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Original article

Clinical, Epidemiological, and Laboratory Profiles of Mediterranean Spotted Fever among Pediatric and Adult Patients in Eastern Libya: A Retrospective Cohort Study

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ABSTRACT

Mediterranean spotted fever (MSF) is a tick-borne rickettsiosis and continues to be endemic in the Mediterranean basin, but relatively little contemporary clinical data exist from Libya. This study characterized the epidemiological, clinical, laboratory, and seasonal profile of clinically diagnosed MSF and identified factors associated with severe disease. A hospital-based retrospective observational study was conducted among consecutive paediatric and adult patients managed at Al-Bayda Medical Center, Libya, from January to December 2024. Data on demographics, epidemiology, clinical characteristics, laboratory findings, treatment, and follow-up outcomes were collected from medical records. Severe disease was defined as admission to the intensive care unit (ICU) or in-hospital mortality. IBM SPSS Statistics version 29.0 was used to analyse the data. A total of 117 patients were included, of whom 87 (74.4%) were under the age of 18 years, and 81 (69.2%) were male patients. A maculopapular rash was noted in all patients, an inoculation eschar in 75 (64.1%), and regional lymphadenopathy occurred in 24 (20.5%). Five patients (4.3%) required ICU admission; no deaths occurred. Compared to paediatric patients, adults had significantly higher C-reactive protein (CRP) concentrations [88.80 mg/L (IQR 54.70–121.93) vs 60.00 mg/L (IQR 40.65–81.25); P = 0.009] and significantly lower platelet counts (146.83 ± 50.57 vs 187.43 ± 50.73 $\times 10^9$/L; P < 0.001). Given the small number of severe cases, multivariable modelling was not performed. More cases clustered in summer (57.3%) and autumn (40.2%). Despite most cases presenting in children and males, MSF appears to follow a relatively benign clinical course in this single-centre Libyan cohort. The inflammatory and haematological disturbance was more prominent in adult than paediatric patients. The small number of severe cases made prognostic modelling impossible. Further prospective multicentre serological and molecular confirmation studies are needed to help define disease burden and prognostic factors in Libya.

Introduction

"Mediterranean spotted fever (MSF) is a zoonotic infection transmitted by ticks and caused by *Rickettsia conorii* subsp. *conorii*. This organism is an obligate intracellular bacterium belonging to the spotted fever group rickettsiae. Its main vector is the brown dog tick, *Rhipicephalus sanguineus* sensu lato." MSF is endemic across much of the Mediterranean region, including North Africa, Southern Europe, and parts of the Middle East [1,2]. The disease was once considered a generally mild infection that resolved without complications. It is now recognised that some patients develop severe vascular injury, multiorgan dysfunction, or other complications requiring intensive care, and a small proportion may die [1,10–13]. "Fever, a maculopapular rash, and an inoculation eschar, or *tache noire*, are commonly described as the characteristic triad of MSF." In clinical practice, however, not every patient presents with all three findings. Headache, myalgia, and regional lymphadenopathy may also occur. "Laboratory abnormalities can include thrombocytopenia, elevated liver enzymes, impaired renal function, and electrolyte disturbances" [1,2,6,9,15]. Because several of these manifestations are nonspecific, the diagnosis may be missed or delayed, particularly when the eschar or rash is absent. Some laboratory abnormalities may also help identify patients at greater risk of a complicated course. Serological testing by indirect immunofluorescence is widely used to confirm the diagnosis. Its value early in the illness is limited, however, because detectable antibodies may not yet have developed. Where suitable facilities are available, polymerase chain reaction testing of blood or material collected from the eschar may provide earlier evidence of infection. Doxycycline remains the preferred treatment for MSF. Starting treatment promptly is important and is usually followed by a rapid fall in temperature and improvement in clinical symptoms [1,20,21]. The epidemiology of MSF differs considerably between endemic areas and across seasons. In a recent Tunisian series of 173 patients, most cases occurred among males and urban residents. Animal exposure was common, and infections were strongly concentrated during the warmer months. Studies from Italy and Spain have also shown that the geographic and seasonal distribution of MSF is not uniform across Southern Europe

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[2,4,5]. Findings from paediatric studies further suggest that children and adults may differ in their clinical manifestations and laboratory abnormalities. Despite environmental conditions that favour the transmission of tick-borne infections in North Africa [6–8], clinical information from Libya remains scarce. Studies directly comparing paediatric and adult cases and examining predictors of severe outcomes are particularly limited. This study therefore aimed to describe the epidemiological, clinical, laboratory, and seasonal characteristics of consecutive paediatric and adult patients clinically diagnosed with MSF at a Libyan tertiary referral hospital over one year. It also compared the findings between the two age groups and investigated factors independently associated with severe disease, defined as admission to the intensive care unit or death during hospitalisation.

Materials and Methods

Study Design and Setting

Methods: A retrospective observational hospital-based study was performed in the Al-Bayda Medical Center, Al-Bayda city, in the Al-Jabal Al-Akhdar region of eastern Libya. This is the most common referral hospital for urban and rural communities. Methods: The study period ran from 1 January 2024 to 31 December 2024.

Study Population and Eligibility Criteria

Inclusion criteria

Consecutive paediatric and adult patients with a clinical diagnosis of MSF, who were admitted during the study period. Eligibility required a presentation that was clinically compatible and epidemiologically consistent with MLI status, plus medical records that provided sufficient completeness. Patients were excluded if: (i) the medical records were materially incomplete; (ii) an alternative confirmed diagnosis best explaining the presentation was available; or (iii) patients had a pre-existing chronic medical condition that could significantly affect the clinical presentation or laboratory indices since such comorbidities are known confounders of severity comparisons in prior series [10-12,20].

Case Definition

The diagnosis of MSF was made based on a compatible clinical syndrome consisting of acute febrile illness, epidemiological exposure consistent with tick contact and at least one characteristic sign (maculopapular rash and/or inoculation eschar) in the presence of or absence of regional lymphadenopathy because systematic confirmatory laboratory testing (serology or PCR) was not generally available at the study site during the study period – this is an identified limitation in resource-constrained settings. A record of a clinical response to empirical doxycycline offered supplementary diagnostic confirmation. This strategy reflects routine practice in endemic settings where serological testing is not available at the point of care [1,7,23].

Data Collection

Data were extracted from inpatient and outpatient medical records using a predesigned, standardised case-report form. Demographic variables included age and sex. Epidemiological variables comprised place of residence (urban or rural), exposure category (permanent residence in an endemic rural area or temporary exposure through travel, picnics, or camping), and the month and season of presentation. Clinical variables included prodromal symptom duration, fever grade, and the presence of a maculopapular rash, inoculation eschar, and regional lymphadenopathy. Laboratory variables included CRP, ESR, WBC count, absolute neutrophil count (ANC), band-cell percentage (B%), haemoglobin concentration, platelet count, and serum AST, ALT, BUN, sodium, and potassium concentrations. Doxycycline treatment, ICU admission, and in-hospital mortality were also recorded.

Outcome Definition

The primary outcome (defined a priori) was severe disease (ICU admission or in-hospital death). Secondary outcomes were also individually described as ICU admission and mortality.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed variables were reported as mean ± standard deviation (SD) and compared using the independent-samples t-test, with Welch's correction applied when variances were unequal. Non-normally distributed variables were reported as median and interquartile range (IQR) and compared using the Mann-Whitney U test. Categorical variables were reported as frequencies and percentages and compared using the chi-square test or Fisher's exact test, as appropriate. Comparisons were performed between paediatric (<18 years) and adult (≥18 years) patients and between the severe and non-severe disease groups. Statistical significance was defined as a two-sided P value < 0.05. Because only five patients met the definition of severe disease,

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multivariable logistic regression was not performed owing to the unreliability of modelling with such a small number of outcome events [16].

Ethical Considerations

This study was conducted in accordance with the Declaration of Helsinki and applicable national and institutional guidelines for retrospective medical-record research. The study protocol was approved by the Research Ethics Committee/Institutional Review Board of Al-Bayda Medical Center on 17 October 2025. The institutional board did not issue a separate approval reference number for this retrospective study. The requirement for individual informed consent was waived because the study involved only anonymised, non-identifiable medical records and included no direct patient contact or intervention. Patient confidentiality was maintained through the use of anonymised study identifiers.

Results

A total of 117 patients fulfilled the eligibility criteria and were included in the analysis. Seventy-seven patients (65.8%) resided in urban areas and 40 (34.2%) in rural areas. Temporary exposure (travel, picnics, or camping in endemic areas) was the most frequently reported risk category (79 patients, 67.5%), followed by permanent rural residence (37 patients, 31.6%); one patient (0.9%) had no identifiable exposure. The median age of the overall cohort was 7.00 years (IQR 4.00–18.00), and 81 patients (69.2%) were male. A maculopapular rash was present in all 117 patients (100%). An inoculation eschar was identified in 75 patients (64.1%), and regional lymphadenopathy was documented in 24 (20.5%). High-grade fever was the predominant fever pattern, occurring in 102 patients (87.2%), whereas 14 (12.0%) had low-grade fever and one (0.9%) presented with hyperpyrexia. The median prodromal symptom duration was 4.00 days (IQR 3.00–5.00). Doxycycline was administered to 116 patients (99.1%). Five patients (4.3%) required ICU admission and were classified as having severe disease; no in-hospital deaths were recorded. Complete demographic and clinical characteristics are presented in (Table 1).

Laboratory Findings

The median CRP concentration was 66.00 mg/L (IQR 43.10–93.20) and the mean ESR was 34.84 ± 14.65 mm/h. The median WBC count was 8.70 × 10^9/L (IQR 7.20–10.10) and the median absolute neutrophil count was 6.10 × 10^9/L (IQR 4.90–7.10). The mean band-cell percentage was 5.49 ± 2.85%, mean haemoglobin concentration was 12.86 ± 1.22 g/dL, and mean platelet count was 177.02 ± 53.52 × 10^9/L. Median AST was 51.00 U/L (IQR 39.00–70.00), median ALT was 44.00 U/L (IQR 31.00–63.00), and median BUN was 16.10 mg/dL (IQR 13.80–19.30). Mean serum sodium was 136.55 ± 3.72 mmol/L and mean serum potassium was 4.00 ± 0.34 mmol/L. Complete laboratory data are summarised in (Table 1).

Comparison Between Severe and Non-Severe Disease

Five patients fulfilled the severe-disease criterion (all by virtue of ICU admission), compared with 112 non-severe patients. Median age was 4.00 years (IQR 4.00–13.00) in the severe group and 7.00 years (IQR 4.00–20.00) in the non-severe group (P = 0.450). Median prodromal duration was 4.00 days in both groups (P = 0.668). Median CRP was 60.00 mg/L (IQR 49.50–160.00) in severe cases versus 66.00 mg/L (IQR 43.08–91.25) in non-severe cases (P = 0.767). Mean serum sodium was numerically lower in the severe group (132.16 ± 5.46 vs 136.75 ± 3.53 mmol/L; P = 0.133), consistent with a trend towards hyponatraemia, although this difference did not reach statistical significance. None of the remaining continuous variables — neutrophil count, haemoglobin, WBC, AST, BUN, platelet count, serum potassium, band-cell percentage, ESR, or ALT — differed significantly between groups. These findings are detailed in Table 2 and must be interpreted in light of the very small number of severe cases (n = 5).

Comparison Between Paediatric and Adult Patients

Of the 117 patients, 87 (74.4%) were paediatric (aged <18 years) and 30 (25.6%) were adults (aged ≥18 years). Male sex was recorded in 57/87 (65.5%) paediatric and 24/30 (80.0%) adult patients; the difference was not statistically significant (P = 0.172; Figure 1). Urban residence was reported in 57/87 (65.5%) paediatric and 20/30 (66.7%) adult patients (P = 1.000; Figure 2). Severe disease occurred in five paediatric patients (5.7%) and no adults (0.0%), a difference that was not statistically significant (Fisher's exact test, P = 0.326; Figure 3). Significant between-group differences were identified for CRP and platelet count. Median CRP was significantly higher in adults than in paediatric patients [88.80 mg/L (IQR 54.70–121.93) vs 60.00 mg/L (IQR 40.65–81.25); P = 0.009]. Conversely, mean platelet count was significantly lower in adults (146.83 ± 50.57 × 10^9/L vs 187.43 ± 50.73 × 10^9/L; P < 0.001). No significant differences were identified for ESR, WBC, neutrophils, band cells, haemoglobin, AST, ALT, BUN, serum sodium, or serum potassium (Table 3).

Seasonal Distribution

The overwhelming majority of cases (114/117, 97.4%) presented during summer or autumn. Summer accounted for 67 cases (57.3%) and autumn for 47 (40.2%), whereas spring and winter each contributed two and one case, respectively

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(Table 4; Figure 4). This pronounced warm-season clustering should be interpreted with caution because calendar months were not uniformly represented in the dataset.

Discussion

This study describes the epidemiological, clinical, laboratory, and seasonal profile of clinically diagnosed MSF in a mixed paediatric-adult cohort from eastern Libya, representing one of the few contemporary clinical series from this North African country. The principal findings were a predominance of paediatric patients and males, near-universal eschar formation, a high doxycycline treatment rate, a low proportion of severe disease, and the absence of in-hospital mortality. Adults demonstrated higher CRP concentrations and lower platelet counts than children, whereas no continuous laboratory variable independently distinguished severe disease in this limited severe-case subgroup. The male preponderance in our cohort (69.2%) is in close agreement with the 67.6% reported in the recent 173-patient Tunisian series by Lamloumi et al. [2] and with the long-term Portuguese series of Crespo et al. [9]. This sex differential may partly reflect greater occupational and recreational exposure to tick-infested environments among males. Urban residence predominated (65.8%), corroborating the observation in the Tunisian cohort that MSF is not restricted to rural settings, probably because urban residents may acquire infection during brief episodes spent in tick-active periurban environments.[2] In our series, temporary exposure through camping, picnics, or rural travel was recorded in 67.5% of patients, underscoring that residential classification does not equate to exposure risk. An inoculation eschar was identified in 64.1% of patients, a proportion strikingly similar to the 63.4% reported among 415 Sicilian children by Colomba et al.[6] and the 60% documented over 24 years in the Portuguese cohort.[9] In the landmark 227-case cooperative study, tache noire was present in approximately three-quarters of patients.[14] The variation across series likely reflects differences in case ascertainment, clinician experience, the timing of presentation relative to eschar evolution, and the anatomical locations examined. Importantly, the absence of an eschar should not exclude the diagnosis, and clinical suspicion must be maintained in endemic areas even when the complete triad is lacking. The finding of universal rash in our cohort, versus 94.5% in the Sicilian paediatric series [6] and 87% in the Portuguese series [9], is most likely attributable to inclusion criteria and documentation practice rather than a genuine biological difference. Paediatric and adult MSF from an endemic region of Bulgaria reported age-related differences in clinical expression.[8] In our study, adults had significantly higher median CRP concentrations and significantly lower mean platelet counts than paediatric patients. These findings suggest a more pronounced systemic inflammatory and haematological response in adults, although they did not translate into a higher observed ICU admission rate. The adult subgroup comprised only 30 patients; therefore, these differences should be regarded as cohort-specific associations pending validation in larger samples. Elevation of inflammatory markers and thrombocytopenia are well-established laboratory features of MSF.[1,9,15] The median CRP of 66.0 mg/L in the overall cohort reflects the systemic inflammatory response driven by endothelial tropism of R. conorii.[1,12] In the recent Tunisian cohort, thrombocytopenia was identified in 48% and elevated CRP in the majority of patients.[2] Crespo et al. likewise identified CRP elevation and thrombocytopenia as the most frequent laboratory abnormalities over 24 years.[9] The significantly lower platelet counts in adults may represent greater endothelial activation or a heightened platelet consumptive process, but the cross-sectional and retrospective nature of this study precludes mechanistic conclusions. Moderate hepatic biochemical abnormalities — median AST 51 U/L and ALT 44 U/L — were common. Transaminase elevation has long been recognised in MSF: abnormal liver function tests were documented in 55% of the 227-case cooperative series,[14] and elevated AST was reported in 50.9% of the Tunisian cohort.[2] The Portuguese long-term series similarly highlighted AST and ALT elevation as frequent findings.[9] In the present study, AST and ALT did not significantly differ between severe and non-severe cases, a finding likely attributable to the very small severe subgroup rather than an absence of biological relevance. Renal and electrolyte parameters — particularly hyponatraemia and uraemia — have been associated with severe and fatal MSF in previous work. De Sousa et al. identified diabetes, vomiting, dehydration, and uraemia as risk factors for death among 105 hospitalised Portuguese patients,[11] and their subsequent multicentre analysis identified acute renal failure and hyperbilirubinaemia as major correlates of fatal disease.[12] Raoult et al. described severe MSF characterised by renal insufficiency, thrombocytopenia, and hyponatraemia in a Marseille case series.[13] In the present cohort, mean serum sodium was lower in severe cases (132.16 ± 5.46 mmol/L vs 136.75 ± 3.53 mmol/L; P = 0.133), consistent with a biologically plausible trend, and BUN did not differ significantly. The study was substantially underpowered to evaluate these markers given only five severe cases, and larger cohorts are needed to examine the prognostic utility of electrolyte and renal indices in Libyan MSF patients. The favourable outcomes observed in the present study — a 4.3% ICU admission rate and no deaths — are consistent with reports from paediatric-predominant or doxycycline-treated cohorts. Crespo et al. reported a 3.6% mortality rate across a 24-year Portuguese series predominantly comprising hospitalised adults [9], whereas selected cohorts dominated by elderly patients with comorbidities have reported substantially higher case-fatality rates, particularly those infected with more virulent strains such as R. conorii subsp. israelensis. [11,12] The high doxycycline utilisation rate (99.1%) in our study likely contributed to the favourable outcome profile; prospective and randomised data firmly establish rapid clinical response to doxycycline-based regimens.[20,21] Notably, the deliberate exclusion of patients with known chronic illnesses produced a lower-risk

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cohort that may underestimate MSF severity in unselected clinical practice. The pronounced warm-season clustering (summer 57.3%, autumn 40.2%) is consistent with established MSF epidemiology. The recent Tunisian study recorded 68.8% of cases during the hot season,[2] the Portuguese 24-year series showed 78% of cases from July through September,[9] and national analyses from Spain and Italy have described strong temporal patterns [4,5]. A plausible biological mechanism is the temperature-mediated increase in the host-seeking behaviour of Rh. sanguineus and the accelerated replication of R. conorii within the tick, as demonstrated by Parola et al. [3]. Nevertheless, because the calendar months represented in our dataset were not uniformly distributed, the observed seasonal pattern reflects the distribution of recorded cases and cannot be extrapolated to population-level seasonal incidence estimates. The absence of systematic serological or molecular confirmation represents an important methodological limitation that warrants explicit discussion. The indirect immunofluorescence assay (IFA) for anti-R. conorii antibodies is the established reference standard for retrospective confirmation; PCR targeting the ompA or ompB gene from blood, eschar swabs, or skin biopsies can provide earlier molecular evidence of acute infection [1]. Neither platform was routinely available at Al-Bayda Medical Center during the study period, a constraint common to resource-limited settings across North Africa and sub-Saharan Africa [1,23]. In such contexts, clinical and epidemiological criteria — applied in conjunction with empirical doxycycline responsiveness — constitute the primary and internationally endorsed basis for diagnosis and early treatment initiation [1,7,23]. As Torpiano and Pace noted in their Maltese series, clinically diagnosed MSF managed with empirical doxycycline is associated with outcomes comparable to laboratory-confirmed cases in endemic settings where clinical expertise is well-developed [23]. Accordingly, the diagnostic approach employed in the present study adheres to established practice for endemic resource-constrained regions. Future Libyan studies should prioritise the integration of paired acute and convalescent IFA serology, alongside PCR from eschar swabs or whole-blood specimens, to strengthen diagnostic specificity and enable microbiologically confirmed surveillance. Until such infrastructure is available, clinical criteria combined with empirical doxycycline therapy remain the cornerstone of management, and withholding treatment while awaiting confirmatory results risks unnecessary morbidity and mortality [1]. Several additional limitations should be acknowledged. First, the retrospective single-centre design constrains generalisability and relies on the completeness of routine clinical documentation, which is inherently variable. Second, despite the diagnostic limitations discussed above, clinical misclassification with other febrile exanthematous illnesses — for example, human monocytotropic ehrlichiosis, secondary syphilis, or viral exanthems — cannot be entirely excluded. Third, only five patients met the severe-disease definition, markedly limiting statistical power for prognostic analysis and rendering multivariable prediction modelling inappropriate. Fourth, the exclusion of patients with chronic medical conditions, while improving cohort homogeneity, may underestimate the true burden and severity of MSF in routine clinical practice, given that comorbidities including diabetes, renal disease, and alcoholism are established determinants of poor outcome [10–12]. Fifth, non-uniform calendar-month representation in the dataset precludes reliable inference about true seasonal incidence. Notwithstanding these limitations, this study has several notable strengths. It provides contemporary clinical data from a country in which MSF publications remain rare, incorporates both paediatric and adult patients, evaluates a comprehensive laboratory profile, and systematically compares age subgroups and disease severity groups. The combination of epidemiological exposure categories, detailed clinical phenotyping, inflammatory and haematological indices, hepatic enzymes, renal and electrolyte parameters, and patient outcomes constitutes a valuable baseline dataset to inform the design of future prospective multicentre surveillance in Libya.

Conclusion

Mediterranean spotted fever in this one-year cohort from Al-Bayda Medical Center was characterised by a predominantly paediatric and male population, frequent inoculation eschar, marked summer-autumn clustering, near-universal doxycycline treatment, and generally favourable outcomes with no in-hospital deaths. Adults exhibited significantly higher CRP concentrations and lower platelet counts than children, suggesting greater inflammatory and haematological perturbation in this age group. No continuous laboratory variable independently distinguished severe disease, a finding constrained by the very small number of severe cases. In resource-limited endemic regions, clinical and epidemiological criteria remain the primary driver for early empirical therapy with doxycycline, pending the establishment of diagnostic infrastructure for serological and molecular confirmation. Prospective multicentre studies with systematic confirmatory testing are needed to delineate the true epidemiological burden of MSF and to define reliable predictors of severe outcomes in Libya.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee/Institutional Review Board of Al-Bayda Medical Center on 17 October 2025. The institutional board did not issue a separate approval reference number for this retrospective study. The requirement for individual informed consent was waived because the study involved only anonymised, non-identifiable

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retrospective medical records and included no direct patient contact or intervention. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable. No individually identifiable patient data are included in this manuscript.

Availability of data and materials

The anonymised dataset supporting the conclusions of this article is available from the corresponding author on reasonable request, subject to institutional data-sharing policy.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AA conceived and designed the study, supervised data collection, interpreted the findings, and drafted the manuscript. SAAA contributed to the study design, clinical interpretation, and critical revision of the manuscript. HAA, MA, and HNS contributed to data collection, data verification, and review of the manuscript. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

Tables

Table 1. Demographic, clinical, and laboratory characteristics of patients with Mediterranean spotted fever (N = 117)

Characteristic	Value
Demographic and clinical characteristics	
Age, years — median (IQR)	7.00 (4.00–18.00)
Male sex, n (%)	81 (69.2)
Female sex, n (%)	36 (30.8)
Urban residence, n (%)	77 (65.8)
Rural residence, n (%)	40 (34.2)
Permanent exposure, n (%)	37 (31.6)
Temporary exposure, n (%)	79 (67.5)
No identifiable exposure, n (%)	1 (0.9)
Rash, n (%)	117 (100)
Inoculation eschar, n (%)	75 (64.1)
Regional lymphadenopathy, n (%)	24 (20.5)
High-grade fever, n (%)	102 (87.2)
Low-grade fever, n (%)	14 (12.0)
Hyperpyrexia, n (%)	1 (0.9)
Prodromal duration, days — median (IQR)	4.00 (3.00–5.00)
Doxycycline received, n (%)	116 (99.1)
ICU admission / severe disease, n (%)	5 (4.3)
In-hospital mortality, n (%)	0 (0)
Laboratory characteristics	
CRP, mg/L — median (IQR)	66.00 (43.10–93.20)
ESR, mm/h — mean ± SD	34.84 ± 14.65
WBC, $\times 10^9$/L — median (IQR)	8.70 (7.20–10.10)
Neutrophils, $\times 10^9$/L — median (IQR)	6.10 (4.90–7.10)
Band cells, % — mean ± SD	5.49 ± 2.85
Haemoglobin, g/dL — mean ± SD	12.86 ± 1.22
Platelets, $\times 10^9$/L — mean ± SD	177.02 ± 53.52
AST, U/L — median (IQR)	51.00 (39.00–70.00)
ALT, U/L — median (IQR)	44.00 (31.00–63.00)
BUN, mg/dL — median (IQR)	16.10 (13.80–19.30)
Serum sodium, mmol/L — mean ± SD	136.55 ± 3.72

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Serum potassium, mmol/L — mean ± SD	4.00 ± 0.34

Note: Data are presented as n (%), mean ± SD, or median (IQR) as appropriate. IQR, interquartile range; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cell count; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; ICU, intensive care unit.

Table 2. Comparison of continuous variables between severe (n = 5) and non-severe (n = 112) disease groups

Variable	Severe (n = 5)	Non-severe (n = 112)	P value	Test
Age, years	4.00 (4.00–13.00)	7.00 (4.00–20.00)	0.450	Mann-Whitney U
Prodromal duration, days	4.00 (3.00–4.00)	4.00 (3.00–5.00)	0.668	Mann-Whitney U
CRP, mg/L	60.00 (49.50–160.00)	66.00 (43.08–91.25)	0.767	Mann-Whitney U
ESR, mm/h	36.80 ± 20.08	34.75 ± 14.48	0.832	Welch t-test
WBC, ×10^9/L	7.20 (6.60–8.50)	8.70 (7.35–10.12)	0.225	Mann-Whitney U
Neutrophils, ×10^9/L	4.40 (3.80–6.60)	6.10 (4.90–7.25)	0.165	Mann-Whitney U
Band cells, %	4.96 ± 4.02	5.52 ± 2.81	0.774	Welch t-test
Haemoglobin, g/dL	12.32 ± 0.77	12.89 ± 1.23	0.179	Welch t-test
Platelets, ×10^9/L	161.80 ± 74.42	177.70 ± 52.75	0.660	Welch t-test
AST, U/L	90.00 (37.00–174.00)	51.00 (39.00–68.50)	0.335	Mann-Whitney U
ALT, U/L	32.00 (27.00–100.00)	44.00 (31.75–63.00)	0.979	Mann-Whitney U
BUN, mg/dL	11.80 (10.80–19.70)	16.30 (13.97–19.30)	0.438	Mann-Whitney U
Serum sodium, mmol/L	132.16 ± 5.46	136.75 ± 3.53	0.133	Welch t-test
Serum potassium, mmol/L	3.94 ± 0.32	4.00 ± 0.34	0.711	Welch t-test

Note: Data are expressed as mean ± SD or median (IQR). No continuous variable reached statistical significance ($P < 0.05$). Results should be interpreted cautiously owing to the very small number of severe cases (n = 5).

Table 3. Comparison of clinical and laboratory characteristics between paediatric (<18 years, n = 87) and adult (≥18 years, n = 30) patients

Variable	Paediatric <18 y (n = 87)	Adult ≥18 y (n = 30)	P value	Test
Categorical characteristics				
Male sex, n (%)	57 (65.5)	24 (80.0)	0.172	Fisher exact
Urban residence, n (%)	57 (65.5)	20 (66.7)	1.000	Fisher exact
Severe disease, n (%)	5 (5.7)	0 (0.0)	0.326	Fisher exact
Continuous laboratory variables				
CRP, mg/L	60.00 (40.65–81.25)	88.80 (54.70–121.93)	0.009*	Mann-Whitney U
ESR, mm/h	34.45 ± 14.10	35.97 ± 16.37	0.652	Welch t-test
WBC, ×10^9/L	8.60 (7.20–9.95)	9.10 (7.30–10.28)	0.512	Mann-Whitney U
Neutrophils, ×10^9/L	6.00 (4.80–6.95)	6.35 (5.00–7.65)	0.480	Mann-Whitney U
Band cells, %	5.47 ± 2.86	5.56 ± 2.88	0.887	Welch t-test
Haemoglobin, g/dL	12.81 ± 1.20	13.01 ± 1.29	0.471	Welch t-test
Platelets, ×10^9/L	187.43 ± 50.73	146.83 ± 50.57	<0.001**	Welch t-test

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AST, U/L	53.00 (39.00–69.00)	47.00 (39.25–70.00)	0.658	Mann-Whitney U
ALT, U/L	42.00 (31.50–63.50)	46.50 (30.00–60.75)	0.925	Mann-Whitney U
BUN, mg/dL	16.10 (12.40–19.30)	16.30 (13.97–19.15)	0.864	Mann-Whitney U
Serum sodium, mmol/L	136.48 ± 3.64	136.77 ± 3.98	0.722	Welch t-test
Serum potassium, mmol/L	4.01 ± 0.35	3.96 ± 0.33	0.543	Welch t-test

*Note: Data are expressed as n (%), mean ± SD, or median (IQR). * P = 0.009; ** P < 0.001. P < 0.05 was considered statistically significant.*

Table 4. Seasonal distribution of Mediterranean spotted fever cases (N = 117)

Season	n	%
Spring	2	1.7
Summer	67	57.3
Autumn	47	40.2
Winter	1	0.9
Total	117	100

Note: Calendar months were not uniformly represented in the dataset; seasonal proportions reflect the distribution of recorded cases and should not be interpreted as population-level seasonal incidence estimates.

Figures

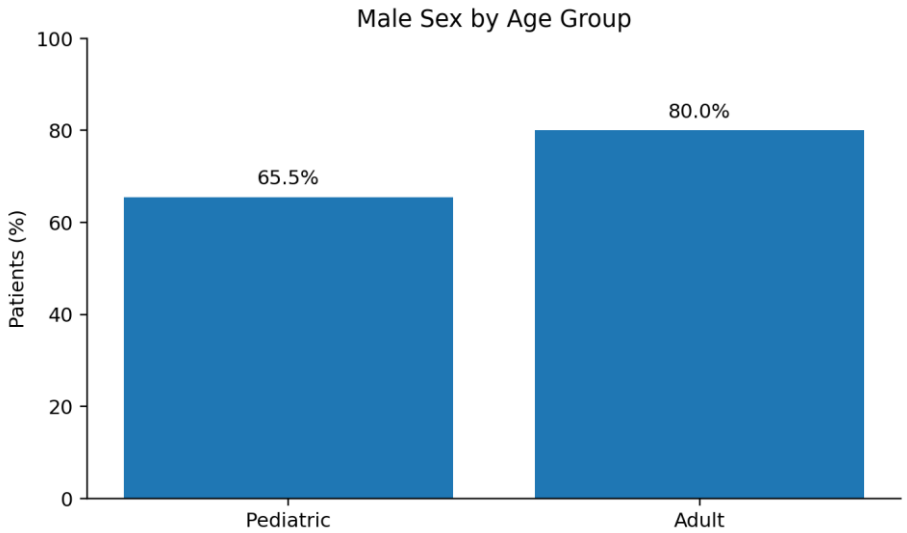

Figure 1. Sex distribution by age group. Male patients accounted for 65.5% of paediatric patients and 80.0% of adult patients (Fisher's exact test, P = 0.172).

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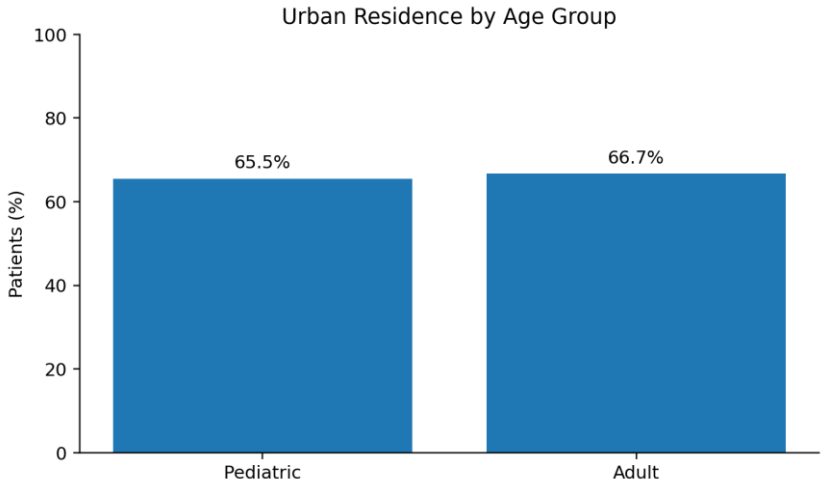

Figure 2. Residence distribution by age group. Urban residence was reported in 65.5% of paediatric patients and 66.7% of adult patients (Fisher's exact test, P = 1.000).

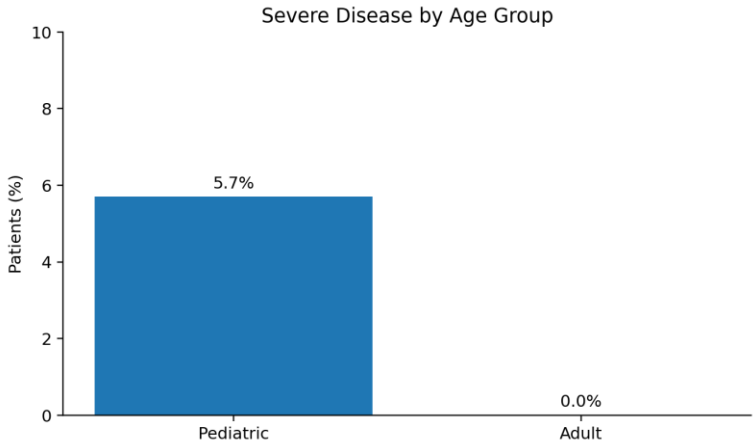

Figure 3. Severe disease distribution by age group. Severe disease (ICU admission) occurred in 5.7% of paediatric patients and in none of the adult patients; the difference was not statistically significant (Fisher's exact test, P = 0.326).

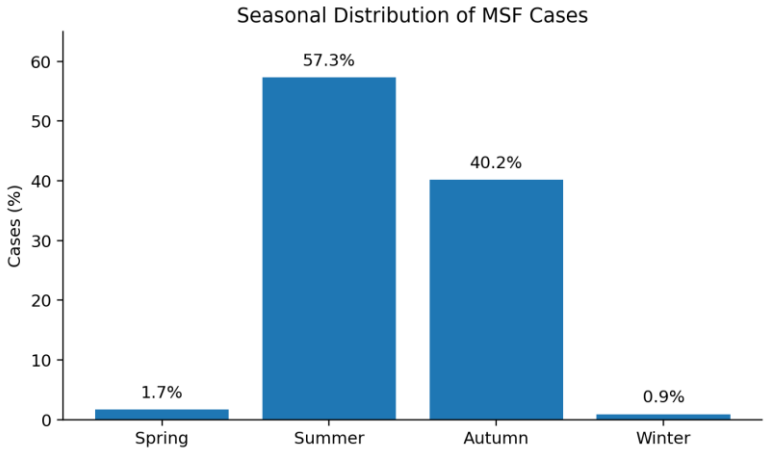

Figure 4. Seasonal distribution of Mediterranean spotted fever cases. Summer accounted for 57.3% of cases and autumn for 40.2%; seasonal interpretation is limited by non-uniform calendar-month representation in the dataset.

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