# Rift valley fever (RVF) and Malaria Co-Infection: A case report

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## **Brief report:**

### Rift valley fever (RVF) and Malaria Co-Infection: A case report

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#### **Consent for Publication**

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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#### Abstract :

Here we report a case of febrile illness that confirmed to be co-infected with malaria and Rift Valley fever. The patient was initially diagnosed with malaria and started on treatment immediately. However, due to the lack of response to the treatment further laboratory investigations were made.

Keywords : Critical care medicine ; Chronic Diseases; Environmental Health; Infectious Diseases; Virology

#### **Background:**

Rift Valley Fever (RVF) is a mosquito-borne zoonotic viral disease that is associated with high morbidity and mortality rates among both human and animals populations in endemic countries [1]. The disease is caused by the Rift valley fever virus (RVFV) that belongs to genus *Phlebovirus* and family *Phenuiviridae* [2]. The disease was described for the first time in 1931 in the Rift Valley area in Kenya; this how the disease obtained its name (Ref). The RVFV is transmitted mainly through several species of *Aedes* and *Culex* mosquitoes, however, other modes of transmission including vertical transmission from mother to child, sexual transmission, and through the consumption of row milk and uncooked meat were documented [3].

In addition to malaria [4,5], Sudan is endemic with several arboviruses including RVF, Chikungunya, Crimean–Congo hemorrhagic fever (CCHF), dengue, and West Nile virus [1, 6 - 11]. Infections with the RVFV were detected in Sudan in early 1930s [3, 12]. Since then, outbreaks of RVF occur frequently in the country [1,13]. The disease is associated with high abortion among human and domestic animals, therefore, in addition to its negative health affects it has devastating socioeconomic impacts on animals-dependent communities in endemic countries [1,13,14]. Recently, several outbreaks of emerging infectious diseases including RVF occurred in Sudan [1,6-11, 13-17]. Additionally, there is rapidly growing evidence about the emergence and spread of invasive diseases vectors in the region including Sudan [10, 18 - 21]. Studies have suggested that the major risk factors that drive this upsurge in the burden and outbreaks of infectious diseases and rapid spread of invasive diseases vectors include Climate change, armed-conflicts and the growing size of population living in humanitarian crisis, globalization, and unplanned urbanization [1,13, 22 - 25]. These risk factors increase the dynamic and the interactions of different populations of human and animals substantially, this in turn magnifies the occurrence of spill over and pathogens sharing events across the different species of diseases-susceptible hosts [26].

Despite the frequent outbreaks of arboviral diseases in Sudan, still there is a huge gap in the local knowledge about the epidemiology, pathology, and the clinical presentation and outcome of patients, particularly in cases of co-infection [3,6]. This gap mainly because of the limited sharing of information about these diseases of local public health and global health concerns [27]. In this communication, we report a case of a differential diagnosis challenge in areas endemic with several causes of febrile illness. Our case, a young (19-year-old) female from central Sudan was confirmed to be co-infected with RVFV malaria.

### Case presentation :

A 19-year-old student female from Kampo five, Kenana, White Nile state (Fig. 1), has arrived at the emergency unit of Kenana. She was presented on 23<sup>th</sup> October 2019; with fever, headache, joint pain, fatigue, and loss of consciousness. The patient is a student resident in kenana district and she reported staying at home for the week before the onset of the symptoms; she reported no contact with sick or apparently ill people or animals. However, she reported being recently exposed to heavy mosquitoes' bites during that time. She complained from fever, severe diffuse throbbing headache, and joint pain specifically in the knee and elbow. These symptoms were also accompanied by progressively fatigue and muscle pain.

On initial examination, she had a normal pulse rate (74/min), respiratory rate (19/min), blood pressure (95/555), and temperature  $(39^{\circ}\text{C})$ . A blood samples were drown from the patient and sent to the local

#### laboratory.

A blood film was made and was positive for the presence of malaria parasite; blood film showed asexual stage trophozoites of *Plasmodium falciparum* and ICT was also positive. She was started on malaria treatment, however, she did not show response to the treatment. Therefore, another sample of blood was taken and sent to the central National Public Health Laboratory (NPHL) in Khartoum to be tested for the major viral infections endemic in the country including dengue, RVF, CCHF, and Chikungunya [3]. Nonetheless, considering the recent reports about RVF outbreaks in different states of the country, namely River Nile and Gedaref (Fig. 1), and a sudden increase in abortion rate among cattle and sheep was reported in the area, the sample was prioritized for testing RVFV infection. The result of the real time–polymerase chain reaction (RT-PCR) confirmed infection with RVFV.

For the treatment, the patient received paracetamol infusion for the pain. For the malaria infection, the patient received artemether/lumefantrine four tablets (20 mg artemether; 120 mg lumefantrine per tablet) orally (PO) as an initial dose, followed by four tablets PO after 8 hours, then four tablets PO twice daily (morning and evening) for two days for a total course of 24 tablets. She was advised to stay all day under mosquito net to avoid infecting mosquitoes with RVFV and maintain the virus transmission in the area and she was followed up closely to monitor her case, she responded well and recovered after three days. After two week follow up, she showed no signs of sequela or any damage.

#### **Discussion:**

Here we report a case of malaria and RVF co-infection that was presented with mild symptoms without involvement of the main characteristics of RVFV infections, namely hemorrhage or neurological syndromes [28]. This none severe presentation of RVF infection has been observed during a recent outbreak in the northern side of the country (Fig. 1) [1]. However, during another outbreak of RVF in the southeastern side of the country during the same year, cases were presented with severe manifestation (Fig. 1) [13]. This difference in the overall manifestation of several patients could be attributed to the sensitivity of the surveillance system and it is capacity to identify and detect none severe cases during the outbreak [3,27]. Therefore, healthcare providers in countries endemic with several causes of febrile illness should pay extra attention during the differential diagnosis and the possibility of co-infection should be high expected in such settings [3,6,7, 29-31]. Particularly, that recently there is a growing evidence about diseases emergence and unusual presentation of endemic diseases [24, 31 - 33]. Alternatively, this difference in the clinical manifestation of RVF infection could be attributed to variation in the virus strains some clads of viruses are more associated with severe clinical presentations of the disease [34 - 36]. Similar situation has been observed during the currently ongoing Mpox outbreak of global concern [37]. Clade IIb of the Mpox virus that diverged from the West African lineage is associated with globally expanded transmission outside the endemic areas with none severe clinical presentation. While on the other hand, the Democratic Republic of Congo/Central African lineage (clade I) is associated with local transmission in Africa and a higher Case Fatality Rate [37].

Interestingly, a substantial increase in outbreaks frequency of endemic and emerging infectious diseases has been observed throughout the country. Several outbreaks of vector-borne diseases including malaria [17], CCHF [11], Chikungunya [10], dengue [29], RVF [1], Leishmaniasis [16], and other zoonotic emerging infectious diseases such as Cholera [38], COVID-19 [39], and hepatitis E [40] were reported in Sudan. These outbreaks were associated with climate change and sudden forcible displacement of human and animals populations as well as international travel and unplanned urbanization [25, 41].

Considering the lack of effective treatment and zoonotic nature of arboviral diseases, their prevention and control rely on the implementation of a transdisciplinary One Health strategy [13,42] including the integration of diseases control programs [43], enhanced surveillance and control of diseases vectors [18, 43,44], improving the water sanitation and hygiene [45], and the use of vaccines [38].

In conclusion, in areas endemic with several infectious diseases like Sudan, co-infection should always be expected and investigated to improve the case management and the clinical outcome. Therefore, investment should be done on training clinical epidemiologists and improving the diagnostic capacity and surveillance system. Additionally, further studies are needed to investigate diseases progress and clinical outcome in case of co-infection with two or more infectious diseases.

#### Key clinical message:

We report a case of febrile illness that was presented with mild symptoms. However, laboratory investigation confirmed a malaria and Rift Valley fever co-infection. Healthcare providers in settings endemic with several infectious diseases should seek rolling out possibilities of other infections prior to starting treatment for achieving effective case management with less resources and better safety of patients.

#### Consent for Publication

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#### **References:**

- Ahmed, A., Ali, Y., Elduma, A., Eldigail, M.H., Mhmoud, R.A., Mohamed, N.S., Ksiazek, T.G., Dietrich, I. and Weaver, S.C., 2020. Unique outbreak of Rift Valley fever in Sudan, 2019. Emerging infectious diseases, 26(12), p.3030.
- 2. Gaudreault, N.N., Indran, S.V., Balaraman, V., Wilson, W.C. and Richt, J.A., 2019. Molecular aspects of Rift Valley fever virus and the emergence of reassortants. Virus genes, 55, pp.1-11.
- 3. Ahmed, A., Dietrich, I., LaBeaud, A.D., Lindsay, S.W., Musa, A. and Weaver, S.C., 2020. Risks and challenges of arboviral diseases in Sudan: the urgent need for actions. Viruses, 12(1), p.81.
- Ageep, T.B., Damiens, D., Alsharif, B., Ahmed, A., Salih, E.H., Ahmed, F.T., Diabaté, A., Lees, R.S., Gilles, J.R. and El Sayed, B.B., 2014. Participation of irradiated Anopheles arabiensis males in swarms following field release in Sudan. Malaria journal, 13(1), pp.1-11.
- Elagali, A., Ahmed, A., Makki, N., Ismail, H., Ajak, M., Alene, K.A., Weiss, D.J., Mohammed, A.A., Abubakr, M., Cameron, E. and Gething, P., 2022. Spatiotemporal mapping of malaria incidence in Sudan using routine surveillance data. Scientific Reports, 12(1), pp.1-13.
- 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. International Journal of Infectious Diseases 2021; 108: 513–6.
- Ahmed A, Elduma A, Magboul B, Higazi T, Ali Y. The First Outbreak of Dengue Fever in Greater Darfur, Western Sudan. Tropical Medicine and Infectious Disease 2019; 4: 43.
- Ahmed A, Ali Y, Elmagboul B, et al. Dengue Fever in the Darfur Area, Western Sudan. Emerging Infect Dis 2019; 25: 2126.
- 9. Ahmed A, Ali Y, Mohamed NS. Arboviral diseases: the emergence of a major yet ignored public health threat in Africa. The Lancet Planetary Health 2020; 4: e555.
- 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. International Journal of Molecular Sciences 2022; 23: 11802.
- 11. 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: 928.

- Findlay, G.J., Stefanopoulo, G.M. and Mac Callum, F., 1936. Présence d'anticorps contre la fievre de la vallée du Rift dans le sang des africains. Bull Soc Pathol Exot, 29, pp.986-996
- 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: 885.
- Baudin, M., Jumaa, A.M., Jomma, H.J., Karsany, M.S., Bucht, G., Näslund, J., Ahlm, C., Evander, M. and Mohamed, N., 2016. Association of Rift Valley fever virus infection with miscarriage in Sudanese women: a cross-sectional study. *The Lancet Global Health*, 4 (11), pp.e864-e871.
- Ahmed A, Ali Y, Siddig EE, et al. Hepatitis E Virus Outbreak among Tigray War Refugees from Ethiopia, Sudan. Emerg Infect Dis 2022; 28: 1722-
- Mohamed NS, Osman HA, Muneer MS, et al. Identifying asymptomatic Leishmania infections in nonendemic villages in Gedaref state, Sudan. BMC Research Notes 2019; 12: 566.
- 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. *The Journal of Infection in Developing Countries*2021; 15 : 168–71.
- 18. Hemming-Schroeder, E. and Ahmed, A., 2022. Anopheles stephensi in Africa: vector control opportunities for cobreeding An. stephensi and Aedes arbovirus vectors. *Trends in Parasitology*.
- Abubakr, M., Sami, H., Mahdi, I., Altahir, O., Abdelbagi, H., Mohamed, N.S. and Ahmed, A., 2022. The phylodynamic and spread of the invasive Asian malaria vectors, Anopheles stephensi, in Sudan. *Biology* , 11 (3), p.409.
- Ahmed, A., Pignatelli, P., Elaagip, A., Hamid, M.M.A., Alrahman, O.F. and Weetman, D., 2021. Invasive malaria vector Anopheles stephensi mosquitoes in Sudan, 2016–2018. *Emerging infectious diseases*, 27 (11), p.2952.
- 21. Ahmed, Selma K. and Elagali, Ahmed and Ali, Faiza F. and Alsagasi, Mohammed A. and Ahmed, Ayman and Elhasan, Sara Salah Mohammed and Rahman, Ahmed H. A., The Spatial Distribution and Prediction of Habitats Suitability of Some Important Aedes Species (Diptera: Culicidae) Vectors of Arboviruses in Sudan. Available at SSRN: https://ssrn.com/abstract=4339988 or http://dx.doi.org/10.2139/ssrn.4339988
- Ahmed, A., Mohamed, N.S., Siddig, E.E., Algaily, T., Sulaiman, S. and Ali, Y., 2021. The impacts of climate change on displaced populations: a call for action. *The Journal of Climate Change and Health* , 3, p.100057.
- Aljak, E.R., Eldigail, M., Mahmoud, I., Elhassan, R.M., Elduma, A., Ibrahim, A.A., Ali, Y., Weaver, S.C. and Ahmed, A., 2021. The first laboratory-confirmed imported infections of SARS-CoV-2 in Sudan. Transactions of The Royal Society of Tropical Medicine and Hygiene, 115 (1), pp.103-109.
- Ahmed, A., Hemaida, M.A., Hagelnur, A.A., Eltigani, H.F. and Siddig, E.E., 2023. Sudden emergence and spread of cutaneous larva migrans in Sudan: A case series calls for urgent actions. *IDCases*, p.e01789.
- 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 May 11:hcad085. doi: 10.1093/qj-med/hcad085. Epub ahead of print. PMID: 37166491.
- Carlson, C.J., Albery, G.F., Merow, C., Trisos, C.H., Zipfel, C.M., Eskew, E.A., Olival, K.J., Ross, N. and Bansal, S., 2022. Climate change increases cross-species viral transmission risk. *Nature*, 607 (7919), pp.555-562.
- Ahmed, A., 2020. Urgent call for a global enforcement of the public sharing of health emergencies data: lesson learned from serious arboviral disease epidemics in Sudan. *International health*, 12 (4), pp.238-240.
- Kahlon SS, Peters CJ, Leduc J, Muchiri EM, Muiruri S, Njenga MK, Breiman RF, White AC Jr, King CH. Severe Rift Valley fever may present with a characteristic clinical syndrome. Am J Trop Med Hyg. 2010 Mar;82(3):371-5. doi: 10.4269/ajtmh.2010.09-0669. PMID: 20207858; PMCID: PMC2829894.
- 29. Elduma AH, LaBeaud AD, A. Plante J, Plante KS, Ahmed A. High Seroprevalence of Dengue Virus Infection in Sudan: Systematic Review and Meta-Analysis. Tropical Medicine and Infectious Disease

2020; 5: 120.

- Rugarabamu S, Rumisha SF, Mwanyika GO, Sindato C, Lim HY, Misinzo G, Mboera LEG. Viral haemorrhagic fevers and malaria co-infections among febrile patients seeking health care in Tanzania. Infect Dis Poverty. 2022 Apr 25;11(1):33. doi: 10.1186/s40249-022-00959-z. PMID: 35462550; PMCID: PMC9036688.
- Ayman Ahmed, Dr. SARAH MISBAH EL-SADIG, Hala Eltigani, et al. Guillain-Barre syndrome associated with COVID-19 and malaria coinfection: A case report. Authorea. March 01, 2023. DOI: 10.22541/au.167767321.12356900/v1
- Ahmed, A, Hagelnur, AA, Eltigani, HF, Siddig, EE. Cutaneous tuberculosis of the foot clinically mimicking mycetoma: A case report. *Clin Case Rep*. 2023; 11:e07295. doi:10.1002/ccr3.7295
- 33. Ahmed, A., El-Amin, R., Musa, A.M., Elsayed, M.A., Fahal, L.A., Ahmed, E.S., Ali, Y., Nebie, I.E., Mohamed, N.S., Zinsstag, J. and Siddig, E.E., 2023. Guillain-Barre syndrome associated with COVID-19 infection: A case series. *Clinical Case Reports*, 11 (2), p.e6988.
- 34. Bird BH, Khristova ML, Rollin PE, Ksiazek TG, Nichol ST. Complete genome analysis of 33 ecologically and biologically diverse Rift Valley fever virus strains reveals widespread virus movement and low genetic diversity due to recent common ancestry. Journal of virology. 2007;81(6):2805–16.
- Bird BH, Ksiazek TG, Nichol ST, MacLachlan NJ. Rift Valley fever virus. Journal of the American Veterinary Medical Association. 2009;234(7):883–93.
- Anywaine Z, Lule SA, Hansen C, Warimwe G, Elliott A. Clinical manifestations of Rift Valley fever in humans: Systematic review and meta-analysis. PLoS Negl Trop Dis. 2022 Mar 25;16(3):e0010233. doi: 10.1371/journal.pntd.0010233. PMID: 35333856; PMCID: PMC8986116.
- 37. Roper, R.L., Garzino-Demo, A., Del Rio, C., Brechot, C., Gallo, R., Hall, W., Esparza, J., Reitz, M., Schinazi, R.F., Parrington, M. and Tartaglia, J., 2023. Monkeypox (Mpox) requires continued surveillance, vaccines, therapeutics and mitigating strategies. *Vaccine*.
- Mohamed, N.S., Ali, Y., Abdalrahman, S., Ahmed, A. and Siddig, E.E., 2022. The use of cholera oral vaccine for containment of the 2019 disease outbreak in Sudan. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, 116 (9), pp.763-766.
- Ahmed, A., Mohamed, N.S., El-Sadig, S.M., Fahal, L.A., Abelrahim, Z.B., Ahmed, E.S. and Siddig, E.E., 2021. COVID-19 in Sudan. *The journal of infection in developing countries*, 15 (02), pp.204-208.
- Ahmed, A., Ali, Y., Siddig, E.E., Hamed, J., Mohamed, N.S., Khairy, A. and Zinsstag, J., 2022. Hepatitis E Virus Outbreak among Tigray War Refugees from Ethiopia, Sudan. Emerging infectious diseases, 28(8), p.1722.
- Ahmed, A., Mohamed, N.S., Siddig, E.E., Algaily, T., Sulaiman, S. and Ali, Y., 2021. The impacts of climate change on displaced populations: a call for action. *The Journal of Climate Change and Health* , 3, p.100057.
- 42. Zinsstag, J., Hediger, K., Osman, Y.M., Abukhattab, S., Crump, L., Kaiser-Grolimund, A., Mauti, S., Ahmed, A., Hattendorf, J., Bonfoh, B. and Heitz-Tokpa, K., 2022. The Promotion and Development of One Health at Swiss TPH and Its Greater Potential. *Diseases*, 10 (3), p.65.
- Ali, Y., Ahmed, A., Siddig, E.E. and Mohamed, N.S., 2022. The role of integrated programs in the prevention of COVID-19 in a humanitarian setting. Transactions of The Royal Society of Tropical Medicine and Hygiene, 116(3), pp.193-196.
- 44. Ahmed, A., Abubakr, M., Ali, Y., Siddig, E.E. and Mohamed, N.S., 2022. Vector control strategy for Anopheles stephensi in Africa. *The Lancet Microbe*, 3 (6), p.e403.
- 45. Ahmed, A., Irish, S.R., Zohdy, S., Yoshimizu, M. and Tadesse, F.G., 2022. Strategies for conducting Anopheles stephensi surveys in non-endemic areas. *Acta Tropica*, 236, p.106671.
- Ahmed, A., Yousif, A., Mohamed, N.S., Zinsstag, J., Siddig, E.E. and Khairy, A., 2023. Hepatitis E Virus Outbreak among Tigray War Refugees from Ethiopia, Sudan (Response). *Emerging infectious diseases*, 29 (2).

## **Figures legends** :

Figure 1 . Map of Sudan shows the area of the current case study highlighted in red and the states (shaded



in blue) where outbreaks of Rift Valley fever were reported during the case presentation.