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Study of usefulness of Weil-Felix test as a simple diagnostic tool for diagnosis of rickettsial fever

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Abstract

Background: Rickettsial infections are the most covert re-emerging infections in present times. They are incapacitating and notoriously difficult to diagnose, Weil-Felix (WF) test is classic serological test which is widely available but not widely acceptable because of its low sensitivity and specificity. Present study was aimed to study of usefulness of Weil-Felix test as a simple diagnostic tool for diagnosis of rickettsial fever.
Material and Methods: Present study was single-center, prospective, observational study, conducted in children < 18 years age, hospitalized with fever and presence of one or more of the following clinical features: Rash, edema, eschar, hepatosplenomegaly, lymphadenopathy OR had history of contact with pets or live stocks and history of tick-bite.
Results: In the present study maximum number of cases were from school going age group (53.5%), male (67.4%), from Rural Areas (88.4%) & Tick bite could be demonstrated in 44.2% cases. Based on clinical features Lymphadenopathy was seen mainly 86.00%, followed by maculopapular rash (76.7%), rash appearing 48-96 hrs. after fever (72.10%), conjunctival congestion (55.80%), hepatomegaly (48.80%), rash on palms & soles, pedal edema (34.9%) & purpura (14%). Out of 43 suspected cases, Weil-Felix test was positive in 31 cases (72.1%) and Negative in 12 cases (27.90%).
Conclusion: Rickettsial disease must be strongly suspected with a triad of fever, rash and lymphadenopathy or having history of tick exposure/ bite and when the cause of fever cannot be established. Weil Felix test can be carried out for early detection of suspicious casein resource limited set up.

Keywords: Rickettsial disease, fever, rash, lymphadenopathy, Weil Felix test

Introduction

Rickettsial infections are the most covert re-emerging infections in present times. They are incapacitating and notoriously difficult to diagnose, if untreated fatality rate is as high as 30-35%. Because of nonspecific signs and symptoms and non-availability of sensitive and specific diagnostic tests, these are difficult to diagnose [1].
The diagnosis of a rickettsial illness is confirmed by serological testing. But serological evidence of infection occurs not earlier than second week of illness in any of the rickettsial diseases and hence a specific diagnosis may not be available until after the patient has fully recovered or worsened [1, 2, 3]. Immunofluorescence Assay (IFA) is the gold standard test for serodiagnosis of rickettsial disease which detects IgG and IgM antibodies, but main

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drawbacks of IFA is that it is very expensive and not widely available [2, 3]. Weil-Felix (WF) test is classic serological test which is widely available but not widely acceptable because of its low sensitivity and specificity. The test should be interpreted in conjugation with history and clinical presentation [2, 3, 4].
The need for this study was to know various clinical manifestations of rickettsial disease in different pediatric age group so that it can be diagnosed early with high index of suspicion and specific treatment is initiated to prevent mortality. Present study was aimed to study of usefulness of Weil-Felix test as a simple diagnostic tool for diagnosis of rickettsial fever.

Material and Methods

Present study was single-center, prospective, observational study, conducted in children admitted in Pediatric ward/Pediatric Intensive Care unit at SSMC hospital, Tumkur, India. Study duration was of 2 years (July 2018 to June 2019). Study was approved by institutional ethical committee.

Inclusion criteria

- Children < 18 years age, hospitalized with fever and presence of one or more of the following clinical features: Rash, edema, Escher, hepatosplenomegaly, lymphadenopathy OR had history of contact with pets or live stocks and history of tick-bite.

Exclusion criteria

- When cause of fever is established.
- Reliable informant not available.
- Refusal for admission

Questions were asked regarding symptoms and signs to patients and relevant investigations carried out based on Rathi Goodman Aghai (RGA) clinical scoring system for spotted fever group.
Data collected was entered in Microsoft excel and analysed using Epi-info 3.5.3. Descriptive statistics like proportion was calculated. Chi-square test was used as test of significance. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

Results

In the present study maximum number of cases (23) were in school going age group (53.5%). More number of cases were in Male (67.4%) as compared to females (32.6%). Based on demographic distribution maximum cases were from Rural Areas (88.4%) as compared to Urban area (11.6%). 90.7% of cases had pets in their home. 88.4% of cases had exposure to ticks. Tick bite could be demonstrated in 44.2% cases.

Table 1: General characteristics

Characteristics	Frequency	Percent
Age group		
Infant	1	2.30%
Preschool	19	44.20%
School going	23	53.50%

ISSN 2515-8260 Volume 09, Issue 02, 2022

Sex		
Female	14	32.60%
Male	29	67.40%
Residence		
Rural	38	88.40%
Urban	5	11.60%
Presence of pets	39	90.70%
Tick Exposure	38	88.40%
Tick bite	19	44.20%

Based on clinical features Lymphadenopathy was seen mainly 86.00%, followed by maculopapular rash (76.7%), rash appearing 48-96 hrs. after fever (72.10%), conjunctival congestion (55.80%), hepatomegaly (48.80%), rash on palms & soles, pedal edema (34.9%) & purpura (14%).

Table 2: Clinical manifestation

Clinical Features	Present	Percentage	Absent	Percentage
Conjunctival congestion	24	55.80%	19	44.20%
Maculopapular rash	33	76.70%	10	23.30%
Purpura	6	14.00%	37	86.00%
Rash 48-96 hrs. after fever	31	72.10%	12	27.90%
Pedal edema	15	34.90%	28	65.10%
Rash on palms/soles	15	34.90%	28	65.10%
Hepatomegaly	21	48.80%	22	51.20%
Lymphadenopathy	37	86.00%	6	14.00%

In Hematological reports Platelets < 1.5 lakh was seen in 30.20% cases followed by Hb < 9 gm% in 11.60%. Biochemical investigations showed serum Sodium < 130meq/L in 30.20%, serum albumin <3gm/dl in 11.60%, SGPT >1000U/Lin 11.60%and urine albumin >2 in 7% of cases. CRP>50 in25.60%.

Table 3: Investigations

Investigations	Present	Percentage	Absent	Percentage
Hb < 9gm%	5	11.60%	38	88.40%
Platelet < 1.5lakh	13	30.20%	30	69.80%
CRP > 50mg	11	25.60%	32	74.40%
Serum albumin <3gm/dl	5	11.60%	38	88.40%
Urine albumin >2	3	7.00%	40	93.00%
SGPT>1000u/l	5	11.60%	38	88.40%
Serum Na<130meq/l	13	30.20%	30	69.80%

Conjunctival congestion was seen in 24 cases of which 14 were in preschool children and 10 in school going age. Of the 21 cases who presented with hepatomegaly 10 cases each in preschool and school going age and 1 case in Infancy were observed. Out of 37 cases of lymphadenopathy 19 cases were in school going age group followed by 17 in preschool group and 1 case in infancy. Of the 33 cases with maculopapular rash 17 cases were from school going age, 15 from preschool age and one from infancy. Pedal edema was seen in 15 cases of which 8 were in school going children and 7 in preschool age group. Of the 6 cases who presented with purpura, 4 were in preschool group and 2 from school going group. Rash appeared 48-96 hrs. After fever in 31 cases of which 16 cases were in school going group and 14 in preschool group.

ISSN 2515-8260 Volume 09, Issue 02, 2022

Table 4: Age wise distribution & clinical features

Age	Conjunctival congestion	Hepatomegaly	Lymphadenopathy	Maculopapular rash	Pedal edema	Purpura	Rash 48-96 after fever
Infant	0	1	1	1	0	0	1
Preschool	14	10	17	15	7	4	14
School going	10	10	19	17	8	2	16
Total	24	21	37	33	15	6	31
Chi-square value	5.14	1.42	0.57	0.45	0.56	1.48	0.48
P value	0.07	0.49	0.75	0.79	0.75	0.47	0.78
Interpretation	Not significant	Not significant	Not significant	Not significant	Not significant	Not significant	Not significant

In the study, out of 43 suspected cases, Weil-Felix test was positive in 31 cases (72.1%) and Negative in 12 cases (27.90%).

Table 5: Positivity of Weil-Felix Test

Weil-Felix	Frequency	Percent
Negative	12	27.90%
Positive	31	72.10%
Total	43	100.00%

Discussion

Most of these patients a history of tick bite or close contact with dogs, cattle, sheep, goats was elicited which are known mammalian reservoirs in life cycle of rickettsial organisms [2]. Initial diagnosis and treatment should be based on a high index of suspicion and appropriate clinical features. The drugs effective against rickettsial infections are Tetracyclines and Chloramphenicol. Doxycycline is the drug of choice for all age group [1, 2, 5].

In the present study 88.40% of cases were from rural areas, majority were between 6-18 years age group (53.5%) followed by 1-6 years age group (44.2%). Contrary to the present study, Palanivel S *et al.*, [6] showed majority of children were in the age group of 1-6 years (68.65%), 11.94% < 1yr and 19.4% above 6 yr. A Study by Inamdar S *et al.* on clinical characteristics and treatment pattern of scrub typhus in tertiary care hospital had most of the cases i.e. 35.5% reported from agriculture exposure [7].

In present study Tick exposure was seen in 88.40% of cases which was similar to study done by Rathi *et al.* (81%) [8]. Tick bite was reported in 44.20% cases. A study by Rathi N *et al.*,[1] noted that since tick bite is painless history of tick bite is present in < 50% of cases, which was consistent with the present study [1]. A Study by Rathi N *et al.* considered animal sheds near houses in rural areas, pets, stray dogs, cattle and long uncut grasses as factors favouring vectors [9].

In the present study fever was present in all cases i.e. 100%, the duration of fever was usually for 3-5 days, high grade. This was consistent with a study done by Palanivel *et al.*, [6] where fever was seen in all children. Inamdar S *et al.*, [7] Udayan U *et al.*, [4] & Dass R *et al.*, [10] also noted that fever was most common symptom.

In the current study lymphadenopathy accounted for 86.00% of cases. This was consistent with a study done by Rathi N *et al.*, [1] and Sirisanthan V *et al.*, [11]. Study by Palanivel S *et al.*, [6] had observed lymphadenopathy in 59.70% of cases in their study [11]. A study by Inamdar *et al.*, [7] reported lymphadenopathy in 52.5% of cases.

Maculopapular rash was seen in 76.70% cases, though rash was more consistent with Rickettsial Fever it appeared only after 48-96 hrs. Which accounted for 72.10% of cases. This feature was similar to the studies done by Rathi N *et al.*, [1] Walker DH *et al.*, [12] Sexton DJ *et*

al., [13] Rash was noted over palms and soles in 34.90% of cases. A study by Rathi N [1] quoted that presence of rash over palms and soles was typical of rickettsial disease. This feature of rash was also supported by Murali N *et al.*, [14].

Conjunctival congestion was seen in 55.80% of cases, which was contrary to Dass R *et al.*, [10] (8.3%) and Kamarasu K *et al.*, [15] (25%). Hepatomegaly was seen in 48.80% of cases. Palanivel S *et al.*, [6] reported hepatosplenomegaly in about 80% of cases. Rathi N [1] also reported hepatosplenomegaly in majority of their cases. But Dass R *et al.*, [10] reported hepatomegaly in 33.3% and splenomegaly in 45.8% separately. Another study by Inamdar *et al.*, [7] reported hepatomegaly alone in 52.5% of cases. Pedal edema accounted for 34.90% of cases in present study, which was also reported in studies done by Kulkarni A [2], Palanivel S. [11].

Platelet count of <1.5 lakh was seen in 30.20% of cases. According to Dass R *et al.*, [10] thrombocytopenia was noted in 26% of cases [10]. Thrombocytopenia was also noted by Rathi N *et al.* [1] Palanivel S *et al.*, [6] & Kulkarni A [2]. Hemoglobin < 9 gm% was seen in 11.60% in present study. Anemia was reported by Rathi B N *et al.*, [1] (8.8%), Kulkarni A[2] & Palanivel S *et al.* [6].

Hyponatremia is seen in 30.20% in present study, reflecting increased vascular permeability [1]. Rathi BN *et al.*, [1] (48%), Dass R *et al.*, [10] (66.7%) & Udayan U *et al.*, [4] (18.75%) also reported hyponatremia in of their study. Hypoalbuminemia was present in 11.60% in present study. The presence of hypoalbuminemia was reported Rathi N *et al.* [1] & Dass R *et al.*, [10].

Weil-Felix test was done in the study and a value of 1:80 or more was considered as significant. Though WF test is not gold standard, in resource limited set up where Immunofluorescence Assay cannot be carried out because of non-availability or cost factor, WF test seems to be the standard diagnostic test for rickettsial fever. Moreover IFA becomes positive only after a period of 5-7 d of illness, the time by which complications may set in. Dass R *et al.*, [10] suggested that WF test helps to detect more cases than misdiagnosed and when positive it is reasonably specific. It also suggested its use in resource limited setup. Study by Kulkarni A[2] and many other studies from India as quoted by Dass R *et al.*, [10] suggested a titer of 1:80 as significant and also its use in resource limited setup as diagnostic for rickettsial when other tests are not available.

Udayan U *et al.*, [4] suggested WF Test as useful and cheapest available tool for laboratory diagnosis of rickettsial disease. Rathi N *et al.*, [1] suggested use of WF test is justified when definitive diagnostic test is not available. Issac *et al.*, [16] demonstrated sensitivity of WF test as 30% at a breakpoint titer 1:80, and specificity and positive predictive value as 100%, hence it is not completely obsolete and has to be interpreted with correct clinical context.

Simple measures like health education to people about mode of transmission of rickettsial disease and its clinical presentation especially at risk groups such as those having pets/ live stocks at their home and those having agriculture exposure may be useful. Disinfection of pets and live stocks, personal protection from ticks, Inspection of body for ticks particularly at risk groups will also be useful. Weil-Felix test can be used as a simple diagnostic tool for early detection of Rickettsial disease although the sensitivity is poor.

Limitations of the study were IFA could not be used because of its non-availability and high cost factor.

Conclusion

Rickettsial disease must be strongly suspected with a triad of fever, rash and lymphadenopathy or having history of tick exposure/bite and when the cause of fever cannot be established. A proper history and careful physical examination help in the diagnosis of Rickettsial disease. Weil Felix test can be carried out for early detection of suspicious casein resource limited set up.

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