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EPIDEMIOLOGICAL TRENDS AND CLINICAL MANIFESTATIONS OF DENGUE IN SUDAN (2009-2015)

By
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AN ABSTRACTOF THE THESIS OF

Magdi Mahgoub Idir Mohammed for Master of Science
Major: Epidemiology

Title:Epidemiological Trends and Clinical Manifestations of Dengue in Sudan (2009-2015)

Background: Dengue fever (DF) is a vector-borne disease, transmitted mainly by the female of the Aedes *aegypti*. The disease has now expanded geographically and by 2011 had reached 128 countries, with estimated that half of the population at risk annually

Objective: To describe the epidemiological characteristics and the clinical manifestation of dengue fever, while highlighting gaps in the quality and completeness of the surveillance reporting over a seven-year period in Sudan.

Methods: All dengue fever (DF) cases reported from 2009 to 2015 at the Sudan Federal Ministry of Health (FMoH) were retrospectively analyzed. Incidence and case-fatality rates were calculated, and described geographically, historically and demographically (age and gender). The clinical and laboratory characteristics of reported DF cases were also tabulated. Finally, variable-specific rates of incomplete reporting in records at the FMoH were studied.

Results: There were 5,923 cases reported from five Sudanese states, especially in two peak outbreak years (2010 and 2014), of which 59% were males and the mean age of cases about 20 years. The highest overall year-to-year incidence rate was 257.6 per 100,000 (95% CI: 249.4-265.8) and the overall case fatality rate was 1.3%. Outbreak case-loads continued a previously recorded decreasing trend. Of cases with laboratory results (55%), 76.5% tested positive for dengue, 62.4% being a primary infection. The classical dengue fever clinical presentation was present in 90% of cases, while the more serious hemorrhagic sub-type composed the remaining 10%. The least completeness report was found for laboratory data (71.5%).

Conclusions: DF outbreaks in the studied years in Sudan are characterized by lower relative severity and low fatality rate. In the five-state involved, two Eastern ones (Red Sea and Kassala) are known to be endemic, while the disease was considered as emergent in three Western states

(North Darfur, South Kordofan and North Kordofan). Outbreaks in the former are linked to peaks occurring regionally, very likely associated with the accelerated life cycle of the mosquito vector under the influence of global warming. In the western states however, the emerging dengue clusters have been attributed to carriers from endemic countries serving in the UN peace-keeping forces stationed there since 2007. Continued vector control efforts are recommended, especially at the household and individual levels. Strict screening for dengue carriage is also recommended when assigning UN forces to areas where the population is still naïve where dengue is concerned.

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LIST OF ABBREVIATIONS

DEN V	Dengue Virus
DF	Dengue Fever
DHF	Dengue HemorrhagicFever
DSS	Dengue Shock Syndrome
ELISA	Enzyme-Linked Immunosorbent Assay
EMRO	Eastern Mediterranean Region Office
FMoH	Federal Ministry of Health
IgM	Immunoglobulins M
IgG	Immunoglobulins G
IHR	International Health Regulations
MENA	Middle East and North Africa
NAMRO-3	US Naval Medical Research Unit No. 3
RNA	Ribonucleic Acid
UNAMID	United Nations Advance Mission in Darfur
WHO	World Health Organization

CHAPTER I

1. INTRODUCTION

1.1. Background

Dengue fever (DF) is a mosquito-borne disease, transmitted mainly by the female of the Aedes *aegypti* and other less common Aedes species. Dengue is an RNA virus disease, with four distinct virus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4) from the Flaviviridae family, Flavivirus genus.[1,2,3]Humans are the primary host of the disease. Infection by any serotype can by asymptomatic or cause the "classical" dengue fever (DF) manifested by fever, severe headache, pain behind the eye ball, joint and bone pain, nausea, vomiting and rash (WHO, 2016). More severe manifestationsare the dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[4]

The virus is absorbed by the mosquito whenfeedingon infected human blood during a febrile period. The virus subsequently experiencesan "extrinsic" incubation period between 10–12 days, then the mosquito becomes infectious. When it bites a healthy human, the virus is inoculated and an "intrinsic"incubation cycle starts which takes 4–13 days (an average of 4–6 days).[4,5]Appendix 1 presents the life cycle of the DF virus.Viral isolation by RT-PCR is the most specific confirmation test, but it is less used than the ELISA serological test, which is more available, cheaper and easier to perform.[6]In the primary infection, dengue-specific IgM antibodies are detected after 3-5 days of illness and decline after 2–3 months, while IgG antibodies start being detected after 7-10days at lower level. Reinfection with different dengue virus serotypes is possible. In case of dengue re-infection, high and early titers of IgG antibodies are detectable, even in the initial phase. IgG activation is life-long, associated with significantly lower level of IgM antibodies.[7,8]DHF was documented for the first time in the Philippines and Thailand during an epidemic in the 1950s.[1]

Despite worldwidecontainment activities to control and eliminate dengue which started in the second half of the 20th century, success has been limited. The worldwide incidence of the disease is believed to have risen dramatically by 30-fold in 50 years.[4]The disease has now expanded geographically and by 2011 had reached 128 countries, with estimated that half of the population at risk annually.[9] Nowadays it is a major cause of infectious morbidity and mortality among children and adults in most Asian and Latin American countries.[1]A compilation of global geo-reports conducted by a research team in Oxford estimated the case-load at 390 million DF cases yearly (95% credible interval 284–528 million), with 96 million symptomatic cases (67–136 million) presenting with different disease severity.[10]The change in dengue global trendsattributed to the rapid, often unplanned, urbanization of the tropical countries leading to geographical extension of adult vectors breeding areas. This is coupled with the proximity of susceptible population in densely crowded cities, with poor prevention and control activities and over-burdened public health services.[11,12]

When accurately diagnosed, DF is relatively easy to treat effectively. Using data from the Institute for Health Metrics and Evaluation, a research team estimated that only 13,586 DF cases out of 58.4 million had died in 2013 (case-fatality 20/100,000). Despite the low case-fatality, the economic burden of DF remains important in view of its relatively large incidence in low-income countries. An average of USD $8,900 million was spent in 2013 on the global cost of DF medical care distributed between hospitalized cases (18%), outpatient care (48%), and non-medical care (34%).[13]In 2013, it was estimated that DF had caused the loss of 1.1 million disability-adjusted life years (DALYs).[14]A new tetravalent vaccine hasbeen marketed since the end of2016, targeting the population of adults 9-60 years in endemic countries. The mainprimary prevention method remains effective vector control measures and good case-management.[15]

1.2. Dengue in TheEastern Mediterranean Region (EMR)

DF was reported in the EMR for the first time at the end of the 19th century.[16]Sudan and Egypt experienced several recognized dengue epidemics in the first half of the 20th century.[17] In 1937, Egypt reported a dengue outbreak in Cairo with 2,600 cases and 55 deaths.[18]A recent systematic review study in the Middle East and North Africa (MENA), revealed that 9 countries had reported DF outbreak between 1941-2015. Two vectors were documented most frequently in MENA: A. *aegypti*in eleven countries and A. albopictusin seven countries. Seven countries did not reportany type of vectors.DF and DHF has been most frequently reported from Pakistan, Saudi Arabia, Yemen and Sudan.[19]DENV serotypes 1-3 were documented in Red Sea countries, but only Pakistan has reportedall four serotypes.[19,20,21]DF case-definition, limited laboratory confirmation capacity, poor surveillance system and unsustainability of well-trained health cadres have been addressed by WHO-EMRO as the main challenges for the prevention and control of dengue in the EMR.[22]

1.3. Dengue in Sudan

Sudan has historically been a country of high DF endemicityparticularly in the humid coastal region.[23,24,25]A.*aegypti* has been documented in Sudan since 1930.[26]The most historically affected area has been Kordofan, in the South part of Sudan. A large“yellow fever” outbreak occurred in Kordofan’s Nuba mountain area in 1940, at a time when differential diagnoses were difficult.[27] An outbreak largely presumed to be of DF was reported again in Kordofan in 1967.[28]However, the documentation of DF in Sudan remained inadequate until the1980s. DEN1, DEN2 and DEN3 serotypes were found as epidemic causative agents in 1986 and again in 2005.[29,30] At the same time, other vector-borne hemorrhagic fevers were also found. In 1989, blood samples were collected during a fever outbreak in the Northern part of Sudan,to be investigated at theUS Naval Medical Research Unit No. 3 (NAMRO-3). The result revealed different types of IgG antibodies for several mosquito-borne diseases. Most frequently detected were West Nile (59%), sand fly fever Sicilian (53%), yellow fever (39%), DEN-2 DF (24%) and chikungunya (12%).[31]

Over the first decade of this millennium, the Eastern part of Sudan has been hit by numerous DFoutbreaks.[32]Few studies have been conducted to analyze main risk factors and the viral serotypes in those Eastern states. During 2014-15, DF expanded geographically to the western part of Sudan, re-emerging in the states of North Darfur, and North and South Kordofan. These states correspond to the borders of Sudan and can be considered as a potential entry points to neighboring countries. Cases emerging in the Red Sea states may have also potential significance for countries in the Arab peninsula on the other side of the narrow waterway. The worst recent DF outbreak occurred in 2010 affected only two states: Red Sea and Kassala, with 3,985 cases and 19 deaths.

Surveillance, case management and vector control are the cornerstone of DF control. In Sudan, epidemiological and entomological surveillance were integrated and showed an effective impact.Control efforts targeting mosquitoes weresuccessful in reducing larval and adult densities, and ultimately the cessation of the DF outbreaks in the Red Sea states in 2010.[32]A major challengeto vector elimination is the low adherence of households to recommendations forregularcleaning, filtering and covering of domestic water storage, despite the important association of poor water storage practices with the increased density of A.

aegypti. Studies in South Kordofan (Lagawa), the Red Sea and Kassala states have consistently associated uncovered indoor water storage containers and jars with the presence of A.*aegypti* within the household. Moreover, DF seroprevalence among individuals who store water at home is double that for those who do not.[33]Other challenges to good vector control are threats to control budget sustainability and trained health worker turnover.[22,32]

1.4. Current status of dengue surveillance in Sudan

While vector control efforts have marked some relative success, epidemiological surveillance is still not adequate. Studies on DF time trends have been lacking. There is no documentation on the evaluation of the routine sources providing data tothe governmental surveillance system. Before 2009, the majority of DF surveillance data was reported on a cumulative weekly basis, after which the surveillance was enlarged to include more variables and reporting became immediate. While the majority of states have been reporting vector-borne fever cases, only 5 states have been specifically reporting a total of 5,923 DF cases at various times between 2009 and 2015. The highest case-load (90.2%) was reported from the Red Sea state, followed by Kassala, North Darfur, South Kordofan and North Kordofan.

1.5. Aims and significance on policies

This is the first analysis of dengue surveillance reports routinely transmitted to the Federal Ministry of Health (FMoH). It aims at highlighting gaps in the quality and completeness in the five states concerned with DF between 2009 and 2015. Findings would ultimately provide policy recommendations to improve the system, and consequently render intervention efforts more targeted and effective. Lessons learned may also be useful to neighboring countries with similar DF context.

1.6. Objectives

I. To determine the incidence and case-fatality rates of dengue in affected states in Sudan during 2009 – 2015, and to describe it by time (years) and place (states).

II. To describe the demographic profile, diagnosis, clinical manifestations and outcomes of dengue cases reported to FMoH.

III. To measure the variable-specific rates of incomplete reporting in records at the FMoH.

CHAPTER II

2. METHODS

2.1. Study Design and Sources of Data

This descriptive study uses secondary data recorded by the Epidemiological Surveillance System at FMoH, Sudan. The study includes all DF records between year 2009 and 2015 in five affected states: Red Sea, Kassala, North Darfour, North Kordofan and South Kordofan (Appendix 2, map of Sudan).

2.2. Study variables

The following variables were extracted as available to achieve our specific objectives:

1. Demographical characteristics of cases: age and gender.

   Age weresubsequently categorized into 5 age-group levels with particular public health significance: 1 year and less (infants), 2-5 years (children less than 5 years), 6-15 years (young adults), 16-45 years (reproductive age) and more than 45 years (older adults).

2. Geographical distribution by state and localities:

   The5affected states represent about 25.3% of the total population of Sudan. A detailed list of localities in those states is provided as Appendix 3.

3. Clinical characteristics:

   Including: date of disease onset, disease outcomes (dead or recovered), laboratory results (ELISA IgM or IgG serology), and clinical manifestation (fever, headache, joint pain & backache, nausea and vomiting, abdominal pain, epistaxis, gum bleeding and vomiting blood).

The population baseline was estimated depending on the Central Bureau of Statistics Census 2008 and the annual health statistic reports.

2.3. Plan of analysis

Data were analyzed using SPSS 20 and STATA 13. Descriptive statistics werepresented in frequency tables with percentages for all research variables.Bivariate associations, when needed, were tested using the Chi-square or the t-test depending on the nature of the independent variable. A p-value$\leq$ 0.05 was considered as the threshold for statistical significance. The outcomes of interest were: disease incidence (IR), outcomes (dead/recovered) and case-fatality rates (CFR). The rate of missing information was calculated per variable.

2.4. Ethical considerations and protecting human subjects

This study is a secondary analysis of de-identified routine surveillance data, with no direct interaction with human subjects. Permission has been received from FMoH-Sudan to access and use the data for the purposes of this analysis with the understanding that results and recommendations will be communicated to the Ministry to improve the general performance regarding dengue control. The study received an IRB clearance at the American University of Beirut (AUB).

CHAPTER III

3. RESULTS

3.1. Incidence and case-fatality of DF in various states

Peaks of DF incidence have been reported in five states in Sudan between 2009 and 2015, with a total of 5,923 cases over the entire period. Of those, a first and highest peak occurred in 2010 (n= 3,985), followed by a lesser one in 2014 (n=1,080 cases). Between these two peaks, less than 300 cases were reported in all, the minimum (22 cases) being reported in 2015(Figure 1).

DF was never signaled in all five involved states simultaneously in any given year. However, both in 2012 and 2014, at least four states were reporting cases. The highest overall year-to-year incidence was 257.6 per 100,000 (95% CI: 249.4-265.8) in 2010, followed by 58.5 (95% CI: 54.4-62.4) in 2014, both in the Red Sea state (Table 1).The lowest incidence was 0.1 per 100,000 in Kassala during 2012 and 2013 and South Kordofan in 2012 (Figure 2). Most cases (90.2%) were reported in the Red Sea state, especially from the state capital city Port Sudan (4,736 cases), followed by Tokar (307 cases). Details on number of reported cases in localities of the five affected states in the study period are presented in Appendix 3.

Seventy-six patients died from DF during that period, for a total CFR of 1.3% (Figure 3). South Kordofan state had the highest overall CFR (8.8%), compared to 0% in North Kordofan. Kassala and North Darfur reported comparable CFR of 5.8% and 5.7%, respectively. For CFR by years, Kassala state obtained the highest rate (15%) in 2012, followed by 13.6% in North Darfur state in 2015 (Table 1).

3.2. Demographic profiles of DF cases

Men were more affected (58.9%) than women (41.1%). Ages ranged from infancy (≤1 year) to 87 years, with a mean age of 20.3 years. Almost half of the cases occurred in adults in the reproductive age-group (16 – 45 years). Only one case was missing information on age. Table 2 presents details on sociodemographic characteristics of cases.

3.3. Laboratory confirmationof DF cases

Among the total registered clinical cases, only 2,636 (44.5%) patients provided blood samples for ELISA test. Most of these patients had a positive confirmation of DF (76.7%), and the highest percentagewas reported from Red Sea state (88.4%). The serological results indicated that the majority ofcases were primary infected with high IgMtiters (62.4%), compared to those with re-infection,as indicated by elevated IgGtiters (34.5%) or combined IgM/IgG elevated titers (3.1%).About 50% of the positive cases were between 16 and 45 years of age, suggesting that there was no age bias in laboratory confirmation (Table 3).

3.4. Clinical manifestations and outcomes

Most cases(89.3%) were diagnosed as classical DF, and only 10.7% as the more severe DHF. Within these relative proportions, historical trends were similar, with a higher peak in 2010 and a lesser one in 2014 (Figure 1).The clinical manifestations of the disease type differedneither by gender nor by age. All registered cases had fever as a presenting symptom. Also, frequently reported wasmusculoskeletal pain,while abdominal pain, nausea and vomiting were less common symptoms. Expectedly, DHF cases reported hemorrhagic episodes more frequently than DF, with nasal bleeding as the most common site, followed by gums. Of all cases, 1% did not survive their clinical episode, but the case-fatality among DHF was seven times higher than in DF(Table 4).

Geographically, the relative proportion of DHF was significantly higher in Kassala (25%) and other states (18%), compared to the Red Sea state (9.5%). Specimen collected also varied by disease severity in various states. In the Red Sea, the majority of specimens corresponded as expected to the predominant DF presentation, while elsewhere specimens from DHF cases were more represented. Finally, while DHF represents about 65% of all deaths, that proportion was highest in the “other” more Western states (Table 5).

3.5. Completeness of data

Reports on persons with suspected DF/DHF are routinely made by clinicians or public health authorities. These reports are sent to the local health surveillance unit at the state level,and thenforwarded to the federal level. Gaps may exist at each level preceding the federal one. Thereporting case investigation form should includebasic demographic information, dates of symptom onset, the residence state, sample collection, laboratory investigations information, case classification (DF and DHF), and the outcome of the disease. Information related to time, onset and demographic characteristics of patientsas well as the overall clinical classification of the disease were almost totally complete. The overall completeness of all the symptoms combined was 78.7%, the most frequently missed (97%) being bleeding from sites other than nose and gums. Laboratory data also displayed lesser completeinformation (71.55%). Details can be found in Table 6.

CHAPTERIV

4. DISCUSSION

4.1. General Features of Dengue Fever in Sudan (2009-2015)

In Sudan, A. *aegypti* and DF have been formally identified and reported since the middle of the 20th century. Vector control and case management remain the main and effective DF outbreak containment activities. Despite progress in DF control, periodical outbreaks have been signaled in recent years mostly in two eastern contiguous states of the country: Red Sea and Kassala, where DF is still endemic. Western states with no previous reports of DF have also been reporting episodic clusters detected by the surveillance system since 2009.

Historically, DF incidence is on the decline, with some peaks recorded throughout the 7-year studyin a small number of states. Two major incidence peaks occurred in 2010 and 2014. Most cases typically occur in males in their 20s, who are very likely more exposed to mosquito bites during outdoor activities. The same gender and age ratios are also found in Saudi Arabia,[34] Bangladesh[35,36], and India.[37]With few variations, the most commonclinical presentation was that of a "classical" DF, with about 10% presenting as the more severe DHF.

Not all cases were confirmed by laboratory testing. Usually, samples were collected from the initial cases to confirm an outbreak. Moreover, in non-endemic areas, samples were more likely to be collected when new cases presented with more serious symptoms such as bleeding. Among samples that tested positive for dengue virus, a majority indicated a recent exposure (IgMtiters), indicating that cases of re-exposure were less likely to be sent for confirmation.

4.2. Potential Limitations

The available data are more likely to be under-estimations of the complete and true dimensions of DF incidence. This is expected as routine surveillance systems usually capture the "tip of the iceberg" representing the relatively more severe cases which required medical attention and subsequent reporting.Nevertheless, fluctuations in numbers of those more severe cases are still valid representations of the unseen aspects of disease dynamics in a given region. However, this limitation may be more important in states with continued experience with DF, where more benign cases due to re-infection are likely to occur. In contrast, the clinical presentation in states where DF is rare is more severe from the outset, attracting more thorough medical attention and resulting in more complete surveillance reporting.

4.3. Distribution of The Incidence and Mortality of Dengue Fever

Red Sea and Kassala states experienced numerous DF outbreaks since 1980s. In this analysis, they also experienced peaks in 2010 and 2014, but the magnitude of these recent outbreaks was much less important than previous ones. This situation may reflect an artifact associated with less reporting of the disease in states where the population is more familiar with its benign signs and symptoms. However, this is very likely not the case, as surveillance has largely improved since the 1980s, and health care workers have become more aware of the importance of reporting. On the other hand, changing conditions in urban lifestyles may have reduced the exposure to infected mosquitos. These include more access to air-conditioning which limits the entrance of flying insects inside homes and work offices, and also increased use of household insecticides in parallel to the decrease in street spraying by municipal authorities.

Episodic re-emergence of DF in recent years in Sudan is not an isolated event. While DF peaks were occurring in the Eastern states nearer to the Red Sea, neighboring countries were also experiencingsimilar outbreaks. Jeddah and Makkah cities in Saudi Arabia, reported about 2,200 cases in 2010, andanother higher peak in 2013 with 4,411 cases.[38] In Eritrea, bordering Red Sea and Kassala states, a DF outbreakoccurred in 2010 with 12,946 cases.[39] In the Red Sea state, the unique location of the outbreaks was the largest sea port of the country. This contributes to the view that outbreaks are regional events, in which infected vectors cross boundaries either on their own or hidden in cargos.[40,41]National and international health regulations are expected to include a set of health prevention activities at entry points, supposed to control such vector moves. All ships coming from endemic areas or areas with ongoing outbreaks undergovector control and detection of symptomatic cases, before theyobtain a health certificate. Despite these efforts, mosquitos seem to be able to fly through on their own over longer distances and longer periods of times. Changes in the capacities of flying vectors have been some of the most nefarious consequences of global warming as signaled by UN agencies. The recent wider spread of Zika infections has also been attributed to these changes in mosquitos' physical attributes.[25]

The interesting finding in this analysis is the recording of small clusters of DF appearing in more Western states, such as North Darfur, where the disease had not been endemic so far. DF vector, A. aegypti had been reported in South Kordofan since 1930,[26] yet mosquito-borne fevers were exceptional, suggesting the absence of human reservoirs to maintain the transmission cycle. New trends have emerged during the last decade in the Darfur and Kordofan regions. Major yellow fever outbreaks, known to be a mosquito-borne fever, were diagnosed in Kordofan and Darfur regions in 2005 and 2012 respectively.[42,43] Clusters of Crimean-Congo hemorrhagic fever and other mosquito-borne fevers, increased or emerged in the same period in those previously disease-free regions.[44,45]Western states which experienced recent clusters of emerging diseases have been provided with higher alert surveillance systems and professional health cadres to detect and report any new alert. Yet in those states, heightened alert is not associated with better detection and confirmation. Apparently clinically serious cases, which remain the smaller portion of the DF presentation in Sudan, attract more investigation then less severe cases.

In attempting to understand these dynamics of DF and other mosquito-borne viral hemorrhagic fevers in Western Sudan, it is important to mention that DFis still highly endemic in several African and Asian countries.[46]These countries, such as Egypt, Nigeria, Kenya, Pakistan, Malaysia and Yemen have contributed large contingents of soldiers to the United Nations Advance Mission in Darfur (UNAMID), which was deployed since the end of 2007. It has been suggested that some of these soldiers who are healthy carriers of viruses have been bitten by locally existing A. *aegypti* mosquitos. This has caused a transmission cycle to emerge and cases to appear among the naïve local population livingin the vicinity of their camps.[43,46]In at least one other situation, the deadly emergence of cholera in Haiti in 2010, has also been attributed to the local presence of UN forces from endemic areas, in this case from Nepal.[47]The longer a new agent is allowed to multiply and circulate, the longer it can start a local endemicity focus. Such a threat is too heavy to bear in struggling countries such as Sudan.

Clinically, theclassical, less severe DF presentation was much more frequent than the more severe DHF, despite of circulation of three dengue virus serotypes (DENV1-3). Some researchers in South America have attributed the resistance of populations to DF exposure to genetic traits within the subgroups from African descent.[48,49,50]The overall CFR of DF was about

1%, which is compatible with early detection and good case management. This figure compares favorably with WHO estimates of 20% CFR.[1]However, CFR were not similar in all Sudanese states concerned with dengue in the years under analysis. CFR was higher in non-endemicstates, most notably South Kordofan(8.8%). This may indicate poor medical management or late case detection associated with no previous familiarity with this disease. DF awareness in the community at large and also among health care providers is important to mitigate the impact of incoming outbreaks.

4.4. Issues Related to Completeness of Reporting

When cases were reported, forms tended to be complete, except for laboratory confirmation data. Within the current design, it is not clear whether laboratory data, when not entered, mean that results were negative OR that they were not reported OR that they were not done. This situation may generate confusion which affects the completeness and accuracy of the data.In addition to the incompleteness of some laboratory report, the reporting system is restricted to two categories of dengueclinical presentation out of three possible ones. To be able to further discriminate in classification, some essential laboratory information like blood platelet count and plasma volumehas to be reported in addition to immunoglobulins data.[8]

CHAPTER V

5. CONCLUSIONS& RECOMMENDATIONS

Vector control, early detection and optimal management of cases remain the main elements of dengue fever control. Nevertheless, vaccines may add an important boost to the control efforts. A live attenuated tetravalent DF vaccine (Dengvaxia®) was marketed recently, and a few endemic countries initiated vaccine programs in their communities, targeting schools first, such as in Philippine. Accordingly, the implementation of DF vaccine in Sudan, at least in the Eastern endemic states, will expand local herd immunity and enhance thevector-control activities.

Municipal vector-control should be reinforced or even replaced by the control at individual levels, such as closing potential domestic breeding sites and using household anti-mosquito products. Community members need to understand their important role in raising their awareness and identifying their responsibilities. WHO recommends this integrated vector control management at all levels to optimize the effects.

No nation is safe from the various negative effects of globalwarming. Most vulnerable are countries where the biological cycles of vectors are activated, while a pool of infectious agent's reservoirs also exists. Such is the case of Sudan and its neighbors. Those countries should be vocal advocates for international control of green-house emissions, while also embracing a vast program for sustainable development and clean electricity generation, to demonstrate their commitment to this goal.

The accuracyof surveillance data is important and used for different purposes such as research, policies and strategies. Moreover, surveillance system need to be qualified and reporting all the cases during outbreak, and not only the serious one. The incompleteness of reporting data indicates a gap in the surveillance system in Sudan, indicating the need of urgent revision of reporting processes and forms by experts. Moreover, conducting training sessions targeting all related health cadres is essential to meet a proper epidemiological surveillance system, especially in states with no previous experience with dengue as an endemic entity.

Early and proper case management is important in DF control. It leads to maintaining low fatality among infected patient. Relatively higher case-fatality rates found in non-endemic states indicate a defect in the health management system due to non-familiarity with the disease. Accordingly, special capacity building of case management staff is important,in parallel with community awareness about early signs and symptoms.

Finally, the hypothesis of the responsibility of UNAMIS soldiers as disease carriers cause dengue fever emergence in some areas should be taken seriously. As a primary precaution and even if evidence is not yet solid, soldiers must be screened for dengue carriage prior to being stationed to Sudan. Their medical clinic should be trained and aware of DF detection and management.

Overall, data indicate that the incidence of DF has been historically decreasing in Sudan as a result of full surveillance, management and vector control efforts. Nevertheless, vigilance is still needed to counter changes in mosquito life cycles, and to prevent the implantation of new foci of endemicity in areas previously free of this disease.

BIBLIOGRAPGY

1. World Health Organization. (2006). Dengue and severe dengue: Fact sheet- updated July 2016. Accessed March 2017 at http://www.who.int/mediacentre/factsheets/fs117/en/
2. Cheah, W. K., Ng, K. S., Marzilawati, A. R., &Lum, L. C. (2014). A review of dengue research in Malaysia. The Medical Journal of Malaysia, 69, 59-67.
3. Calisher, C. H., Karabatsos, N., Dalrymple, J. M., Shope, R. E., Porterfield, J. S., Westaway, E. G., & Brandt, W. E. (1989). Antigenic relationships between flaviviruses as determined by cross-neutralization tests with polyclonal antisera. Journal of General Virology, 70(1), 37-43.
4. World Health Organization, Special Programme for Research, Training in Tropical Diseases, Department of Control of Neglected Tropical Diseases, Epidemic & Pandemic Alert. Dengue: guidelines for diagnosis, treatment, prevention and control (2009). Accessed October 2016 at www.who.int/iris/bitstream/10665/44188/1/9789241547871_eng.pdf
5. Watts, D. M., Burke, D. S., Harrison, B. A., Whitmire, R. E., &Nisalak, A. (1986). Effect of temperature on the vector efficiency of Aedes aegypti for dengue 2 virus. Army Medical Research Inst Of Infectious Diseases Fort Detrick MD, 36(1), 143-152.
6. Guzman, M. G., Halstead, S. B., Artsob, H., Buchy, P., Farrar, J., Gubler, D. J., ... & Nathan, M. B. (2010). Dengue: a continuing global threat. Nature Reviews Microbiology, 8, S7-S16.
7. Mandavdhare, H. S., & Sharma, V. (2016). Differentiating primary and secondary dengue infections: Why and how? Medical Journal of Dr. DY Patil University, 9(5), 594.
8. World Health Organization. (2014). Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever: Revised and Expanded Edition. WHO Regional Office for South East Asia; 2010. Accessed in Jan 2017 athttp://apps.searo.who.int/pds_docs/B4751.pdf

9. Brady, O. J., Gething, P. W., Bhatt, S., Messina, J. P., Brownstein, J. S., Hoen, A. G., ... &Hay, S. I. (2012). Refining the global spatial limits of dengue virus transmission by evidence-based consensus. PLoSNegl Trop Dis, 6(8), e1760
10. Bhatt, S., Gething, P. W., Brady, O. J., Messina, J. P., Farlow, A. W., Moyes, C. L., ... &Myers, M. F. (2013). The global distribution and burden of dengue. Nature, 496(7446), 504-507.
11. Kyle, J. L., & Harris, E. (2008). Global spread and persistence of dengue. Annu. Rev. Microbiol., 62, 71-92.
12. Gubler, D. J. (1998). Dengue and dengue hemorrhagic fever. Clinical microbiology reviews, 11(3), 480-496
13. Shepard, D. S., Undurraga, E. A., Halasa, Y. A., &Stanaway, J. D. (2016). The global economic burden of dengue: a systematic analysis. The Lancet Infectious Diseases, 16(8), 935-941.
14. Stanaway, J. D., Shepard, D. S., Undurraga, E. A., Halasa, Y. A., Coffeng, L. E., Brady, O. J., ... & Chuang, T. W. (2016). The global burden of dengue: an analysis from the Global Burden of Disease Study 2013. The Lancet infectious diseases, 16(6), 712-723.
15. World Health Organization. (2016). Dengue vaccine: WHO position paper – July 2016. Accessed Jan 2017 at http://www.who.int/wer/2016/wer9130.pdf?ua=1
16. Gratz, N. G., Knudsen, A. B., & World Health Organization. (1996). The rise and spread of dengue, dengue haemorrhagic fever and its vectors: a historical review (up to 1995). Available at http://apps.who.int/iris/bitstream/10665/64454/2/CTD_FIL(DEN)96.7_pp101-197.pdf
17. Van Rooyen, C. E., & Rhodes, A. J. (1948). Virus Diseases of Man. Virus Diseases of Man, (2nd Edition).
18. Kuno, G. (2009). Emergence of the severe syndrome and mortality associated with dengue and dengue-like illness: historical records (1890 to 1950) and their compatibility with current hypotheses on the shift of disease manifestation. Clinical microbiology reviews, 22(2), 186-201.

19. Humphrey, J. M., Cleton, N. B., Reusken, C. B., Glesby, M. J., Koopmans, M. P., & Abu-Raddad, L. J. (2016). Dengue in the Middle East and North Africa: A Systematic Review. PLOS Neglected Tropical Diseases, 10(12), e0005194.
20. Suleman, M., Faryal, R., Alam, M. M., Sharif, S., Shaukat, S., Aamir, U. B., ... & Arshad, Y. (2017). Dengue Virus Serotypes Circulating in Khyber Pakhtunkhwa Province, Pakistan, 2013-2015. Annals of Laboratory Medicine, 37(2), 151-154.
21. Haider, Z., Ahmad, F. Z., Mahmood, A., Waseem, T., Shafiq, I., Raza, T., ... &Humayun, M. A. (2015). Dengue fever in Pakistan: a paradigm shift; changing epidemiology and clinical patterns. Perspectives in Public Health, 135(6), 294-298.
22. World Health Organization. (2012). Report on the sub-regional meeting on dengue fever in the Red Sea rim, Cairo, Egypt, 20–22 July 2011. Accessed Jan 2017 at http://apps.who.int/iris/bitstream/10665/116078/1/IC_Meet_Rep_2012_EN_14470.pdf
23. Seidahmed, O. M., Hassan, S. A., Soghaier, M. A., Siam, H. A., Ahmed, F. T., Elkarsany, M. M., &Sulaiman, S. M. (2012). Spatial and temporal patterns of dengue transmission along a Red Sea coastline: a longitudinal entomological and serological survey in Port Sudan City. PLoSNegl Trop Dis, 6(9), e1821.
24. Thai, K. T., & Anders, K. L. (2011). The role of climate variability and change in the transmission dynamics and geographic distribution of dengue. Experimental Biology and Medicine, 236(8), 944-954.
25. Hales, S., De Wet, N., Maindonald, J., & Woodward, A. (2002). Potential effect of population and climate changes on global distribution of dengue fever: an empirical model. The Lancet, 360(9336), 830-834.
26. Lewis, D. J. (1955). The Aedes mosquitoes of the Sudan. Annals of Tropical Medicine & Parasitology, 49(2), 164-173.
27. Kirk, R. (1941). An epidemic of yellow fever in the Nuba Mountains, Anglo-Egyptian Sudan. Annals of Tropical Medicine & Parasitology, 35(1), 67-112.
28. Malik, A., Earhart, K., Mohareb, E., Saad, M., Saeed, M., Ageep, A., ... &Soliman, A. (2005). Dengue hemorrhagic fever outbreak in Port Sudan. Sudanese Journal of Paediatricians, 9, 60-65.

29. Malik, A., Earhart, K., Mohareb, E., Saad, M., Saeed, M., Ageep, A., &Soliman, A. (2011). Dengue hemorrhagic fever outbreak in children in Port Sudan. Journal of Infection and Public Health, 4(1), 1-6.
30. Hyams, K. C., Oldfield, E. C., Scott, R. M., Bourgeois, A. L., Gardiner, H., Pazzaglia, G. ... &Daniell, F. D. (1986). Evaluation of febrile patients in Port Sudan, Sudan: isolation of dengue virus. The American Journal of Tropical Medicine and Hygiene, 35(4), 860-865.
31. Watts, D. M., El-Tigani, A., Botros, B. A., Salib, A. W., Olson, J. G., McCarthy, M., &Ksiazek, T. G. (1994). Arthropod-borne viral infections associated with a fever outbreak in the northern province of Sudan. The Journal of Tropical Medicine and Hygiene, 97(4), 228-230.
32. Seidahmed, O. M. E., Siam, H. A. M., Soghaier, M. A., Abubakr, M., Osman, H. A., Abd Elrhman, L. S., ... &Velayudhan, R. (2012). Dengue vector control and surveillance during a major outbreak in a coastal Red Sea area in Sudan. Eastern Mediterranean Health Journal, 18(12), 1217-1224.
33. Soghaier, M. A., Mahmood, S. F., Pasha, O., Azam, S. I., Karsani, M. M., Elmangory, M. M., ... &Eltigai, E. (2014). Factors associated with dengue fever IgG sero-prevalence in South Kordofan State, Sudan, in 2012: Reporting prevalence ratios. Journal of Infection and Public Health, 7(1), 54-61.
34. Alzahrani, A. G., Al Mazroa, M. A., Alrabeah, A. M., Ibrahim, A. M., Mokdad, A. H., &Memish, Z. A. (2013). Geographical distribution and spatio-temporal patterns of dengue cases in Jeddah Governorate from 2006–2008. Transactions of The Royal Society of Tropical Medicine and Hygiene, 107(1), 23-29.
35. Rahman, M., Rahman, K., Siddque, A. K., Shoma, S., Kamal, A. H., Ali, K. S., ... &Breiman, R. F. (2002). First outbreak of dengue hemorrhagic fever, Bangladesh. Emerging Infectious Diseases, 8(7), 738-740.
36. Nimmannitya, S. (2002). Dengue HemorrhagicFever: current issues and future research. Asian-Oceanian Journal of Paediatrics and Child Health, 1, 1-21.
37. Gupta, E., Dar, L., Kapoor, G., &Broor, S. (2006). The changing epidemiology of dengue in Delhi, India. virology Journal, 3(1), 92. http://www.virologyj.com/content/3/1/92

38. Alhaeli, A., Bahkali, S., Ali, A., Househ, M. S., & El-Metwally, A. A. (2016). The epidemiology of Dengue fever in Saudi Arabia: A systematic review. Journal of Infection and Public Health, 9(2), 117-124.
39. Usman, A., Ball, J. D., Rojas, D. P., Berhane, A., Ghebrat, Y., Mebrahtu, G., ... &Haque, U. (2016). Dengue fever outbreaks in Eritrea, 2005–2015. Global Health Research and Policy, 1(1), 17.
40. Colón-González, F. J., Lake, I. R., & Bentham, G. (2011). Climate variability and dengue fever in warm and humid Mexico. The American Journal of Tropical Medicine and Hygiene, 84(5), 757-763.
41. Lu, L., Lin, H., Tian, L., Yang, W., Sun, J., & Liu, Q. (2009). Time series analysis of dengue fever and weather in Guangzhou, China. BMC Public Health, 9(1), 395.http://doi.org/10.1186/1471-2458-9-395
42. Gould, L. H., Osman, M. S., Farnon, E. C., Griffith, K. S., Godsey, M. S., Karch, S., ... &Brair, M. E. (2008). An outbreak of yellow fever with concurrent chikungunya virus transmission in South Kordofan, Sudan, 2005. Transactions of the Royal Society of Tropical Medicine and Hygiene, 102(12), 1247-1254.
43. Soghaier, M. A., Hagar, A., Abbas, M. A., Elmangory, M. M., Eltahir, K. M., &Sall, A. A. (2013). Yellow Fever outbreak in Darfur, Sudan in October 2012; the initial outbreak investigation report. Journal of Infection and Public Health, 6(5), 370-376.
44. Ibrahim, A. M., Adam, I. A., Osman, B. T., &Aradaib, I. E. (2015). Epidemiological survey of Crimean Congo hemorrhagic fever virus in cattle in East Darfur State, Sudan. Ticks and Tick-Borne Diseases, 6(4), 439-444.
45. Abdelhakam, H. A. A., & Taha, M. A. (2014). Crimean-Congo hemorrhagic fever (CCHF) in Southern Kordofan. Sudanese Journal of Paediatrics, 14(1), 81.
46. Amarasinghe, A., Kuritsky, J. N., Letson, G. W., & Margolis, H. S. (2011). Dengue Virus Infection in Africa. Emerging Infectious Diseases, 17 (8), 1349–1354.
47. KATZ, J. M. (2010, November 03). Experts ask: Did U.N. troops infect Haiti? Retrieved April 21, 2017, from http://www.nbcnews.com/id/39996103/ns/healthinfectious_diseases/t/experts-ask-did-un-troops-infect-haiti/#.WPiFNE2wecw.
48. Sierra, B. D. L. C., Kouri, G., & Guzmán, M. G. (2007). Race: a risk factor for dengue hemorrhagic fever. Archives of Virology, 152(3), 533.

49. Halstead, S. B. (2006). Dengue in the Americas and Southeast Asia: do they differ? RevistaPanamericana de SaludPublica, 20(6), 407-415.

50. Guzmán, M. G., Kouri, G. P., Bravo, J., Soler, M., Vazquez, S., &Morier, L. (1990). Dengue hemorrhagic fever in Cuba, 1981: a retrospective seroepidemiologic study. The American Journal of Tropical Medicine and Hygiene, 42(2), 179-1

TABLES

Table 1

Incidence (IR) per 100,000 (95% ci) and case fatality rates (CFR) (%) of dengue fever in selected states in Sudan (2009-2015) *

STATES		Red Sea	Kassala	North Darfour	SouthKordofan	NourthKordofan
2009	Cases	388				
	IR	29.2(26.3-32.1)				
	CFR	1.0				
2010	Cases	3803	182			
	IR	257.6 (249.4-265.8)	9.6(8.2-11)			
	CFR	0.4	2.2			
2011	Cases	204	80			
	IR	15.4(13.3-17.5)	4(3.1-4.9)			
	CFR	3.4	15.0			
2012	Cases	39	3		2	10
	IR	2.9(2-3.8)	0.1(0 -0.4)		0.1(0.0-0.3)	0.3(0.1-0.5)
	CFR	2.7	0		0	0
2013	Cases	48	2			
	IR	3.5(2.5-4.4)	0.1 (0-0.3)			
	CFR	4.2	0			
2014	Cases	819	58	137	66	
	IR	58.4(54.4-62.4)	3(2.8-3.7)	6.1(5.1-7.1)	5.7(4.3-7.1)	
	CFR	0.9	5.2	4.4	9.1	
2015	Cases			22		
	IR			1(0.6-1.4)		
	CFR			13.6		
Total	Cases	5,301	325	159	68	10
	IR	64.3 (63 -66)	3.2 (2.7-3.5)	3.5 (3-3.9)	2.3 (1.7-2.8)	0.3 (0.1-0.5)
	CFR	0.7	5.8	5.7	8.8	0

*Shadowed areas correspond to periods of zero-case reports

Table 2

Sociodemographic characteristics of dengue fever in selected states in Sudan (2009-2015) (n=5923) *

VARIABLE	**Frequency**	**%**
GENDER (n=5923)		
Male	3,491	58.9
Female	2,432	41.1
AGE GROUPS (years) (n=5922)		
Infants (≤1 year)	268	4.5
Children (2 – 5)	656	11.1
Youth (6 – 15)	1,768	29.9
Adults in reproductive age (16-45)	2,855	48.2
Older adults (>45)	375	6.3
Mean age in years (SD)20.3 (15.2) [Range ≤1 year-87]		

* Totals do not add up because of missing data

Table 3

Laboratory confirmation of dengue fever in selected states in Sudan (2009-2015) (n=5,923)

Variable	Frequency	Percentage
Blood Sampling		
Taken	2,636	44.5
Not taken	3,287	55.5
Sample Results (**N=2,636**)		
Positive	2,021	76.7
Negative	615	23.3
Positive samples per age group(**N= 2,021**)		
≤1 year	59	2.9
(2 – 5) year	199	9.8
(6 – 15) year	574	28.4
(6-45) year	1056	52.3
>45 year	133	6.6
Positive samples per serological results(**N=2,021**)		
IgG	697	34.5
IgM	1261	62.4
IgM/IgG	63	3.1
Positive samples in states (**N= 2,021**)		
Red Sea	1786	88.4
Kassala	186	9.2
Other states*	49	2.4

* Other states are North Kordofan, South Kordofan and North Darfur

Table 4

Clinical manifestations and outcomes of dengue fever in selected states in Sudan (2009-2015) (n=5,923)

Variables	**DF**		**DHF**		**Total**	
n (%)	**5288 (89.3)**		**635 (10.7)**		**5923(100)**	
Symptoms						
Fever	5,288	100	635	100	5,923	100
Musculoskeletal pain	2,076	39.3	234	36.6	2,310	39.0
Headache	1,973	37.3	251	39.3	2,224	37.5
Nausea and vomiting	380	7.2	57	8.9	437	7.4
Abdominal pain	30	0.6	4	0.6	34	0.6
Impaired consciousness	4	0.1	1	0.2	5	0.1
Respiratory distress	1	0.0	2	0.3	3	0.1
Bleeding	417	7.9	617	97.2	1034	17.5
Bleeding sites						
Nasal	239	4.5	302	47.6	541	9.1
Gum	144	2.7	260	40.9	404	6.8
Gastrointestinal	33	0.6	13	2.0	46	0.8
Hematuria	0	0.0	18	2.8	18	0.3
Eye	0	0.0	11	1.7	11	0.2
Vaginal	0	0.0	7	1.1	7	0.1
Ear	1	0.0	3	0.5	4	0.1
Skin bleeding	0	0.0	3	0.5	3	0.1
Deaths (CFR %)	27	0.5	49	7.7	76	1.3
Gender						
Male	3,110	58.8	381	60.0	3,491	58.9
Female	2,178	41.2	254	40.0	2,432	41.1
Mean Age (SD)	20.3 (15.3)		20.2 (13.5)		20.3 (15.2)	

DF= classical dengue fever; DHF= dengue hemorrhagic fever

Table 5
Dengue fever presentation in selected states in Sudan by geographical distribution (2009-2015)

Variables	Disease				Total	P-value
	DF		DHF			
	n	%	n	%		
Clinical presentation						
Kassala	258	75.4	84	24.6	342	<0.001
Red Sea	4,835	90.5	508	9.5	5,343	
Other states*	194	81.9	43	18.1	237	
Total	**5287**	**89.3**	**635**	**10.7**	**5922**	
Deaths						
Kassala	7	35.0	13	65.0	20	0.336
Red Sea	17	41.5	24	58.5	41	
Other states*	3	20.0	12	80.0	15	
Total	**27**	**35.5**	**49**	**64.5**	**76**	
Specimens sent to laboratory						
Kassala	115	58.4	82	41.6	197	<0.001
Red Sea	2007	85.0	355	15.0	2362	
Other states*	47	61.0	30	39.0	77	
Total	**2169**	**82.3**	**467**	**17.7**	**2636**	

* North Darfur, South Kordofan and North Kordofan
DF= classical dengue fever; DHF= dengue hemorrhagic fever

Table 6

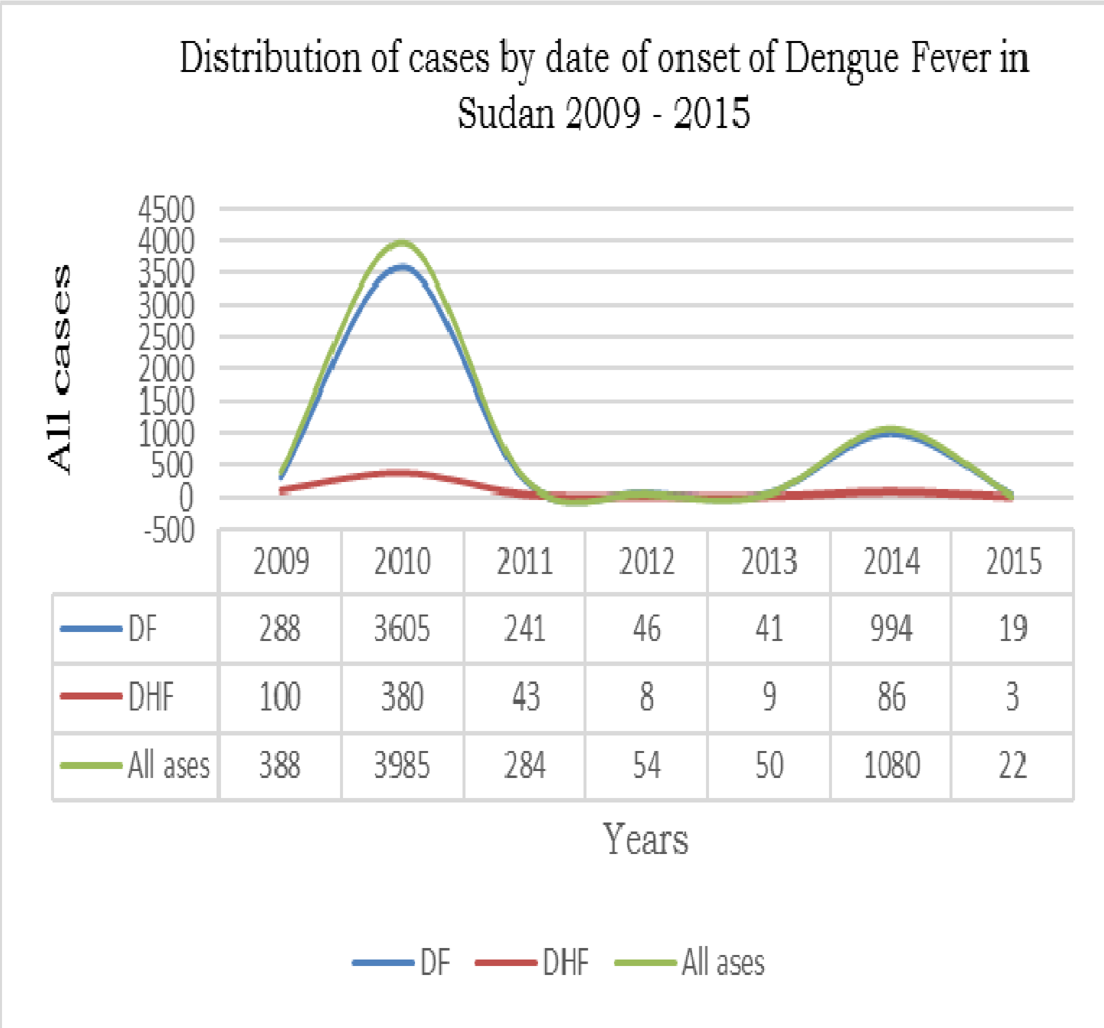
Variable-specific rates of incomplete reporting of dengue fever cases in selected states in Sudan (2009-2015) (n=5,923)

Category	Variable	Records available	Missed	Missing % by variable	Completeness % by variable	Completeness % by category
Time	Date of onset	5,863	60	1.01	98.99	98.99
Place	State	5,922	1	0.02	99.98	99.98
	Locality	5,922	1	0.02	99.98	
Person	Age	5,922	1	0.02	99.98	99.99
	Gender	5,923	0	0.00	100.00	
	Outcome	5,922	1	0.02	99.98	
Laboratory	Result (confirmation)	4,238	1685	28.45	71.55	71.55
Disease	Disease classification	5,923	0	0.00	100.00	78.73
	Fever	5,923	0	0.00	100.00	
	Headache	4,598	1325	22.37	77.63	
	Musculoskeletal pain	4,040	1883	31.79	68.21	
	Nausea&vomiting	4,836	1087	18.35	81.65	
	Abdominal pain	5,455	468	7.9	92.1	
	Epistaxis	4,640	1283	21.66	78.34	
	Gum bleeding	5,259	664	11.21	88.79	
	Vomiting blood	5,789	134	2.26	97.74	
	Other bleeding sites	166	5757	97.2	2.8	

FIGURES

FIGURE 1

Distribution of cases by date of onset of dengue fever reported in selected states in Sudan (2009-2015) (n=5,922) *



	2009	2010	2011	2012	2013	2014	2015
DF	288	3605	241	46	41	994	19
DHF	100	380	43	8	9	86	3
All ases	388	3985	284	54	50	1080	22

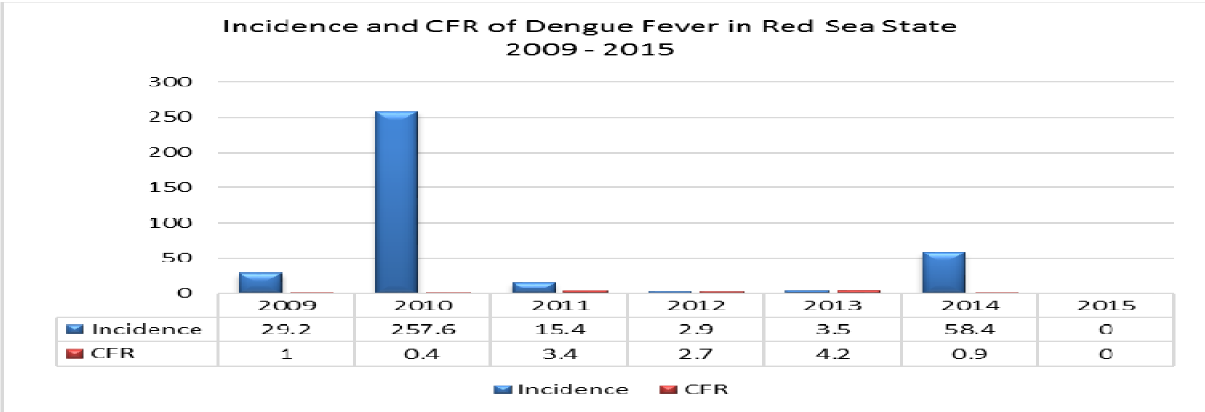
d

DF= classical dengue fever; DHF= dengue hemorrhagic fever

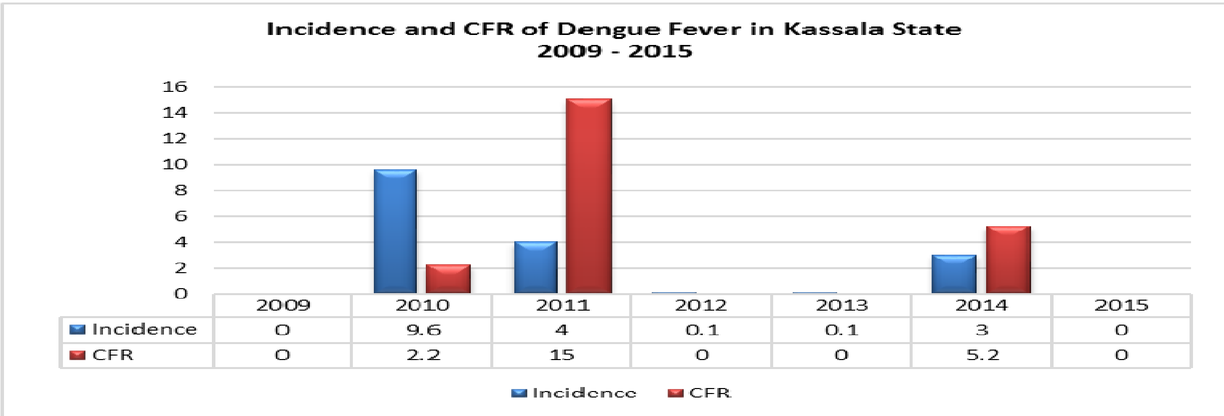
Figure 2

Incidence (IR) per 100,000 and case fatality rates (CFR) (%) of dengue fever by selected states in Sudan (2009-2015)

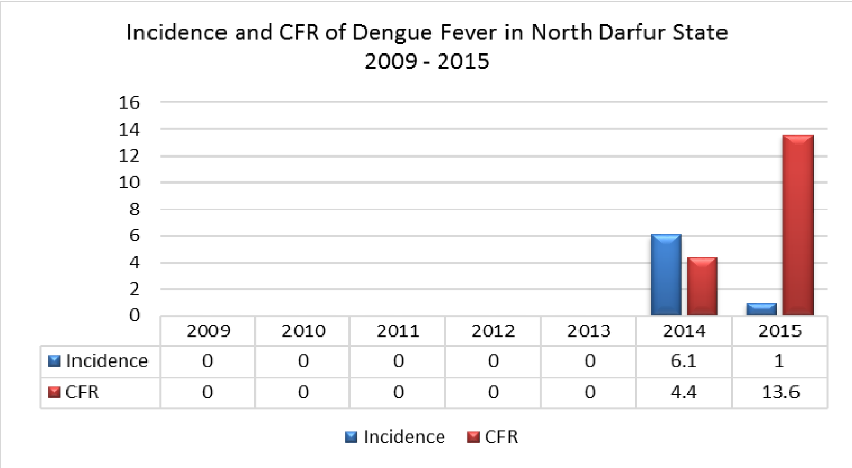
1. RED SEA STATE

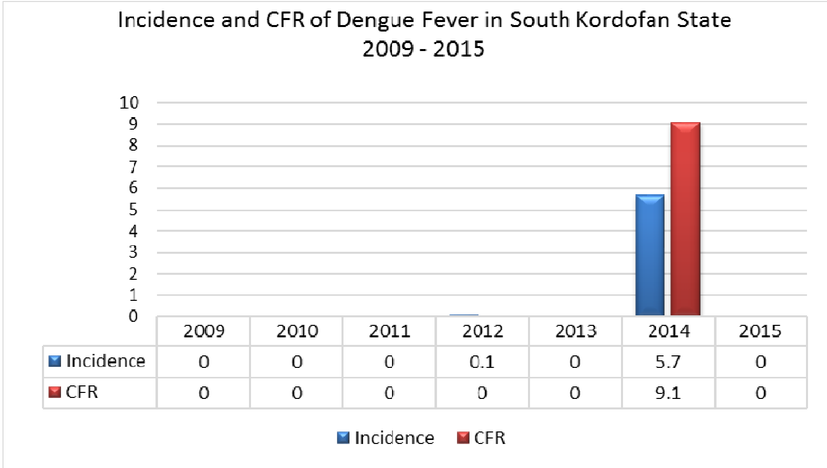


2. KASSALA STATE



3. NORTH DARFUR STATE4. SOUTH KORDOFAN STATE





5.NORTH KORDOFAN STATE

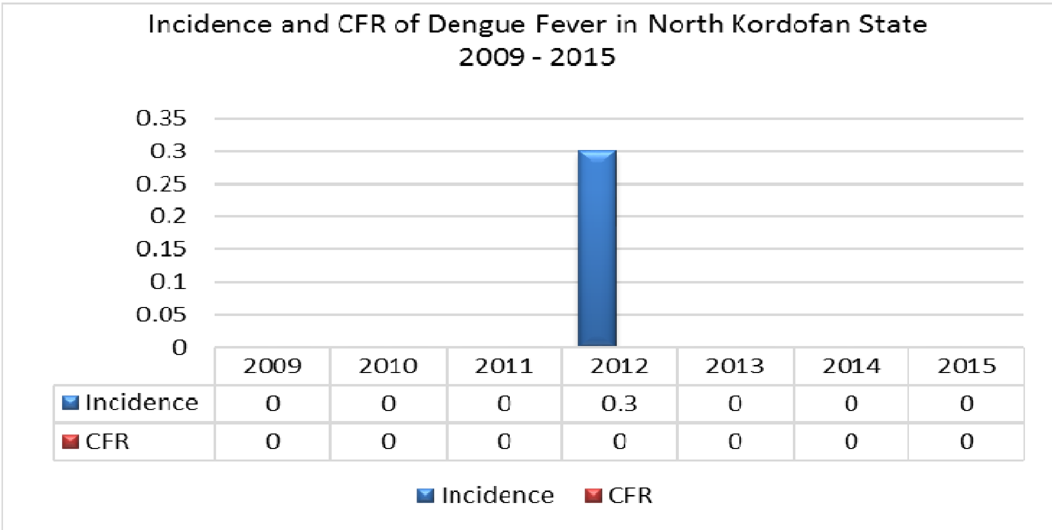
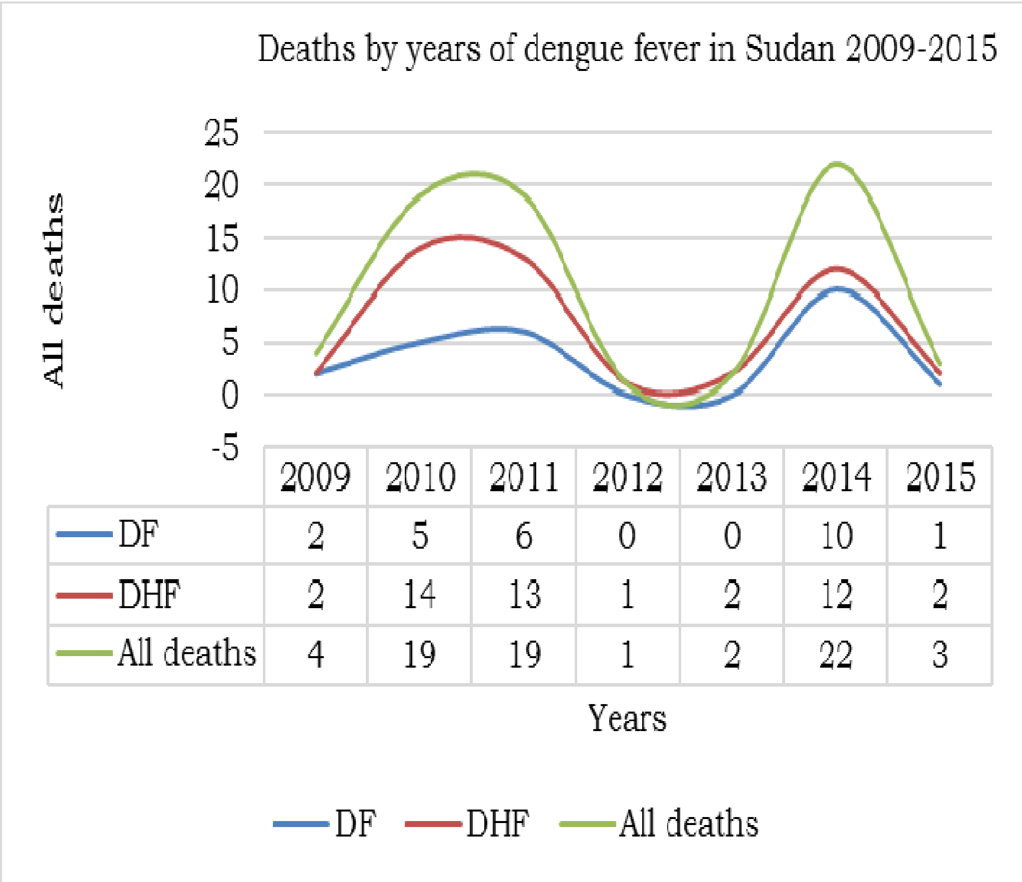


Figure3

Distribution of deaths by year of dengue fever cases reported in selected states in Sudan (2009-2015) (n=70) *



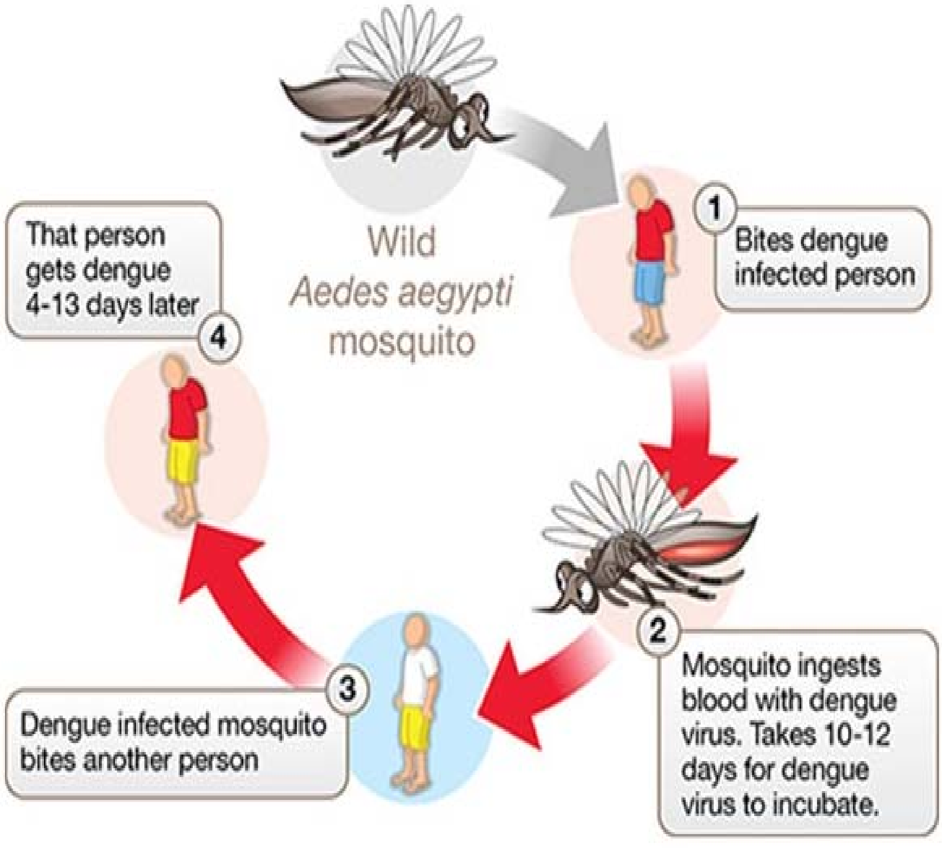
* Six cases missed

DF= classical dengue fever; DHF= dengue hemorrhagic fever

APPENDICES

Appendix 1

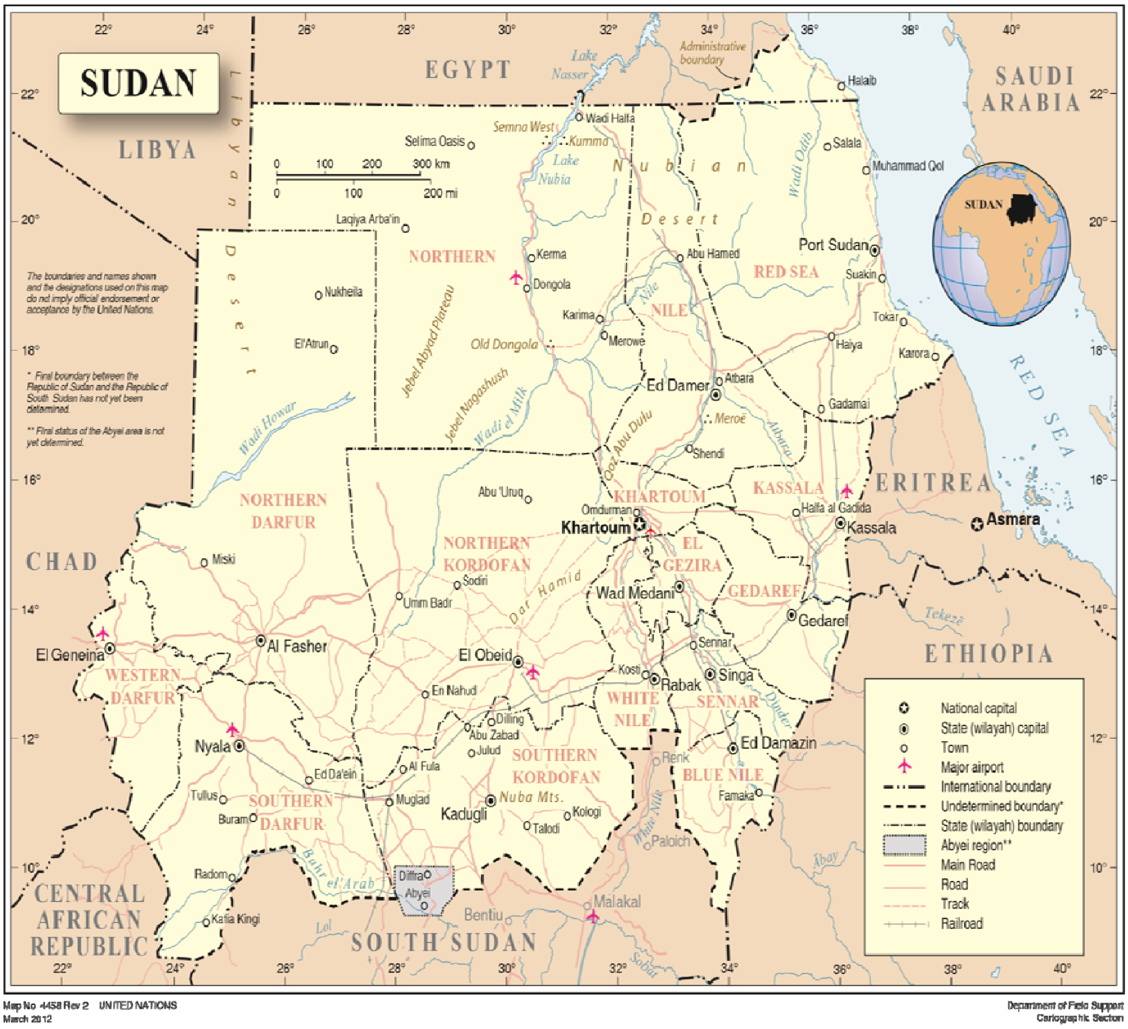
Life cycle of dengue fever virus in mosquitos (extrinsic) and humans (intrinsic)



Retrieved from http://www.eliminatedengue.com/our-research/dengue-fever

Appendix 2

Sudan map with states & states capitals



Retrieved from:[UN Cartographic Sectionhttp://www.un.org/Depts/Cartographic/map/profile/sudan.pdf](http://www.un.org/Depts/Cartographic/map/profile/sudan.pdf)

Appendix3

Detailed geographical distribution of dengue fever cases in Sudan by states and localities (2009-2015) (n=5923) *

States and localities	Frequency	%
Red Sea		
Alganab and Aloleeb	25	0.4
Halaib	1	0.0
Sinkat	65	1.1
Tokar	307	5.2
Aggig	2	0.0
Hayaa	6	0.1
Port Sudan	4,736	80.0
Sawakin	201	3.4
Total	**5,343**	**90.2**
Kassala		
Aroma	4	0.1
Halfa	15	0.3
Hamashkoraib	3	0.1
Kassala	224	3.8
KhashmAlgerba	2	0.0
Nahr Atbara	3	0.1
Rifi Kassala	80	1.4
Wad Alhelaw	9	0.2
Wadsharefai	2	0.0
Total	**342**	**5.8**
North Darfur		
AlFasher	130	2.2
Alkoma	4	0.1
Alseraif	2	0.0

Altenna	7	0.1
Dar Alsalam	9	0.2
Karnawi	2	0.0
Kotoom	2	0.0
Tawella	3	0.1
Total	**159**	**2.7**
South Kordofan		
Abo Gebaiha	2	0.0
Alabasia	1	0.0
Aldalang	2	0.0
Habella	49	0.8
Kadogli	14	0.2
Total	**68**	**1.1**
North Kordofan		
Aledaia	1	0.0
Alnohood	3	0.1
Hegleeg	1	0.0
Wad Banda	5	0.1
Total	**10**	**0.2**
Grand total	**5,922**	**100.0**

* One case missed