

Challenges and epidemiological implications of the first outbreak of dengue and chikungunya in Sudan

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Abstract

Background: Dengue and chikungunya are mosquito-borne infections that are spreading rapidly worldwide. The highest burden lies in tropical and subtropical countries. In 2022 Sudan encountered the most widespread infection of both diseases.

Aim: To describe the magnitude of the first outbreak of dengue and chikungunya infections in Tandalti Town, White Nile State, southern part of Sudan.

Methods: Following the report of a high number of undifferentiated febrile illnesses in 32 health clinics in Tandalti Town, an area with high densities of *Aedes aegypti*, we collected blood samples from symptomatic suspected cases. The samples were tested for major arboviral infections using arboviral-specific enzyme-linked immunosorbent assays (IgM capture ELISA), and serologically positive samples were confirmed using commercially available Real Time RT-PCR Kits.

Results: Out of 773 suspected cases, 63 (8.15%) were confirmed. Eleven (17.46%) of the confirmed cases were DENV, 49 (77.77%) were CHIKV, and 3 (4.76%) were DENV and CHIKV co-infections. The outbreak started at the beginning of October and ended by mid December 2022. Both dengue and chikungunya infection was higher (41(65.08%)) among young females than males (22 (34.92%)).

Conclusions: White Nile State may experience larger outbreaks of dengue and chikungunya in the future, there is, therefore, an urgent need for proper vector control interventions in the state and nearby states.

Key words: dengue, chikungunya, fever, Sudan, *Aedes aegypti*

Citation: Aljaily SM, Hamed IAY, Mustafa KS, Ishag OSB, Musa EAE, Ahmed AK, et al. Challenges and epidemiological implications of the first outbreak of dengue and chikungunya in Sudan. East Mediterr Health J. 2024;30(1):53–59. <https://doi.org/10.26719/emhj.24.007>

Received: 07/02/23; Accepted: 08/10/23

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Introduction

Dengue virus (DENV) and Chikungunya (CHIKV) infections are fast-growing mosquito-borne arboviral diseases. The spread of both diseases is increasing worldwide and is a growing public health threat for many continents, including the Americas (1). The most affected areas are tropical and subtropical Africa. DENV varies in presentation from asymptomatic infections to dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS), which are the most serious forms of the disease. CHIKV infection is characterized by an abrupt onset of fever, frequently accompanied by debilitating joint pain. Occasional cases of eye, cardiological, and neurological complications have been reported with CHIKV infections.

The history of arboviral infections in Sudan dates back to the past century with noticeably increased outbreaks of viral haemorrhagic fevers since the 1970s (2). In Sudan, arboviral infections include yellow fever, Rift Valley fever, Crimean-Congo haemorrhagic fever, DENV and CHIKV. DENV and CHIKV are spreading across the country more rapidly than other arboviral diseases. DENV has received more attention than CHIKV,

as CHIKV is usually considered a mild condition of short duration (3-5). CHIKV was first reported in sporadic cases in South Kordofan or rare cases in central and eastern Sudan (6,7), but outbreaks have dramatically increased. In 2018/2019, the Kassala area in eastern Sudan experienced the largest epidemic of CHIKV in Africa to date, with a greater incidence of severe illness, fatality, and longer-term disability (8-10).

Outbreaks of DENV have increased dramatically during the past 20 years. Several outbreaks of DENV and DHF were reported in Port Sudan in the Red Sea State in 2004, 2005, and 2010 (11-13). DENV was then reported in other cities in eastern Sudan suggesting the significant circulation of the disease and difficulties in differentiating it from other diseases, including measles, during diagnosis. (14-18). Outbreaks of DENV and DHF were also reported in northern, central and Darfur states (19-25). In 2020, the presence of DENV infections was documented in 11 of the 18 states in Sudan (26). The study (26) concluded that DENV is circulating countrywide with a significant spatiotemporal variation in the disease seroprevalence.

The main vector associated with the transmission of both DENV and CHIKV infections in Sudan is *Aedes aegypti* (10,13,18,27,28). The main sources of *Aedes aegypti* immatures are man-made larval habitats used for the preservation of water for domestic use.

This study reports the first outbreak of DENV and CHIKV in White Nile State which is located in the southern region of Sudan and borders Khartoum, the capital city, in the northeast.

Methods

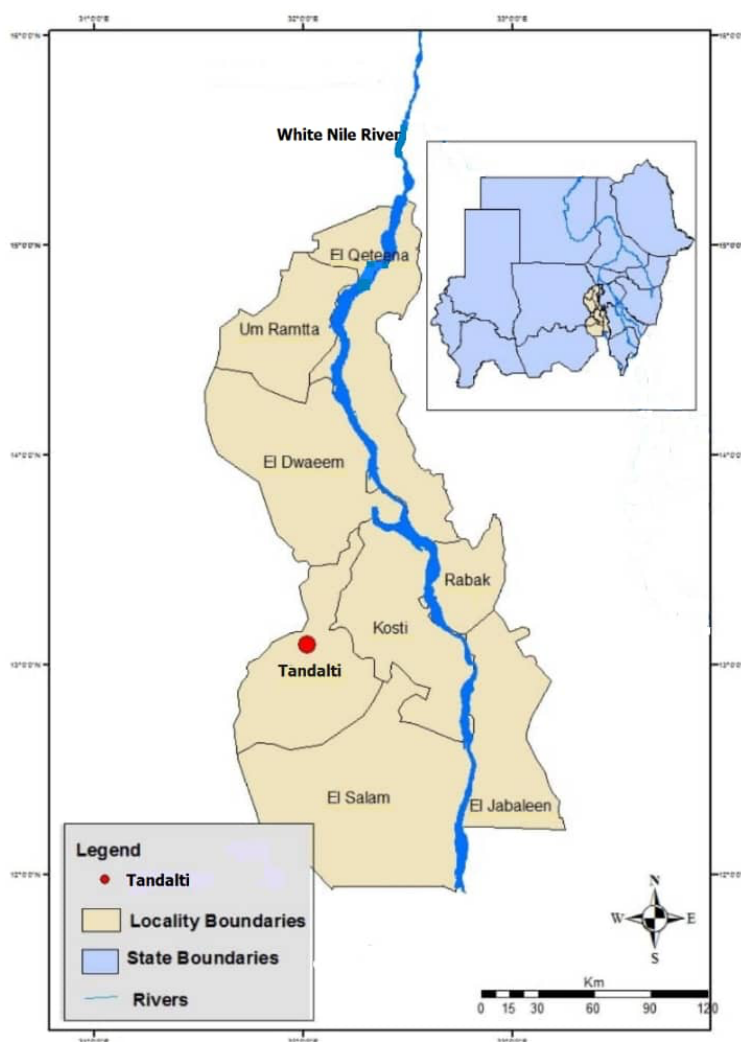
By the beginning of October 2022, the White Nile State Ministry of Health reported an unusually high number of cases of non-malaria febrile illness in the Tandalti locality (map 1), accompanied by high densities of *Aedes aegypti* (unpublished data of the Integrated Vector Management Unit). An outbreak investigation team was sent to the area by the Federal Ministry of Health, in collaboration with the White Nile State Ministry of Health and the WHO. Suspected cases of arboviral infections were identified in 34 health clinics. Blood samples were collected from suspect symptomatic patients and tested for major

arboviral infectious agents of dengue fever, yellow fever, Rift Valley fever, Crimean–Congo Hemorrhagic Fever, West Nile virus, CHIKV, and Zika virus.

Arboviral-specific enzyme-linked immunosorbent assays (IgM capture ELISA) were performed using commercially available kits and following the manufacturer's instructions (Panbio, Inverness Medical Innovations Australia Pty Ltd, Brisbane, Australia). Serologically positive samples were confirmed by using commercially available RT-PCR Kits (Shanghai ZJ Bio-Tech Co., Ltd, Shanghai, China) following the manufacturer's guidelines. All serological and molecular assays were conducted at the Sudan National Public Health Laboratory/Federal Ministry of Health. Descriptive statistics, mainly frequencies and percentages, were applied using Microsoft Excel 2016 to describe the magnitude of outbreaks.

A package of interventions was implemented to control the outbreaks of both diseases, including house-to-house inspections to destroy main larval habitats and to control vector populations (Aqua-Reslin) in all affected areas, health education sessions, and medical care for all suspect cases.

Map 1 Landsat map showing the geographical location of Tandalti town in White Nile State, Sudan



Results

Seven hundred and seventy-three suspect cases of hemorrhagic fever were identified within Tandalti Town and the 32 villages surrounding it, with the majority of the cases reported in the villages. The first suspected case appeared on 4 October 2022, and the last was reported during the first week of December 2022, with the peak of the outbreak in November (Figure 1). Out of 773 suspect cases, 63 (8.15%) were confirmed; 11 (17.46%) were DENV, 49 (77.77%) were CHIKV and 3 (4.76%) were co-infected with DENV and CHIKV. For DENV, 5 (45%) were males while 6 (55%) were females. For CHIKV, 16 (33%) were males and 33 (67%) were females. For mixed infections, 1 case (33%) was male while 2 (67%) cases were females. Most of the DENV and CHIKV cases were in young females between the ages of 1 and 19 years (Table 1).

The clinical presentation of CHIKV showed that all cases (100%) presented with fever and the majority presented with headache (86%), joint pain (79%), muscle pain (78%) and back pain (75%). Sixty-two percent had loss of appetite/anorexia, 6% were in coma, and 4% had convulsions. For DENV; 91% of the cases presented with both fever and headache, 45% had bleeding, 73% had both joint and muscle pain, 36% had loss of appetite, and 55% had back pain. The mortality rate was 0% for DENV, CHIKV and co-infection.

Discussion

DENV and CHIKV infections in Sudan are associated with the presence of *Aedes aegypti*, the main vector (10,13,18, 27, and 28). The abundance of *Aedes aegypti* in the Tandalti locality (unpublished data) indicates the urgent need for vector surveillance and control in the area and is associated with increased risk of transmission of DENV, CHIKV and other arboviral diseases.

We believe that the magnitude of the outbreak may have been underestimated due to several reasons that were previously given in similar outbreaks of DENV and/or CHIKV infections in western and eastern Sudan e.g. passive surveillance and reliance on the attendance of patients to health centres, home treatment due to the cost and limited treatment options, limited diagnostic

resources, and absence of data collection in private clinics (9,14,24).

The high infection rate suggests that people are vulnerable to these infections. The risk of DENV and CHIKV infections followed a spatial pattern and was higher in villages surrounding Tandalti Town. The same spatial pattern was reported in eastern Sudan by Seidahmed et al., who showed a spatiotemporal pattern of DENV transmission in Port Sudan City with higher DENV prevalence in lower and mid classes of neighborhood strata (13).

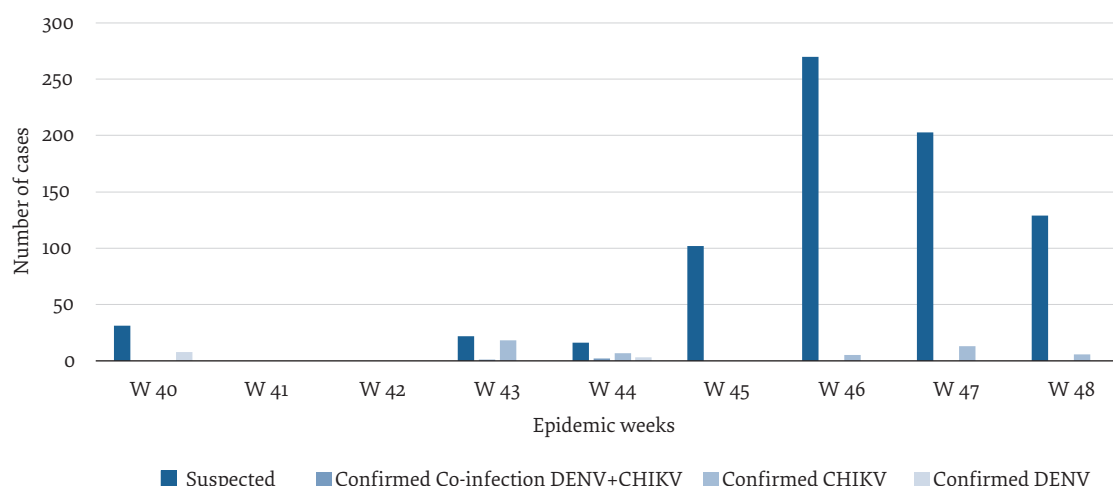
This study showed that for both DENV and CHIKV infections, females were slightly more affected than males and the outbreak affected all age groups with higher rates among the younger populations between the ages of 1 and 19 years. This is in agreement with Ahmed et al., who documented an outbreak of DENV in western Sudan (24). However, higher prevalence among males were reported in eastern Sudan by Seidahmed et al., (13). The latter study reported that DENV affected all groups with a higher infection rate among young age groups; between 6 and 39 years. This is consistent with the epidemiologic features of the CHIKV outbreak in eastern Sudan (9), which can be explained by the fact that women and young people stay at home during the day and are therefore more exposed to bites of *Aedes aegypti* inside houses (9,10).

The clinical presentation of both DENV and CHIKV cases in this outbreak was severe and suggests a lack of previous exposure and/or, for DENV, co-infection of 2 serology types. The latter is well documented in Sudan (10). The shared clinical signs between DENV and CHIKV and the fact that they are transmitted by the same vector within the same area increases the risk of misdiagnosis and under-reporting of CHIKV, as previously reported by Hassan et al (8). White Nile State has a high prevalence of malaria (29) and it is possible that these arboviral infections were mistakenly unidentified or/and misdiagnosed with malaria and/or other diseases e.g., measles (15).

CHIKV disease can be divided into 4 phases based on its clinical presentation and immunopathology (30). Supportive care and treatment guidance of different at-risk populations is complicated by the lack of high-quality clinical management guidelines for different at-risk

Table 1 Age group of confirmed cases of DENV and CHIKV diseases in White Nile State, southern Sudan

Age group (years)	DENV	CHIKV	Co-infection DENV+CHIKV
Total number (%)			
1–9	4 (36.36)	5 (10.20)	2 (66.67)
10–19	3 (27.27)	19 (38.78)	1 (33.33)
20–29	1 (9.09)	6 (12.24)	0 (0.00)
30–39	1 (9.09)	9 (18.37)	0 (0.00)
40–49	1 (9.09)	6 (12.24)	0 (0.00)
50–59	1 (9.09)	3 (6.12)	0 (0.00)
60–69	0 (0.00)	1 (2.04)	0 (0.00)
Total	11 (100.00)	49 (100.00)	3 (100.00)

Figure 1: Frequency of suspected and confirmed cases of DENV and CHIKV diseases

populations (31). Recent outbreaks of CHIKV in eastern Sudan have also challenged the view that CHIKV is a mild condition of short duration. Bower et al., reported life-threatening clinical presentations in the outbreak of CHIKV in Kassala that included haematemesis, oral bleeding, epistaxis, petechiae, haemoptysis, and melena, in addition to one fatal case who died from sepsis complicated by disseminated intravascular coagulation and acute kidney injury (9).

White Nile State borders South Sudan, and many areas serve as customs centres and routes for immigrants, displaced persons, and refugees of both countries. It hosts most of South Sudanese refugees and camps in Al Salam (29). This is an area characterized by agricultural as well as grazing land and the old nomadic route across the state into South Sudan. It has a high incidence of malaria disease (32). Both arboviral diseases could be mistakenly diagnosed as malaria. All above mentioned factors could

have serious implications and increase the risk of future outbreaks in the area and the possibility of transmission of the disease in refugee camps in White Nile State and cross-border transmission into South Sudan.

Conclusion

There is an urgent need for strategic vector control interventions to prevent future outbreaks of DENV and CHIKV infections in White Nile State, which hosts most of South Sudanese refugees. Both arboviral diseases could be mistakenly identified as malaria, therefore, attention should be paid to the diagnosis of these diseases in White Nile State.

Funding: None.

Competing interests: None declared.

Défis et conséquences épidémiologiques liés à la première flambée épidémique de dengue et de chikungunya au Soudan

Résumé

Contexte : La dengue et le chikungunya sont des infections transmises par les moustiques qui se propagent rapidement dans le monde entier. Les pays tropicaux et subtropicaux sont les plus touchés. En 2022, le Soudan a connu la plus importante survenue de ces deux infections.

Objectif : Décrire l'ampleur de la première flambée épidémique de dengue et de chikungunya dans la ville de Tandalti, dans l'État du Nil Blanc, au sud du Soudan.

Méthodes : Suite au signalement d'un nombre important de cas de maladies fébriles non différenciées dans 32 centres de santé de la ville de Tandalti, une zone à forte densité d'*Aedes aegypti*, nous avons prélevé des échantillons de sang sur des cas suspects symptomatiques. Les échantillons ont été testés afin de détecter les principales arboviroses à l'aide de tests d'immunoabsorption enzymatique (test ELISA pour la détection des IgM) spécifiques à ces infections, et les échantillons séropositifs ont été confirmés au moyen de kits RT-PCR en temps réel disponibles dans le commerce.

Résultats : Sur 773 cas suspects, 63 (8,15 %) ont été confirmés. Onze (17,46 %) des cas confirmés étaient des infections à DENV, 49 (77,77 %) étaient des infections à CHIKV, et 3 (4,76 %) étaient des co-infections à DENV et à CHIKV. La flambée a commencé au début du mois d'octobre et s'est terminée au milieu du mois de décembre 2022. Le nombre

d'infections par le virus de la dengue et du chikungunya était plus élevé chez les jeunes femmes (41 [65,08 %]) que chez les hommes (22 [34,92 %]).

Conclusion : L'État du Nil Blanc pourrait connaître à l'avenir des flambées plus importantes de dengue et de chikungunya. Il est donc urgent de mettre en œuvre des interventions appropriées de lutte antivectorielle dans cet État et dans les États voisins.

التحديات والتداعيات الوبائية لأول فاشية لحمى الضنك والشيكونجونيا في ولاية النيل الأبيض، السودان

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الخلاصة

الخلفية: حمى الضنك والشيكونجونيا هما حالتا عدوى تنقلها البعوض وتنتشر بسرعة في جميع أنحاء العالم. ويقع العبء الأكبر للعدوى في البلدان المدارية وشبه المدارية. وفي عام 2022، عانى السودان من أكثر حالات العدوى انتشاراً لكلا المرضين.

الأهداف: هدفت هذه الدراسة إلى وصف حجم الفاشية الأولى لعدوى حمى الضنك والشيكونجونيا في مدينة تندلي، بولاية النيل الأبيض، في الجزء الجنوبي من السودان.

طرق البحث: عقب الإبلاغ عن وجود عدد مرتفع من حالات الحمى غير المتمايزة في 32 عيادة صحية بمدينة تندلي، وهي منطقة بها كثافة عالية من بعوض الزاعجة المصرية، جمعنا عينات الدم من الحالات المصحوبة بأعراض المشتبه في إصابتها. واختبرت العينات للكشف عن حالات العدوى المنقولة بالمفصليات الرئيسية باستخدام مقاييس المُنْتَرِ المناهض المرتبط بالإنزيم الخاصة بالأمراض الفيروسية التي تنقلها المفصليات (اللاقط للجلوبولين المناهض M)، وأكدت الإيجابية المصلية للعينات بمجموعات اختبار تفاعل البوليميراز التسلسلي باستخدام إنزيم النسخ العكسي في الوقت الحقيقي المتاحة تجارياً.

النتائج: من بين 773 حالة مشتبه في إصابتها، تأكدت إصابة 63 حالة (8,15٪). وكانت إحدى عشرة حالة (1,74٪) من الحالات المؤكدة مصابة بحمى الضنك، و49 حالة (7,77٪) مصابة بالشيكونجونيا، و3 حالات (4,76٪) مصابة بعدوى حمى الضنك المصحوبة بالشيكونجونيا. وبدأت الفاشية في أوائل أكتوبر/ تشرين الأول وانتهت بحلول منتصف ديسمبر/ كانون الأول 2022. وكانت العدوى بكل من حمى الضنك والشيكونجونيا أعلى [41 (65,08٪)] بين الإناث الشباب منها بين الذكور [22 (34,92٪)].

الاستنتاجات: قد تشهد ولاية النيل الأبيض في المستقبل فاشيات أكبر لحمى الضنك والشيكونجونيا، ولذلك، هناك حاجة ملحة لوضع تدخلات مناسبة لمكافحة النواقل في هذه الولاية والولايات المجاورة.

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