

MEDITERRANEAN SPOTTED FEVER IN ALGERIA: A CRITICAL REVIEW OF EPIDEMIOLOGICAL TRANSITIONS, EMERGING PATHOGEN DIVERSITY, AND THE CASE FOR A ONE HEALTH STRATEGY

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ABSTRACT

Mediterranean Spotted Fever (MSF) is an endemic tick-borne disease in Algeria caused by *Rickettsia conorii*, yet its true burden remains largely underestimated due to diagnostic and surveillance gaps. This review summarizes available data on the epidemiology, vectors, and emerging challenges associated with MSF in Algeria. *Rhipicephalus sanguineus* is identified as the primary vector, with other local tick species found infected and potentially involved in transmission cycles. Recent studies highlight genetic variability among *R. conorii* strains, potential acaricide resistance in tick populations, and the influence of climate change on vector distribution and seasonal disease patterns. Effective control of MSF requires a multifaceted approach, integrating enhanced epidemiological monitoring, molecular identification of vectors, public health education, and community engagement. Interdisciplinary collaboration and

international data sharing are crucial to anticipate disease trends and implement targeted prevention strategies.

Keywords: Mediterranean Spotted Fever, *Rickettsia conorii*, Algeria, One Health.

1. INTRODUCTION: BEYOND THE CLASSICAL PARADIGM

Mediterranean spotted fever (MSF) is a zoonotic tick-borne disease caused by *Rickettsia conorii* and transmitted mainly by the brown dog tick, *Rhipicephalus sanguineus*. Across the Mediterranean basin, MSF has long been recognized as one of the most frequent rickettsioses, affecting both urban and rural populations and remaining a persistent public health concern in many endemic countries [1, 2].

Clinically, MSF is traditionally described as a febrile illness characterized by headache, myalgia, a maculopapular rash, and the presence of an inoculation eschar at the site of the tick bite. In everyday clinical practice, however, this "classical" presentation is not always observed. Increasing evidence shows that MSF can evolve toward atypical or severe forms, including neurological, renal, and systemic involvement, particularly when diagnosis is delayed or clinical suspicion is low [3-5]. These severe presentations challenge the widespread perception of MSF as a benign and self-limiting disease.

Although MSF has historically been associated with southern Europe and North Africa, recent reports have revealed natural foci beyond its classical geographic boundaries. The identification of MSF cases in Asia and the detection of *R. conorii* in captive non-human primates suggest a broader and more dynamic distribution of the pathogen than previously assumed [6, 7]. Such observations underline the role of ecological changes, human activity, and animal-vector interactions in shaping the epidemiology of rickettsial diseases.

In Algeria, MSF has been reported for several decades and remains endemic. Clinical, serological, and molecular studies have documented infections in both adults and children, highlighting the persistent circulation of *R. conorii* in diverse regions of the country [8-10]. More recent molecular investigations confirm that human infections coexist with widespread rickettsial circulation in tick vectors, reinforcing the public health relevance of MSF in Algeria [11, 12]. Despite this long-standing presence, the true burden

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of MSF remains difficult to assess, largely due to underdiagnosis, underreporting, and limited access to molecular diagnostic tools.

Another layer of complexity arises from the diversity of spotted fever group (SFG) rickettsiae circulating in Algeria. Beyond *R. conorii*, several pathogenic or potentially pathogenic rickettsial species have been detected in ticks, fleas, domestic animals, and wildlife [13-15]. Moreover, molecular studies have demonstrated that *R. conorii* is not exclusively associated with *R. sanguineus* but may also be detected in other tick species, suggesting a broader ecological range of potential vectors [16]. This diversity complicates clinical diagnosis and epidemiological interpretation and increases the risk of misclassification between MSF and other SFG rickettsioses.

In this context, continuous surveillance and molecular characterization of circulating strains are essential to better understand the epidemiology of MSF and related rickettsioses [10, 17].

2. LITERATURE SEARCH METHODOLOGY

This narrative review was conducted following a systematic literature search to ensure comprehensive coverage of the topic. We searched PubMed, Scopus, and Web of Science databases for studies published up to December 2024. The search strategy combined terms related to the pathogen ("*Rickettsia conorii*", "Spotted Fever Group *Rickettsia*"), the disease ("Mediterranean spotted fever", "boutonneuse fever"), the vector ("tick", "*Rhipicephalus sanguineus*"), and the geographic focus ("Algeria", "North Africa", "Maghreb") using Boolean operators (AND, OR). We also manually screened the reference lists of included articles to identify additional relevant studies. We included original research articles, reviews, case reports, and epidemiological reports (including Monthly Epidemiological Reports) that provided data on the epidemiology, vectors, clinical presentation, diagnosis, or molecular characterization of SFG rickettsiae in Algeria. Studies not focused on Algeria or those focusing solely on non-SFG rickettsiae were excluded.

3. THE EPIDEMIOLOGICAL RECORD: WHAT WE KNOW AND WHAT WE DO NOT

Mediterranean spotted fever is considered endemic in Algeria, with reported human cases across multiple provinces. Data derived from Monthly Epidemiological Reports [18] and published clinical studies in-

dicate a heterogeneous spatial distribution of cases, reflecting marked regional differences in surveillance intensity, diagnostic capacity, and research coverage rather than true absence of disease circulation.

As illustrated in Figure 1, reported MSF cases and molecular detections of *Rickettsia* spp. are unevenly distributed across the country, with a predominance of data originating from northern regions. It is important to emphasize that this uneven distribution reflects the locations where research has been conducted rather than the true geographic range of pathogen circulation. Several provinces with no published data (grey areas) may still harbor circulating rickettsiae, as suggested by the presence of suitable tick vectors and ecological conditions similar to neighboring regions with documented cases.

The map summarizes published evidence of human Mediterranean spotted fever (MSF) cases and molecular detection of spotted fever group *Rickettsia* spp. across Algerian provinces. Blue areas indicate provinces with reported human MSF cases based on epidemiological surveillance or clinical studies. Yellow hatched areas represent provinces where *Rickettsia* spp. were detected exclusively in tick vectors or animal hosts. Green hatched areas indicate provinces with both reported human MSF cases and molecular detection of *Rickettsia* spp. Grey areas correspond to provinces for which no published epidemiological or molecular data were available. The observed spatial heterogeneity reflects differences in surveillance intensity, diagnostic capacity, and research coverage rather than the true absence of pathogen circulation.

3.1. Historical Data and Diagnostic Evolution

Mediterranean spotted fever, caused by *Rickettsia conorii*, has long been considered an endemic tick-borne disease in Algeria. The earliest records related to rickettsial infections date back to the mid-20th century, notably the experimental studies conducted by Blanc (1951) on *Rickettsia (Coxiella) burnetii* in Algeria and neighboring regions [19]. Subsequently, Bernard et al. (1963) provided a comprehensive review of the epidemiological status of rickettsioses in Algeria, laying the groundwork for future investigations and the development of epidemiological knowledge on these infections [20].

Clinically documented human cases of MSF in Algeria were first reported in the late 20th century. Mouffok et al. (2006) described the re-emergence of rickettsioses in Oran, affecting both paediatric and adult

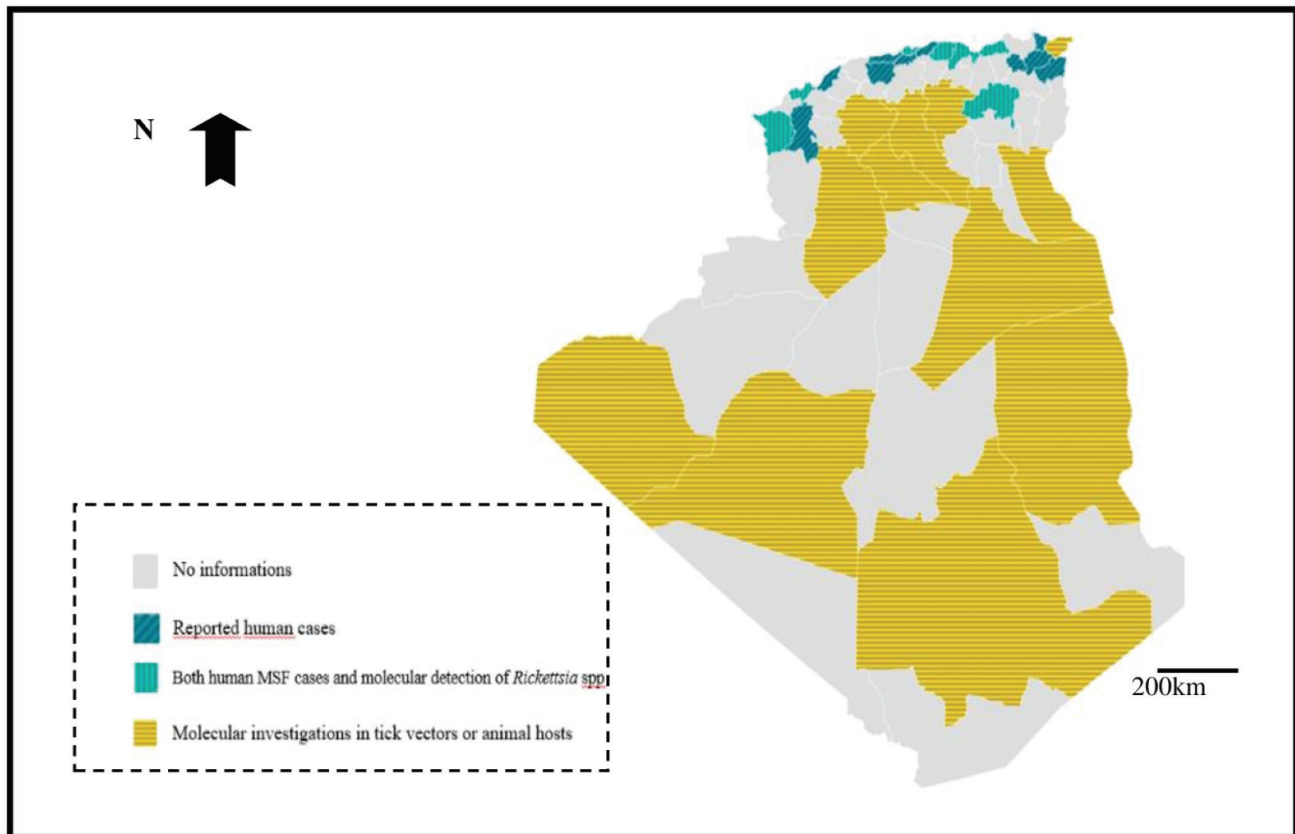


Figure 1. Geographical distribution of published studies on Mediterranean spotted fever and SFG rickettsiae in Algeria. Blue areas indicate provinces with reported human MSF cases based on epidemiological surveillance or clinical studies. Yellow hatched areas represent provinces where *Rickettsia* spp. were detected exclusively in tick vectors or animal hosts. Green hatched areas indicate provinces with both reported human MSF cases and molecular detection of *Rickettsia* spp. Grey areas correspond to provinces for which no published epidemiological or molecular data were available.

Crucially, this map reflects the distribution of research and surveillance effort, not the true distribution of disease risk. The absence of data in grey areas should not be interpreted as the absence of pathogen circulation, but rather as a critical gap in knowledge. The observed spatial heterogeneity is primarily driven by differences in surveillance intensity, diagnostic capacity, and research activity rather than genuine epidemiological patterns.

patients presenting with typical clinical features such as fever and rash [21]. Shortly thereafter, Benabdelah et al. (2007) reported the clinical and laboratory characteristics of 34 paediatric MSF cases hospitalized in Oran, with confirmation of *R. conorii* as the causative agent [8]. These pioneering studies clearly established MSF as a relevant public health issue in both urban and rural settings.

Subsequent molecular and serological investigations provided further evidence of the continuous circulation of *R. conorii* among human populations and tick vectors across different regions of Algeria. In particular, applied multispacer typing (MST) to *R. conorii* strains isolated from patients, offering valuable insights into strain diversity and geographic distribution. Together, these historical and early epidemiological data form the basis for understanding the current epidemiological situation of MSF in Algeria

and underscore the need for sustained surveillance and research on emerging rickettsial infections [10].

3.2. Geographic Distribution: A Map of Surveillance Effort, Not Disease Risk

At present, Mediterranean spotted fever remains endemic in multiple regions of Algeria, affecting both urban and rural populations. Epidemiological information is mainly derived from hospital-based clinical studies, serological surveys, and molecular investigations conducted on humans, ticks, and animal hosts. Although these studies consistently demonstrate the circulation of *R. conorii*, they do not allow a reliable estimation of population-level incidence, strongly suggesting that MSF is underdiagnosed and underreported.

The main vector, *Rhipicephalus sanguineus*, has been consistently identified as playing a central role in the transmission of *R. conorii* to humans [10, 13].

In addition to *R. sanguineus*, molecular studies have identified several other tick species harbouring rickettsial pathogens in Algeria, including *Hyalomma aegyptium*, *Hyalomma dromedarii*, and *Ixodes ricinus*, which carry *Rickettsia aeschlimannii*, *Rickettsia massiliae*, and *Rickettsia monacensis*, respectively [13, 14, 22].

In the north of Algeria, particularly the coastal and sub-coastal regions have been the most extensively investigated. Serological and molecular studies have confirmed MSF among patients presenting with febrile illnesses, including atypical and severe clinical forms [9, 12]. Similar findings have been reported in eastern regions such as Batna and El Tarf, where both human cases and infected ticks have been documented [23, 24].

Beyond the northern regions, molecular surveys conducted in steppe and high plateau areas, as well as in southern and semi-arid zones, have revealed the circulation of *R. conorii* and other spotted fever group rickettsiae in ticks collected from domestic animals, particularly dogs and livestock [15, 25]. These observations broaden the recognized geographic range of

rickettsial circulation and indicate that MSF risk is not confined to traditionally endemic coastal areas.

Ecological and climatic factors influencing tick abundance and seasonal activity likely contribute to regional variations in MSF occurrence. Northeastern Algeria, in particular, shows a high diversity of rickettsial species within tick populations, including *R. slovaca*, *R. aeschlimannii*, and *R. massiliae*, detected in *Hyalomma* and *Ixodes* ticks collected from domestic animals and wildlife [26, 27].

Overall, available evidence suggests that MSF may be widely distributed across diverse ecological zones in Algeria, but this interpretation is based on fragmented studies and remains insufficiently quantified by comprehensive national surveillance. The lack of nationwide surveillance systems and population-based studies severely limits accurate estimation of disease burden, reinforcing the classification of MSF as a likely underdiagnosed and underreported zoonosis.

As summarised in Table 1, epidemiological studies conducted in Algeria between 2006 and 2025 encompass human clinical cases, serological surveys,

Table 1. Summary of epidemiological studies on Mediterranean spotted fever and related rickettsioses in Algeria (2006-2025)

provinces / Area (study site)	Study type / metric	Main findings	Rickettsia species detected	Study (year)
Oran (hospital cases)	Clinical series (serology)	Clinical features of 34 paediatric rickettsiosis cases confirmed by IF	<i>R. conorii</i> (human MSF cases)	[3]
Oran region	Hospital-based surveillance	Re-emergence of rickettsioses; recurrent clinical cases; mortality reported	<i>R. conorii</i> (clinical/molecular diagnosis)	[4, 5]
El Tarf (NE Algeria)	Tick survey (PCR prevalence)	Seasonal and species-dependent PCR positivity in <i>I. ricinus</i> and <i>R. bursa</i>	<i>R. helvetica</i> , <i>R. monacensis</i> , <i>R. raoultii</i> , <i>R. massiliae</i>	[20]
Steppe and high plateau (dogs)	MIR / % positive pools in ticks	Rickettsial DNA detected in <i>R. sanguineus</i> s.s. from dogs (MIR $\approx$ 6.3%)	<i>R. conorii</i> , <i>R. massiliae</i> , other SFG	[21]
Multiple provinces (multi-biotope survey)	Molecular screening (ticks and fleas)	Overall MIR $\approx$ 6.37%; <i>R. massiliae</i> in ticks; <i>R. felis</i> in fleas; novel <i>Rickettsia</i> sp.	<i>R. massiliae</i> , <i>R. felis</i> , novel <i>Rickettsia</i> sp.	[7]
Batna (Eastern Algeria)	Clinical surveillance	Human rickettsial infections detected; molecular confirmation	<i>Rickettsia</i> spp. (MSF included)	[19]
Kabylie (dogs)	PCR screening in dogs	Vector-borne pathogens detected in dogs; rickettsiae reported in associated ectoparasites	Not specified	[37]
Various regions (wildlife and livestock)	Molecular detection in ticks/hosts	Detection in wild boar, hedgehogs, camels; host- and site-specific distribution	<i>R. slovaca</i> , <i>R. aeschlimannii</i> , <i>R. africae</i>	[9, 27, 29]
Northern Algeria (meningeal syndrome patients)	Serology / PCR in humans	Recent clinical study showing rickettsial infection among patients with meningeal syndrome	<i>Rickettsia</i> spp.	[11]

MIR: minimum infection rate; IF: immunofluorescence; PCR: polymerase chain reaction; SFG: spotted fever group

Note: Studies marked with serology alone may overestimate *R. conorii* prevalence due to cross-reactivity with other SFG species.

Table 2. Annual distribution of reported Mediterranean spotted fever cases by provinces in Algeria, 2000-2002

provinces	2000	2001	2002	Total	Trend
Tindouf	0	0	118	118	Abrupt emergence
Tlemcen	59	7	43	109	Marked fluctuation
Tipaza	35	3	39	77	Stable with rebound
Boumerdès	34	1	26	61	Moderate decline then increase
Oran	22	0	7	29	Decreasing
Sidi Bel Abbès	18	0	1	19	Sharp decrease
Béjaïa	13	0	4	17	Low and sporadic
Algiers	12	0	15	27	Variable
Aïn Témouchent	0	0	9	9	Single-year reporting
Jijel	6	0	12	18	Increasing
Blida	5	1	1	7	Low and stable
Mostaganem	5	0	7	12	Slight increase
Aïn Defla	55	1	0	56	Sharp decrease
Sétif	4	0	2	6	Low-level fluctuation
Médéa	4	0	4	8	Stable
Guelma	3	0	7	10	Increasing
Bordj Bou Arréridj	3	0	0	3	Single-year reporting
Chlef	2	0	0	2	Single-year reporting
Bouira	2	0	0	2	Single-year reporting
Skikda	2	0	0	2	Single-year reporting
Tizi Ouzou	1	0	6	7	Re-emergence
Saïda	0	0	1	1	Sporadic
Annaba	1	0	0	1	Sporadic
Constantine	1	0	0	1	Sporadic
Souk Ahras	1	0	7	8	Increasing
Total Algeria	238	13	309	560	Marked interannual variability

Source: Monthly Epidemiological Reports (REM), 2000-2002 [22]

and molecular investigations of tick vectors and animal hosts. Collectively, these studies highlight a fragmented epidemiological landscape characterized by heterogeneous methodologies, uneven geographic coverage, and a predominance of descriptive rather than analytical approaches.

Historical surveillance data further illustrate temporal variability in reported MSF cases. Table 2 presents the annual distribution of MSF cases by provinces in Algeria between 2000 and 2002, based on Monthly Epidemiological Reports (REM). These data reveal marked interannual and regional variability, suggesting fluctuations in reporting and surveillance sensitivity.

This temporal variability is further illustrated in Figure 2, which shows the overall annual trend in reported MSF cases at the national level. Reported human cases were extracted from Monthly Epidemiological Reports (REM). A marked interannual variability is observed, with a sharp decrease in 2001 followed by a peak in 2002.

It is crucial to emphasise that the data presented in Figure 2 and Table 2, spanning 2000-2002, represent the only publicly available nation-wide surveillance dataset for MSF in Algeria. The absence of consolidated national data beyond this period is not an oversight, but rather a direct consequence of

the very limitations this review seeks to highlight: underreporting, lack of a standardized national surveillance system, and decentralization of diagnostic capabilities.

While more recent clinical and molecular studies, such as the detailed investigation of 167 patients in Oran between 2004-2005 by Mouffok et al. [9], provide invaluable insights into disease presentation and local epidemiology, they do not constitute a continuous national dataset. Currently, MSF is a notifiable disease in Algeria, but in practice, reporting is passive and incomplete. Diagnosis is often clinical, and confirmed cases requiring laboratory notification are significantly underreported, especially from the private health sector and rural areas.

Therefore, the 2000-2002 data are presented here not as a reflection of current incidence, but as a historical benchmark illustrating the chronic instability and unreliability of reporting systems. The marked interannual variability observed—a sharp decrease in 2001 followed by a peak in 2002—almost certainly reflects changes in surveillance sensitivity and reporting practices rather than true fluctuations in disease incidence. This historical perspective reinforces the urgent need for renewed, consistent national surveillance as advocated throughout this review.

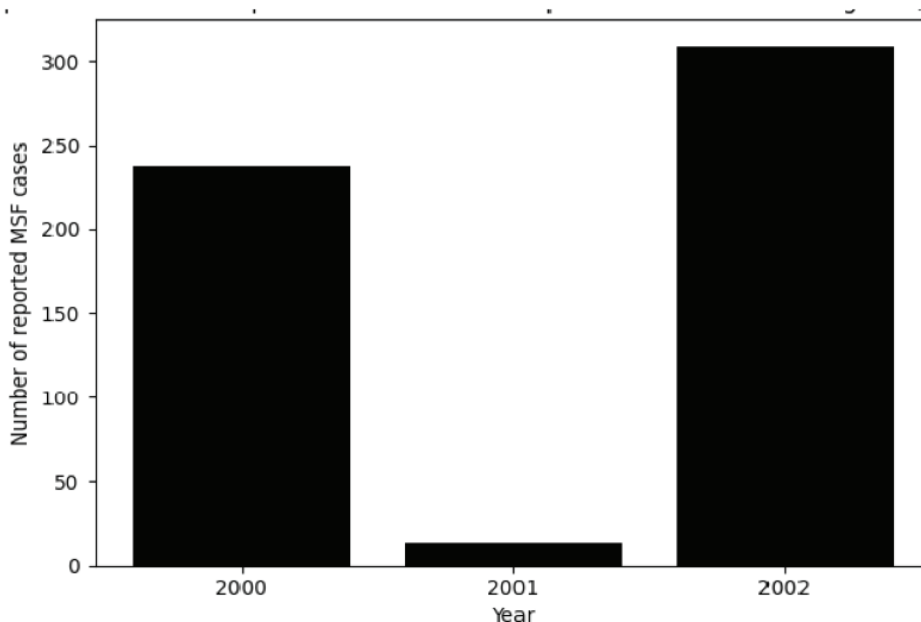


Figure 2. Temporal variation of reported Mediterranean spotted fever cases in Algeria (2000-2002). Reported human cases were extracted from Monthly Epidemiological Reports (REM). A marked interannual variability is observed, with a sharp decrease in 2001 followed by a peak in 2002. This pattern likely reflects changes in surveillance sensitivity and reporting practices rather than true fluctuations in disease incidence.

4. VECTORS, HOSTS, AND PATHOGEN DIVERSITY: A SYSTEM IN FLUX

4.1. *Rhipicephalus sanguineus*: The Primary but Not Sole Actor

Ticks are the primary vectors of Mediterranean spotted fever (MSF) in Algeria, and their geographic distribution strongly influences transmission risk. The brown dog tick, *Rhipicephalus sanguineus* sensu lato, remains the main vector of *R. conorii* and studies have documented its presence in urban, peri-urban, and rural areas across multiple provinces [10, 13, 17]. However, comprehensive nationwide mapping of tick distribution and infection rates is still lacking. Its close association with domestic dogs facilitates frequent human exposure.

Multiple molecular studies in Algeria have confirmed the circulation of *R. conorii* in *R. sanguineus* ticks collected from dogs in northern regions, the steppe, and high plateau areas [15, 25]. Infection rates in questing ticks remain generally low, likely due to limited transovarial transmission and ecological constraints affecting pathogen persistence [17].

4.2. Genetic Diversity of *Rickettsia conorii* in Algeria

Recent molecular studies have revealed significant genetic diversity among *R. conorii* strains circulating in different regions of Algeria [15, 25]. Analyses of multiple loci, including *ompA*, *ompB*, and *gltA*, indicate the presence of distinct haplotypes within local tick populations, suggesting microevolutionary pro-

cesses shaped by geographic and ecological factors. This genetic variability may influence the pathogenicity, the transmission efficiency by *R. sanguineus*, and the spectrum of clinical manifestations in humans.

The coexistence of multiple strains in a single region could contribute to variability in disease severity and complicate diagnostic efforts, particularly when serological assays cannot distinguish closely related genotypes. Understanding local strain diversity is crucial for epidemiological surveillance, risk mapping, and vector control strategies, and it may inform the development of targeted diagnostic tools or vaccines. Continuous molecular monitoring is therefore essential to track the evolution of *R. conorii* populations and detect the emergence of novel or potentially more virulent variants.

The detection of multiple SFG rickettsiae in ticks and animal hosts across Algeria [14, 15, 22, 24-27] raises important questions about their potential role in human disease. While *R. conorii* is the classic agent of MSF, other SFG species such as *R. aeschlimannii*, *R. massiliae*, and *R. slovaca* have been associated with human illness in other countries and may contribute to the burden of undifferentiated febrile illness in Algeria. The clinical similarities between infections caused by different SFG species mean that cases attributed to MSF in the literature, particularly those diagnosed by serology alone, may represent a mix of etiologies. This fact highlights the need for molecular

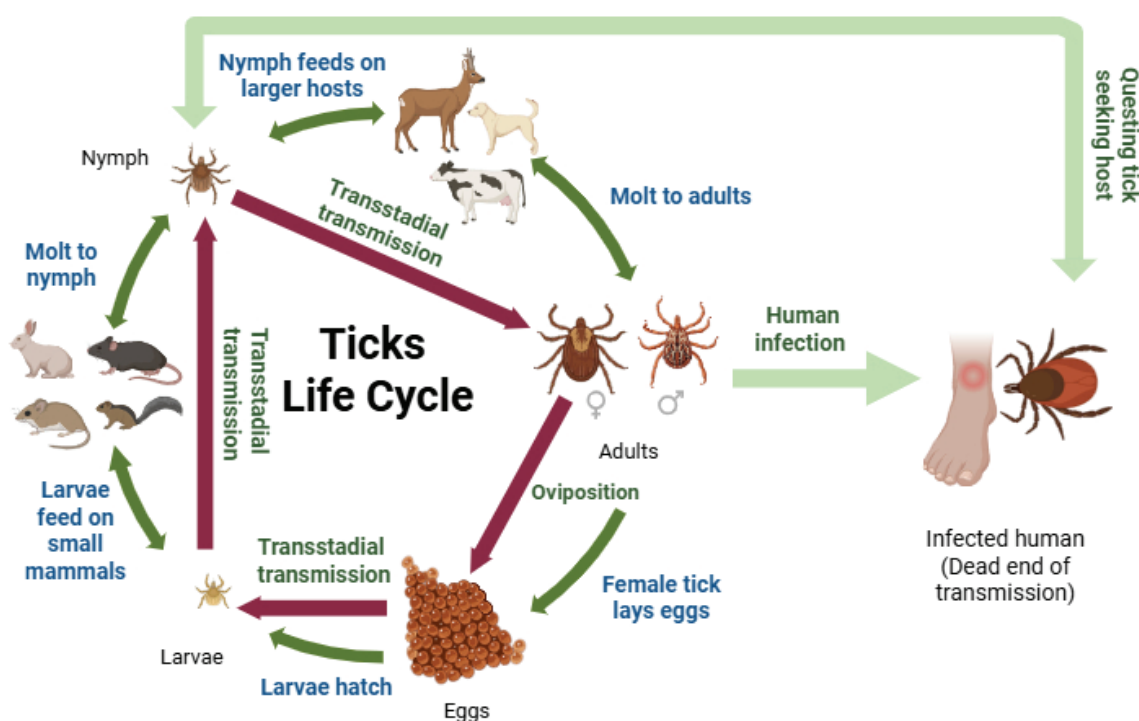


Figure 3. Transmission cycle of *Rickettsia* spp. in Algeria (created with BioRender). Includes *Rhipicephalus sanguineus* and other tick vectors, domestic animals (dogs, livestock), wildlife (wild boars, hedgehogs), and pathogen diversity across geographic regions.

surveillance to determine the true distribution and clinical impact of each SFG species in Algeria.

Beyond *R. sanguineus*, several other tick species in Algeria harbour spotted fever group rickettsiae. *Hyalomma aegyptium* and *H. dromedarii* have been found infected with *Rickettsia aeschlimannii*, *R. massiliae*, and *R. africae*, particularly in ticks collected from livestock and camels in northern, steppe, and sub-Saharan regions [14, 26, 27]. Although their role in classical MSF transmission remains uncertain, their presence suggests potential alternative transmission pathways and SFG rickettsioses that may present with MSF-like clinical features.

In northern Algeria, *Ixodes ricinus* has been reported to carry *Rickettsia monacensis* and *R. helvetica*, further expanding the spectrum of rickettsial agents circulating in local tick populations [22, 24]. Additionally, *Dermacentor* species have been implicated in the circulation of spotted fever group rickettsiae in limited surveys [14]. This diversity of potential vectors underscores the importance of effective tick control. However, data on acaricide resistance in Algerian tick populations are currently limited, highlighting a critical knowledge gap that hinders the optimization of vector control strategies.

4.3. Domestic Animals as Reservoir Hosts

Domestic animals play a crucial role in MSF epidemiology in Algeria by sustaining infected tick populations and facilitating zoonotic transmission. Dogs are of particular importance as primary hosts of *R. sanguineus* and frequently live in close proximity to humans. Molecular evidence of spotted fever group rickettsiae in ticks collected from dogs has been consistently reported across different regions of Algeria, supporting their role as key sentinels and amplifying hosts [15, 25, 28].

Livestock animals, including sheep, cattle, and camels, also contribute to rickettsial maintenance by hosting large populations of *Hyalomma* ticks. Molecular detection of *R. aeschlimannii*, *R. massiliae*, and *Candidatus Rickettsia barbariae* in ticks collected from livestock highlights the epidemiological importance of pastoral systems, particularly in rural and semi-arid regions [27, 30]. Although these animals often remain asymptomatic, their role as reservoirs or amplifying hosts increases the risk of human exposure, especially in settings where animal husbandry overlaps with human habitation.

4.4. Wildlife and Sylvatic Cycles

Wildlife plays a significant role in the maintenance of spotted fever group rickettsiae in Algeria. Molec-

ular investigations have documented the presence of rickettsial agents in ticks and ectoparasites collected from wild boars, hedgehogs, and other wild mammals, providing strong evidence for sylvatic transmission cycles [26, 31, 32].

Wild boars have been shown to harbour *Rickettsia slovaca* in internal organs, indicating active infection rather than passive carriage [26]. Hedgehogs and their ectoparasites have been associated with multiple rickettsial species, including *R. aeschlimannii* and *R. felis*, particularly in peri-urban and forested environments [31, 32]. The coexistence of domestic and sylvatic cycles increases the risk of spillover to human populations, especially in regions where anthropogenic activities encroach upon natural habitats. This ecological overlap likely contributes to the persistence, diversification, and potential geographic expansion of rickettsial agents in Algeria, although longitudinal studies are needed to confirm these dynamics. Figure 3 illustrates the transmission cycle of *Rickettsia* spp. in Algeria, highlighting the main tick vectors, domestic and sylvatic hosts, and the interactions between domestic and wildlife cycles that contribute to human exposure. The figure also reflects the diversity of rickettsial strains detected in different tick species across regions.

5. CLINICAL SPECTRUM: RETHINKING SEVERITY

Based on published clinical series, Mediterranean spotted fever (MSF) in Algeria presents a broad clinical spectrum, ranging from mild febrile illness to severe and potentially life-threatening disease. However, the true range of clinical presentations in community settings remains unknown due to underdiagnosis. The classical form is characterized by acute onset of fever, headache, myalgia, maculopapular rash, and the presence of an inoculation eschar (tache noire). These manifestations have been consistently reported in Algerian patients, confirming the endemic circulation of *R. conorii*. Other SFG rickettsiae (*R. aeschlimannii*, *R. massiliae*, *R. monacensis*, *R. slovaca*) have also been detected in Algeria and may cause similar clinical presentations [8, 9, 21].

5.1. Clinical Presentation in Children and Adults

Paediatric MSF represents a significant proportion of reported cases in Algeria. Hospital-based studies conducted in Oran described classical febrile exanthematous illness in children, with serological confirmation of MSF and generally favorable outcomes following

appropriate antibiotic treatment [8, 9]. These findings highlight the importance of including MSF in the differential diagnosis of febrile illnesses in children, particularly during the summer season and in areas with high tick exposure.

In adults, MSF shows greater clinical heterogeneity. Epidemiological investigations in northern and western Algeria have documented recurrent cases and re-emergence of rickettsioses in both urban and peri-urban settings [21]. Delayed diagnosis remains common due to non-specific early symptoms and limited clinical suspicion, contributing to increased disease severity.

5.2. Severe and Atypical Clinical Forms

Although MSF is often considered benign, severe and atypical forms have been increasingly reported in Algeria. Neurological involvement constitutes one of the most serious complications, including meningitis, meningoencephalitis, and other central nervous system manifestations. Clinical studies from northern Algeria have documented rickettsial involvement in patients with neurological symptoms, emphasising the neurotropic potential of SFG rickettsiae [9, 11].

Rare neurological complications, such as peripheral facial nerve palsy, have also been described, expanding the clinical spectrum and illustrating the potential for focal neurological deficits [5]. Recent serological and molecular evidence from northern Algeria confirmed *Rickettsia* spp. in patients presenting with meningeal syndrome, suggesting that severe complications related to SFG rickettsioses may be more frequent than previously assumed [12]. In the absence of species-level identification, it remains unclear whether these cases were caused by *R. conorii* or other SFG species. It is important to note that serological tests such as indirect immunofluorescence assay (IFA) cannot reliably distinguish between *R. conorii* and other closely related SFG rickettsiae due to cross-reactivity. Therefore, some historical cases reported as MSF based on serology alone may actually have been caused by other SFG species circulating in Algeria, including *R. aeschlimannii*, *R. massiliae*, *R. monacensis*, or *R. slovaca*. In addition to neurological involvement, renal dysfunction and other systemic complications have been reported, particularly in elderly patients or in cases with delayed initiation of doxycycline therapy.

5.3. Disease Severity, Mortality, and Prognostic Factors

Although overall mortality associated with MSF remains relatively low, fatal outcomes have been reported, especially in severe or untreated cases. Poor prognosis is associated with advanced age, delayed doxycycline administration, absence of early clinical suspicion, and the presence of neurological or renal complications [9].

The detection of *Rickettsia* spp. among patients with meningeal syndrome further indicates that the true burden of severe MSF and related rickettsioses may be underestimated. Limited access to molecular diagnostics and lack of systematic surveillance likely contribute to underreporting of severe and atypical forms.

5.4. Clinical and Public Health Implications

The diversity of clinical manifestations observed in Algeria underscores the need for increased clinical awareness of MSF among healthcare providers. Early recognition based on epidemiological exposure, seasonal patterns, and compatible clinical features is essential to ensure prompt initiation of appropriate antibiotic therapy.

Figure 4 illustrates the clinical spectrum and severity of MSF in Algeria, depicting the progression from mild febrile illness to severe neurological or systemic complications. This severity pyramid highlights the importance of early diagnosis and timely treatment to prevent progression to life-threatening disease.

Strengthening diagnostic capacities and including rickettsial infections in the routine differential diagnosis of febrile and neurological syndromes could

significantly reduce morbidity and prevent severe outcomes.

6. DIAGNOSTIC APPROACHES AND CHALLENGES IN ALGERIA

The diagnosis of Mediterranean spotted fever in Algeria remains challenging due to non-specific clinical presentation, limited laboratory infrastructure, and restricted access to molecular diagnostic tools. Consequently, MSF and other rickettsioses are likely underdiagnosed and underreported, particularly outside major urban centers.

6.1. Clinical Diagnosis

In routine practice, MSF is frequently diagnosed on clinical and epidemiological grounds, relying on the association of fever, rash, eschar, and a history of tick exposure. However, this approach has important limitations, as rash and eschar may be absent or atypical, and early symptoms often mimic viral infections or other bacterial diseases [9, 21]. These limitations are particularly problematic in atypical and severe cases, including neurological presentations.

6.2. Serological Diagnosis

Serology, mainly based on indirect immunofluorescence assay (IFA), remains the most commonly used laboratory method for MSF diagnosis in Algeria. Several studies have relied on serological confirmation to diagnose MSF and other rickettsioses in hospitalised patients [8, 23]. However, serology lacks sensitivity during the early phase of infection and is affected by cross-reactivity among SFG rickettsiae, preventing re-

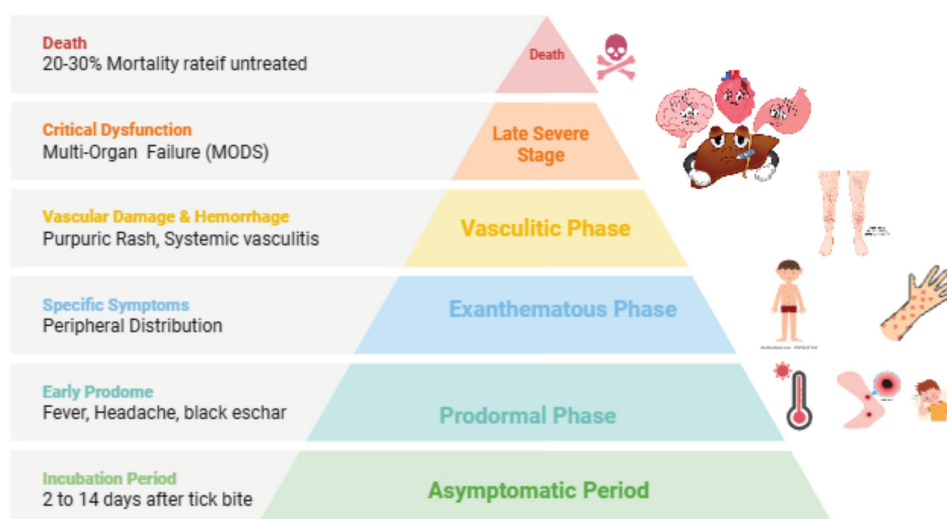


Figure 4. Clinical Spectrum of Spotted Fever (Severity Pyramid), created with BioRender. The image illustrates the progression of a tick-borne illness through various clinical phases, from mild febrile illness to severe neurological or systemic complications.

liable species-level identification.

This limitation has important epidemiological implications. Because IFA cannot reliably distinguish between *R. conorii* and other closely related SFG species, it is highly probable that some historical infections reported as MSF based on serology alone were, in fact, caused by other SFG rickettsiae circulating in Algeria, such as *R. aeschlimannii*, *R. massiliae*, *R. monacensis*, or *R. slovaca*. The increasing use of molecular tools in recent years has revealed this complex picture, demonstrating that multiple SFG species coexist in the same geographic regions and tick populations. Consequently, the true relative contribution of *R. conorii* versus other SFG species to human disease in Algeria remains unknown and requires further investigation using species-specific molecular diagnostics. The use of serological diagnosis has a long history in Algeria. Early investigations conducted during outbreaks of epidemic typhus demonstrated both the value and limitations of serodiagnosis in non-vaccinated populations [33, 34]. Subsequent reports of imported and autochthonous typhus cases further confirmed the persistence of rickettsial infections and the reliance on serology in the absence of molecular tools [35, 36].

6.3. Molecular Diagnostic Methods

Molecular techniques, particularly PCR-based assays, have significantly improved the detection and characterisation of rickettsial infections in Algeria. PCR has been successfully applied to human samples, ticks, fleas, and animal reservoirs, contributing to a better understanding of disease epidemiology.

PCR performed on eschar swab samples has been shown to be a reliable and minimally invasive diagnostic method, allowing early confirmation of rickettsioses without the need for invasive sampling [37]. In addition, genotyping approaches such as multispacer typing (MST) have demonstrated the genetic diversity of *Rickettsia conorii* strains circulating in Algeria [10]. Despite these advances, culture-based isolation remains limited to specialized laboratories, as illustrated by rare successful isolations using shell vial techniques [38].

Recent studies combining serological and molecular approaches have highlighted the diagnostic benefit of integrated strategies, particularly in severe clinical presentations such as meningeal syndromes [12].

6.4. Diagnostic Gaps and Perspectives

Despite methodological advances, major diagnostic

gaps persist in Algeria. Molecular diagnostics remain largely confined to research laboratories, and standardized diagnostic algorithms are lacking. Advances in vector identification and pathogen detection, including the use of MALDI-TOF mass spectrometry for arthropods and the identification of novel *Rickettsia* species in soft ticks, illustrate the complexity of rickettsial transmission cycles and emphasize the need for integrated diagnostic and surveillance approaches [39, 40].

7. EMERGING CHALLENGES AND FUTURE PERSPECTIVES FOR MEDITERRANEAN SPOTTED FEVER IN ALGERIA

Mediterranean spotted fever (MSF) in Algeria faces a set of emerging challenges that extend beyond the classical epidemiological framework. Although the disease has been recognized for decades, recent clinical, entomological, and molecular data indicate that MSF and other spotted fever group (SFG) rickettsioses are evolving in terms of transmission patterns, clinical severity, and diagnostic complexity.

7.1. Underdiagnosis and Underreporting

One of the major challenges in Algeria is the underdiagnosis of MSF. The non-specific nature of early clinical symptoms, combined with limited access to laboratory confirmation, likely leads to frequent misclassification or missed diagnoses. It is probable that many cases are treated empirically or remain unrecognized, particularly in rural and semi-urban areas, although the exact magnitude of underdiagnosis cannot be quantified with current data. This issue is further compounded in atypical and severe presentations, such as neurological forms, where MSF is not routinely considered in the differential diagnosis.

Recent molecular and serological evidence demonstrating *Rickettsia* spp. infections in patients with meningeal syndrome highlights that the true burden of severe rickettsioses in Algeria is likely underestimated. The absence of systematic national surveillance prevents accurate assessment of incidence, trends, and disease impact.

The persistent underdiagnosis of rickettsioses is not unique to Algeria but reflects a global pattern, as tick-borne rickettsioses continue to challenge traditional clinical and diagnostic concepts worldwide [41, 42].

7.2. Expanding Diversity of Rickettsial Agents and Vectors

Another emerging challenge is the increasing di-

versity of rickettsial agents detected in Algeria. Beyond *Rickettsia conorii* (the agent of classic MSF), multiple SFG rickettsiae have been identified in ticks, fleas, and animal hosts, including *R. aeschlimannii*, *R. massiliae*, *R. monacensis*, *R. slovaca*, and potentially pathogenic novel species. This diversity complicates the epidemiological picture and raises questions regarding the clinical significance of non-classical rickettsial species in human disease.

Changes in land use, urban expansion, animal husbandry practices, and climate conditions may further influence vector distribution and host-vector interactions. These factors could contribute to the emergence of new transmission cycles and increase human exposure to infected arthropods.

Ecological studies conducted in diverse geographical regions have demonstrated that rickettsial distribution and diversity are strongly influenced by environmental and climatic factors, leading to dynamic and region-specific transmission patterns [43, 44].

Furthermore, the coexistence of multiple SFG species in the same regions complicates the interpretation of historical epidemiological data. Many earlier studies relied exclusively on serology, which cannot differentiate between SFG species. Therefore, the perception that *R. conorii* is the dominant or sole cause of SFG rickettsioses in Algeria may be an artifact of diagnostic limitations rather than an accurate reflection of the true pathogen landscape. Future studies employing molecular diagnostics are essential to reassess the relative importance of each SFG species and to understand their respective clinical and epidemiological features.

7.3. Diagnostic and Laboratory Capacity Limitations

Despite advances in molecular diagnostics, access to PCR and genotyping tools remains limited in routine clinical practice in Algeria. Most molecular investigations are confined to research laboratories, and standardized diagnostic algorithms integrating clinical, serological, and molecular data are lacking. As a result, species-level identification is rarely achieved, hindering accurate epidemiological surveillance and risk assessment.

The limited use of innovative tools for vector identification and pathogen detection further constrains the ability to monitor emerging rickettsial threats. Strengthening laboratory capacity and ensuring equitable access to diagnostic technologies remain critical priorities.

Advances in the understanding of rickettsial pathogenesis underscore the need for improved diagnostic tools capable of capturing early host-pathogen interactions, a challenge emphasized by recent experimental and translational studies [42].

7.4. Public Health and Clinical Implications

From a public health perspective, MSF continues to be perceived as a benign and self-limiting disease, which may delay medical consultation and appropriate treatment. However, accumulating evidence of severe and atypical forms challenges this perception and underscores the need for improved clinician awareness.

Educational initiatives targeting healthcare professionals, particularly in endemic regions, are essential to promote early recognition and timely treatment. Integrating MSF and other rickettsioses into national infectious disease surveillance programs would represent a major step forward in improving disease control and prevention.

From a public health perspective, the control of rickettsioses requires an integrated One Health approach that considers human, animal, and environmental components, as highlighted in veterinary and vector-borne disease frameworks [45].

7.5. Future Directions

Future research on Mediterranean spotted fever in Algeria should move beyond fragmented or cross-sectional approaches toward integrated, longitudinal, and multidisciplinary frameworks. Priority should be given to long-term epidemiological studies combining human, animal, and vector data to better characterize transmission dynamics, seasonal patterns, and risk factors across diverse ecological settings. Such approaches are essential to capture the complexity of rickettsial circulation and to anticipate shifts driven by environmental change.

Advances in molecular biology offer important opportunities to explore the genetic diversity, pathogenic potential, and evolutionary dynamics of both classical and emerging rickettsial species. Improved understanding of host-pathogen and vector-pathogen interactions, particularly during early stages of infection, will be critical to refine diagnostic tools and identify biomarkers of disease severity. Experimental and translational studies should therefore be encouraged to bridge the gap between basic research and clinical application.

In parallel, the absence of effective vaccines against

rickettsial diseases remains a major unmet need. Although antimicrobial therapy is generally effective when administered early, prevention strategies based on vaccination represent a promising yet largely underexplored avenue. Renewed research efforts in this area, supported by advances in immunology and genomics, could substantially strengthen future control strategies.

Overall, Mediterranean spotted fever in Algeria should no longer be regarded as a fully characterised or static disease entity. The convergence of diagnostic gaps, ecological transformations, and expanding rickettsial diversity underscores the necessity of translating future-oriented research into coordinated public health action.

7.6. Strategic Recommendations for an Integrated National Response

Building on these future directions, a coordinated and integrated national response is essential to address the evolving challenges posed by Mediterranean spotted fever in Algeria. Strengthening epidemiological surveillance at the national level should be considered a priority in order to accurately assess disease burden, identify high-risk areas, and monitor temporal trends. Surveillance systems should encompass both human cases and tick vector populations and be supported by standardized diagnostic algorithms integrating clinical evaluation, serology, and molecular tools.

Expanding molecular investigations represents a critical component of this strategy. The implementation of advanced techniques such as genetic sequencing and multiplex PCR would allow precise identification of *Rickettsia* species and strains, facilitate detection of genetic variability, and enable early recognition of emerging or potentially more virulent variants. Parallel molecular identification of tick vectors and monitoring of acaricide resistance are necessary to inform and adapt vector control strategies.

Integrated vector management should be promoted through a combination of rational acaricide use, environmental management, and community-based interventions aimed at reducing human exposure to infected arthropods. These measures must be adapted to local ecological and socio-economic contexts to ensure effectiveness and sustainability.

Public health education also plays a pivotal role. Increasing awareness among healthcare professionals, particularly in endemic regions, is essential to im-

prove early recognition of typical and atypical clinical presentations and to ensure prompt treatment. At the community level, targeted educational initiatives can enhance knowledge of preventive measures and encourage timely medical consultation.

Finally, sustained interdisciplinary collaboration among entomologists, epidemiologists, clinicians, veterinarians, and public health authorities is indispensable. Data sharing and cooperation with other Mediterranean countries would further strengthen regional preparedness and facilitate anticipation of future challenges related to climate change, ecological shifts, and human mobility.

8. CONCLUSION

Mediterranean Spotted Fever is not a new disease in Algeria, but this review underscores that it represents a dynamic and evolving public health challenge based on the available fragmentary evidence. The convergence of endemic *Rickettsia conorii* transmission, the apparent expanding diversity of SFG rickettsiae in an increasing number of documented vectors and hosts, and the persistent gaps in diagnosis and surveillance creates a complex scenario that warrants urgent attention. The evidence clearly shows that MSF and related rickettsioses are significantly underdiagnosed, and their severe neurological and systemic forms are underappreciated. Moving forward, a passive, fragmented approach is insufficient. The path to effective control lies in the urgent implementation of a coordinated One Health strategy. This must be built on strengthened national surveillance, equitable access to molecular diagnostics, continuous vector and pathogen monitoring, and sustained education for both healthcare professionals and communities. By prioritizing these integrated measures, Algeria can transform its response to MSF, shifting from managing sporadic cases to proactively reducing the disease burden and mitigating the risks posed by this and other emerging tick-borne threats.

Author Contributions

Assia Beneldjouzi: study conception and design, literature search, data collection, data analysis and interpretation, manuscript writing. Lydia Hamrioui: contribution to literature search, participation in data analysis, critical revision of the manuscript. Naouel Eddaikra: participation in data interpretation, scientific revision of the manuscript. Idir Bitam: scientific supervision, final validation of the content, critical

revision and approval of the manuscript. All authors read and approved the final version of the manuscript.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

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