Rickettsial Infections in Goa—Not Just Scrub Typhus!

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Abstract

Background and Objectives: Rickettsial infections are an important cause of undifferentiated febrile illness in tropics. While scrub typhus was reported from Goa, other rickettsial infections have not been reported earlier. The present study was planned to identify pattern of rickettsial infections in Goa.

Materials and Methods: All patients presenting with undiagnosed acute febrile illness were recruited over a two-year period. Other causes of febrile illness were ruled out by appropriate tests. Sera of the patients were subjected to Weil Felix testing. Patients were labelled as probable rickettsial infection if the titres to any one antigen was >1:80 as per DHR-ICMR guidelines. Clinical details were obtained retrospectively from case records.

Results: Sixty-one patients met inclusion criteria, of which six were excluded because of alternative diagnosis. Out of remaining patients, 32 were positive by Weil Felix test (positivity rate 58.18%). Eighteen were males; there was no age predilection. Twenty-one patients were positive for OXK (scrub typhus); of these, 13 were positive for other antigens also. Of the remaining, 6 were positive for OX2 alone, 2 were positive for OX 19 alone, one patient was positive for both OX2 and OX19 and 2 were positive for all three antigens. Most patients had non-specific clinical presentation. Two patients in scrub typhus group and one in spotted fever group died (mortality rate =9.5% and 11.1 %).

Interpretation and Conclusion: Our study shows that rickettsial infections other than scrub typhus are also prevalent in Goa. Weil Felix test is useful in diagnosis; however, there is cross reactivity between various antigens of the test, hence differentiation into various groups of rickettsiosis should not be done based on Weil Felix test alone.

Introduction

Rickettsiosis is an under recognised cause of acute febrile illness in the tropics, owing to non-specific clinical features as well as due to lack of access to diagnostic modalities.1 However, in last few years, there have been multiple reports of occurrence of the disease from different parts of the country.2–8 Though the prevalence of scrub typhus was reported earlier from Goa,6 data on other rickettsial diseases was not available from this part of the country.

The present work was undertaken to study the prevalence of rickettsial infections amongst patients presenting with undiagnosed fever to our Institution. The primary aim was to ascertain the pattern of rickettsial infections in Goa. We also aimed to study the utility of Weil Felix test in diagnosis of the disease.

Materials and Methods

This study was conducted at a tertiary care institution in the state of Goa. All patients who had presented to our institution with an undiagnosed acute febrile illness over a two year period were included in the study. Other causes of acute febrile illness such as malaria, leptospirosis, dengue, chikungunya, bacterial sepsis, etc were ruled out by appropriate investigations. The sera of patients who remained undiagnosed were collected after informed consent and stored at -70°C. These samples were subjected for Weil Felix...

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Received: 25-09-2016; Accepted: 30-03-2017
testing in batches. The test was performed and interpreted as per the instructions of the manufacturer (PROGEN, Tulip Diagnostics, Goa). Positivity titre of equal to or more than 1:80 was considered significant as per the DHR-ICMR guidelines for the diagnosis and treatment of rickettsial infections.\textsuperscript{10} The clinical profile of the positive patients was retrospectively obtained from their case records and entered in a proforma and analysed.

The study was approved by institutional Ethics Committee.

### Results

Sixty-one patients met the inclusion criteria and were screened for the present study; out of which 6 patients were excluded as they had an alternative diagnosis. The remaining 55 patients were tested for rickettsial diseases with Weil-Felix test. Thirty-two patients were found to be positive (positivity rate =58.18%). Of this, 18 patients were males; there being no specific predisposition for any age group. The youngest patient was 13 years while the oldest was 61 years of age. Twenty one patients were positive for OXK suggesting scrub typhus, of which, 8 were positive forOXK alone while remaining 13 were positive for other antigens also. Out of the remaining 11 patients, 6 were tested positive forOX2 alone, 2 were positive forOX 19 alone, and one patient was positive for both OX2 andOX19 suggesting that all these patients had rickettsial diseases other than scrub typhus. Remaining 2 patients had positivity for all three antigens, however both of them had high titres ofOX19 andOX2 and had petechial rash, hence they were also labelled as spotted fever group (SFG) rickettsiosis.

The pattern of positivity for different antigens of Weil-Felix is given in Table 1.

All 32 patients tested positive by Weil Felix had fever, additionally 7 patients in scrub typhus group, 4 patients in spotted fever group and 1 patient in typhus group also had rash. Eschar was seen in 4 patients of scrub typhus, none of the cases of other rickettsial infections had eschar. Hepatitis and acute kidney injury were the most common complications. Two patients in scrub typhus group and one patient in spotted fever group succumbed to the illness, giving a mortality rate of 9.5% and 11.1% respectively.

### Discussion

Rickettsial infections are one of the common causes of undiagnosed febrile illness in the tropics.\textsuperscript{1,11-16} These diseases have a high mortality if the diagnosis and treatment are delayed.\textsuperscript{16} Rickettsial infections are diagnosed mainly by serological assays or DNA-PCR,\textsuperscript{17,18} which are expensive and unavailable in most parts of our country. As a result, these infections remain grossly under diagnosed and underreported.\textsuperscript{1} In the last 2 decades, the outbreaks of rickettsial diseases have been reported from various parts of India.\textsuperscript{2-6,19-21} The prevalence of scrub typhus in Goa was reported earlier,\textsuperscript{2} however, the presence of other rickettsial diseases was not documented from our State. This study was therefore aimed to identify the presence of various rickettsial diseases in Goa.

A confirmed case of rickettsial disease is diagnosed by the presence of either rickettsial DNA on PCR or rising antibody titres on indirect immune fluorescence assay (IFA).\textsuperscript{10,22} Weil Felix test is a cheap alternative in resource poor settings and is mostly used for the diagnosis in our country.\textsuperscript{4,7,20,25,27} Though the test lacks sensitivity, it is relatively specific.\textsuperscript{1,25-27} In the present study, Weil Felix test was used for the diagnosis. A titre of 1:80 or above for any of the three antigens was considered as a probable case of rickettsial infection.\textsuperscript{10}

Based on pattern of positivity to the various antigens on Weil Felix testing, the patients can be classified into three categories.OX19 reacts strongly with serum from patients of typhus fever group (also Rocky Mountain Spotted Fever),OX2 reacts with serum from patients having spotted fever group rickettsiosis (except Rocky Mountain Spotted Fever) andOXK reacts with serum from scrub typhus patients.\textsuperscript{25} We have also used the same pattern for classifying our patients. However, as can be seen from Table 1, majority of our patients had positive titres for more than one antigen. Further, though scrub typhus was believed to give positive reaction forOXK alone,\textsuperscript{25} in our study many of the probable scrub typhus patients (13 out of 21) had positivity to other antigens. This shows that there can be a cross reactivity to the different antigens.
of Weil Felix test. However, as we have not done specific IgM ELISA or DNA-PCR tests for scrub typhus, we will have to interpret this finding with caution. Such cross reactivity has been reported in many other studies,4,7,24 which suggests that differentiation of rickettsial infections into various groups such as scrub typhus, spotted fever group and typhus group based on pattern of agglutination in Weil Felix test is not specific.

The other reason for the positivity to different antigens could be the possibility of mixed infections with scrub typhus and other rickettsiosis26 however; this again needs to be confirmed by specific tests.

As Weil Felix test uses antigens from Proteus species, the test may give false positivity.25 Hence, the test is not confirmatory for rickettsial diseases. The specificity of the test could be increased by repeating it in convalescent sera. In our study, we could not obtain convalescent sera. We have not used any other gold standard tests for confirmation. However, most of our patients have shown positivity to higher dilutions; some even to 1:640 or 1:1280, which rules out false positivity. Positivity rate of 56% in undiagnosed febrile illness shows that rickettsial infections are prevalent in Goa and should be considered in the differential diagnosis of any acute febrile illness. Further, there is cross reactivity to various antigens in a positive case; hence, categorisation into various groups based on Weil Felix testing alone may not be specific.

Limitations of the Study

We have not used any of the Gold standard tests to confirm the diagnosis of rickettsial disease, thus all patients were categorised as “probable” cases as per DHR-ICMR guidelines.10 The small sample size is also a major limitation of the study.

Conclusion

In conclusion, our study shows that not only scrub typhus but also other types of rickettsial infections are prevalent in Goa and should be considered in the differential diagnosis of any acute febrile illness. Further, there is cross reactivity to various antigens in a positive case; hence, categorisation into various groups based on Weil Felix testing alone may not be specific.

References

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