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SCRUB TYPHUS SEROPOSITIVITY IN DIFFERENT AGE GROUPS AND THEIR CORRELATION WITH OTHER LAB PARAMETERS FROM RURAL BASED TERTIARY CARE CENTER IN WEST BENGAL: A RETROSPECTIVE STUDY.

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Abstract

Scrub typhus, a re-emerging zoonotic infection caused by *Orientia tsutsugamushi*, is a significant public health concern in India, particularly in endemic regions like northern West Bengal. This retrospective study, conducted at Raiganj Government Medical College from January to December 2024, analyzed 1,185 acute febrile illness (AFI) cases, of which 244 (20.59%) were confirmed positive for scrub typhus via IgM ELISA. Clinical, biochemical, and hematological data were examined to identify age-related variations and potential predictors of disease severity. While several biochemical markers—including bilirubin, AST, albumin, globulin, creatinine, and potassium—showed statistically significant variation across age groups, others such as ALT, urea, sodium, and ALP did not. Hematological parameters, including platelet count, total leukocyte count, and hemoglobin, showed minimal age-related differences. Anemia (78.99%) and thrombocytopenia (79.41%) were common findings. Notably, elevated AST and thrombocytopenia were linked with more severe outcomes, particularly in children aged 10–14 years. However, multivariate analysis revealed that age alone was not a major determinant of changes in laboratory parameters, suggesting that other clinical factors may play a more critical role in disease progression. These findings highlight the need for early recognition of biochemical changes to improve prognosis and support further multi-centric prospective studies.

Keywords: Scrub typhus, Lab Parameters, Biomarkers.

1. Introduction

Scrub typhus is endemic in different parts India and of course in Bengal, but reported from only certain parts. It is a well known cause of acute febrile illness (AFI) and also comes as an etiology of acute encephalitis syndrome (AES).The disease is caused by a bacteria Orientia tsustsugamushi a small intracellular gram negative bacteria and transmitted by bite of larva of trombiculid mite (chiggers).[1,2] The clinical feature of fever, joint pain are present often , but the classical eschar or blackening of skin are less common in dark skinned population and often missed. The children of 0-14 yrs age are commonly affected. Among them under 5 children have protracted outcomes.[3] Rickettsial diseases are re-emerging in the Indian subcontinent with a more varied geographic distribution. Scrub Typhus, although a common rickettsial disease in India, is one of the neglected zoonoses of public health importance. Scrub typhus gained research focus after the thousands of confirmed cases and several deaths in 2023, in India in particular. Confirmed human cases of this zoonotic disease were reported throughout India, with 17 deaths. [4] It affects a large part of northern and eastern India (Kashmir, Himachal Pradesh, Assam and Sikkim) and some parts of southern India (Eastern and Western Ghats) and is considered to reappear in the eastern and southern parts. [5] As a common entity in the tropics, scrub typhus should be suspected in patients from endemic areas with a high risk of environmental exposure and acute febrile illness. The prevalence of scrub typhus cases was 10 %. Most cases were post-monsoon leading into winter, which coincides with increased scrub vegetation and favors vector growth. [6] High fever with or without classic eschar was observed in cases. Scrub typhus is a multi-organ dysfunctional syndrome that often affects multiple organs during treatment, and complications usually develop during the first week of illness. Patient outcomes may vary depending on doxycycline regimen.[7] The outcome depends on the circulating burden of O. tsutsugamushi, early or late presentation, and the method of treatment. High mortality is mainly due to delayed presentation or diagnosis and organ dysfunction.[8] The diagnosis of scrub typhus is quite difficult in India due to its non-specific clinical picture, the absence of eschar in a large number of patients and the lack of availability of specific tests The effect of climate change and human expansion into afforested areas has increased the incidence and re-emergence of the disease.[9] A high index of suspicion and careful clinical, laboratory and epidemiological evaluation is an essential tool for the early diagnosis of scrub typhus in resource-limited countries such as India. The bacteria are very difficult to stain as they lack a proper cell wall and also do not grow on cell free culture media. The mainstay of the diagnosis therefore is mostly serological detection of antibody in patients' sera or molecular detection. Data on correlation with other lab parameters and Seropositivity for Scrub Typhus cases is lacking.[10] This study was undertaken to correlate and analyze the biochemical parameters with seropositivity and patient age. It could also give insight to the disease process.

2. Materials and Methods

The study was conducted at the department of Microbiology, Raiganj Government Medical College and Hospital in collaboration with the Department of Biochemistry and central lab for last one year (1/1/2024- 31/12/2024). Ours is a rural tertiary care hospital in the Northern part of Bengal, caters the needs of patients from the neighboring districts of this region and also from neighboring states of Bihar, as well as Bangladesh. The local area is humid having moderate to heavy rainfall, plenty of paddy fields and wetlands and forests.[11,12] In Patients with AFI were enrolled in the study and their IgM ELISA test [J.Mitra Scrub Typhus IgM ELISA kit and InBios ELISA kits] the result for scrub typhus with a sensitivity of 91% and a specificity of 99% was used for diagnostic testing. The IgM ELISA test was performed using manufacturer's test instructions. The samples were tested on Erba Lisa wash™ and Lisa Scan™ [make Erba Manheim]A sample absorbance value>0.5was established as the cutoff criteria based on the local healthy normal sera. The other hematological and biochemical parameters were tested using Cobas Auto analyser and Sysmex 5 part machines. The demographic data including address, age, gender, duration of fever, and other available lab parameter were collected in a standard proforma. Patients with other established causes of pyrexia other than scrub typhus such as SARS CoV-2, malaria, dengue, leptospirosis, enteric fever, viral hepatitis and

viral meningitis, incomplete case records, unwilling patients were excluded from the study. The study was approved prior by the institutional ethics committee (vide ethical number [IEC.11/2023(03) DATE: 30/11/2023]). Waiver of consent was obtained from the Institutional Ethics Committee because this was a retrospective chart review. The data were entered in a data recording form and then transcribed to MS Excel data and analyzed using SPSS, Version 27.0 (SPSS Inc., Chicago, IL). Descriptive data were represented by frequency, percentage, and mean ± SD. Regression analysis, specifically a general linearized model (GLM) with posthoc analysis was performed to assess the correlation between the mentioned lab parameters among different age groups. The associations of clinical and laboratory variables were studied by multivariate regression and analysis. $p< 0.05$ was considered statistically significant.

3. Results

A total of 1,185 clinically suspected acute febrile illness (AFI) patients were tested for Scrub Typhus IgM ELISA. Among them, 244 cases (20.59%) were confirmed positive. The overall mortality rate among positive cases was 2.45% (n = 244), with a total of six deaths. The primary causes of mortality were pneumonia (n = 2, 33.6%), myocarditis (n = 1, 16.6%), and meningoencephalitis (n = 3, 50%). Patients who succumbed to the disease were excluded from the age-related analysis of biochemical and hematological parameters.

Clinical Features and Seasonal Variation: All Scrub Typhus-positive patients presented with fever, chills, and rigor upon hospital admission. The distribution of clinical features among positive cases is illustrated in **Figure 1**. A significant seasonal variation was observed, with the highest number of cases recorded in October and November (**Figure 2**). The positive cases were evenly distributed between indoor and outpatient settings, and no significant gender differences were noted among the confirmed cases. The duration of fever varied among cases, with the majority (65%) experiencing fever for 7–14 days.

Biochemical Marker Analysis Across Age Groups: The biochemical parameters were analyzed across three age groups: 0–5 years, 6–14 years, and above 14 years (N = 238, after excluding deceased patients). The analysis revealed that several biochemical markers, including direct bilirubin (D_Bilirubin), indirect bilirubin (I_Bilirubin), serum glutamate pyruvate transaminase (SGOT_Or_AST), albumin (AI), globulin (GI), creatinine, and potassium, exhibited significant variations among different age groups. In contrast, other biochemical markers such as serum glutamate oxaloacetate transaminase (SGPT_Or_ALT), urea, sodium, and alkaline phosphatase (ALP) did not show substantial age-related differences.

The distribution of these biochemical markers across age groups demonstrated varying proportions in different categories (normal, below normal, and above normal). For instance, in the direct bilirubin category for the 6–14 years age group, 30% of individuals had normal levels, 40% had below-normal levels, and 30% had above-normal levels. A similar trend was observed for other biomarkers such as indirect bilirubin, SGOT_Or_ALT, and ALP, indicating that most individuals fell within normal or below-normal ranges for these biochemical markers. These findings highlight the importance of age as a factor influencing biochemical variations in Scrub Typhus patients.

Hematological Parameter Analysis Across Age Groups: The hematological parameters analyzed in the same age groups (N=238) included platelet count, total leukocyte count (TLC), and hemoglobin (HB). The mean platelet counts are 106033.2/µl, and across the three age groups they were similar, suggesting no substantial differences. The TLC values exhibited a slight increase with age, with the highest mean observed in the 15+ years group [7843cell/µl], followed by the 6–14 years group[6906 cell/µl] and the lowest in the 0–5 years group [6954 cell/µl] . Mean hemoglobin levels were 9.9 across all age groups, with the lowest mean recorded in the 6–14 years group and the highest in the 15+ years group.

Multivariate analysis using Pillai's Trace and other statistical tests revealed that the intercept test was highly significant ($p < 0.0001$), indicating a strong overall effect of the model. However, the age group variable did not significantly impact the combined hematological parameters (platelet count,

TLC, and HB) (p = 0.163). This suggests that while some differences exist in TLC values between age groups, the overall influence of age on hematological parameters is minimal, with most comparisons showing no significant effects.

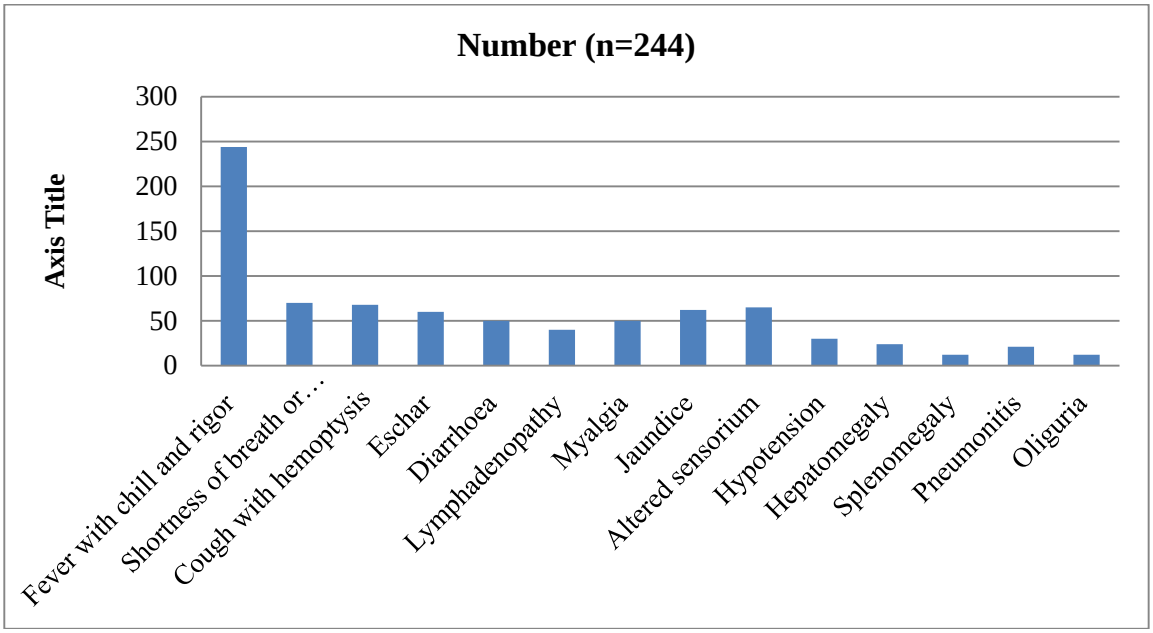

Figure 1 Distribution of Scrub Typhus Cases According to Clinical Feature.

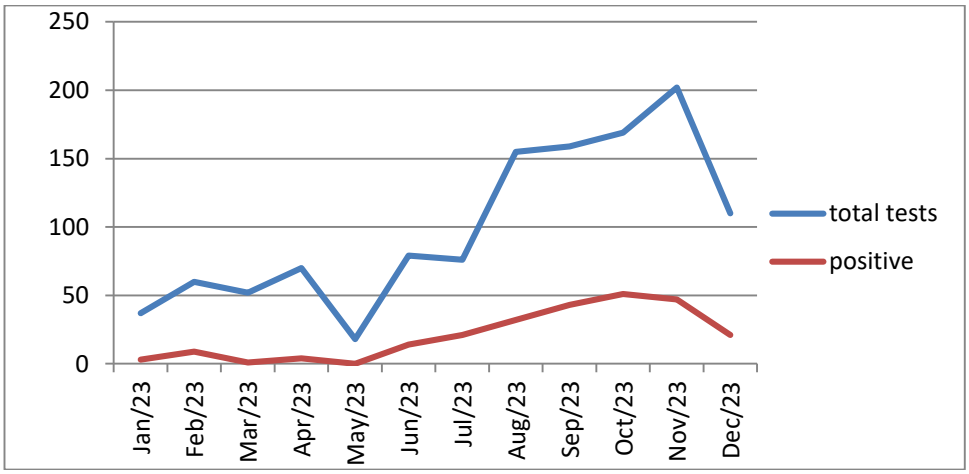

Figure 2 Distribution of Scrub Typhus Cases According to month of the year

4. Discussion

Scrub typhus is a febrile disease that is endemic in Asian-Pacific areas, including the Korean Peninsula. It is a clinically important disease because of its high incidence in endemic areas and associated with many serious complications. In our study 59% of patients were in age group of 15 to 60 years, people of this age group are mostly involved in agricultural activities or visit the forest/grass fields to collect grass. In our study about 54% cases were females; the higher incidence in females may be due to the fact that females in this region actively participate in the agricultural or horticultural work. The typical working position of females in a squatting position, with bare hands in the fields or cutting grass predisposes them for exposure to infected mites which inhabiting soil and scrub vegetation. Mahajan et al in their study noted that more than 2/3rdof patients were female. The diseases affected 40 % of cases of under 15 years of age but 67% case fatality were in this age group.[13] Thus we endeavored to identify any biochemical or hematological parameter alteration in different age group in scrub typhus cases for prediction of fatal outcome if any. In our study, duration of symptoms was 7-14 days in 65% of patients, < 7 days in 21.5% patients, >14 days in 12.5 % of

patients. Eschar is fpound only in 56 cases (23%) and was lesser than other studies. It may be that eschar is less frequent in South Asians, especially in dark skinned people.[14]

Our study suggested the prevalence of anemia (haemoglobin <11.0 g/dl) as 78.99% (188/238) and abnormal liver function in 60.08% (143/238) cases. Thrombocytopenia and leukocytosis were found in 79.41% (189/238) and 22.27% of cases. Immune thrombocytopenia may be the cause of thrombocytopenia in scrub typhus. Palanivel et al. from Chennai, India, revealed that 83% of the people they studied had anemia, which is consistent with the findings of the present study. [15]

The analysis revealed that several biochemical markers, including direct bilirubin (D_Bilirubin), indirect bilirubin (I_Bilirubin), serum glutamate pyruvate transaminase (SGOT_Or_AST), albumin (AI), globulin (GI), Creatinine, and potassium, exhibited significant variations among different age groups.[16] In contrast, other biochemical markers such as serum glutamate oxaloacetate transaminase (SGPT_Or_ALT), urea, sodium, and alkaline phosphatase (ALP) did not show substantial age-related differences. This finding predicts a reversal of the A/G ratio suggesting acute hepatocellular injury. Hypoalbuminemia causes decreased plasma colloidal oncotic pressure, increases hydrostatic pressure causing endothelial permeability, and fluid leakage to the interstitial space resulting in peripheral edema and intravascular hypovolemia. Few studies in our areas had been undertaken but not covered the sero-biochemical correlation.[12,17] Our study identified elevated aspartate aminotransferase liver enzyme levels and thrombocytopenia as predictors of complication due to scrub typhus. An elevated aspartate aminotransferase liver enzyme level as a determinant of severe scrub typhus has been re-established by our study. This was similar to the studies by Kispotta et al and Sharma et al. [18,19]. A few studies from south Bengal in pediatric age group especially infants (1-12 months) found that thrombocytopenia, hypoalbuminemia, and hyponatremia predict risk for poor outcome. In our study the 6 fatal cases were mostly 4 (66.67%) in the age group of 10-14 yrs and had similar biochemical parameters. [20,21]

This was a retrospective and a single-center study, a large prospective randomized controlled multi-centric study is needed to investigate further whether could predict the severity and course of the disease.

5. Conclusion

Overall, age group does not significantly influence the various biochemical parameters when controlling for other factors in the model. The significant findings related to the intercept indicate that there are overall differences in these health measures, but these differences are not explained by the age grouping. Only Creatinine (with a borderline significance level) shows a small age-related trend, which could warrant further investigation. In conclusion, age does not appear to have a major impact on the health parameters included in this analysis, suggesting that other factors might be more relevant in explaining variability in these health measures.

6. Acknowledgement

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7. Conflict of Interest

None.

8. Funding

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9. References

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