ABSTRACT

Background: Rickettsial infections are the most common re-emerging infections in the recent times especially Scrub typhus. If untreated, fatality rate is as high as 30-35%. Scrub typhus can cause changes in hematological and biochemical parameters. The need for this study is to correlate the laboratory investigations in patients with scrub typhus, so that early diagnosis and appropriate treatment can be done.

Methods: This prospective observational study was carried out in children admitted in the pediatric ward/ pediatric ICU of RMMCH who were diagnosed to have Scrub typhus by positive ELISA test. Their basic laboratory investigations are categorized and correlated.

Results: Normal Leukocyte count was seen in 48% (n=24) of the cases, leucocytopenia 30% (n=15), leucocytosis 22% (n=11). Platelets <1.5 lakhs were seen in 72% (n=36) and none of the cases had platelets less than 80000. Hb<9gm/dl was seen in 44% (n=22). Hyponatremia in 24% (n=12). CRP was positive in 28% (n=14). Hypoalbuminemia was seen in 22% (n=11). Renal function test was normal in all the cases.

Conclusions: This study discusses the various biochemical and hematological changes in patients with Scrub typhus. Pancytopenia is rare in patients with Scrub typhus. Abnormalities in renal and liver function tests may indicate the progression to complications. Normal WBC count with hyponatremia and hypoalbuminemia with related symptoms and signs can be used to diagnose the disease at earlier stages.

Keywords: Hypoalbuminemia, Hyponatremia, Laboratory investigations, Rickettsia, Scrub Typhus

INTRODUCTION

Rickettsial infections are the most common re-emerging infections in the recent times. They are incapacitating and notoriously difficult to diagnose. If untreated, fatality rate is as high as 30-35%. Rickettsial infections have been one of the great scourges of mankind, occurring in devastating epidemics during times of war and famine. Because of non-specific signs and symptoms and non-availability of sensitive and specific diagnostic tests, these are difficult to diagnose.

If diagnosed properly they are easily treatable. Immunofluorescence assay (IFA) is the gold standard test for Sero-diagnosis of rickettsial disease which detects IgG and IgM antibodies. Weil-Felix (WF) test is a classic serological test which is widely available but not reliable because of its low sensitivity and specificity. But in developing countries where specific diagnostic tests are not widely available WF can be used as screening test. The test should be interpreted in conjugation with history and clinical presentation.

Initial diagnosis and treatment should be based on a high index of suspicion and appropriate clinical features. The drugs effective against rickettsial infections are tetracyclines, Azithromycin and chloramphenicol. Doxycycline (2mg/kg/dose bid PO or IV, maximum
200mg/day) is the drug of choice for all age group. Alternate regimens include tetracycline (25-50 mg/kg/day divided every 6 hr PO, maximum 2g/day) or Chloramphenicol (50-100mg/kg/day divided every 6 hr IV, maximum 3g/24hr).^4

This study is done to correlate the biochemical and hematological changes in patients with Scrub typhus. Positive clinical signs and symptoms with appropriate changes in laboratory investigations can be used to diagnose the disease where there are limited facilities for serological and immunological investigations.

METHODS

Data was collected from patients and/or their informants (reliable) who were admitted in the pediatric ward/ pediatric intensive care unit at Rajah Muthiah Medical College and hospital in Chidambaram, from September 2015 to October 2017. Totally 50 patients were studied.

This prospective observational study was carried out in the children admitted in pediatric ward/ pediatric ICU of RMMCH. Children of pediatric age group who are diagnosed to have scrub typhus by positive ELISA test were taken up for the study. Informed consent was obtained from the parents/guardians of the study population. Children of both sexes were included. Children more than 12 years of age and with co-morbid illness like Dengue, Leptospirosis, Typhoid were not included in the study.

Detailed history was obtained from the patients taken into study. Thorough Clinical examination was done. Complete hemogram, blood glucose, Bleeding time, Clotting time, blood urea, serum creatinine, serum electrolytes were studied. The symptoms, signs and laboratory investigations were analyzed and compared with the study population. The complications occurring were also studied.

RESULTS

The patients positive for Scrub typhus through ELISA were taken into the study. Their clinical features, biochemical and hematological changes were studied. In the present study, 84% cases were from rural areas/ living in farms and 16% cases were from urban areas. Majority of the children i.e. 54% were in school going group i.e., between 6-12 yrs, 28% in pre-school group i.e. 3-6yrs, 14% in toddler group i.e. 1-3 yrs. The lowest age reported was 8 months.

Among the cases, fever was seen as major presenting symptom (100%) followed by hepatomegaly (82%), Eschar (76%), lymphadenopathy (60%), Rash (26%), distress (10%), abdominal distension (6%), edema (4%), seizures (2%) were seen. In hematological reports, normal leukocyte count was seen in 48% (n=24) of the cases, leucocytopenia 30% (n=15), leucocytosis 22% (n=11). Platelets <1.5 lakhs were seen in 72% (n=36) and none of the cases had platelets less than 80000. Hb< 9gm/dl was seen in 44% (n=22). Pancytopenia was seen in 8% (n=4), Hyponatremia in 24% (n=12). CRP was positive in 28% (n=14). Hypoalbuminemia was seen in 22% (n=11). Renal function test was normal in all the cases.

DISCUSSION

This study was done on 50 cases who were admitted with symptoms of scrub typhus, positive for scrub typhus by ELISA method and negative for other co morbid illness. Children were examined for the following clinical features: rash, eschar, lymphadenopathy, hepatosplenomegaly, edema, history of insect bite. Tick exposure was said to occur when ticks were seen on clothes of child or inside the house or history of playing in an area where ticks were seen.

The pathogenesis of scrub typhus is uncertain but recent studies have indicated that the process is stimulated by a disseminated rickettsial infection of vascular endothelial cells that corresponds to the distribution of disseminated vasculitic and perivascular inflammatory lesions observed in histopathologic examinations. The major result of the vascular injury appears in autopsy series to be hemorrhage. However, it is very likely that the vascular injury initiated by the rickettsial infection results in significant vascular leakage and compromise. It is further confounded by the waxing immune and inflammatory reactions. The net result is significant vascular compromise and ensuring end organ injury, most often manifested in the brain and lungs, as with other vasculotropic rickettsioses.^4
In India Rickettsial infections have been reported from Karnataka, Maharashtra, Tamil Nadu, Kerala, Jammu and Kashmir, Uttarakhand, Himachal Pradesh, Rajasthan, Assam and West Bengal. Rickettsial diseases were reported from various districts of Tamil Nadu and in and around Chidambaram, where the study was conducted.

In the present study, 84% cases were from rural areas/living in farms and 16% cases were from urban areas. Majority of the children i.e. 54% were in school going group i.e., between 6-12yrs, 28% in pre-school group i.e. 3-6yrs, 14% in toddler group i.e. 1-3yrs. The lowest age reported was 8 months.

**Laboratory findings**

*Hematology*

Hemoglobin: Anemia (Hemoglobin <9gm%) was seen in 22 cases (44%) in present study. Platelets-Platelet count of <1.5 lakh was seen in 36 of cases i.e. 72%. Leukocyte count: normal leukocyte count was seen in 48% (n=24) of the cases, leukocytopenia 30% (n=15), leucocytosis 22% (n=11).

*Biochemistry*

Serum sodium: Hyponatremia (serum sodium less than 130meq/ l) is seen in 12 cases i.e. 24% in present study. Hyponatremia was due to increased vascular permeability. Albumin-Hypoalbuminemia was seen in 22% (n = 11) mainly due to increased vascular permeability. CRP-elevated C-reactive protein was present in 14 cases i.e., 28% in the present study.

According to Rathi N et al total leucocyte count, during early course of the disease, was normal to low normal with marked shift to left. Later in the course of the disease, it shows leucocytosis in 30% of cases. The study also said hyponatremia and hypoalbuminemia, reflecting increased vascular permeability, were sometimes helpful in differentiating rickettsial infections from other acute infections.

In Kulkarni A et al study initially there was normal to low leucocyte count. Leukocytosis occurred when the disease progress. A study by Udayan U et al also reported thrombocytopenia and hyponatremia. According to a study done by Palanivel S et al, Hemoglobin 11 gm% was reported in 83.58%, leukocytosis was seen in 49% of the cases. Thrombocytopenia, Hyponatremia, Hypoalbuminemia was also seen. Anemia in 8.8% of cases, hyponatremia, elevated CRP was reported in a study by Rathi BN et al. According to a study done by Dass R et al thrombocytopenia was noted in 26% of cases. Comparing with dengue and other viral infections, platelet count less than 80000 and bleeding manifestations was not noted in this study. Total leucocyte count was normal at presentation in 58.3% cases, high in 25% and low in 16.7% cases. Hypoalbuminemia which is one of the important laboratory finding was observed in 52.2% of cases. Hyponatremia was also seen.

Thrombocytopenia and hyponatremia was also noted in a study by Kulkarni A et al. In a study done by H. R. Somashekar et al, thrombocytopenia was seen in 74% cases and leukocytosis in 40% of the cases. Thrombocytopenia, Anemia, Pancytopenia were seen in nearly 4% of the patients according to the study done by Gurung S et al.

**CONCLUSION**

This study was done in RMMCH, Chidambaram on patients diagnosed to be positive for scrub typhus by ELISA method. This study was done to correlate the laboratory findings with the progression of the disease in order to diagnose much earlier to prevent mortality and morbidity. Among the cases, fever was seen as major presenting symptom (100%) followed by hepatomegaly (82%), Eschar (76%), lymphadenopathy (60%), Rash (26%), distress (10%), abdominal distension (6%), edema (4%), seizures (2%) were seen.

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

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