Dahman et al, 2017;3(1):92–98.
https://doi.org/10.24911/IJMDC.1.3.8

ORIGINAL RESEARCH

Clinical spectrum of dengue fever in hospitalized children in Mukalla city, Yemen after the attack of Chapala cyclone Nov. 2015

Haifa Ali Bin Dahman[1]*, Eman Awadh Hatem[2]

ABSTRACT

Background: Dengue is a serious public health threat with a variable clinical course ranging from self-limited illness to fatal complications. Atypical manifestations and uncommon clinical pattern of presentations have been observed during the recent past.

Methodology: A retrospective study was conducted for all pediatric patients admitted to Mukalla and university hospital from December 2015 to March 2016 with a suspicion of dengue infection after the attack of Chapala cyclone in November 2015 to determine the common clinical presentations and recognize any atypical manifestations of dengue infection. Data collected included age, gender, monthly distribution, duration of symptoms on admission, common presentations, associated co-morbidities, complications, and outcome.

Results: The sample consisted of 123 patients (32 cases confirmed, 91 cases probable) including 59 males and 64 females. The most common age group of presentation was between 9 and 12 years. Classic DF was present in 120 cases (97.6%) and only one case (0.81%) had dengue shock syndrome. The most common manifestations included fever (100%), vomiting (64.2%), anorexia (52%), abdominal pain (48%), and general weakness (42.3%). Hemorrhagic manifestations were present in (17%) of cases. Unusual presentation included upper respiratory manifestations (20.3%), pleural effusion (3.2%), hypotension (22%), tachycardia (16.3%), bradycardia (13.6%), and hematuria (1.6%). Seizures (4.1%) were the commonest neurological presentation. Two patients had coma and one patient died.

Conclusion: High index of suspicion, especially among the healthcare personnel at primary health centers, is needed to ensure prompt recognition, early management, avoid fatal complications and improve the outcome of dengue infection.

Keywords: Atypical manifestation, Chapala cyclone, dengue, dengue virus, Yemen.

Introduction

Dengue is one of the major global health problems in the world [1,2]. It has been considered as the fastest spreading mosquito-borne viral disease by the World Health Organization (WHO) [1,3]. Two-fifths of the world's population in tropical and subtropical countries are at risk, with an annual estimation of 50 million newly infected cases worldwide [3]. Around 500,000 cases of dengue hemorrhagic fever (DHF) requiring hospitalization [4]; 90% of them are in the pediatric age group [5]. DF is caused by one of the four serotypes of a single-stranded RNA flavivirus [5], which is transmitted by the bite of female *Aedes aegypti* and *Aedes albopictus* mosquitos [1], both have high vectoral competency but variable capacity to dengue virus (DENV) [3]. Transmission of the DENV is sensitive to climate. Temperature, rainfall, and humidity affect the breeding cycle, survival and biting rates of the mosquito vectors (principally *Aedes aegypti*). Higher ambient temperatures favor rapid development of the vector, increase the frequency of blood meals, and reduce the extrinsic incubation period. Non-climatic factors (viral strain, competent vector, and human susceptibility) are

Correspondence to: Haifa Ali Bin Dahman
*Department of Pediatric, Hadhramaut University College of Medicine (HUCOM), Hadhramaut Governorate, Yemen.
Email: bin_dahman.h@hotmail.com
Full list of author information is available at the end of the article.
Received: 17 April 2017 | **Accepted:** 2 July 2017

important in determining the extent and maintenance of an epidemic [3,6].

From 1870 to 1873, dengue-like epidemics occurred in the Arabian Peninsula in Yemen (Aden) and Saudi Arabia (Makkah, Madinah, and Jeddah) [6,7]. An increasing number of dengue cases in Yemen occur simultaneously with the expanding geographic spread of epidemic dengue [1].

In general, Yemen lacks quality healthcare service and adequate infrastructure facilities, and concerns are usually focused on crisis management of the dengue epidemics rather than implementing a strategy to control dengue epidemics in the long run [8].

Hadhramaut is the largest governorate in the republic of Yemen. It lies in the south of Yemen along the Gulf of Aden in the Arabian Sea and extends eastwards to the borders of Dhofar region of Oman. Al-Mukalla is the main Sea Port and the capital city of Hadhramaut. The tropical hot weather in Hadhramaut during Summer (temperature reaching 40°C) with moderate temperature in the coastal area and the large areas of standing water and sewage following rainy seasons [7] provide a suitable habitat for dengue vector. In November 2015, an increasing number of dengue cases were reported by the Ministry of Health in Hadhramaut following the tropical Chapala cyclone [9]. Unfortunately, the true burden of dengue epidemic cannot be estimated due to under-recognition or under-reporting because of limited resources or problems of accessibility [8].

DF is usually a non-specific and self-limiting biphasic febrile illness [3,10,11], but outbreaks of dengue infection with increasing number of atypical or unusual clinical manifestations in addition to multisystem involvement all raise challenges in terms of diagnosis and treatment and cause difficulty in predicting diagnosis [2,12]. In 2011, the WHO classification guidelines for dengue were revised and dengue was divided into DF, DHF without shock or with shock, and the expanded dengue syndrome [3]. With rising disease burden, atypical manifestations are also on the rise but are underreported and often missed due to the lack of awareness among health care personnel [3].

The aim of this study was to document the common clinical presentations, as per WHO definition, and recognize any atypical manifestations of dengue patients admitted to the pediatric ward in Al-Mukalla city after the strike of Chapala cyclone in November 2015.

Methods

A record-based descriptive study was conducted to determine the clinical profile and outcome of all pediatric patients admitted to University Hospital, Mukalla, with the diagnosis of suspected DF from December 2015 to March 2016 after the attack of Chapala cyclone in November 2015.

A total of 123 hospitalized patients with the suspicion of DF were included. A detailed history was obtained; data analyzed included the age, gender, monthly distribution, duration of symptoms on admission, common presentations, associated co-morbidities, complications that developed after admission and the outcome. General and systemic clinical examinations were carried out. Case definition and diagnosis of dengue infection were based on the revised WHO guidelines 2011 for DF [3]. Confirmation of DF was proven by dengue serology for Immunoglobulin M (IgM) and Immunoglobulin G (IgG) antibodies (Onsite Dengue IgG/IgM Combo rapid test-CTK Biotech.) and/or DENV NS1Ag rapid test. Probable dengue cases were considered if acute febrile illness with two or more of the following: headache, retro-orbital pain, myalgia, arthralgia/bone pain, rash, hemorrhagic manifestations, leucopenia (White blood cell $\leq$ 5,000 cells/mm^3), thrombocytopenia (platelet count < 150,000 cells/mm^3), rising hematocrit (5%–10%), and at least one of following: 1) supportive serology on single serum sample: titer $\geq$1,280 with hemagglutination inhibition test, comparable IgG titer with enzyme-linked immunosorbent assay, or testing positive in IgM antibody test, and 2) occurrence at the same location and time as confirmed cases of DF (WHO 2011) [3]. Patients lacking typical clinical features of DF with negative anti-dengue serology were not included in the study.

Hypotension by age was defined as systolic pressure <80 mm Hg for those aged <5 years or 80–90 mm Hg in older children. Bleeding manifestations were recorded when petechia, epistaxis, gum bleeding, hematemesis, melena, or a positive tourniquet test was observed. Circulatory failure was recorded when the patient had cold, clammy skin and restlessness, tachycardia and weak pulse with pulse pressure <20 mm Hg. The data were analyzed using SPSS 17.0 statistical software.

Results

In our study, we revised the clinical presentation of all pediatric patients admitted to University Hospital in Mukalla with the suspicion of DF from December 2015 to March 2016 after the attack of Chapala cyclone. The total number of cases was 123 patients (32 confirmed cases, 91 probable cases; 15 cases with negative dengue serology (<5 day fever), 76 cases (serology was not done)). The case definition of confirmed or probable cases was according to the revised WHO guidelines 2011 [3]. Classic DF was considered in 120 cases (97.6%), two cases (1.6%) fit the definition of DHF and only one case (0.81%) had dengue shock syndrome (DSS). All cases were distributed over four months with decreasing frequencies: December 56 cases (45.5%), January 46 cases (37.4%), February 20 cases (16.2%), and March 1 case (0.88%), Figure 1. There were 59 boys and 64 girls, with a ratio of 0.9:1. The age ranged from 14 months to 14 years, with the commonest age group affected between 9 and 12 years (mean 8.88 ± 3.44), Figure 2. An underlying chronic hemolytic disease (sickle cell anemia and thalassemia) was present in 12 cases (9.75%). All

cases of DF were admitted for the first time apart from six cases (4.9%) who were readmitted from another hospital.

For patients presented with fever, minimum duration was 1 day and maximum duration was 21 days (mean 4.7 days ± 2.6), and 23 patients were associated with chills (18.7%). Other general complaints with decreasing frequencies were headache in 37 cases (30.1%), periorbital pain in 13 cases (10.6%), injected conjunctiva in six cases (4.9%), blurring vision in four cases (3.3%), and maculopapular skin rash in two cases (1.6%).

Variable involvement of other systems was noticed with the gastrointestinal (GI) manifestations presented in 108 patients (87.8%) followed by musculoskeletal involvement in 71 patients (57.7%), cardiovascular system in 54 cases (43.9%), respiratory system in 25 cases (20.3%), bleeding tendency in 21 cases (17.1%), and central nervous system in eight cases (6.5%).

GI involvement showed vomiting in 79 cases (64.2%), anorexia in 64 cases (52%), abdominal pain in 59 cases (48%); with diffuse tenderness in 52.5% of cases (Table 1), nausea in 35 cases (28.5%), altered taste in 15 cases (12.2%), and diarrhea in 23 cases (18.7%). Hepatomegaly and splenomegaly were detected in 16 patients (13%) and three patients (2.4%), respectively (either as a new finding or increasing in size in cases with chronic hemolytic disease).

General weakness noticed in 52 patients (42.3%) was the common complaint in the musculoskeletal system, followed by arthralgia in 34 patients (27.6%), backache in 22 patients (17.9%), and myalgia in 18 patients (14.6%).

Cardiovascular system was manifested with hypotension in 27 cases (22%), tachycardia in 20 patients (16.3%), and bradycardia in 17 cases (13.6%).

A sore throat, cough, chest pain, and inflamed pharynx formed about 20.3%. Pleural effusion was detected in four patients (3.2%) and pneumonia in three cases (2.4%).

Bleeding tendency from multiple sites was noticed in 21 cases (17.1%): gum bleeding in nine cases (7.3%), epistaxis in eight cases (6.5%), and hematemesis in six cases (4.9%). Petechia was noticed in five patients (4.1%) and hematuria in two cases (1.6%).

Eight patients (6.5%) showed central nervous system involvement, seizures were noticed in five cases (4.1%), followed by disturbance in consciousness in four patients (3.3%) and coma in two patients (1.6%).

All patients were treated symptomatically with bed rest, antipyretics, and cautious IV fluid administration according to the WHO protocol [3]. Only one patient (0.8%) died with multisystem involvement.

Discussion

Dengue is an important emerging disease of the tropical and subtropical regions [5]. It is the most rapidly spreading mosquito-borne viral disease [3] with annual seasonal variation related to environmental and climatic

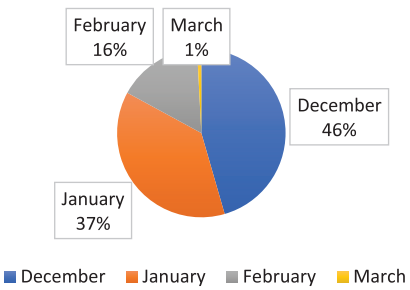

Figure 1. *Month distribution of dengue cases.*

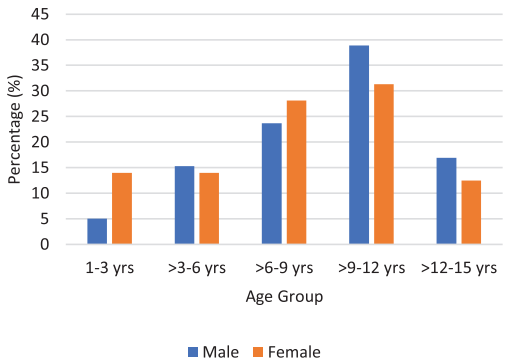

Figure 2. *Age and sex distribution of dengue patients.*

Table 1. *Character of abdominal pain among dengue patients.*

Character of abdominal pain	Frequency	Percent (%)
Diffuse	31	25.2
Epigastric	11	8.9
Periumbilical	1	0.8
Right upper quadrant	8	6.5
No abdominal pain	72	58.5

factors and human and vector behaviors [1,6]. Globally, 30-fold increments in incidence were reported over the last five decades [3]. Annually, more than 50–100 million people were infected with dengue, around two-and-a-half billion people living mainly in urban areas of tropical and subtropical regions are at risk of infection [3,4,13]. Dengue is a leading cause of pediatric hospitalization and child mortality in several Asian and South American countries [13]. It is caused by four closely related, antigenically similar serotypes of DENV 1–4 [3]; an enveloped, single-stranded RNA virus of filoviridae family [1]. Transmission to humans occurs by the bite of the female *Aedes aegyptis* and *Aedes albopictus* mosquitoes infected by one of four viral serotypes. Patients can develop long-term immunity to infection with one serotype while only short-term immunity to the other serotypes. Subsequent infection with a different type increases the risk of severe complications [3,7,13].

The historic record of dengue infection in Yemen goes back to the 19th century when a severe outbreak was reported in 1870–1873 [6]. More frequent outbreaks of dengue have emerged since 2000, and documented outbreaks were in Shabwah governorate (1994), Hadhramaut/ Mukalla (2005) and Al-Hudeidah governorate (1994, 2000, 2004, and 2005). Other outbreaks were not well documented as was the case in Shabwah governorate, Aden, and Taiz [1,8]. In 2010, another outbreak was reported in Al-Mukalla, Hadhramaut [7,8], and most cases in Hadhramaut occurred in the spring and summer [8]. This seasonal variation is similar to the pattern of dengue occurrence in Saudi Arabia [14].

Since November 2015, the Ministry of Health in Hadhramaut has documented more than 1,000 suspected and 280 confirmed cases of DF, with at least seven deaths attributed to an outbreak of DF resulting from large areas of standing water and sewage following the tropical Chapala cyclone [9].

Four DF serotypes were identified. DENV-4 was the predominant serotype at 31.88% followed by DENV-2 at 23.18%, DENV-3 at 20.28%, and DENV-1 at 10.14% [15]. DENV-1 was confirmed in Alhodeidah governorate, whereas DENV-3 was confirmed in Hadhramaut governorate in the 2010 outbreak [7,8].

Clinical presentation in dengue infection depends on the age, the virus strain and the immune status of the host with genetic predisposition that can provide protection and also induce more severe forms of the disease [1,3]. Despite the presence of WHO guidelines for dengue disease, it remains a difficult task clinically to differentiate dengue infection from other causes of febrile illness, especially during the early phase of illness [1,16]. In 2011, dengue was classified into DF, DHF without shock or with shock, and the expanded dengue syndrome based on the revised WHO guidelines for dengue. DHF was divided into four grades according to severity [3]. Wide spectrum involvement of GI, hepatic, neurological, pulmonary, and renal systems was considered as an unusual manifestation of expanded dengue syndrome [2].

Our study was conducted to detect the most common clinical presentations and recognize any atypical manifestations of pediatric patients with DF admitted to Al-Mukalla University Hospital after the strike of the Chapala cyclone in November 2015.

A total of 123 patients were included in the study, all were considered as dengue cases (either confirmed or probable) based on the case definition in the revised WHO guidelines 2011, with the highest number of admissions during December 45.4% (Figure 1). Different studies showed increased frequency in male patients [10,15,17] including a study done in Hadhramaut 2010 [8]. But our results showed the reverse as male-to-female ratio was 0.9:1. This could be related to the limited population included in our study or we might consider a similar risk of exposure to mosquito bite for both pediatric genders in our community. The commonest age group affected was between 9 and 12 years (mean 8.88 ± 3.44, Figure 2) which is consistent with other studies [10,17].

Early diagnosis of DF is considered challenging [16] due to the wide spectrum of disease severity ranging from asymptomatic or an influenza-like illness (DF) to the life-threatening DHF/DSS [4,18,19] and the possibility of late serological diagnosis of dengue [16]. In our study, 120 (97.6%) patients had classic DF, two cases (1.6%) fit the definition of DHF and only one case (0.81%) had DSS. This might be related to infection with one serotype of DENV [18].

In DF, the clinical signs are always initiated by fever, headache, myalgia, anorexia, retro-orbital pain, nausea, prostration, vomiting, diarrhea, and rash in lower percentage [16,19].

In this study, all patients presented with fever (100%) similar to other studies [11,17,20–22] and in contrast to others in which fever forms 94.6% [23] and 66.6% [19] of patients. Headache in 37 cases (30.1%) was the second most common general manifestation in our study followed by retro-orbital pain, injected conjunctiva, blurring vision, and maculopapular skin rash in a lower percentage.

Ahmed [19] reported similar results regarding headache (34.85%). Pothapregada et al. [23] and Pai Jakribettu et al. [11] reported high percentage of 75.1% and 52.16%, respectively. Low frequency of headache was reported in Mumbai [20], Saudi Arabia [19], and Thailand [24].

Skin rash was less frequent in our study (1.6%) in comparison to 18.18% and 13.51% reported in Saudi Arabia during 2006 and 2008, respectively [19] and 33.8% in Thailand [24]. No skin rash was reported in Saudi Arabia during 2005 or 2007 [19].

Systemic involvement in our study was more frequent in the GI system followed by musculoskeletal involvement, while hemorrhagic and neurological manifestations were less common.

Vomiting, abdominal pain, and anorexia were most frequent GI manifestations; this was in consistent with the results

reported previously [22] and in contrast to low frequency reported by Pancharoen et al. [24]. Hepatomegaly and splenomegaly were prominent physical signs in 13% and 2.4% of cases, respectively. WHO 2011 reported hepatomegaly in 90%–98% of patients at any stage of the disease [3]. Previous studies reported hepatomegaly in 43.8%, 97.4%, 90%, and 62.5% cases [17,20,22,25], respectively. Splenomegaly results from the presence of DENV antigen in the lymphoreticular cells [26]. Previous studies reported splenomegaly in 21.2%, 28.2%, 6.15%, and 11.8% of cases [10,20,26,27], respectively. Higher incidence of 60% was reported in a study conducted in Lucknow [25] in contrast to the low incidence in our study. Diarrhea was not recognized as a common clinical manifestation in dengue infection [10,16,23,25]. Duangmala et al. [21] reported an increasing incidence of diarrhea reaching 28.8% among dengue patients, with 19% of them having diarrhea as the main presenting symptom. In our study, diarrhea was an associated complaint in 18.7% of cases. Lymphadenopathy is common [16,23]. Narayanan et al. [27] reported this finding in 10% of cases. No cases were reported in our study.

DF, break-bone fever, is characterized by bone ache, myalgia, and arthralgia [3,7]. None of these manifestations were reported in Saudi Arabia [19]. General weakness (42%) was the commonest musculoskeletal manifestation in our study followed by arthralgia.

Muscle injury in DF results either from direct invasion of the muscle fibers or release of myotoxic cytokines [2,26] causing myalgia and fatigability during and weeks after illness [2]. Our results showed lower incidence (14.6%) of myalgia, and this was inconsistent with Pawaria et al. [26], where muscle weakness was uncommon manifestation and contradictory to the incidence of 100% [11], 81.9% [23], and 76.8% [17] as reported in other studies.

Cardiac manifestations of dengue are usually asymptomatic and have a benign, self-limiting course with resolution of infection [2]. In our results, tachycardia was present in 20 cases (one DSS, one DHF) and bradycardia in 17 cases (one DHF). Hypotension was present in 27 cases (22%) (one DSS, two DHF). Other studies reported hypotension in 65% and 5% of cases [22,28], respectively.

Upper respiratory tract manifestations collectively formed 20.3% of cases in comparison with 79.7% [23], 52.5% [24], and 8.2% [14] reported previously. Pneumonia was observed in three patients. Pleural effusion in DF, which occurs probably due to increased vascular permeability, plasma leakage, abnormalities of hemostasis and protein-losing shock syndrome [29], was observed in 100% of DHF and 1.67% of DF patients. Variable incidence of pleural effusion was reported in previous reports [18,28,29].

Bleeding tendency from multiple sites was noticed in 17.1% of patients, this was inconsistent with 19.9% [23] reported previously. Gum bleeding was the most common hemorrhagic manifestation, while petechia [16,17], epistaxis [28], melena [20], and hematemesis [27] were the commonest in other reports. Other studies reported higher [20] and lower frequencies of hemorrhagic manifestations [19]. Hematuria is a rare and an infrequent manifestation [3,16]. Our study showed hematuria in 1.6% of cases.

Different pathogeneses contribute to central nervous system involvement in DF, causing a wide range of neurological manifestations including non-specific symptoms, disturbance of consciousness, seizures, coma, meningitis, polyneuropathies, Guillain–Barre Syndrome, and transverse myelitis [30]. Disturbed level of consciousness was reported as the commonest neurological manifestation [21]. In our study, seizure was the commonest finding followed by the disturbance of consciousness. Pothapregada et al. [10,23] reported similar observation.

Frequently reported rare and atypical manifestations of DF [2,10,12] might be explained by severe, profound shock, associated underlying host conditions, diseases, and co-infections [2].

The majority of dengue cases have a self-resolving course [1], but multisystem involvement can account for significant mortality [12]. Overall, mortality was reported as 7.6% [20] and 4.1% [21]. Other studies showed no significant mortality [11,17]. In our study, there was no significant mortality; from one point of view, this could be related to increasing awareness among people in Mukalla, early suspicion of diagnosis; especially we were in an endemic area and proper management. Infection with one DENV serotype may be a contributing factor, but this information cannot be confirmed due to lack of facilities in our area. From another point of view, we might consider low mortality registered in this study due to the limited population included in the study, unreported cases from poor rural areas related to decreased awareness about DF manifestations due to lack of audiovisual facilities or their inability to reach hospitals for medical care.

Our study had the following limitations:

1. This study was conducted in two public hospitals. Outpatient clinics and private hospitals were not included.
2. Poor supply of dengue kit and the high cost of the test in the private laboratories limited the possibility for serological confirmation of probable cases.
3. No facility to isolate and determine the serotype of the virus.

Conclusions

Dengue is one of the dreaded fevers for the pediatric age group, with increasing incidence of atypical and uncommon clinical pattern of presentations. Our study showed an increasing incidence of vomiting, anorexia, general weakness, and upper respiratory tract manifestations. The most common atypical manifestations were seizures, pleural effusion, hypotension, bradycardia, and hematuria. A high index of suspicion is required;

especially among the healthcare staff at primary health centers from where these cases are more often referred, in order to ensure prompt recognition and early management to avoid fatal complications and improve the outcome.

Acknowledgements
We are thankful for all the junior doctors who helped in data collection and the patient families who were cooperative to supply us with needed information.

List of Abbreviations

DENV	Dengue virus
DF	Dengue fever
DHF	Dengue hemorrhagic fever
DSS	Dengue shock syndrome
GI	Gastrointestinal
WHO	World health organization

Funding
The authors have declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Conflict of Interests
The authors have declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Availability of data and material
The data and materials are available.

Authors' contribution
Haifa A. Bin Dahman performed the data collection, analysis, discussion, figures, and critical revision of the manuscript. Eman A. Hatem performed the data collection and manuscript revision. All authors approved the final form of the manuscript.

Competing interests
The authors have declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval
Our study is a retrospective record based study. A formal approval was sought from hospital managers and statistical department. The methods employed in this study were carried in accordance with the approved research guidelines of Hadhramaut University (College of Medicine).

Consent for publication
Not applicable.

Author details
Haifa A. Bin Dahman[1], Eman Awadh Hatem[2]
1. Department of Pediatric, Hadhramaut University College of Medicine (HUCOM), Hadhramaut governorate, Yemen.
2. Department of Pediatric, M.C.H Hospital, Hadhramaut Governorate, Yemen.

References

1. TDR. Dengue—guidelines for diagnosis, treatment, prevention and control [Internet]. WHO; 2009 [cited 2017 April 11]. Available from: http://www.who.int/tdr/publications/training-guideline-publications/dengue-diagnosis-treatment/en/
2. Gulati S, Maheshwari A. Atypical manifestations of dengue. Trop Med Int Health 2007; 12:1087–95. https://doi.org/10.1111/j.1365-3156.2007.01891.x
3. World Health Organization. Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever [Internet]. SEARO, WHO, Regional Office for South-East Asia; 2011 [cited 2017 April 11]. Available from: http://www.searo.who.int/vector_borne_tropical_diseases/documents/SEAROTPS60/en/
4. World Health Organization. WHO|dengue and severe dengue [Internet]. Geneva, Switzerland: WHO; 2017 [cited 2017 April 11]. Available from: http://www.who.int/mediacentre/factsheets/fs117/en/
5. Kumar A, Rao CR, Pandit V, Shetty S, Bammigatti C, Samarasinghe CM. Clinical manifestations and trend of dengue cases admitted in a tertiary care hospital, udupi district, karnataka. Indian J Community Med 2010; 35:386–90; https://doi.org/10.4103/0970-0218.69253
6. Van Kleef E, Bambrick H, Hales S. The geographic distribution of dengue fever and the potential influence of global climate change. TropIKA.net 2010. pp 1–22.
7. Madani TA, Abuelzein E-TME, Al-Bar HMS, Azhar EI, Kao M, Alshoeb HO, et al. Outbreak of viral hemorrhagic fever caused by dengue virus type 3 in Al-Mukalla, Yemen. BMC Infect Dis 2013; 13:136. https://doi.org/10.1186/1471-2334-13-136
8. Bin Ghouth AS, Amarasinghe A, Letson GW. Dengue outbreak in Hadramout, Yemen, 2010: an epidemiological perspective. Am J Trop Med Hyg 2012; 86:1072–6. https://doi.org/10.4269/ajtmh.2012.11-0723
9. USAID. Yemen|complex emergency|fact sheet #4, fiscal year (FY) 2016. United States Agency International Development (USAID) Center for International Disaster Information; 2016.
10. Pothapregada S, Kamalakannan B, Thulasingam M. Clinical profile of atypical manifestations of dengue fever. Indian J Pediatr 2016; 83:493–9. https://doi.org/10.1007/s12098-015-1942-9
11. Pai Jakribettu R, Boloor R, Thaliath A, Yesudasan George S, George T, Ponadka Rai M, et al. Correlation of clinicohaematological parameters in paediatric dengue: a retrospective study. J Trop Med 2015; 2015:647162. https://doi.org/10.1155/2015/647162
12. Gangasiddaiah N, Nanjundaiah N. Dengue fever: atypical manifestation. Int J Res Med Sci 2014; 2:1804–6.
13. Guha-Sapir D, Schimmer B. Dengue fever: new paradigms for a changing epidemiology. Emerg Themes Epidemiol 2005; 2:1. https://doi.org/10.1186/1742-7622-2-1
14. Shahina W, Nassara A, Kalkattawia M, Bokharia H. Dengue fever in a tertiary hospital in Makkah, Saudi Arabia. Dengue Bulletin 2009; 33:34–43.
15. Alahdal M, Al-Shabi J, Ogaili M, Abdullah QY, Alghalibi S, Jumaan AO, et al. Detection of dengue fever virus

serotype—4 by using one-step real-time RT-PCR in Hodeidah, Yemen. Br Microbiol Res J 2016; 14:1–7.

16. GUBLER DJ. Chapter 72—dengue and dengue hemorrhagic fever. In: Guerrant RL, Walker DH, Weller PF, editors. Tropical infectious diseases. 2nd ed. Philadelphia, PA: Churchill Livingstone; 2006. pp. 813–22. Available from: https://doi.org/10.1016/B978-0-443-06668-9.50077-6
17. Mishra S, Ramanathan R, Agarwalla SK. Clinical profile of dengue fever in children: a study from Southern Odisha, India. Scientifica 2016; 2016:e6391594. https://doi.org/10.1155/2016/6391594
18. Neeraja M, Iakshmi V, Teja VD, Lavanya V, Priyanka EN, Subhada K, et al. Unusual and rare manifestations of dengue during a dengue outbreak in a tertiary care hospital in South India. Arch Virol 2014; 159:1567–73. https://doi.org/10.1007/s00705-014-2010-x
19. Ahmed MM. Clinical profile of dengue fever infection in King Abdul Aziz University Hospital Saudi Arabia. J Infect Dev Ctries 2010; 4:503–10.
20. Shah I, Deshpande GC, Tardeja PN. Outbreak of dengue in Mumbai and predictive markers for dengue shock syndrome. J Trop Pediatr 2004; 50:301–5.
21. Duangmala T, Lumbiganon P, Kosalaraksa P. Unusual clinical manifestations of dengue infection in children in a tertiary care hospital in northeast Thailand. Asian Biomed 2017; 8:97–103. https://doi.org/10.5372/1905-7415.0801.267
22. Choudhury J, Mohanty D, Routray SS. Clinical profile and outcome of dengue fever and dengue haemorrhagic fever in pediatric age group. International Journal of Contemporary Pediatrics. 2016;3:442–4. https://doi.org/10.18203/2349-3291.ijcp20161025
23. Pothapregada S, Kamalakannan B, Thulasingham M, Sampath S. Clinically profiling pediatric patients with dengue. J Glob Infect Dis 2016; 8:115–20. https://doi.org/10.4103/0974-777X.188596
24. Pancharoen C, Mekmullica J, Thisyakorn U. Primary dengue infection: what are the clinical distinctions from secondary infection? Southeast Asian J Trop Med Public Health 2001; 32:476–80.
25. Rashmi Kumar C, Jyotsana Agarwal G, Nagar R, Jain A. Changing clinical manifestations of dengue infection in north India. Dengue Bulletin 2008; 32:118–25.
26. Pawaria A, Mishra D, Juneja M, Meena J. Atypical manifestations of dengue fever. Indian Pediatr 2014; 51:495–6.
27. Narayanan M, Aravind MA, Thilothammal N, Prema R, Sargunam CSR, Ramamurty N. Dengue fever epidemic in Chennai—a study of clinical profile and outcome. Indian Pediatr 2002; 39:1027–33.
28. Jain H. Clinical profile and outcome of dengue fever in hospitalized children of South Rajasthan, India. Int J Contemp Pediatr 2016; 3:546–9. https://doi.org/10.18203/2349-3291.ijcp20161035
29. Venkata Sai PM, Dev B, Krishnan R. Role of ultrasound in dengue fever. Br J Radiol 2005; 78:416–8. https://doi.org/10.1259/bjr/54704044
30. Misra UK, Kalita J, Syam UK, Dhole TN. Neurological manifestations of dengue virus infection. J Neurol Sci 2006; 244:117–22. https://doi.org/10.1016/j.jns.2006.01.011