

Original Article

Assessment of Clinical Manifestation of Rickettsial Infection and its Correlation with Weil-Felix Test

Shiva Prasada T¹, Krishna Kumar Naik T²

¹Senior Resident, ²Assistant Professor, Department of General Medicine, KIMS, Koppal, Karnataka, India.

Abstract

Background: Rickettsial diseases are some of the most covert re-emerging infections of the present times. They are generally incapacitating and notoriously difficult to diagnose and untreated cases can have fatality rates as high as 30-35% but when diagnosed properly, they are often easily treated. **Objective:** To assess the clinical manifestation of rickettsial infection and its Correlation with Weil-Felix test. **Setting:** This prospective observational study was conducted in the department of general medicine, KIMS, HUBLI. **Participants:** 60 subjects. **Sampling:** convenient sampling. **Statistical Analysis:** Chi square test was used to test statistical significance.

Results: The study has included 60 cases of clinically confirmed rickettsial disease, who were presented to a tertiary care teaching hospital between November, 2015 to January, 2017. The key findings of the study were only 40% and 20% respectively in Weil felix test, 21 (35%) had 80 titre, the number of cases with titre 160, 320 and 640 were 19 (31.67%), 13 (21.67%) and 7 (11.67%) respectively

Conclusion: The study has highlighted the need to have a high index of suspicion to enhance the diagnosis of rickettsial diseases and also the strong association between weil felix titre and liver and renal dysfunction.

Keywords: Rickettsial diseases, weil felix test, weil felix titre, clinical manifestation.

Introduction

Rickettsia disease is zoonotic where human beings are accidentally involved in a chain of transmission between trombiculid mites (chiggers), ticks or fleas and animals (most commonly rodents). Rickettsial infection is caused by a variety of intracellular, gram negative bacteria from genera Rickettsia, Oriental, Ehrlichia, Neorickettsia, Neoehrlichia and Anaplasma, belonging to the Alphaproteobacteria.¹

The rickettsial disease commonly presented with symptoms like fever, rashes, eschar, cough, breathlessness, nausea, vomiting, myalgia^{2,3} and in

untreated cases patient may develop the complications like jaundice, renal failure, pneumonitis, acute respiratory distress syndrome (ARDS), septic shock, myocarditis and meningoencephalitis are various complications known with this disease.⁴

Rickettsial infections are grossly under-diagnosed in India. As no single laboratory finding is specific for early diagnosis, treatment needs to be started empirically on clinical and epidemiological suspicion. In view of low index of suspicion, nonspecific signs and symptoms and absence of widely available sensitive and specific diagnostic test, these infections are extremely difficult to diagnose but treatment is easy, affordable and often successful with dramatic response to antimicrobials.

Today rickettsial infection can be accurately diagnosed by immunofluorescence and ELISA. But these tests are very expensive and are not easily available. As a result, the main diagnostic tool in the clinician's hand is

Corresponding Author :

Dr. Krishna Kumar Naik T

Department of General Medicine, KIMS, Koppal,
Karnataka, India 583231. Phone : 9686647369 (M)
Email: dr.krishnakumarnaikt@gmail.com

still the weil-felix test. Weil felix test has less sensitivity but the specificity has been proven to be quite acceptable. Isaac .et. al., have demonstrated that the sensitivity of Weil-Felix was 30% at a breakpoint titre of 1:80, but the specificity and positive predictive value were 100%. Hence Weil-Felix test is still not entirely obsolete but has to be interpreted in the correct clinical context. ⁵

But there are very limited number of studies conducted on Indian population, which have documented the association between weil felix reaction and various clinical and laboratory parameters in rickettsial disease. Hence the current study was conducted to fulfill this knowledge gap. Thus, the present study was designed to assess the clinical manifestation of rickettsial infection and its correlation with Weil-Felix test

Materials and Method

This prospective observational study was conducted in the department of general medicine, KIMS, HUBLI. The study population included all the patients presenting fever, rash and were diagnosed with rickettsial disease by clinical examination. The data collection for the study was conducted between November 2015 to January 2017.

Inclusion criteria- Clinical features consistent with rickettsial infection and positive weil felix test

Exclusion criteria -1. Subjects who do not consent to the study.

2. Cases with other established causes of infection.

Sample size:

A total of 60 subjects, satisfying the inclusion and exclusion criteria were included in the final analysis. The sample size was calculated assuming the expected proportion of rickettsial infection as 11% among fever cases as per previously published studies, with a precision of 8% and 95% confidence level, using the following formula. $n=Z^2(1-P)d^2$

Where n = Sample size

Z = Z statistic for a level of confidence= 1.96

P = Expected prevalence of proportion

(If the expected prevalence is 11% then $P= 0.11$)

d = Precision (If the precision is 8% then $d=0.08$).

The required sample size, as per the above mentioned calculation was 59. To account for a 5% nonparticipation rate it was decided to sample 63 subjects, so that final analysis can include not less than 59 subjects. The final analysis has included 60 subjects at the end of data collection period.

Sampling method: All the eligible study subjects, satisfying inclusion and exclusion criteria were recruited into the study by convenient sampling.

Method of collection of data: Cases of fever admitted in the study period in our hospital were followed up on the basis of weil felix positivity. The clinical presentation and multiple organ dysfunctions in these patients were evaluated with a special focus on the renal manifestation and hepatic manifestations.

Data collection tools:

The data was collected using a structured proforma, which has documented the following details

1. Socio-demographic information
2. Clinical presentation
3. Weil Felix reaction positivity pattern
4. Other laboratory parameters

Ethical considerations

Clearance was obtained from ethical committee. Written and informed consent was sought from the patients. They were given the option of quitting from the study if so desired by them. No element of compulsion was exerted. All data were kept confidential.

Statistical methods:

Weil-Felix was considered as the primary outcome variable. Symptoms of disease and blood pressure were considered as an explanatory variable. Demographic age and gender were considered as other explanatory variables.

Descriptive analysis: Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables.

Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots.

Inferential statistics: The association between quantitative blood pressure variables and any positive weil felix was assessed by comparing the mean values. The mean differences along with their 95% CI were presented. ANOVA was used to assess statistical significance.

The association between all symptoms of the disease and weil felix titre was assessed by cross tabulation and comparison of percentages. Chi square test was used to test statistical significance.

P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis. ⁶

Results

The mean of age was 36.75 years with a standard deviation of 17.81. The youngest person was 13 years old and the oldest person was 75-years-old. Among the study population, 36 (60%) were male and 24 (40%) were female. Among the study population, 24 (40%) was an indoor occupation and 36 (60%) were an outdoor occupation. Among the study population, 46 (76.67%) were rural and 14 (23.33%) were urban. (Table 1)

Table 1: Descriptive analysis of socio-demographic characteristics in study population (N=60)

Socio-Demographic Characteristics	Frequency	Percentage
Gender		
Male	36	60.00%
Female	24	40.00%
Occupation		
Indoor	24	40.00%
Outdoor	36	60.00%
Residence		
Rural	46	76.67%
Urban	14	23.33%

Among the study population, 57 (95%) people had headache. The number of congestion of eyes, rash, cough, pain abdomen, tick bite, bleeding manifestations, eschar, hepatosplenomegaly, icterus, myalgia, fever and others symptoms was 56 (93.33%), 55 (91.67%), 54 (90%), 24 (40%), 22 (36.67%), 12 (20%), 42 (70%), 30 (50%), 60 (100%) and 57 (95%) respectively. Among the study population, 50(83.33%) people had no Pleural effusion and 10 (16.67%) people had Pleural effusion. (Table 2)

Table 2: Descriptive analysis of symptoms in study population (N=60)

Symptoms	Frequency	Percentage
Tick bite	24	40.00%
Fever	60	100.00%
Rash	55	91.67%
Myalgia	60	100.00%
Headache	57	95.00%
Cough	54	90.00%
Pain abdomen	46	76.67%
Congestion of eyes	56	93.33%
Bleeding manifestations	22	36.67%
Eschar	12	20.00%
Icterus	30	50.00%
Lymphadenopathy	40	66.7%
Hepatosplenomegaly	42	70.00%
Others	57	95.00%

Among the study population, 15 (25%) people had no Weil Felix OX2 titre. The number of people with 80, 160 and 320 Weil Felix OX2 titre was 21 (35%), 14 (23.33%) and 10 (16.67%) respectively. (Table 3)

Table 3: Descriptive analysis of Weil Felix OX2 titre in study population (N=60)

Weil Felix OX2 titre	Frequency	Percentage
No	15	25.00%
80	21	35.00%
160	14	23.33%
320	10	16.67%

Among the study population, 36 (60%) people had no Weil Felix OXK titre. The number of 80, 160 and 320 Weil Felix OXK titre was 19 (31.67%), 4 (6.67%) and 1 (1.67%) respectively. (Table 4)

Table 4: Descriptive analysis of Weil Felix OXK titre in study population (N=60)

Weil Felix OXK titre	Frequency	Percentage
No	36	60.00%
80	19	31.67%
160	4	6.67%
320	1	1.67%

Among the study population, 35(58.33%) people had no weil felix OX19 titre. The number of 80, 160, 320 and 640 Weil Felix OX19 titre was 6 (10%), 8 (13.33%), 4 (6.67%) and 7 (11.67%) respectively. (Table5)

Table 5: Descriptive analysis of Weil Felix OX19 titre in study population (N=60)

Weil Felix OX19 titre	Frequency	Percentage
No	35	58.33%
80	6	10.00%
160	8	13.33%
320	4	6.67%
640	7	11.67%

Among the study population, 21 (35%) people had 80 titres any positive weil felix. The number of overall Weil Felix titre 160, 320 and 640 Overall Weil Felix titre was 19 (31.67%), 13 (21.67%) and 7 (11.67%) respectively.

Discussion

mean of age was 36.75 years with a standard deviation of 17.81. The youngest person was 13 years old and the oldest person was 75 years-old. In contrary, Thomas R. et. al., have studied children below 18 years who were hospitalized for suspected rickettsial fever.⁷ Contradicting to this, a study by Lindblom. et. al., have recruited participants whose median age was 64 years.⁸ Of the study population, 36 (60%) were male and 24 (40%) were female. This is dissimilar to the 82 (37.6%) men and 136 (62.4%) women who were enrolled in Lingblom. et. al., study.⁸ Among the study population, 24 (40%) was an indoor occupation and 36 (60%) were an outdoor occupation. Among the study population, 46 (76.67%) were rural and 14 (23.33%) were urban.

In the study population, 57(95%) people had headache. The number of congestion of eyes, rash, cough, pain abdomen, tick bite, bleeding manifestations, eschar, hepatosplenomegaly, icterus, myalgia, fever and others symptoms was 56 (93.33%), 55 (91.67%), 54 (90%), 24 (40%), 22 (36.67%), 12 (20%), 42 (70%), 30 (50%), 60 (100%) and 57 (95%) respectively. Among the study population, 50 (83.33%) people had no Pleural effusion and 10 (16.67%) people had Pleural effusion. In our study population, 15(25%) people had no Weil Felix OX2 titre. The number of people with 80, 160 and 320 Weil Felix OX2 titre was 21 (35%), 14 (23.33%) and 10 (16.67%) respectively. Among the study population, 36 (60%) people had no Weil Felix OXK titre. The number of 80, 160 and 320 Weil Felix OXK titre was 19 (31.67%), 4 (6.67%) and 1 (1.67%) respectively. Among the study population, 35 (58.33%) people had no Weil Felix OX19 titre. The number of 80, 160, 320 and 640 Weil Felix OX19 titre was 6 (10%), 8 (13.33%), 4 (6.67%) and 7 (11.67%) respectively.

Among the study population, 21 (35%) people had 80 titre any positive Weil Felix. The number of overall Weil Felix titre 160, 320 and 640 Overall Weil Felix titre was 19 (31.67%), 13 (21.67%) and 7 (11.67%) respectively. Thomas R. et. al., have found Weil Felix positivity in 1:160 titre among 70% cases, while elevated OX-K titre in 80% cases.⁷ In a study by Amano K. et. al., about 80% sera were positive for the Proteus OXK antigen.⁹ Lindblom. et. al., have described 44% of participants who had seropositivity for Rickettsial species. In addition, during follow-up of the seropositive cases about 18.3%, had raised titre which indicated

recent infection.⁸

Of the people with a tick bite, 3 (12.5%) people had 80 Overall Weil-Felix titre. The number of people with 160, 320 and 640 Overall Weil Felix titre was 4 (16.66%), 10 (41.66%) and 7 (29.16%) respectively in people with a tick bite. Among people without tick bite higher proportion of people had 80 and 160 titre. None of them had 640 titre. The ticks bitten participants who were included in the Lindblom. et. al., a study has shown 8.3%(39) of ticks (brought by them) that were Rickettsial sp positive and about 31.3% (five out of 16) participants bitten by Rickettsiae infected ticks were seroconverted.⁸ In those subjects with fever, 5 (12.5%) people had 80 Overall Weil-Felix titre.

The number of people with 160, 320 and 640 Overall Weil Felix titre was 15 (37.5%), 13 (32.5%) and 7 (17.5%) respectively in people with fever. In a study by Mathai E. et. al., fever more than one week duration was found to be the commonest manifestation of the patients admitted and it was accounted in about 52% of the cases.¹⁰ One study has had 96.3% of cases with fever while 61.0% had fever accompanied by chills.¹¹

Conclusion

This study has insisted the suspicion of Rickettsial infection when a person presents with fever with rashes and associated constitutional symptoms like headache, congestion of eyes, cough, myalgia. Clinical findings like hepatosplenomegaly, lymphadenopathy, icterus, bleeding manifestations were also moderately correlated with the disease condition while pleural effusion was least correlated.

Weil Felix OX2 titre had more than one-third of the subjects in the 80 group and OXK titre remained nil in about two-thirds of the cases, alike was the titre for OX19 test. Though the tick bite had a higher association with the Weil Felix titre of 320 followed by 640, rashes had an only modest correlation with Weil Felix titre of 80, 160 and 320 similar to the eschar with titre of 320 and 640. This shows the lesser sensitivity of this test in diagnosing the disease state.

Ethical Approval: Permission for the study was obtained from the College authorities prior to commencement.

Source of Funding: This research received no specific grant from any funding agency in the public,

commercial or not-for-profit sectors.

Conflict of Interest: None to declare.

Acknowledgement: I would like to express my profound gratitude to all the participants for their co-operation and for their immense faith they reposed in me.

References

1. Varghese GK. Rickettsial Diseases in India: Not as Uncommon as Believed. *J Assoc Physicians India*. 2014;62(12):9-10.
2. Mahajan SK. Rickettsial diseases. *J Assoc Physicians India*. 2012;60:37-44.
3. Mohta A. Rickettsial diseases in central India. *Indian Pediatr*. 2012;49(3):251; discussion -2.
4. Snowden J, Bhimji SS. Rickettsial Infection. *StatPearls*. Treasure Island (FL): StatPearls Publishing StatPearls Publishing LLC.; 2017.
5. Botelho-Nevers E, Socolovschi C, Raoult D, Parola P. Treatment of Rickettsia spp. infections: a review. *Expert Rev Anti Infect Ther*. 2012;10(12):1425-37.
6. Machines IB. IBM SPSS Statistics for Windows, Version 22.0. IBM Corp Armonk, NY; 2013.
7. Thomas R, Puranik P, Kalal B, Britto C, Kamallesh S, Rego S, et al. Five-year analysis of rickettsial fevers in children in South India: Clinical manifestations and complications. *J Infect Dev Ctries*. 2016;10(6):657-61.
8. Lindblom A, Wallmenius K, Sjowall J, Fryland L, Wilhelmsson P, Lindgren PE, et al. Prevalence of Rickettsia spp. in Ticks and Serological and Clinical Outcomes in Tick-Bitten Individuals in Sweden and on the Aland Islands. *PLoS One*. 2016;11(11):e0166653.
9. Amano K, Suzuki N, Hatakeyama H, Kasahara Y, Fujii S, Fukushi K, et al. The reactivity between rickettsiae and Weil-Felix test antigens against sera of rickettsial disease patients. *Acta Virol*. 1992;36(1):67-72.
10. Mathai E, Rolain JM, Verghese GM, Abraham OC, Mathai D, Mathai M, et al. Outbreak of scrub typhus in southern India during the cooler months. *Ann NY Acad Sci*. 2003;990:359-64.
11. Chang K, Chen YH, Lee NY, Lee HC, Lin CY, Tsai JJ, et al. Murine typhus in southern Taiwan during 1992-2009. *Am J Trop Med Hyg*. 2012;87(1):141-7.