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CASE REPORT

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Severe coinfection of dengue and malaria: A case report

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Key Clinical Message

In countries like Sudan, where several infectious diseases are prevalent, health care providers should not be satisfied with initial detection of a single pathogen and whenever it is feasible, they should investigate coinfections. Infections with high mortality or severe morbidity should be prioritized during the differential diagnosis particularly for diseases with similar clinical manifestations to reduce the death and disability rates. However, this requires substantial improvement in the diagnostic capacity.

Abstract

Here we report a case of dengue and malaria coinfection from the southeast region of Sudan, bordering Ethiopia and Eritrea. A 25-year-old male from Sudan presented with symptoms of fever, chills, vomiting, and muscle and joint pain. Laboratory investigations confirmed a coinfection of dengue and malaria, which is assumingly not uncommon in areas heavily syndemic with several diseases but it is severely under-detected, underreported, and underestimated. The case has fully recovered after the supportive care for dengue and chemotherapy treatment for malaria. In such a case, it was important to monitor the patient's recovery and the treatment outcome through clinical indicators and laboratory parameters to update the treatment course whenever needed, according to response. The increasing burden and outbreaks of vector-borne diseases including dengue and malaria in Sudan, indicates the need for improving the implementation of the global vector control response that established by the World Health Organization. Additionally, the increasing prevalent of coinfections is urging substantial improvement in the diagnostic capacity in endemic countries.

KEYWORDS

arboviral diseases, coinfection, global vector control response, malaria, Sudan, vector-borne diseases

Emmanuel Edwar Siddig and Ayman Ahmed contribute equally to this work.

1 | INTRODUCTION

Malaria and dengue, two mosquito-borne diseases, have significant implications for human health and pose global public health challenges in endemic countries[1,2]; particularly that their co-burden is increasingly growing in Sub-Saharan Africa including Sudan.[3–5] Malaria is caused by *Plasmodium* parasites transmitted by several species of *Anopheles* mosquitoes. Five species of *Plasmodium* cause malaria to humans with *P. falciparum* and *P. vivax* being the most prevalent species.[6,7] On the other hand, dengue is caused by four distinct closely related serotypes of dengue virus, a flavivirus that is primarily transmitted by *Aedes* mosquitoes.[8–11] Dengue is considered a major arbovirus in terms of morbidity and mortality, and it is the most rapidly spreading disease worldwide.[12,13]

In tropical regions, the distribution and transmission areas of these diseases often overlap, this commonly results in coinfections.[4,5,14] Factors such as climate change,[9] urbanization, deforestation, and agricultural settlements in peri-urban areas increase the emergence and spread of infections.[15] Malaria is a major public health problem in Sudan, while dengue is rapidly spreading throughout the country, this indicated the growing epidemics.[4,11,16,17] Noteworthily, outbreaks of dengue in Sudan have been attributed to the circulation of DENV 1, 2, and 3 serotypes in various regions of the country.[12 – 14] An analysis of health records from Sudan revealed that over 80% of cases tested for dengue in West Darfur, 58% in Central Darfur, and 33% in East Darfur also tested positive for malaria.[18] This significant rate of malaria coinfection among Sudanese patients emphasizes the importance of considering malaria and other highly prevalent infectious diseases in the initial diagnosis.[5] Specifically, molecularly investigating patients hospitalized and treated for malaria has revealed high rate of coinfection or single infection with an arboviral disease that was mistakenly diagnosed as malaria.[4,5,19]

However, diagnosing coinfections is an additional challenge with limited resources settings due to the similarities in clinical characteristics between the two diseases and the common assumption that the firstly detected infection is the final diagnosis.[8,9] Furthermore, additional investigations come with additional cost that is commonly beyond the capacity of the poor patients. However, it is crucial to differentiate between the two diseases because delays in diagnosis and administering the appropriate treatment can worsen outcomes, leading to increased morbidity, mortality, and socioeconomic impacts.

In this communication, we are presenting a case of dengue and malaria coinfection in Sudan. We will discuss the clinical and laboratory investigations that were conducted to better understand this unique case and highlight the importance of accurate diagnosis and appropriate management strategies.

2 | CASE HISTORY

A 25-year-old male from Galabat, Gedaref State (Figure 1) presented on September 8, 2023, with 10 days history of fever accompanied by chills and rigors,

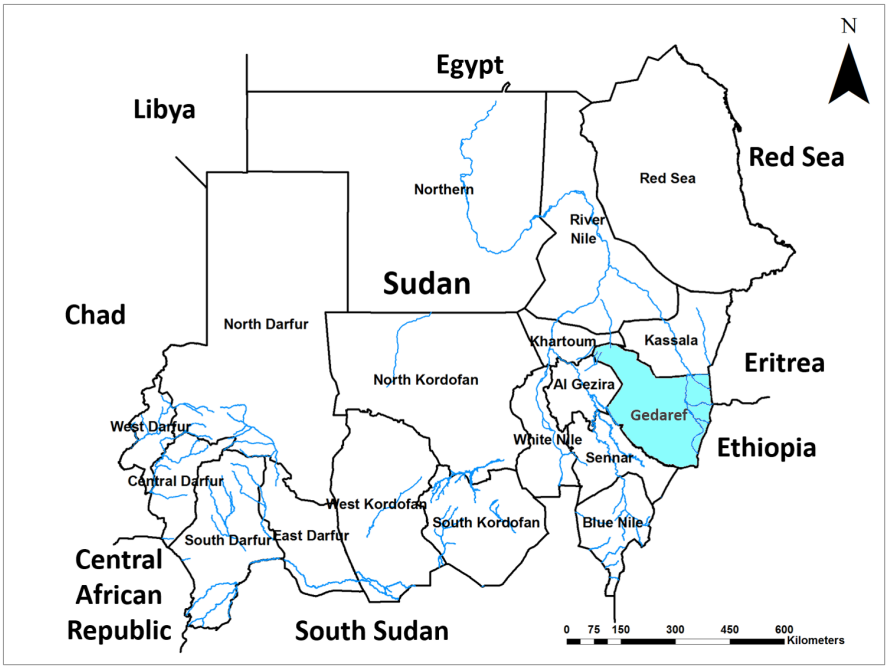

FIGURE 1 Map of Sudan shows the state where the patient lives.

vomiting, and muscle and joint pain. His recorded temperature was 39°C. He displayed tachycardia with a heart rate of 115 beats per minute (bpm) and low blood pressure (BP) of 95/56 mmHg. The tourniquet test was positive.

3 | METHODS

A blood sample was collected and sent to the laboratory for investigation. The patient tested positive for the NS1 Ag, confirming infection with dengue virus. It is essential to note that, infection with arboviruses was prioritized during the investigations, because of recent reports about arboviral infection in the area and the alerts issued by WHO and Ministry of Health about epidemics of arboviruses including dengue in the region.[20,21] The blood sample tested negative for Rift Valley fever and chikungunya; however, the NS1 Ag test was positive, confirming current infection with dengue virus in the patient. Additionally, laboratory results revealed thrombocytopenia, anemia, and lymphocytosis. The peripheral blood smear confirmed the presence of trophozoite and schizonts of *Plasmodium falciparum*, indicating coinfection with malaria. Details of the laboratory investigation's results are shown in Table.1.

Further examination through an abdominal ultrasound showed an enlarged spleen measuring 12 cm, this prompted investigating leishmaniasis as it is endemic in the area,[22] but the sample tested negative.

TABLE 1 Demonstration of the laboratory investigation results of the patient.

Lab parameter	Result
Hemoglobin (Hb)	10.9 g/dL
Packed cell volume (PCV)	33.8%
Total white blood cells count (TWBCs)	6800 cell/μL
Differential leukocyte count	Neutrophils = 43 Lymphocytes = 48 Monocytes = 8 Eosinophils = 1
Platelets	92,000/μL
Urea	37 mg/dL
Creatinine	1.3 mg/dL
Total bilirubin	6.4/3.8 mg/dL
Conjugated bilirubin	3.3 mg/dL
NS1 Ag/IgG for dengue	Positive
NS1 Ag/IgM for dengue	Positive
Blood film for malaria	Positive

4 | CONCLUSION AND RESULT

To stabilize the patient's condition, he was given a bolus of normal saline, which improved his hemodynamic stability. Adequate hydration was continued thereafter, and the patient's clinical indicators and laboratory parameters began to improve. In addition, the patient was started on treatment with artesunate injection (2.4 mg/kg/dose). The injections were administered at regular intervals, starting with a dose on admission (H0), followed by doses at 12 h (H12) and 24 h (H24) after admission. Afterward, the patient received once-daily injections for 3 days, followed by a 3-day course of an artemisinin-based combination drug orally. Two weeks after discharge, the patient had no symptoms, and all laboratory parameters had returned to normal range.

5 | DISCUSSION

We present a severe case of a patient presented with 10 days history of fever accompanied by chills, rigors, vomiting, and muscle and joint pain. Laboratory investigations confirmed infection with dengue. Further investigations confirmed coinfection with malaria, specifically *Plasmodium falciparum*. Such malaria and dengue coinfections are increasingly reported worldwide.[18,23–27]

Africa is heavily burdened with malaria, however, recently the burden of arboviral diseases is rapidly growing throughout the region including Sudan, mainly due to the widespread of invasive diseases vectors.[11,14,28] In Sudan, the transmission and burden of arboviruses are rapidly growing, therefore, coinfections of malaria and arboviruses including dengue is a serious challenge for the health system with limited diagnostic capacity and conflict.[29–34] This challenge is indicated by the substantial delay in reaching final diagnosis that is reflected in a proper case management highlighted with better clinical outcomes.[4,5,14] However, these coinfections are often not detected, thus they are underreported; this in turn, is resulting in poor case management and severe clinical outcomes.[35] One of the main difficulties in addressing this issue is that malaria and dengue coinfections have similar symptoms, which makes it challenging to differentiate them clinically or pursue final diagnosis following initial detection of the other.[36–38]

In this particular case, the patient displayed symptoms consistent with both dengue and malaria, such as fever, muscle and joint pain, as well as thrombocytopenia, anemia, and lymphocytosis. These findings align with other studies that have noted an increased likelihood of experiencing fatigue, joint, and muscle pain in individuals with malaria and dengue coinfections.[2,13,18,23] This observation

is further supported by a study conducted in Nepal, which found an association between malaria and dengue coinfections and symptoms like fatigue, joint pain, and chills.[2] Therefore, it is crucial to understand the prevalence of these coinfections in order to improve the diagnostic capacity and implement appropriate treatment measures. Moreover, to avoid further complications due to this coinfection and ensure successful case management, the clinical indicators and laboratory parameters of the patient was closely monitored. This was particularly important to avoid malaria treatment failure due to drug resistance.[39]

Considering that currently there is no treatment for dengue, the health care approach is focused on stabilizing the patient's hemodynamic status by administering a bolus of normal saline for fluid resuscitation. Adequate hydration is crucial in managing dengue fever to prevent hypovolemia and shock caused by plasma leakage. Additionally, treatment with artesunate, an artemisinin derivative, was initiated to target the malaria parasite per the recent recommendation of the WHO.[40] The patient's response to treatment was monitored through the assessment of clinical symptoms and laboratory parameters. Improved condition and normalized laboratory parameters indicated an effective response to treatment. It is important to remain vigilant for potential complications during and after treatment especially with coinfections, such as severe dengue, organ dysfunction, or recurrence of malaria.[37] The successful management of the coinfection was evident as the patient was discharged symptom-free with normal laboratory parameters.

Dengue and malaria are both vector-borne diseases, therefore, effective prevention and control strategies should be built on the comprehensive implementation of the global vector control response (GVCR) 2017–2030.[41] More investment should be made in effective implementation of GVCR, including universal coverage with integrated vector surveillance and control, and giving proper attention to invasive diseases vectors.[7,25,41,42] People living in humanitarian crisis settings should be prioritized due to their high vulnerability and should be protected from living at high risk of disease epidemics and outbreaks.[20,43–45]

It is imperative for stakeholders in the health, humanitarian, and development sectors to invest in long-term and comprehensive solutions. These include addressing peace and social issues, improving living conditions, and implementing national actions plans for climate change adaptation and mitigation. Such investments have the potential to yield greater rewards in the long term and contribute significantly to achieving the Sustainable Development Goals (SDGs).[46,47]

In conclusion, when managing patients in regions like Sudan where multiple infectious diseases are endemic, considering and investigating the possibility of coinfection is essential for optimizing case management and improving clinical outcomes. Therefore, investing in training clinical epidemiologists, improving diagnostic capacity, and strengthening surveillance systems is crucial. Additionally, further research is needed to explore the progression of diseases and clinical outcomes in cases of coinfection involving two or more infectious diseases.

AUTHOR CONTRIBUTIONS

Emmanuel Edwar Siddig: Conceptualization; investigation; methodology; supervision; validation; visualization; writing – original draft; writing – review and editing. **Nouh Saad Mohamed:** Methodology; supervision; validation; visualization; writing – review and editing. **Ayman Ahmed:** Conceptualization; investigation; methodology; supervision; validation; visualization; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest in this work.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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REFERENCES

1. Zaki SA. Malaria and dengue co-infection. *Ann Indian Acad Neurol*. 2011;14(2):141-142.
2. Gautam A, Aryal U, Bhandari S, et al. Dengue and malaria coinfection: the first case report in Nepal. *Oxf Med Case Rep*. 2022;2022(3):omac022.
3. Elagali A, Ahmed A, Makki N, et al. Spatiotemporal mapping of malaria incidence in Sudan using routine surveillance data. *Sci Rep*. 2022;12(1):14114.

4. Ahmed A, Eldigail M, Elduma A, et al. First report of epidemic dengue fever and malaria co-infections among internally displaced persons in humanitarian camps of North Darfur, Sudan. *Int J Infect Dis*. 2021;108:513-516.
5. Ali Y, Siddig EE, Mohamed N, Ahmed A. Rift Valley fever and malaria co-infection: a case report. *Clin Case Reports*. 2023;11(9):e7926.
6. Altahir O, AbdElbagi H, Abubakr M, Siddig EE, Ahmed A, Mohamed NS. Blood meal profile and positivity rate with malaria parasites among different malaria vectors in Sudan. *Malar J*. 2022;21(1):124.
7. Ahmed A, Abubakr M, Ali Y, Siddig EE, Mohamed NS. Vector control strategy for Anopheles stephensi in Africa. *Lancet Microbe*. 2022;3(6):e403.
8. Hamid Z, Hamid T, Alsedig K, et al. Molecular investigation of dengue virus serotype 2 circulation in Kassala state, Sudan. *Jpn J Infect Dis*. 2019;72(1):58-61.
9. Elduma AH, LaBeaud AD, Plante JA, Plante KS, Ahmed A. High seroprevalence of dengue virus infection in Sudan: systematic review and meta-analysis. *Trop Med Infect Dis*. 2020;5(3):120.
10. Ahmed A. Urgent call for a global enforcement of the public sharing of health emergencies data: lesson learned from serious arboviral disease epidemics in Sudan. *Int Health*. 2020;12(4):238-240.
11. Ahmed A, Abubakr M, Sami H, Mahdi I, Mohamed NS, Zinsstag J. The first molecular detection of Aedes albopictus in Sudan associates with increased outbreaks of chikungunya and dengue. *Int J Mol Sci*. 2022;23(19):11802.
12. Rodriguez-Tan RS, Weir MR. Dengue: a review. *Tex Med*. 1998;94(10):53-59.
13. Kok BH, Lim HT, Lim CP, Lai NS, Leow CY, Leow CH. Dengue virus infection - a review of pathogenesis, vaccines, diagnosis and therapy. *Virus Res*. 2023;324:199018.
14. Ahmed A, Dietrich I, LaBeaud AD, Lindsay SW, Musa A, Weaver SC. Risks and challenges of arboviral diseases in Sudan: the urgent need for actions. *Viruses*. 2020;12(1):81.
15. Whiteman A, Loaiza JR, Yee DA, et al. Do socioeconomic factors drive Aedes mosquito vectors and their arboviral diseases? A systematic review of dengue, chikungunya, yellow fever, and zika virus. *One Health*. 2020;11:100188.
16. Ahmed A, Ali Y, Elmagboul B, et al. Dengue fever in the Darfur area, Western Sudan. *Emerg Infect Dis*. 2019;25(11):2126.
17. Elaagip A, Alsedig K, Altahir O, et al. Seroprevalence and associated risk factors of dengue fever in Kassala state, eastern Sudan. *PLoS Negl Trop Dis*. 2020;14(12):e0008918.
18. Magalhães BM, Siqueira AM, Alexandre MA, et al. P. Vivax malaria and dengue fever co-infection: a cross-sectional study in the Brazilian Amazon. *PLoS Negl Trop Dis*. 2014;8(10):e3239.
19. Ahmed A, Elduma A, Magboul B, Higazi T, Ali Y. The first outbreak of dengue fever in greater Darfur, Western Sudan. *Trop Med Infect Dis*. 2019;4(1):43.
20. Ahmed A, Mahmoud I, Eldigail M, Elhassan RM, Weaver SC. The emergence of Rift Valley fever in Gedaref state urges the need for a cross-border one health strategy and enforcement of the international health regulations. *Pathogens*. 2021;10(7):885.
21. Ahmed A, Ali Y, Mohamed NS. Arboviral diseases: the emergence of a major yet ignored public health threat in Africa. *Lancet Planet Health*. 2020;4(12):e555.
22. Mohamed NS, Osman HA, Muneer MS, et al. Identifying asymptomatic leishmania infections in non-endemic villages in Gedaref state, Sudan. *BMC Res Notes*. 2019;12(1):566.
23. Ahmed A, Mohamed NS, Siddig EE, Algaily T, Sulaiman S, Ali Y. The impacts of climate change on displaced populations: a call for action. *J Climate Change Health*. 2021;3:100057.
24. Selvaretnam A, Sahu P, Sahu M, Ambu S. A review of concurrent infections of malaria and dengue in Asia. *Asian Pac J Trop Biomed*. 2016;6(7):633-638.
25. Alsedig K, Eldigail MH, Elduma AH, et al. Prevalence of malaria and dengue co-infections among febrile patients during dengue transmission season in Kassala, eastern Sudan. *PLoS Negl Trop Dis*. 2023;17(10):e0011660.
26. Epelboin L, Hanf M, Dussart P, et al. Is dengue and malaria co-infection more severe than single infections? A retrospective matched-pair study in French Guiana. *Malar J*. 2012;11:142.
27. Sudan: Humanitarian Update, 23 August 2023 [EN/AR] – Sudan. 2023 ReliefWeb. Retrieved April 7, 2024, from https://reliefweb.int/report/sudan/sudan-humanitarian-update-23-august-2023-enar
28. Hemming-Schroeder E, Ahmed A. Anopheles stephensi in Africa: vector control opportunities for cobreeding an. Stephensi and Aedes arbovirus vectors. *Trends Parasitol*. 2023;39(2):86-90.
29. Abdallah ATH, Abdelkhalig RE, Hamid E, Ahmed A, Siddig EE. Recurrent abdominal wall mass in a hepatitis B-positive male: an unusual case of lumbar mycetoma. *Clin Case Rep*. 2023;11(12):e8275.
30. Ahmed A, El-Sadig SM, Eltigani HF, Bongomin F, Siddig EE. The first helicobacter pylori-induced Guillain-Barré syndrome in Sudan. *Clin Case Rep*. 2023;11(11):e8204.
31. Siddig EE, Eltigani HF, Ahmed A. Healing the unseen wounds: Sudan's humanitarian crisis traumatizing a nation. *Asian J Psychiatr*. 2023;89:103764.
32. Abdallah ATH, Abdelkhalig RE, Hamid E, Ahmed A, Siddig EE. Unusual manifestation of cystic mycetoma lesions: a case report. *Clin Case Reports*. 2023;11(10):e8054.
33. Alfadul ESA, Alrawa SS, Eltigani HF, Ahmed A, Siddig EE. The unraveling of Sudan's health system: catastrophic consequences of ongoing conflict. *Med Confl Surviv*. 2023;39(4):364-368.
34. Siddig EE, Eltigani HF, Ahmed A. Urgent call to protect children and their health in Sudan. *BMJ*. 2023;382:1799.
35. Salam N, Mustafa S, Hafiz A, Chaudhary AA, Deeba F, Parveen S. Global prevalence and distribution of coinfection of malaria, dengue and chikungunya: a systematic review. *BMC Public Health*. 2018;18(1):710.
36. Mandage R, Kaur C, Pramanik A, et al. Association of dengue virus and Leptospira Co-infections with malaria severity. *Emerg Infect Dis*. 2020;26(8):1645-1653.
37. Chong SE, Mohamad Zaini RH, Suraiya S, Lee KT, Lim JA. The dangers of accepting a single diagnosis: case report of concurrent plasmodium knowlesi malaria and dengue infection. *Malar J*. 2017;16(1):2.
38. Abdul-Ghani R, Mahdy MAK, Alkubati S, et al. Malaria and dengue in Hodeidah city, Yemen: high proportion of febrile outpatients with dengue or malaria, but low proportion co-infected. *PLoS One*. 2021;16(6):e0253556.
39. Mohamed NS, Abdelbagi H, Osman HA, et al. A snapshot of plasmodium falciparum malaria drug resistance markers in Sudan: a pilot study. *BMC Res Notes*. 2020;13(1):512.

40. Zoller T, Junghanss T, Kapaun A, et al. Intravenous artesunate for severe malaria in travelers. *Europe Emerg Infect Dis*. 2011;17(5):771-777.
41. World Health Organization and UNICEF. Global vector control response 2017–2030. 2017.
42. Ahmed A, Irish SR, Zohdy S, Yoshimizu M, Tadesse FG. Strategies for conducting Anopheles stephensi surveys in non-endemic areas. *Acta Trop*. 2022;236:106671.
43. El-Sadig SM, El-Amin SO, El-Amin RO, Siddig EE, Ahmed A. Humanitarian crisis in Sudan: the collapsed health system threats the public and global health. *QJM*. 2023;116(9):810.
44. Mohamed NS, Ali Y, Muneer MS, Siddig EE, Sibley CH, Ahmed A. Malaria epidemic in humanitarian crisis settings the case of South Kordofan state, Sudan. *J Infect Dev Ctries*. 2021;15(1):168-171.
45. Ahmed A, Ali Y, Salim B, Dietrich I, Zinsstag J. Epidemics of Crimean-Congo hemorrhagic fever (CCHF) in Sudan between 2010 and 2020. *Microorganisms*. 2022;10(5):928.
46. Ahmed A, Elbashir A, Mohamed AA, et al. Socioeconomic impacts of elimination of onchocerciasis in Abu-Hamed focus, northern Sudan: lessons after elimination. *BMC Res Notes*. 2020;13(1):256.
47. Ali Y, Ahmed A, Siddig EE, Mohamed NS. The role of integrated programs in the prevention of COVID-19 in a humanitarian setting. *Trans R Soc Trop Med Hyg*. 2022;116(3):193-196.

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