



R FACTOR AS MEASURE OF SEVERITY IN SCRUB TYPHUS- A NEW USABLE TOOL

General Medicine

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ABSTRACT

INTRODUCTION: Scrub typhus is acute febrile illness caused by *Orientia tsutsugamushi* an endemic disease occurring throughout the Indian subcontinent.(1) Incidence of scrub typhus has risen many times in Himachal Pradesh mainly during rainy season due to exposure to vegetation while working in fields. Acute onset fever, headache, Eschar and rash are clues for early diagnosis. Several factors have been suggested to be associated with severe complications(14). We carried out this study to study a new usable tool R factor as prognostic indicator in patients of scrub typhus.

RESULTS: A total of sixty patients were studied who presented with acute onset fever and were IgM scrub positive. Patients were studied for outcome which was discharge or death which ever was earlier. Patients were studied for outcome which was discharge or death which ever was earlier. In patients who expired mean R-factor was 5.1 (hepatocellular) and the one who survived mean R factor was 1.02 (cholestatic). Over all the R-factor was found to be significant ($p=0.17$) for death in scrub typhus.

CONCLUSION: This study explicitly explains the usefulness of R factor as a prognostic marker in patients with scrub typhus. Hepatocellular injury was found to be most important and had a poor prognosis

KEYWORDS

Scrub Typhus, R Factor, Prognostic Marker

INTRODUCTION :

Scrub typhus is acute febrile illness caused by *Orientia tsutsugamushi* an endemic disease occurring throughout the Indian subcontinent.(1) Incidence of scrub typhus has risen many times in Himachal Pradesh mainly during rainy season due to exposure to vegetation while working in fields. Rise in cases is mainly because of early presentation, recognition of eschar and point of care tests with high sensitivity. Acute onset fever, headache, Eschar and rash are clues for early diagnosis. ELISA test for IgM scrub has been used mainly to diagnose cases of scrub. Severe complications such as pneumonia, meningitis/encephalitis, septic shock, myocarditis, and acute renal failure and MODS can lead to death.(2-4). The case-fatality rate for untreated cases varies widely from 3% to 60%. (1) Several factors have been suggested to be associated with severe complications(14). Plasma rickettsial load is associated with disease severity in adults.(5) Clinical characteristics such as older age, underlying diseases, and delay of appropriate antibiotics administration seems to contribute to the severity.(6,7) Laboratory markers such as increased transaminases, hypoalbuminemia, leucocytosis, thrombocytopenia and elevated serum creatinine have been reported to be associated with the disease severity.(8-10)

R factor primarily used for drug induced liver injury was studied in this study as a severity index as well as prognostic marker in patients presenting with scrub typhus. R factor is calculated as ratio of alanine aminotransferase ALT/ALT upper limit normal divided by the alkaline phosphatase (ALP) divided by ALP upper limit normal and is used to differentiate hepatocellular from cholestatic liver injury, the ratio is typically >5 in hepatocellular injury, <2 in cholestatic injury and between 2-5 in mixed injury. We carried out this study to study a new usable tool R factor as prognostic indicator in patients of scrub typhus.

MATERIAL AND METHODS-

This study was conducted prospectively in department of Medicine DRPGMCH Tanda at Kangra. Sixty patients were enrolled between months of April to December 2018.

Inclusion criteria –

- 1) Patients aged >18 years
- 2) Patients presenting with acute febrile illness and IgM scrub positive with or without multiorgan dysfunction syndrome.

Exclusion criteria-

- 1) All other febrile illness IgM scrub negative.
- 2) Patients aged ≤ 18 years.

The chief complaint of the patients were recorded as fever, headache, jaundice, eschar, rash and multiple organ failure. The subjects were analyzed for biochemical, clinical profile, etiology and outcome. Samples for IgM scrub, liver function tests, and other relevant investigations were sent. IgM scrub typhus was done by kit method manufactured by In Bios International, Inc. This was a qualitative ELISA for the detection of IgM antibodies to *O. tsutsugamushi* in serum. R factor was calculated as ratio of alanine aminotransferase ALT/ALT upper limit normal divided by the alkaline phosphatase (ALP) divided by ALP upper limit normal. Chest radiograph and ABG were done. All the patients were treated as per set protocols for the disease. Patient outcomes included discharge from hospital or death which ever occurred earlier. Written consent was taken from all patients

STATISTICAL ANALYSIS:

The data as analyzed as per SPSS version 16. Univariate vs odd's ratio was calculated. Parametric or nonparametric tests were used according to the distribution of variables. Differences in categorical variables were analysed using the Chi-square. Significant value of p was taken as <0.05 . ROC (receiver operating characteristic) curve was plotted.

RESULTS:

A total of sixty patients were studied who presented with acute onset fever and were IgM scrub positive. Out of these 32 (53%) were females and 28 (47%) were males. 44 (73%) patients were in the age group of 30-50 yrs. Patients were studied for outcome which was discharge or death which ever was earlier.

Out of 60 patients, 26 (43%) patients died and 34 (57%) were discharged. Outcome was studied as per individual liver enzymes (ie SGOT (aspartate amino transferase), SGPT (alanine aminotransferase), ALP). Mean SGOT in patients who survived was 255 and who died was 207. mean value of SGPT in patients who died was 101 and who survived was 199. mean value of alkaline phosphatase in patients who survived was 233 and who died was 551. It was found to be statistically significant in relation to death with a p value of 0.010 Ratio of SGOT/SGPT in patients who died was 2 in

contrast to patients who survived in which it was 1.2. Ratio was not found to be statistically significant. R-factor was calculated for all patients. In patients who expired mean R-factor was 5.1 (hepatocellular) and the one who survived mean R factor was 1.02 (cholestatic). It was found that out of 26 patients who died, 21(81%) had hepatocellular dysfunction, 5(19%) had mixed and nil had cholestatic dysfunction. In 34 patients who were discharged 19(56%) had hepatocellular, 11(32%) had mixed and 5(12%) patient had cholestatic dysfunction. Overall 67% patients had hepatocellular dysfunction, 27% patients had mixed dysfunction and 8% had cholestatic dysfunction. The patients who died mainly had hepatocellular dysfunction (56%) and the patients who survived also were having mainly hepatocellular dysfunction (73%) which was not statistically significant independently. Over all the R-factor was found to be significant ($p=0.017$) for death in scrub typhus. ROC curve was plotted (figure1) which showed area under the curve of .837 thus proving our hypothesis that R factor can be used as an independent marker to predict mortality in scrub typhus patients. A pattern of hepatocellular injury was found but was not statistically significant.

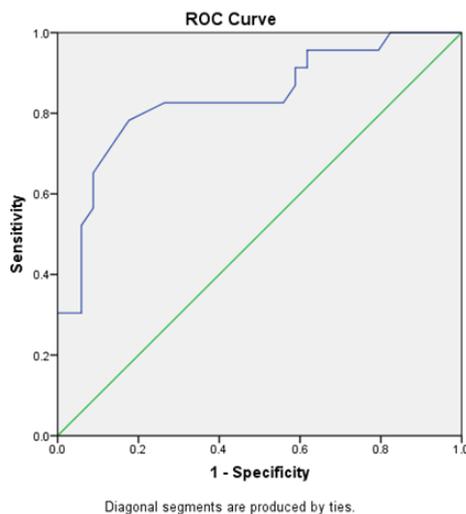
DISCUSSION:

Scrub typhus has been responsible for many deaths in patients presenting with febrile illness with rash. Very few studies have looked into prognostic factors leading to death in these patients. This study was carried out for using a tool which was used in other illnesses to use as a prognostic factor for predicting outcome in scrub. no study has discussed R- factor as prognostic marker in scrub. In a study by ritesh et al(1) in journal of association of physicians of India hepatic dysfunction was found to be one of the poor prognostic factor in scrub but R factor was not calculated in that study. In a study by park et al(2) liver enzymes SGOT/PT were raised in patients with scrub but none were found to be independently associated with poor prognosis in scrub. The basis for liver injury in scrub has been studied extensively and differentiates it from viral injury. O. tsutsugamushi hepatitis is speculated to cause primarily intrahepatic sinusoidal endothelial vasculitis and thus in turn increases the serum levels of AST, ALT and γ -GTP (glutamyltransferase) due to direct cytopathic liver damage(6) thus inciting hepatocellular injury unlike that of viral hepatitis which has both hepatocellular and cholestatic injury. Previous studies have reported that hepatic dysfunction in patients with scrub typhus was found to be mainly hepatocellular-patterned abnormality.(3,4,5,11) This has been proven beyond doubt in our study since most of the patients presented with hepatocellular injury.

The infection of *Orientia tsutsugamushi* is characterized pathologically by focal or disseminated vasculitis and perivasculitis on the involved organs(15). Thus, scrub typhus infected in liver is speculated to cause mild focal inflammation due to intrahepatic sinusoidal endothelial vasculitis and to increase the levels of aminotransferases due to direct cytopathic liver damage.(3,12,13)

CONCLUSION:

This study explicitly explains the usefulness of R factor as a prognostic marker in patients with scrub typhus. Hepatocellular injury was found to be most important and had a poor prognosis. Further studies are required to study this factor.



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