Original Article

A Study on Clinical Profile and Complications of Acute Rickettsial Diseases in Children at A Tertiary Care Hospital of Western Maharashtra

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Abstract

Background: Rickettsial infections are progressively becoming a major cause of acute febrile illness in the paediatric age group, especially in a few endemic regions of India. The multi-organ involvement in these infections is often common and can get complicated if diagnosis and treatment are not done promptly. The objective is to compose the clinical presentation and complications of the rickettsial infection in hospitalized children in a tertiary care hospital in Westerly, Maharashtra. **Material and Methods:** We conducted a retrospective study of serologically confirmed rickettsial infections in children aged 1 month to 18 years. Demographic data, clinical manifestations, laboratory parameters, and complications were retrieved from the medical records database through search and analysis. **Results:** 61 children were included per the inclusion criteria, with a slight male bias (54.1%). A larger part of them (37.7%) were below 5 years old. Fever persisted in all these cases, with prolonged fever (>5 days) observed in 60.7% of children. Escher was detected in 59% of the children; common manifestations were gastrointestinal (vomiting: 54.1% and hepatosplenomegaly: 50.8%), dermatological (rash: 39.3%), and neurological (altered sensorium: 27.9% and convulsions: 13.1%). When laboratory parameters were evaluated, anemia was 88.5%, thrombocytopenia 77%, leukocytosis 72.1%, and hypoalbuminemia 75.4%. The prevalent complications reported were meningoencephalitis (29.5%), shock (26.2%), acute hepatitis (24.6%), acute kidney injury (19.7%), pneumonia (16.4%), myocarditis (11.5%), and ARDS (8.2%). **Conclusion:** Pediatric rickettsial infections can present through a wide range of clinical presentations, and often, multi-organ involvement is likely to exist. Early detection of key clinical manifestations and laboratory abnormalities can serve as a predictive marker for early diagnosis and timely treatment, helping achieve better outcomes. The study validates the pertinence of recognizing pediatric rickettsial disease as an endemic and the necessity of combining early diagnosis and risk-stratification approaches in the practice of modern pediatrics.

Keywords: Acute Rickettsial Diseases, Pediatric Rickettsial Infections, Clinical Profile, Complications, Children, Tertiary Care Hospital, Western Maharashtra, Scrub Typhus, Febrile Illness, Pediatric Infectious Diseases.

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Introduction

Rickettsial diseases represent a heterogeneous group of zoonotic, arthropod-borne agents with a substantial global public health impact.[1] However, in recent years, rickettsial infections have acquired a new level of relevance in the Indian subcontinent, as they are a prominent etiology of an acute undifferentiated febrile disease, especially in children.[2] The epidemiological evidence present in most sections of the nation suggests the endemicity and significance of the rickettsial disease in large geographical areas of India. It is pervasive and has existed between the south (Kerala, Tamil Nadu, Maharashtra, and Karnataka) and northern India (Himalayan foothills).[3]

The most common rickettsioses in the Asia-Pacific region, in terms of distribution, include scrub typhus and spotted fever group rickettsiae.[4] The Orientia tsutsugamushi is causative of scrub typhus and is serologically specific to the OX-K antigen of the Weil-Felix test.[5] Rickettsia conorii is attributed to the cause of Indian tick typhus, and is positive to the OX-2 antigen of the Weil-Felix test.[6]

The laboratory parameters in children with rickettsial fever show results that are more or less stereotypical, consistent with an infectious process of a specific pattern. They are likely to manifest as anemia, thrombocytopenia, leukocytosis, elevated C-reactive protein, electrolyte abnormalities (most commonly hyponatremia), elevated serum aminotransferases, and low serum albumin.[7] These are predictable parameters, as they imply generalized infectious and inflammatory reactions that often lead to physiologic alterations in blood vessels, resulting in vasculitis. The fatal complications of Rickettsial infections are most likely to occur in the second week of the illness. They encompass severe thrombocytopenia, which is followed by disseminated intravascular coagulation and shock. Interstitial pneumonitis, non-cardiogenic pulmonary oedema, meningoencephalitis (central nervous system), acute renal

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failure, hepatic dysfunction, myocarditis, and, in rare cases, purpura fulminans.[7,8]

The immunofluorescence antibody (IFA) test is considered the gold standard for diagnosing acute rickettsial fever. However, it is very expensive, and its use is not feasible in most health centers due to the need for a high-power fluorescence microscope. Hence, the Weil-Felix test, a variant of the heterophile agglutination assay, remains the minimum-stay confirmatory test for rickettsial infection, as it is relatively inexpensive and readily available in most hospitals.[9]

As rickettsial infections have the potential for rapid progression and a high morbidity rate, increased clinical awareness and timely, appropriate treatment by pediatricians will substantially improve outcomes.

Materials and Methods

Study Design and Institutional Setting

It is a retrospective analytical study conducted in a tertiary care hospital in Western Maharashtra. This study comprised hospital records of pediatric patients aged 1 month to 18 years who were hospitalized between January 2018 and December 2020 and discharged with a diagnosis of rickettsial fever or rickettsial infection. Before data collection for the study, prior approval from the institutional Ethics Committee was obtained.

Eligibility Criteria and Case Identification

Medical records were screened to identify children with a clinical presentation consistent with rickettsial illness and supportive serological evidence. Inclusion was done if Weil-Felix test titers were 1:160 or higher for OX-19, OX-K, or OX-2 antigens. The cases were analyzed only if both clinical and laboratory criteria were met.

Exclusion Criteria

Records were excluded from the study if

1. Discharged against medical advice before completion of treatment.
2. Inadequate or incomplete clinical or laboratory documentation was done.
3. Children were diagnosed with concurrent infections such as viral haemorrhagic fever (Dengue), leptospirosis, malaria, viral hepatitis, enteric fever, or other infectious diseases.

Data Extraction and Variables Assessed

For information retrieval, the predetermined data collection format was used. The variables were demographic variables and the duration of febrile disease, along with associated symptoms, including rash, eschar, myalgia, vomiting, and headache, which were accompanied by other clinical symptoms. Vital signs recorded during admission, general physical examination, and general system examination findings were noted. The analyzed laboratory parameters were complete blood counts, serum electrolytes, renal function tests, liver function tests, and other routine investigations, followed by the Weil-Felix test report. Chest radiography findings were also documented whenever possible.

Operational Definitions of Complications

The identification of the Standardized Clinical complications was achieved in the following way:

- **Acute Kidney Injury (AKI):** Defined according to recent Acute Kidney Injury Network (AKIN) guidelines.
- **Acute Hepatitis:** Defined by the high level of serum transaminases over fourfold above the upper limit of normal
- **Acute Respiratory Distress Syndrome (ARDS):** Defined by acute bilateral lung infiltrates in the chest X-ray, along with or without the pO2 /FiO2 in the ABG lower than 300.
- **Myocarditis:** defined by clinical findings suggestive of left ventricular dysfunction or 2D-Echo report consistent with findings of myocarditis or significantly elevated creatine kinase-MB levels, irrespective of accompanying electrocardiographic abnormalities.
- **Meningitis/Meningoencephalitis-** defined as the presence of fever and vomiting with meningeal signs, with or without CSF abnormalities, and/or altered sensorium with or without seizure activity.
- **Pneumonia:** respiratory (cough or dyspnea), audible (auscultation) (crepitus), and radiological (pulmonary consolidation) symptoms.
- **Shock:** defined when the values of systolic blood pressure were lower than the 5th percentile for age, sex, and height.

Results

A 2-year study enrolled 61 children who met our inclusion criteria. Males were more affected than females (33 [54.1%] and 28 [45.9%], respectively), with a male-to-female ratio of 1.2:1.

Table 1: Demographic profile of Children with Acute Rickettsial infection.

Parameters	n	%
Male	33	54.1
Female	28	45.9
Age (y)		
<5 years	23	37.7
5 years - 10 years	21	34.4
10 years- 18 years	17	27.9

Most commonly affected children belonged to age group of 1 month to 5 years followed by age group of 5-10 years (37.7% and 34.4% respectively). It implied maximum children were below 10 years (72%) which is a sizable proportion.

Table 2: Clinical profile of acute rickettsial infection.

Clinical manifestations	n	%
Fever	61	100
< 5 days	24	39.3
> 5 days	37	60.7

Cough	28	45.9
Breathlessness	23	37.7
Vomiting	33	54.1
Abdominal Pain	18	29.5
Jaundice	6	9.9
Hepato-splenomegaly	31	50.8
Maculopapular Rash	24	39.3
Eschar	36	59
Lymphadenopathy	12	19.6
Myalgia	13	21.3
Headache	14	23
Convulsions	8	13.1
Altered Sensorium	17	27.9
Oliguria	13	21.3

Fever was present in all children (100 %), and a longer duration of fever (>5 days) was noted in the largest number of children (60.7 %). Eschar was present in 36 children (59%), most commonly in the groin, followed by the axilla. Gastrointestinal manifestations were also common, with vomiting occurring in 33 children (54.1%) and abdominal pain (29.5%). Respiratory symptoms, such as cough, were present in 28 children (45.9%), followed by breathlessness (37.7%). A maculopapular rash was present in 24 children (39.3%), and lymphadenopathy was observed in only 1/5 cases (19.6%) during routine general examination. Neurological symptoms manifested with altered sensorium in 17 children (27.9%) and convulsions in 8 children (13.1%). Hepatosplenomegaly was documented in 31 children (50.8%), although jaundice was noted only in 6 children (9.9 %). Oliguria was present in 13 children (21.3%).

Table 3: Haematological and biochemical parameters in acute rickettsial infections.

Variables	n	%
Hematologic parameters		
Hb < 11g/dl	54	88.5
WBC (per mm3)		
< 4000	5	8.2
>11,000	44	72.1
Platelets (per mm³)		
>150,000	14	23
<150,000	47	77
Biochemical Parameters		
Raised creatinine	12	19.7
Hypoalbuminemia	46	75.4
Raised AST	24	39.3
Raised ALT	15	24.6
Total bilirubin >1.2 mg/dl	8	13.1
Hyponatremia	23	37.7
Raised CRP	41	67.2
INR > 1.4	9	14.8

Hematological derangements were very commonly encountered in acute rickettsial infections. The proportion of them with anemia was very high, at 88,5% (54/61). Another significant observation was thrombocytopenia (77%), followed by leukocytosis (72.1%)

Derangements in biochemical parameters were often suggestive of multisystem involvement. Acute renal failure, usually associated with increased creatinine, was noted in 19.7% of children. AST and ALT were significantly elevated (39.3% and 24.6%, respectively), indicative of hepatic dysfunction. Another significant observation was hypoalbuminemia, which was present in 75.4% of children, consistent with fatal complications and morbidity. Electrolyte disturbances, especially hyponatremia, were encountered in 37.7% of children.

Whereas CRP was elevated in 67.2% of children, indicative of an inflammatory process, and Coagulopathy (INR >1.4) was noted in 14.8%. Collectively, these findings reflect the common hematologic and biochemical disturbances characterizing acute rickettsial infections.

Table 4: complications associated with rickettsial infections.

Complications	n	%
Acute Renal Failure	12	19.7
Hepatitis	15	24.6
ARDS	5	8.2
Pneumonia	10	16.4
Myocarditis	7	11.5
Meningo-encephalitis	18	29.5
Shock	16	26.1

Complications involving multi-organ involvement were frequently encountered. The neurological manifestation was most common in 18 children (29.5%) diagnosed with meningoencephalitis. Hemodynamic instability in the form of shock was documented in 16 children (26.2%). Hepatic dysfunction in the form of acute hepatitis was noted in 15 children (24.6%), whereas 12 children (19.7%) developed acute renal failure. The respiratory complications manifested in 16.4 % (10/61) of children as pneumonia, while five children (8.2%) advanced to acute respiratory distress syndrome. Seven children (11.5%) developed myocarditis as a cardiac complication, which was relatively less frequent compared to other complications.

Discussion

It was observed that acute rickettsial infections can manifest with a broad spectrum of clinical manifestations in children and are likely to develop serious systemic complications, as supported by the available literature in India and other rickettsial-endemic countries. Even an observational study in Odisha by Tiwari et al. suggests that scrub typhus may account for more than one-fourth (28.46%) of unexplained fevers without focus.[10] Even, sometimes it can account for 50% of cases of fever of unknown origin (FUO) in the pediatric age group, based on clinical relevance in endemic areas.

Rickettsial infections are caused by the obligatory intracellular, pleomorphic, Gram-negative, coccobacilli that need hematophagous arthropods [ticks, mites, fleas, or lice].[11] Inoculation results in a high level of relative affinity of these pathogens for the vascular endothelium and reticuloendothelial cells. The outcome is a cascade of endothelial inflammatory and coagulation abnormalities, resulting in systemic vasculitis. The importance of the clinical presentations of rickettsial infections, such as cutaneous eruptions, interstitial oedema, inadequate tissue oxygenation, microvascular thrombosis, and multi-organ involvement, lies in the pathology of this vascular damage. Molecularly, Rickettsial species encode numerous chemokine-regulating genes, which are susceptible to enhancement of microvascular damage, only a few of which are regulated by the transcription factor activator protein-1.[12,13]

The specificity of fever and a prolonged duration that exceeds five days, along with the frequent occurrence of the eschar (59 %), also coincide with the findings of Varghese et al. (2014), which stated that eschar was documented in half of all cases (>50%) of scrub typhus in children in the south.[14] Likewise, in our study, gastrointestinal (54.1% vomiting) and respiratory-related (45.9% cough) symptoms are most common, as in the case of Kumar et al. (2018), which implies Rickettsial disease manifests with multi-organ involvement in children.[15]

The neurological involvement in the form of meningoencephalitis was the most frequently encountered complication, which was 29.5 % of the cases. This finding aligns with the research by Palanivel et al. (2012), which revealed that central nervous system involvement was present in 26% of pediatric patients with scrub typhus, a finding the authors attribute to endothelial dysfunction and resulting vasculitis.[16] Our research also demonstrates that the incidence of shock (26.2%) and acute hepatitis (24.6%) was considerably significant, which aligns with trends in Chrispal et al. (2010); the authors revealed that the determinants of serious illnesses and mortality among Indian children were hepatic malfunction and circulatory collapse.[17] These uncanny similarities substantiate the global data according to which rickettsial infections are the etiology of acute febrile disease with a high morbidity in developing and underdeveloped countries due to a lack of awareness and poor access to early diagnostics and treatment.

In our study, hematologic abnormalities, including thrombocytopenia (77%) and anemia (88.5%), were very common. A survey by Varghese et al. reported results similar to ours, with thrombocytopenia (81%) as a significant hematological abnormality.[13] One important finding in our study was the presence of hypoalbuminemia in 75.4% of children, which is comparable with Khichar et al, in which the incidence of hypoalbuminemia was 75%.[18] It is observed that severe hypoalbuminemia at any stage of rickettsial infection is associated with morbid complications and poor prognosis. In addition to this, the fact that multi-organ involvement such as acute kidney injury (19.7%) and cardiac complications in form of myocarditis (11.5%) also speaks in favor of the fact that rickettsial organisms play a vital role in developing diffuse endothelial inflammation and microvascular thrombosis, the pathogenesis of which can be successfully elaborated in the frames of the global pathophysiological models.[19]

These trends in our study population call for heightened clinical suspicion, timely diagnosis, and intervention, even if supported by positive Weil-Felix serology titers (>1:160), especially in endemics where confirmatory tests like IFA or PCR are not routinely performed. Despite resource-limited settings, Cox and Tadi (2020) demonstrate that the sensitivity of the Weil-Felix test is low, yet it remains a resource-saving, cost-efficient diagnostic tool.[20]

The evidence from our study suggests that rickettsial infections should be considered in the differential diagnosis of children with prolonged fever, especially when eschar is present, along with laboratory findings such as thrombocytopenia, hypoalbuminemia, and hyponatremia. Thus, the timely diagnosis and prompt treatment can avert morbid complications and improve the prognosis of the disease.

Limitations

There are a few limitations in our study. It was confined to a retrospective character and was consequently constrained by inherent weaknesses in the design, such as lapses in available data and limited ability to control confounding variables. In terms of sample size, it is relatively small and cannot justify statistical power, control for variability, or control for bias. Lastly, the rickettsial infection diagnosis was established by combining clinical examination, supportive laboratory parameters, and the Weil-Felix test, which was not as accurate as the gold standard for diagnosis, namely, immunofluorescence assay (IFA) or polymerase chain reaction (PCR). These are what must be taken into consideration whenever quoting our study findings.

Conclusion

Pediatric rickettsial infection presents with a broad spectrum of clinical manifestations, often leading to complications involving multiple systems. Early detection of key clinical features, such as persistent fever and eschar, along with characteristic laboratory features, such as hypoalbuminemia, thrombocytopenia, and elevated CRP, is a useful tool for timely diagnosis and appropriate treatment, helping achieve a better prognosis and averting fatal complications.

It is imperative that meticulous clinical care planning and early antimicrobial treatment be initiated at the earliest, as high morbidity is primarily linked to neurological, renal, circulatory, and cardiovascular complications. Our study, henceforth, emphasizes raising awareness of the morbidity associated with pediatric rickettsial infections in endemic areas. Thus, prompt diagnosis of acute rickettsial infection and risk-stratification should be incorporated into the routine pediatric practice to decrease the burden of the disease.

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Conflicts of interest

There are no conflicts of interest.

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