



Rickettsial Infection in Patients with Acute Febrile Illness at a Tertiary Care Hospital in Bengaluru, India - Serological, Demographic and Clinical Profile

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Authors' contributions

This work was carried out in collaboration between all authors. Author SKC designed the study and wrote first draft of the manuscript. Author JVS wrote the protocol and performed statistical analysis. Author RA performed analysis of study and did the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background and Objectives: Rickettsial infections are under recognised cause of acute febrile illness (AFI) in India. The reason being low index of suspicion, the absence of specific signs/symptoms and lack of access to confirmatory laboratory tests. These diseases have a high mortality, which can be averted if diagnosed and treated early. Weil- Felix test is the cheapest and widely used test for diagnosis in India. The present study was undertaken with the objective of evaluating the patients with AFI, for rickettsial infection using Weil- Felix test and study their demographic and clinical profile.

Materials and Methods: One hundred Patients with AFI, from June 2015 to December 2016 were evaluated for Rickettsial infection. Detailed history, signs, symptoms were recorded. The serum samples were analysed by Weil-Felix test.

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Results: Of the 100 patients, 69 showed a titre of 1:80/>>. The disease was more common in children and in the cooler months. Rash, headache, vomiting, pain abdomen and altered sensorium were common symptoms. Most common signs were hepatomegaly/ splenomegaly (51%), rash (40%), CNS involvement (26%). All 69 patients diagnosed with Rickettsial infection, were started on Doxycycline, however 07% of patients succumbed.

Interpretation and Conclusions: Rickettsial infection should be considered in the differential diagnosis of AFI, especially when associated with rash, gastrointestinal symptoms, seasonality etc. Weil Felix test is useful for initial diagnosis and timely treatment of Rickettsial infection. Delay in diagnosis and treatment can lead to increased mortality.

Keywords: Rickettsial infection; acute febrile illness; Weil Felix test; doxycycline; India.

1. INTRODUCTION

Burden of rickettsial diseases in India largely remains unmeasured. They are prevalent in India as an important cause of acute febrile illness (AFI). They have been reported from various parts of India, including Karnataka [1]. Rickettsial infections are re-emerging but are under diagnosed, leading to high mortality in untreated cases [2].

In India, Scrub typhus seems to be the most common rickettsial infection, followed by Indian tick typhus (spotted fever group). Scrub typhus is transmitted by chigger *Leptotrombidium deliense* and Indian tick typhus by tick *Rhipicephalus sanguineus*. Epidemic typhus transmitted by body louse *Pediculus humanus corporis*, Endemic typhus transmitted by rat flea *Xenopsylla cheopis* are also reported from various parts of India [3]. Under diagnosis in rickettsial infections is due to the low index of suspicion and absence of signs or symptoms specific enough to make a clinical diagnosis early in the course, when treatment is likely to be highly rewarding. The absence of easy availability of sensitive and specific tests further adds to diagnostic dilemma. However, if diagnosed in time, they are easily treatable conditions with rapid improvement on treatment with appropriate antibiotics [4]. During the course of illness, the infection clinically manifests as non-specific febrile illness, with headache, myalgia, rash, often accompanied by systemic involvement, which may lead to multi-organ dysfunction and death in untreated cases [5]. All clinical manifestations of rickettsial diseases are due to infective vasculitis and perivascular inflammatory response leading to occlusion of vascular lumen and vascular leakage [1].

The mainstay of diagnosis in Rickettsial infection is serology [6]. In resource limited settings like ours, Weil- Felix test is widely used as it enables the clinician to initiate treatment and assess

prognosis of the infection. While the cost of the definitive diagnosis of rickettsial infections by Immunofluorescence assay (IFA) or PCR runs into several thousands, the cost of Weil Felix test and complete treatment with doxycycline is meager.

With this background, the present study was undertaken with the aim of evaluating the patients with AFI attending our tertiary care hospital for presence of rickettsial infection by using Weil- Felix test and study their demographic and clinical profile.

2. MATERIALS AND METHODS

Prospective cross-sectional study was conducted in a tertiary care hospital from June 2015 to December 2016. Institutional Ethical committee (Bangalore Medical College and Research Institute) approval was taken. Informed consent from patients was obtained. Study was conducted among 100 consecutive patients as per inclusion criteria [7].

Inclusion criteria: All patients with AFI, with fever of 5 days or more, with or without eschar, headache, rash, lymphadenopathy, multi-organ involvement like liver, lung and kidney involvement were clinically suspected as cases of Rickettsial infection and included in the study after ruling out other common causes of fever as per DHR-ICMR guidelines.

Exclusion criteria: AFI due to other causes of fever like malaria, enteric fever, dengue, leptospirosis.

Detailed clinical history, demographic details were taken, signs and symptoms were recorded. The serum samples were analysed for rickettsial infection by Weil-Felix test. Weil Felix test was performed using commercially available kit (Omega Diagnostics Ltd. Scotland, UK) as per manufacture's instruction for OX K, OX19 and OX 2. Titre of $\geq 1: 80$ was taken as significant.

3. RESULTS

Weil Felix test was performed using serum samples in 100 patients as per our inclusion criteria. A titre of 1: 80 / > was taken as suggestive of rickettsial infection. A total of 69/100 (69%) patients showed a titre of 1:80/>. Of 69 cases, 45/100 (45%) showed a titer of 1:80/> for OX K suggestive of Scrub typhus and 24/100 (24%) a titre of 1:80/> for OX 19 and OX 2 alone or both, suggestive of other Rickettsiae (Spotted fever group and Typhus group).

Out of 69 patients in whom rickettsial infection was diagnosed, 38 (55%) were males and 31 (45%) were females. The age of patients varied from 04-63 years, 39 (57%) were pediatric patients and 30 (43%) were adults. The maximum number of cases 47 (68%) were seen during the rainy season (June- September), followed by 20 (29%) during winter (October-February) and least 02 (03 %) during summer (March to May) (Fig. 1).

Most of the patients 23 (33%) were from Bengaluru, followed by 13 (19%) from Chikballapura, 13 (19%) from Tumkur, 05 (07%) from Ramnagar and 15 (22%) from other places like Mandya, Doddaballapur, Chitradurga, Bidar, Hindupur (Fig. 2).

All the patients had fever. Rash, headache, vomiting, pain abdomen and altered sensorium were other common symptoms. On examination rash was seen in 28 (40%), pallor in 11 (16%), icterous in 06 (09%) and eschar in 04 (06%). Systemic examination by the clinician revealed hepatomegaly with or without splenomegaly in 35 (51%), signs of CNS involvement in 18 (26%) and pleural effusion in 02 (03%) patients (Table 1).

Doxycycline was started for all the 69 patients diagnosed with rickettsial infection, of which 62 (90%) improved, 05 (07%) patients succumbed, whereas 02 (03%) were lost for follow up.

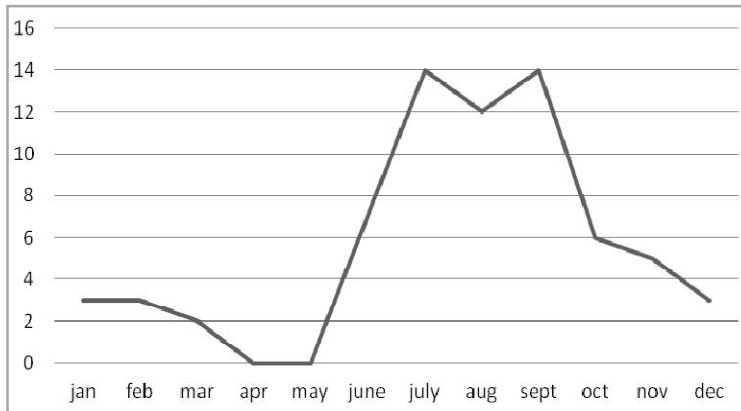


Fig. 1. Seasonal variation of Rickettsial infection

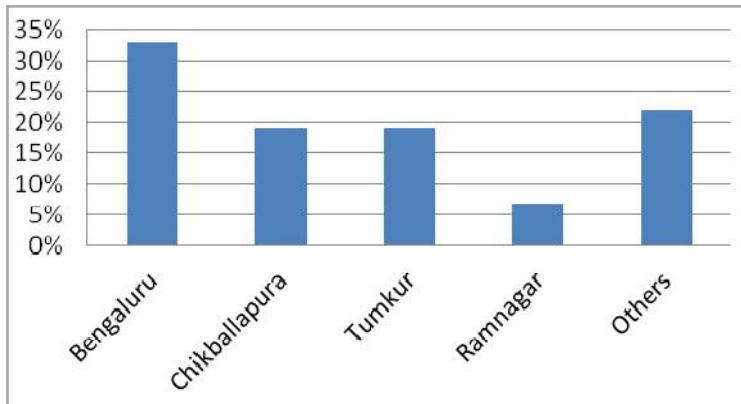


Fig. 2. Geographical distribution of cases

Table 1. Clinical parameters of patients

	Clinical parameters	Percentage (n= 69)
Symptoms	Fever	100
	Rash	40
	Headache	26
	Vomiting	23
	Pain abdomen	19
	Altered sensorium	10
Signs	Rash	40
	Pallor	16
	Ictericus	09
	Eschar	06
	Hepatomegaly /Splenomegaly	51
	CNS involvement	26
	Pleural effusion in	03
Weil Felix test (titre ≥ 1: 80)	OX K	45
	OX 19 and 2	24

4. DISCUSSION

In India, rickettsial infections constitute re-emerging group of zoonosis [5]. Its presence has been reported from various parts of India [8,9]; Bengaluru being no exception as shown in the present study. In our study, 69% of the cases with AFI were found to be due to Rickettsiosis, which is quite significant. Other studies have reported 12-50% rickettsial infection in a similar cohort [2,5,8,10]. Disease was more common among males and in paediatric population. Increased outdoor activity may be the reason for this gender and age bias. Majority of the cases were seen during rainy season (68%) followed by (29%) in winter, similar observation has been made in other studies as well [5,8,11]. This seasonality may be attributed to change in climate. After the rainfall, hatching of mite eggs into larvae (chiggers) responsible for the disease transmission may be favoured by increased humidity [11,12]. Awareness of seasonality is essential for taking up preventive measures.

Our cases were from both urban and rural Bengaluru and surrounding areas. Presence of disease in urban areas is reported in another study as well [5]. Though traditionally rickettsial infections are known to be predominantly rural [8], its presence in urban areas cannot be ruled out and should be looked for.

Non specific clinical features like fever, rash, headache, vomiting, pain abdomen and altered sensorium were common symptoms seen, as documented in other studies [1,5]. Awareness regarding nonspecificity of clinical features helps clinicians to have high index of suspicion to

consider possibility of the rickettsial infection in cases of AFI. An algorithmic or stepwise approach can be used for the diagnosis of rickettsial diseases in a resource poor setting [1,4].

Other common clinical findings encountered in the study were rash, hepatosplenomegaly, signs of CNS involvement and pleural effusion. Similar findings have been reported in other studies [2,5,10]. Eschar which is considered as pathognomic of scrub typhus was seen only in 06%. But eschar may be a highly variable finding, may not be found even when present, unless thoroughly searched for.

In the present study, 62 patients showed good clinical response on treatment with Doxycycline. All of them improved without any sequelae. Rapid defervescence with an appropriate antibiotic like Doxycycline can be taken as diagnostic of rickettsial infection [1]. Five patients who succumbed to death in the present study were critical and had complications at the time of admission to hospital. Among them, 01 patient developed disseminated intravascular coagulation, another progressed to multi organ dysfunction following acute kidney injury and 03 patients developed meningoencephalitis and succumbed. Mortality in our study (07%) was slightly lower than that reported in other studies [10,13,14]. This may be due to prompt therapy with doxycycline.

Rickettsial infections are diagnosed mainly by serological assays or PCR [15,16]. However, the cheapest and widely used test in our country is Weil- Felix test. A titre of 1:80 or above for any of

the three antigens (OX K, OX 19, OX 2) is considered as a probable case of Rickettsial infection [7]. In our study, out of 69 cases of Rickettsiosis, 45 cases showed titer of 1:80/> for OX K suggestive of scrub typhus and 24 patients showed titre of 1:80/> for OX 19 and or OX 2 suggestive of other rickettsial infection (Spotted fever group and Typhus group).

Though Weil-Felix test is not considered very useful, comparative evaluation of Weil-Felix test and IgM ELISA for diagnosis of scrub typhus carried out at NCDC, India, showed that it is equally sensitive with specificity of 89% [3]. The test is useful in circumstances where IFA or PCR are not accessible. It has to be interpreted in the proper clinical context and is not outmoded [17].

5. CONCLUSION

In conclusion, our study shows that rickettsial infections are re-emerging. They should be considered in the differential diagnosis of AFI, especially when associated with rash, gastrointestinal symptoms, seasonality etc. Delay in diagnosis and treatment may lead to complications and higher mortality. Early recognition and treatment with doxycycline are the key factors for a favourable outcome. Weil Felix test is useful for initial diagnosis in resource poor settings, where confirmatory tests are not accessible. In view of low specificity/ sensitivity, results of Weil Felix test should be interpreted in right clinical perspective. Confirmatory tests such as Immunofluorescence assay or PCR should be performed whenever feasible for specific diagnosis.

CONSENT

Informed written consent from patients was obtained.

ETHICAL APPROVAL

Institutional Ethical Clearance (Bangalore Medical College and Research Institute) obtained.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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