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Dengue hemorrhagic fever outbreak in children in Port Sudan

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KEYWORD
Dengue Port-Sudan

Summary Dengue fever (DF)/dengue hemorrhagic fever (DHF) has emerged as a global public health problem with countries in Asia and the Pacific sharing more than 70% of the disease burden. In 2004—2005 a total of 312 cases admitted to Pediatric and Sea Port Hospitals in Port Sudan were clinically diagnosed as DHF. The mortality rate recorded was 3.8% ($n = 12$). Of the cases 73.4% were patients 5—15 years of age. A total of 91.2% of cases were admitted during May and June 2005 with 49.4% residing in the eastern region of Port Sudan. Dengue shock syndrome was observed in 37 of 312 (11.9%). All patients had thrombocytopenia with platelets count ranged from <100,000 to <150,000 cell/mm^3. Of the 40 sera tested using RAPID-cassette test in the Khartoum Central Public Health Lab, 36 (90%) were dengue IgM positive. A subset of these sera ($n = 23$) were sent to NAMRU-3 and confirmed by IgM-capture ELISA; 9 of 23 were PCR positive for dengue serotype 3.

Introduction

Dengue fever (DF) is the most important disease caused by the dengue (DEN) virus of family *Flaviviridae* and transmitted by the *Aedes aegypti* mosquito. Dengue virus exists as four distinct serotypes, DEN-1—4. DF, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) have emerged as a global public health problem in recent decades. DHF and DSS are most commonly observed in children under 15 years, but they also occur in adults [1]. Infection with one serotype gives life-long immunity for that serotype but not to the others. Secondary infection with a heterologus serotype from the primary infection enhances the risk of developing DHF/DSS [2]. Dengue is

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known to occur in Sudan, however, reporting is subject to limited diagnostic capacity. DEN-2 was first reported in Port Sudan in 1986 [3]. An outbreak of acute febrile illness occurred later in 1989 in the Northern Province of Sudan and the prevalence of DEN-2 antibody was 24% [4]. Additional serological evidence of DEN-2 infection in Sudan was reported 1995 [5]. The aim of this study was to describe the etiology and clinical findings of dengue cases admitted to main hospitals in Port Sudan from November 2004 to June 2005.

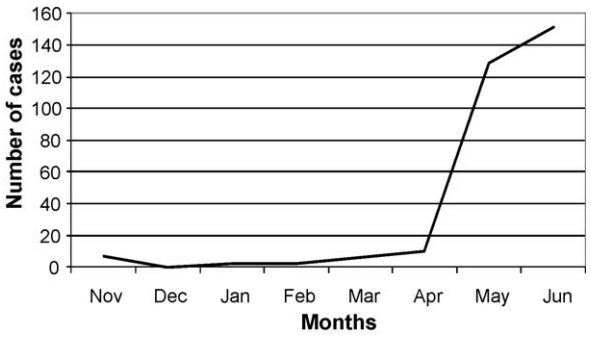

Figure 1 Distribution of DHF cases during November 2004—September 2005.

Materials and methods

Clinical and demographic data were collected from each child admitted to the Pediatric Emergency and Red Sea Port hospitals in Port Sudan with suspected dengue infection during (as per WHO case definition) November 2004 to September 2005. Blood samples were collected for platelet count. Serum samples were tested at the Central Public Health Laboratory (CPHL) in Khartoum for DEN-IgM antibodies using RAPID-Cassette test (PanBio, Brisbane QLD, Australia) kits. Frozen aliquots of sera were sent to NAMRU-3 for confirmation using DEN-IgM-capture-ELISA (PanBio). RNA extractions were conducted on sera using Qiagen Viral RNA Mini Kits, nested PCR amplification of the C gene (~0.3 kb) [6] and direct sequencing of PCR products using the ABI 3100 genetic analyzer (Applied Biosystems, Foster City, CA., USA).

Results

A total of 312 patients with clinically suspected DHF were admitted to the pediatric and Red Sea Port hospitals during the study period. The majority of the patients ($n = 229$, 73.4%) were between 5 to 15 years of age, while the remaining ($n = 83$, 26.6%) were below 5 years of age, 59.6% of the patients were males. Patients were predominantly (91.2%) admitted to the hospitals during the months of May and June 2005 (Fig. 1), 49.4% of them were from Eastern region (close to the Red Sea port) and 32.4% (101/312) were from local tribes living in Port Sudan. The clinical manifestations of the DHF cases are summarized in Table 1. Fourteen cases developed convulsions and 4 had cerebral hemorrhage. The mortality rate recorded was 3.8% ($n = 12$), of which 11 (91.7%) had typical DSS. Eight of 12 mortalities (66.7%) recorded were among the 10—15 years age group. Patients with DSS received oxygen, intravenous fluids, plasma, platelets, fresh blood and supportive medicine each case as required. Response of these patients to treatment was adequate in some despite of high mortality in this group of patients. A total 37 of 312 (11.9%) hemorrhagic cases developed DSS. Thrombocytopenia of <100,000 cell/mm^3 was recorded in 75.6% of cases while 25.4% had mild thrombocytopenia (100,000 to <150,000), 49 cases received fresh blood transfusion, 22 received plasma and platelets and 13 cases received both fresh blood and platelets. Only 40 serum samples were tested in CPHL in Khartoum due to lack of testing facilities and transportations from Port Sudan to Khartoum, of these samples 90% were dengue IgM positive by RAPID-cassette test. Of 40 serum samples 23 had enough volume for further confirmation at NAMRU-3 and all were confirmed by IgM-capture ELISA kits. Nine of 23 were PCR positive for DEN virus serotype 3 (DEN-3). Blast search of the PCR product sequences showed a 99% identity (288 bp fragment) to DEN-3 isolated during dengue outbreak in India in 2003 and to DEN-3 detected during the outbreak in Yemen in 2004/2005 (Figs. 2—6).

Figure 2 Sub conjunctival hemorrhage.

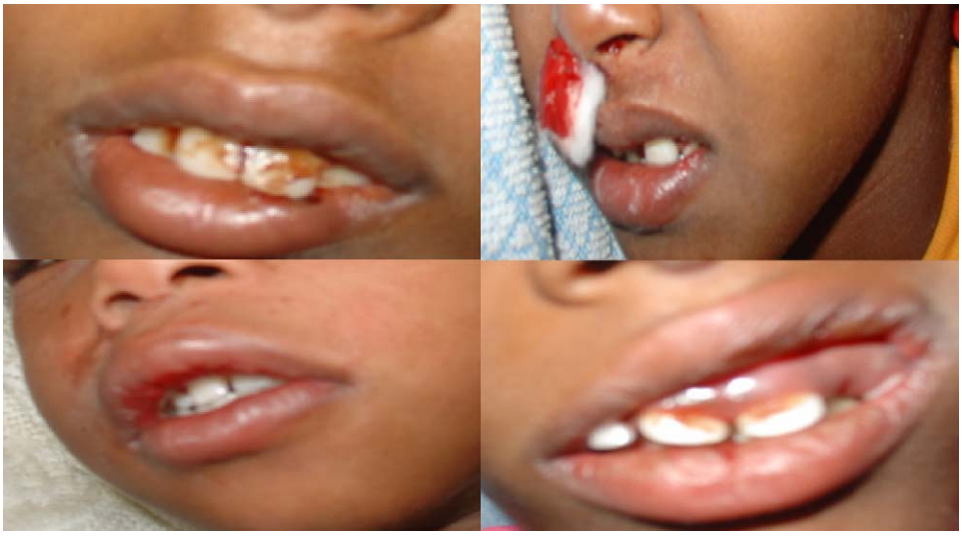

Figure 3 Red mouth, gum bleeding, epistaxis and cracked lips.

Discussion

An outbreak of a febrile disease consistent with DHF was identified in May and June of 2005 in Port Sudan. Testing of a subset of patients confirmed this outbreak to be dengue fever. Onset in May coincided with a brief rainy season [7]. No further cases were noted in July, however, much of the population of Port Sudan leave the city during July and August to escape the extreme heat.

All patients admitted had clinical picture consistent with DHF. Clinical manifestations and mortality were consistent with previously published findings [8]. Convulsions reported in some patients could be due to fever or other diseases, the cerebral hemorrhage was diagnosed clinically for no access to

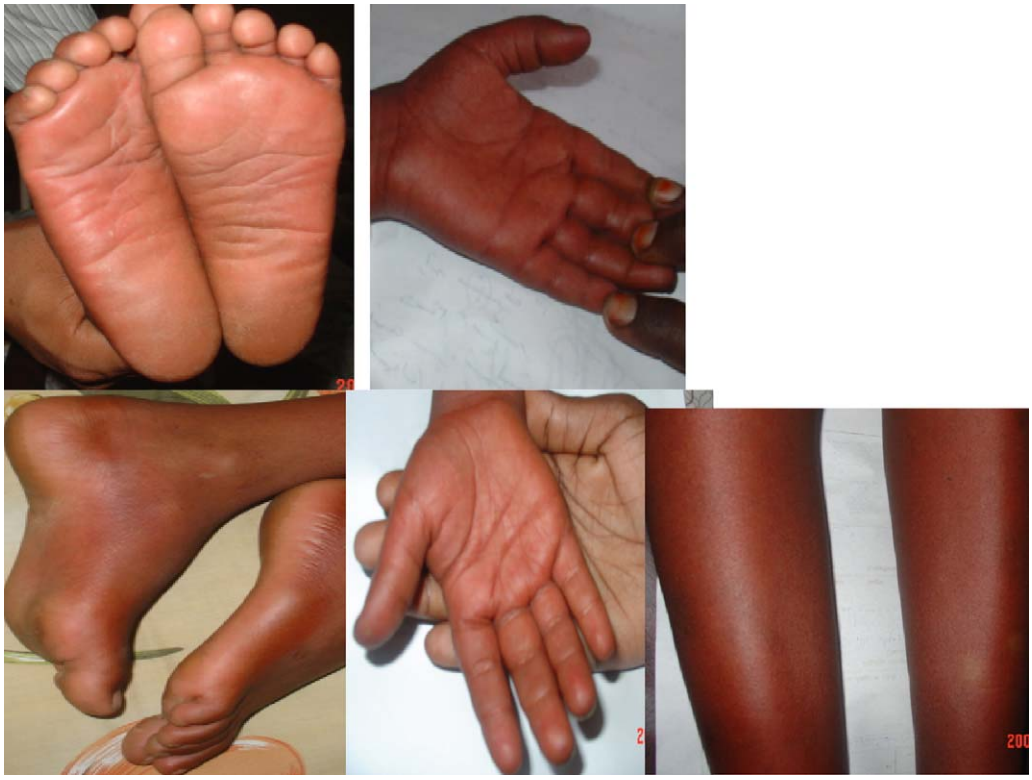

Figure 4 Plethoric hands, legs and feet at the end of the disease.

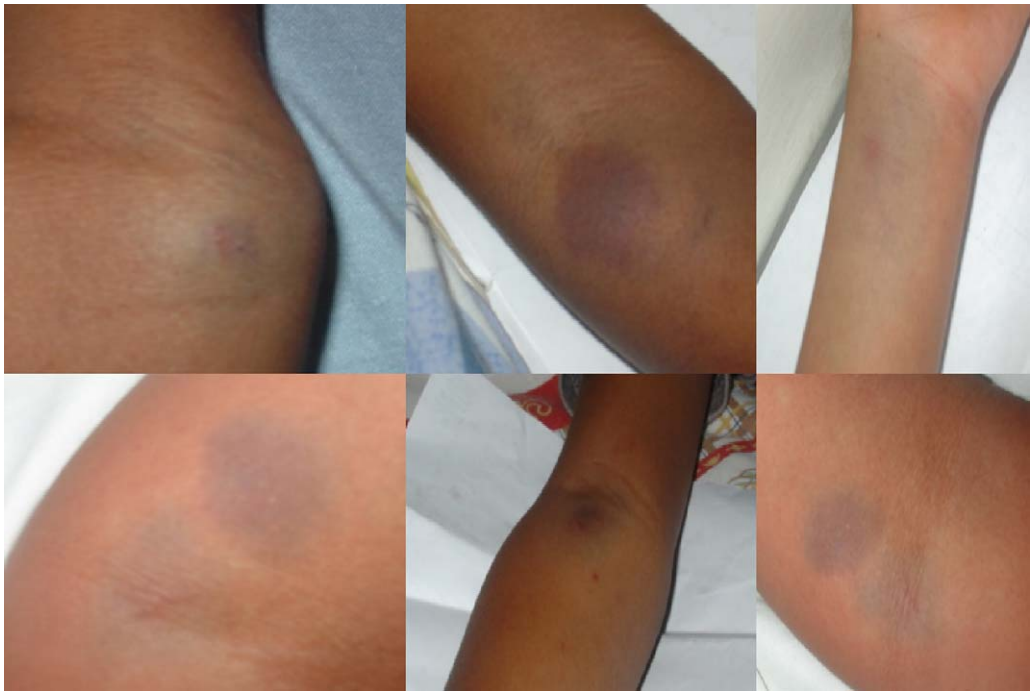

Figure 5 DHF with ecchymosis cases.

neuroimaging but cases were associated with low platelets count (<14000). It is worth mentioning that, cases with hematemesis or melena associated with fever had no previous history of GIT problems, cases were diagnosed clinically with no need for endoscopy. Schistosomiasis that may cause portal hypertension is not circulating in the region and the relatively high rate of hematemesis or melena could be due to new serotype of DHF virus or the extensive use of steroids to control fever before admission to the hospital. In general, patients with mild disease either do not present to the hospital, or are managed as outpatients. There is very limited capacity for both inpatient care (no ICU) and laboratory diagnosis in Port Sudan. All patients admitted were age 15 or less. This reflects the age of the population served by the hospitals and pediatrician conducting the evaluations. No clinical information was available on disease among adults.

The dengue serotype causing this outbreak was DEN-3. Although dengue fever is known to occur in Port Sudan, DEN-3 had not previously been detected. Introduction of DEN-3 helps explain the high number of cases of DHF. In November of 2004,

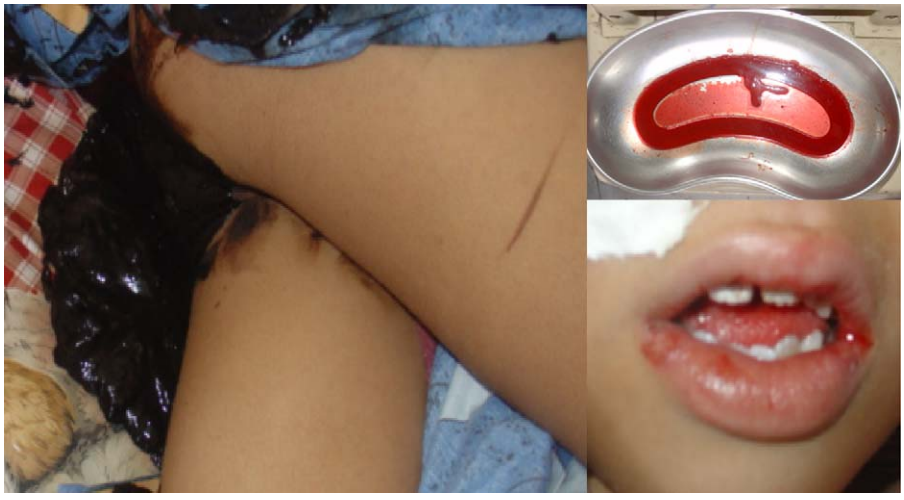

Figure 6 Fatal melena and mouth bleeding.

Table 1 Demographic and clinical data of DHF patients.

Demographic and clinical data	DHF patients $n = 312$ N (%)
Age in years	
<1	9 (2.9)
1 to <5	74 (23.7)
5 to <10	117 (37.5)
10—15	112 (35.9)
Male gender	186 (59.6)
Race/ethnicity/tribe	
Hadandaw	53 (17.0)
Rashiada	1 (0.3)
Bani Amer	45 (14.4)
Aritrian	2 (0.6)
Others	211 (67.6)
Residence in Port Sudan	
Eastern	154 (49.4)
Northern	39 (12.5)
Southern	60 (19.2)
Central	49 (15.7)
Sawakin	5 (1.6)
Missing	5 (1.6)
Bleeding manifestations	
Hematemesis	115 (36.9)
At venipuncture	111 (35.6)
Epistaxis	108 (34.6)
Melena	102 (32.7)
Pupura	14 (4.5)
Gum bleeding	14 (4.5)
Other sites	11 (3.5)
Clinical manifestations	
Fever	312 (100.0)
Abdominal pain	163 (52.2)
Skin rash	84 (26.9)
Plethora[a]	68 (21.8)
Hepatomegaly	28 (8.9)
Hemorrhagic manifestation in fatal cases ($n = 12$)	
Melena	11 (91.7)
Shock	11 (91.7)
Hematamesis	8 (66.7)
Epistaxis	2 (16.7)
Age distribution in fatal cases ($n = 12$)	
<5 years	1 (8.3)
>5 to <10 years	3 (25.0)
>10—15 years	8 (66.7)

[a] An excess of blood in one area of the body.

Yemen experienced onset of an outbreak of DEN-3 that coincided with this outbreak (unpublished data). Over the past two decades, dengue virus serotype 3 (DENV-3) has caused unexpected epidemics of DHF in Sri Lanka, East Africa, and Latin America. The emergence of DHF in Sri Lanka in 1989 correlated with the appearance there of a new DENV-3, subtype III variant. This serotype likely spread from the Indian subcontinent into Africa in the 1980s and from Africa into Latin America in the mid-1990s [9].

Following this outbreak in Port Sudan, cases of DHF were anecdotally reported from as far East as Kassala and Central as Kordofan (Ministry of Health, Sudan). *Aedes* mosquitoes have been reported from many different regions of Sudan (personal communications). Much of the population of Sudan is at risk for dengue infection. Introduction of new serotypes into the region increases the chances of the population suffering from DHF. There is a need for enhanced the laboratory diagnostic capacity and implementation of preventive measures like vectors control and quarantine at the ports and programs to include different governmental sectors in the country (Ministries of health, environment, agriculture, and interior) particularly in high risk areas like Port Sudan.

Conflict of interest

Funding: This work was supported by the US Military Infectious Diseases Research Program, Work Unit No. 600 RADI. A.E. 403.

Competing interest: Authors have no conflict of interest to declare in relation to this study.

Ethical approval: The study protocol was approved by the Naval Medical Research Unit No. 3 Institutional Review Board (IRB #: 179) in compliance with all applicable Federal regulations governing the protection of human subjects.

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prepared by a military service member or employee of the U.S. Government as part of that person's official duties.

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