevant investigations including CBC, Dengue serological test, Widal test, urine routine examination and C/S, blood C/S, chest x-ray were done. Patients not responding to conventional antibiotic therapy and having persistent fever were further investigated for typhus fever with Weil-Felix test.

Results: Out of 50 patients 35 were male; age range was 2 to 12 years. Mean duration of fever was 10 days. Blood for CBC showed nonspecific findings, Blood culture and urine for c/s were negative for bacterial growth, dengue serological tests were negative, chest x-ray were normal (except 2 patients had pneumonia). Weil-Felix tests were positive in all cases. 12 cases were positive for both Widal test and Weil-Felix test and in 8 cases blood c/s were also positive with Weil-Felix test. Treatment changed to Doxycycline or Azithromycin in cases of typhus fever.

Conclusion: Typhus fever should be taken into account in the management of febrile illness who were admitted without a confirmed cause of fever.

Keywords: Typhus fever, Weil-Felix test, Typhoid fever.

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Introduction:

Typhus fever is a group of rickettsial disease which include epidemic typhus, murine typhus & scrub typhus. Salmonella Enterica serotype typhi is often responsible for Typhoid fever which cause multisystem infection by bacterial blood stream invasion.^{1,2} Epidemic typhus may be misdiagnosed as typhoid fever.^{1,3} Rickettsia is emerging in this subcontinent

as a cause of clinically nonspecific febrile illness.⁴ Rickettsia prowazekii causes epidemic typhus in which the vector is body louse. It is the most virulent form with worldwide distribution.⁵ Murine typhus due to Rickettsia typhi is a small obligate intracellular bacterium transmitted by rat flea. It has a worldwide distribution particularly in tropical countries. In Asia, the pacific region and Australia typhus is endemic in nature. One million cases of scrub typhus occur annually in South-east Asia and there are 50000-80000 death per year caused by this disease.^{6,7} The etiology of febrile illness remains poorly characterized in many places in developing world.^{4,8} The causative agents are usually not identified and patients are often treated empirically with antimicrobial therapy.⁸

So typhus is an important cause of febrile illness in south-east Asia and pacific, could be emerging cause in Middle –East and South Asia.^{7,8} Scrub typhus and Murine typhus should be considered as possible

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causes of infection in Bangladesh also.⁸⁻¹⁰ In Murine typhus the clinical features are non-specific and these mimic typhoid fever.^{11,12} In Bangladesh two case reports of co-infection with typhoid and typhus have been reported in 2008 and 2013. Clinical suspicions is the key in the diagnosis of both typhoid and typhus fever.^{11,12} Co-infection of scrub typhus with diseases such as typhoid fever, may be overlooked and masked in view of overlapping clinical features.^{11,13} Patient with murine typhus exhibits symptoms such as rash, myalgia, vomiting, cough, headache, diarrhea, abdominal pain, petechial rash etc.¹⁴ High continued fever, headache, myalgia are usually present in both typhoid and typhus fever.¹⁵ Proper clinical evaluation, positive Weil Felix test and other causes of fever should be ruled out before starting the treatment.¹⁶ In Typhus fever rising titer of OXK,OX2,OX19 antigens supports the diagnosis but confirmation of diagnosis is done by Polymerase chain reaction.^{12,17} Here fifty cases of typhus fever were presented who were suffering from fever for more than seven days.

Materials & Method:

This was a prospective observational study conducted in Kurmitola General Hospital, Dhaka, Bangladesh from January to December 2019. A total fifty patients between 2-12 years age groups were taken randomly, who were suffering from fever for more than seven days. Some relevant investigations like complete blood count (CBC), C- reactive protein (CRP), Dengue serological test, Widal test, blood culture and sensitivity (C/S), urine for routine and C/S and X-ray chest were done. Due to persistence of fever, conventional antibiotic therapy was given and further investigation like Weil-Felix test, ICT for Kala-azar, ICT for Malaria, Montaux test, USG of whole abdomen, rheumatoid factor (RF), ASO titre were done.

Patients with positive Weil-Felix test were considered as cases of typhus fever along with clinical suspicions. These patients were treated with Doxycycline (4 mg/kg twice daily for 7 days) or Azithromycin (10 mg/kg once daily for 5 days). Patients with Typhoid fever in addition to typhus fever were treated with injection Ceftriaxone along with Doxycycline or Azithromycin and typhus fever with pneumonia were treated by injection Flucloxacillin in addition to Azithromycin. Informed written consent was taken from parents and a structural questionnaire was used to collect samples. The patients who were very sick, convulsive, unconscious were excluded from the study. Ethical

permission was taken from the local institutional ethical committee.

Results:

Total 50 cases were included in this study. Among them 35 were male and 15 were female. All the patients had fever. Other top three clinical features were vomiting in 42%, abdominal pain in 32% & headache in 26% cases. (Fig-1) Besides, 4% patients presented with pneumonia. After doing investigations (Table-I) 100% cases showed positive Weil-Felix test, 24% cases showed positive Weil-Felix with positive widal test and 16% patient also showed salmonella infection by blood culture. About 4% cases had consolidation in the lung with positive Weil-Felix. Scrub Typhus was present in 42% cases, dual pathology in 40%, Indian tick typhus in 18% cases (Fig.-2). All the patients were treated by either Doxycycline or Azithromycin alone or in with combination with other antibiotics in 28% of cases (shown in Table-II). All patients were discharged from hospital after remission of fever.

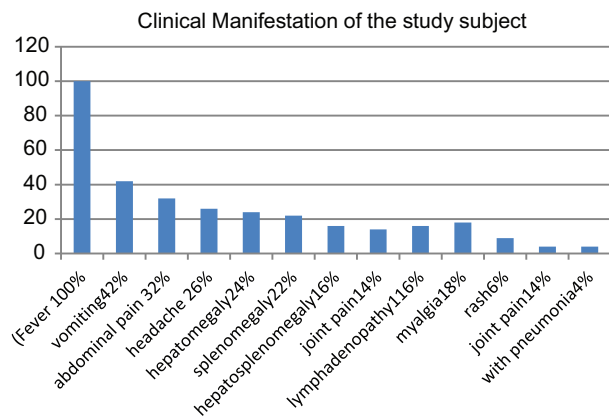


Fig.-1: Clinical Manifestations of the study subject (n=50)

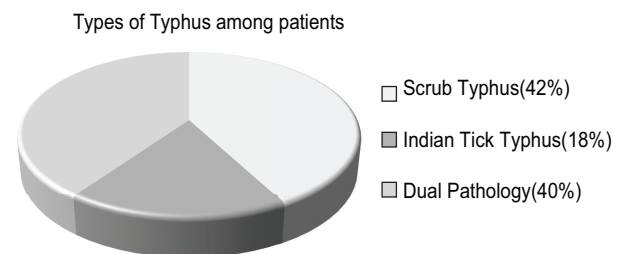


Fig.-2: Types of Typhus among patients (n=50)

Table I*Laboratory parameter of the study subject (n=50)*

Name of the test	No. of patient (%)
Weil- Felix (positive)	50 (100%)
Weil-Felix with widal positive	12(24%)
Weil-Felix with blood c/s positive	8(16%)
Weil- Felix with pneumonia	2(4%)

Table II*Treatment pattern of study subjects (n=50)*

Antimicrobial used	No. of Cases
Doxycycline	17 (34%)
Doxycycline + Ceftriaxone	8 (16%)
Azithromycin	19 (38%)
Azithromycin + Ceftriaxone	4 (8%)
Azithromycin + Flucloxacillin	2 (4%)

Discussion:

Clinical suspicion is important to diagnose of typhus fever.^{4,8} In this study, initially typhoid fever was suspected as the cause of fever, while typhus was overlooked. Similar results were seen in study of Mazumder RN.⁵ Here, in some cases, typhus infection was present along with typhoid fever. Similar observation was seen in study of Vigna SRV.¹⁵ As treatment, either Doxycycline or Azithromycin was administered in all cases. Vivekanandan M also found that, both Doxycycline and Azithromycin were sensitive to typhus.¹⁸

Regarding the infection pattern, in this study, scrub typhus was present in 42% cases, dual pathology in 40%, Indian tick typhus in 18% which are similar to study of Miah MT.⁴ From above study, it can be said that, typhus is another cause of febrile illness in Bangladesh which is missed in many cases. Again, here, concomitant infections were searched with Typhoid. Thus, suspected cases of Typhus were confirmed by Weil-Felix test. Early consideration of typhus co-infection is of clinical significance as it is treatable.¹⁹ A systematic review of mortality from untreated scrub typhus suggested that while mortality is lower than commonly reported estimates morbidity is significant.⁸ The complications of typhus fever are vasculitis, hepatitis, GIT hemorrhage, hypovolemia,

electrolyte imbalance, multi organ involvement including CNS and kidneys.⁵ In this study, two patients had pneumonia as secondary infection though Mazumder RN found pneumonia as an uncommon feature in typhus fever.⁵ However, other complications like myocarditis, respiratory distress syndrome had been observed in the study of Seow CWXS,¹¹ though we didn't get that type of complications.

Conclusion:

Typhus is an emerging infectious disease and sometimes overlooked and misdiagnosed as typhoid fever, moreover, co-infection of typhus and typhoid fever is commonly observed. Weil- Felix test was positive in all the cases and most of the patients were responsive to azithromycin and doxycycline.

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