University of Khartoum  
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Prevalence and clinical criteria predicting diagnosis and outcome of dengue infection among Sudanese patients

A thesis submitted in partial fulfillment for the requirements of the Degree of Clinical MD in Medicine.  
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( وإذا مرضت فهو يشفين )

صدق الله العظيم
سورة الشعراء آية رقم(80)
Dedication

To

My parents, brother and sisters

ELTAYEB
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ABSTRACT

This is a prospective case controlled hospital based study done in Khartoum teaching hospital in the period Feb 2004-Aug 2004. The aim of the study was to assess the prevalence and clinical presentation of Dengue fever and to determine morbidity and mortality among febrile patients. 107 patients of age ranged between (15-60) years and who had fever for less than two weeks duration were selected for the study. A written consents were obtained from all patients and controls. Base line data was collected through a questionnaire that included the history of illness and clinical examination for each patient. Investigations were done for all patients including blood film for malaria , ICT for malaria, white blood count and urine analysis. All patients and control were tested for IgG and IgM antibodies against Dengue virus by rapid test.

Significant immuno globulin M (IgM) was detected in (10.28%) of the study group (febrile patients).

- No positive result for immune globulin G (IgG) against dengue virus was detected neither in febrile patients nor in controls.

The study showed a significant association between presence of IgM antibody against Dengue virus and the following symptoms.

- Fever between (37-38.5°C)
- Headache and cough (100%)
- Myalgia (90.9%)
- Neck pain (63.3%)

While diarrhea, retro-orbital pain and photophobia were less likely presentation (27.3%). Lymphadenopathy (cervical & submandibular) was detected in (99%) of the study group and in all IgM positive patients suggesting other infections beside Dengue fever.

No haemorrhagic signs were detected in the study and all patients recovered in 1-2 weeks with only supportive treatment.
ملخص الاجراة

هذه دراسة مستقلة محكم بها اجريت في مستشفى الخرطوم التعليمي في الفترة من فبراير 2004 وحتى أغسطس 2004 م.

الهدف من الدراسة معرفة معدل انتشار مرض حمي الضنك الوبائي والامراضية ومعرفة حالته السريرية المختلفة.

حيث قمت بدراسة 107 حالة من المرضى الذين تتراوح اعمارهم بين 15-60 عاماً ويعانون من الحمي لفترة اقل من أسبوعين مع استبعاد أي أسباب اخرى للحمى، وكذلك تم جمع العينات من 107 أشخاص لاعيان من المحمي.

تم جمع المعلومات بعد مل اقرار مكتوب عن طريق تعنيه استمارة استببان شاملة على التاريخ المرضي وفحص السريري لكل حالة بالإضافة إلى اخذ ثلاث مل مدم من كل مريض لإجراء الفحوصات العملية الخاصة مثل الدم للملاريا ، الدم الابيض ، تحليل البول

لاستبعاد بعض انواع الحمي تم فحص عينات الدم لمضادات مناعية الفيروس "ج" و"م" عن طريق الفحص السريع.

 نسبة وجود المضادات المناعية من نوع "م" يمثل 10.28% من مجموع الدراسة ولم يوجد اي نتيجة ايجابية للمضادات المناعية من نوع "ج" في أي من المجموعتين مما يدل الى ان فيروس العدوى الأولي أكثر حدوثاً من العدوى الثانوي في هذه الدراسة.

 اوضحت الدراسة وجود علاقة وطيدة بان ايجابية البروتين المناعي "م" ضد فيروس الطنكة والاعراض الاتية :-

  • الحمي بين (37-38 درجة منوية).
  • والرأس والسعال (100%)
  • الم عضلات (90.9%) %
  • الرقبة (63.3%) %

بينما السعال والدم خلف العينين وعدم تحمل الضوء تمثل (27.3%) من ضمن الاعراض المحتملة وهي اقل اهمية في تشخيص الحالات في هذه الدراسة، لوحظ أيضاً ان حدوث تضخم الغدد الالافمية ( الرقبة تحت الفك ) بنسبة عالية في مجموع الدراسة (99%) وكذلك ايجابيا.
في كل المجموعة (100%) ايجابية مضادات الدم المناعية من نوع "م"، مما يزيد احتمالية حدوث تضخم هذه الغدد مع حمي الضنك والاسباب الاخرى للحميات.

- لم تلاحظ أي اعراض نزفية في مجموعة الدراسة.
- كل المرضى زالت الحمي والاعراض خلال مدة تتراوح بين 1-2 اسبوع دون علاجات.
Dengue causes more illness and death than any other arboviral infection, there are at least 20 million infections in the world each year and several hundred thousand cases of a severe, life-threatening syndrome known as dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS).

In recent years, the geographical range of dengue has extended and DHF/DSS is occurring in new areas and with increased incidence. The reasons for the resurgence are complex, but parallel demographic changes and reduced efforts towards disease control.\textsuperscript{1}
Dengue Viral Fever:

Dengue virus (DV) is the causative agent of dengue fever (DF) and dengue hemorrhagic fever (DHF) and consists of four distinct serotypes (DEN-1, DEN-2, DEN-3, and DEN-4). Symptoms include sudden onset of fever, intense headache, and muscle and lower back pain. The duration of illness is usually 1–2 weeks. During the 1995 outbreak in Palau, disease was mild and hemorrhagic manifestations were rare. Although the symptoms associated with dengue 4 virus infections have been reported as being milder than symptoms associated with infections with the other subtypes (with outbreaks being characterized by a majority of dengue fever rather than dengue hemorrhagic fever), infections with dengue 4 virus can also be associated with severe and fatal disease. DHF, the potentially fatal form of dengue virus infection, was first recognized in Bangkok, Thailand, in 1958. Since then, dengue disease incidence has increased from 9/100,000 in 1958 to 189/100,000 in 1998, with the
largest reported incidence of 325/100,000 in 1987. Dengue has thus become a severe and intractable public health problem in Thailand. ²

Dengue haemorrhagic fever (DHF) first emerged as a public health problem in 1954, when the first epidemic occurred in Manila. This gradually spread to other countries in the region. Major epidemics occurred in other regions of the world in the 1980s and 1990s and were caused by all four dengue viral serotypes. While the predominant serotype in the 1980s and the early 1990s was DEN-2, in recent years it has changed to the DEN-3 serotype. In 1998, a pandemic of dengue viral infections occurred, where 1.2 million cases of dengue fever and DHF were reported from 56 countries worldwide. The world population was exposed to a new subtype of the DEN-3 virus (subtype III), which originated in the Indian subcontinent and later spread to involve other continents. Exposure of a non-immune population to this new subtype of DEN-3 may have been the cause of this pandemic. A situation of comparable magnitude was also seen in 2001–02. ⁴ In most of the tropical and subtropical world, dengue fever is a leading cause of morbidity and mortality, particularly among children. ³
In the last four decades the incidence of dengue fever has increased 30-fold worldwide, and over half the world's population is now threatened with infection from one or more of four co-circulating viral serotypes (DEN-1 through DEN-4).  

**Clinical Epidemiology:**

During the 19th century, dengue was considered a sporadic disease, causing epidemics at long intervals. However, dramatic changes in this pattern have occurred and currently, dengue ranks as the most important mosquito borne viral disease in the world. In the past 50 years, its incidence has increased 30-fold with significant outbreaks occurring in five of six World Health Organisation (WHO) regions. At present, dengue is endemic in 112 countries in the world.

Around 2.5 to 3 billion people, living mainly in urban areas of tropical and subtropical regions, are estimated to be at risk of acquiring dengue viral infections. Estimates suggest that annually 100 million cases of dengue fever and half a million cases of dengue haemorrhagic fever (DHF) occur in the world with a case fatality in Asian countries of 0.5%–3.5%. Of those with DHF, 90% are children less than 15 years of age. Although the mosquito vector and all four
dengue viral serotypes are present in the African region, to date an epidemic of DHF has not occurred. Since DHF is less frequent among black persons living in areas that experience epidemics of DHF, it is possible that individuals of African origin may have a degree of inherent resistance to the disease.³ Dengue is an acute febrile disease caused by infection with any of four serotypes of dengue virus (DEN), a flavivirus. It is a public health problem of growing importance in areas where the insect vector, Aedes aegypti and related species, is abundant. Although most DEN infections present as a benign illness with low mortality, many countries report increasing incidences of severe manifestations, i.e. dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). DEN infections have been identified as a cause of febrile illness in travellers. The clinical-to-subclinical infection rate was 1 :3.3. The risk of infection showed marked seasonal variation. DEN infections are frequent in travellers to endemic areas in Asia; most remain subclinical. 45% of cases of fever in travellers returning from endemic areas.⁶

Depending on the population studied and the laboratory methods used, serological evidence of recent DEN infection was
found in 7–45% of cases of fever in travellers returning from endemic areas. Mechanisms of disease transmission in human outbreaks of HFVs are still poorly understood. Clarification of the role of airborne transmission is vital. Rapid diagnostic methods need to be developed for all of the HFVs. Methods to safely handle potentially infected specimens in a clinical laboratory should be developed.  

**Characteristics of Dengue Virus:**

The dengue virus is a single stranded RNA virus belonging to the flaviviridae family. There are four serotypes (DEN 1–4), classified according to biological and immunological criteria. The viral genome is approximately 11 kb in length. The mature virion consists of three structural (core, membrane associated, and envelope) and seven non-structural (NS1, NS2a, NS2b, NS3, NS4a, NS4b, and NS5) proteins. The envelope protein is involved in the main biological functions of the virus. It binds to receptors on host cells, allowing the virus to be transported through it. In addition, the envelope protein is associated with haemagglutination of erythrocytes, induction of neutralising antibodies and protective immune responses. Non-structural proteins (NS1–NS5) expressed as both membrane
associated and secreted forms have also been implicated in the pathogenesis of severe disease. Unlike other viral glycoproteins, NS1 does not form a part of the virion but gets expressed on the surface of infected cells. Preliminary evidence suggests its involvement in viral RNA replication. Plasma levels of secreted NS1 (sNS1) correlate with viral titres, being higher in patients with DHF compared with dengue fever. Moreover, elevated free sNS1 levels within 72 hours of onset of illness identify patients at risk of developing DHF. Very high levels of NS1 protein are detected in acute phase samples from patients with secondary dengue infections but not primary infections. This suggests that NS1 may contribute to formation of circulating immune complexes, which are thought to have an important role in the pathogenesis of severe dengue infections.

The dengue virus shares antigenic epitopes with other flaviviruses such as Japanese encephalitis virus. These shared epitopes may lead to production of cross reactive antibodies and hence interfere with serological diagnosis. However, antibodies directed to the prM protein of dengue viruses are species specific (not cross reactive with those of other flaviviruses) and may be useful for
Clinical Manifestations Of Dengue Infection:

The clinical features of dengue vary with the age of the patient and, in addition to clinically inapparent infections, can be classified into five presentations: non-specific febrile illness, classic dengue, dengue haemorrhagic fever, dengue haemorrhagic fever with dengue shock syndrome, and other unusual syndromes such as encephalopathy and fulminant liver failure. Young children with dengue often have an undifferentiated febrile illness with a maculopapular rash. Upper respiratory infections, especially pharyngitis, are common. Most infections in children under 15 years are asymptomatic or minimally symptomatic; a study of schoolchildren in Thailand found only 13% of those infected missed more than one day of school because of illness. Classic dengue is more commonly seen among older children, adolescents, and adults. They are less likely to be asymptomatic. Dengue is abrupt in onset, typically with high fever accompanied by severe headache, incapacitating myalgias and arthralgias, nausea and vomiting, and sero epidemiological studies in dengue (especially in countries where other flaviviruses are endemic).
rash. Rash, typically macular or maculopapular, often becoming confluent and sparing small islands of normal skin, has been reported in over half of infected people. Other signs and symptoms include flushed facies, sore throat, cough, cutaneous hyperaesthesia, and taste aberrations. Recovery may be prolonged and include depression. 9

Undifferentiated Fever:

This usually follows a primary infection but may also occur during a secondary infection. 4 Most dengue viral infections are clinically inapparent or result in a mild, flu-like (viral syndrome) illness, particularly in young children. The incubation period ranges from 3 to 14 days (average = 4–7 days) 1 Dengue fever, may present as a spectrum of illness that ranges from asymptomatic infection to severe hemorrhagic diathesis. Most dengue viral infections are clinically inapparent or result in a mild, flu-like (viral syndrome) illness, particularly in young children. Risk factors that influence disease severity include the strain of virus, and the age, immune status, and genetic background of the host. The incubation period ranges from 3 to 14 days (average = 4–7 days) 10
**Dengue Fever:**

Dengue fever may occur either during primary or secondary infections. Patients with DF could not be distinguished from other febrile patients on clinical grounds alone. Infection results in a viremia that lasts from 2 to 12 days (average = 5 days). Generally, older children and adults more frequently experience classic dengue fever, an acute febrile illness of several days’ duration. The onset is sudden with high fever, severe headache (especially in the retro-orbital area), arthralgia, myalgia, anorexia, abdominal discomfort, and sometimes a macular papular rash. The fever may be biphasic and tends to last for 2–7 days. Flushing, a characteristic feature is commonly observed on the face, neck, and chest. Coryza may also be a prominent symptom especially in infants. Younger children tend to present with coryza, diarrhoea, rash and seizure, and less commonly with vomiting, headache, and abdominal pain. Although, haemorrhagic manifestations are uncommon in dengue fever, petechiae / pupura, gastrointestinal bleeding, epistaxis, and gingival bleeding have been observed in some individuals. A positive
tourniquet test has been reported in many individuals with dengue fever possibly due to reduced capillary fragility. Recovery from dengue fever is usually uneventful, but may be prolonged especially in adults. In a large prospective study of pediatric dengue, no clinical or basic laboratory parameters clearly differentiated between children with and without dengue, although petechiae and hepatomegaly were independently associated with the diagnosis. Dengue fever (DF) with acute acalculous cholecystitis is rarely reported.

**Dengue Haemorrhagic Fever:**

DHF usually follows secondary dengue infections, but may sometimes follow primary infections, especially in infants. In such infants, maternally acquired dengue antibodies are presumed to enhance primary infections. Such a phenomenon has not been described in human infections other than dengue. Dengue haemorrhagic fever is primarily a disease of children under 15 years in hyperendemic areas. Black populations may be at decreased risk. The disease is characterised by increased capillary permeability and haemostatic changes. If major plasma leakage occurs, it usually develops 24 hours before to 24 hours after defervescence. Patients
may develop effusions and ascites with a variable amount of bleeding. Enlargement and tenderness of the liver has been reported in up to 40% of patients. Mortality can be as high as 10-20% (over 40% if shock occurs) without early appropriate treatment, but it is as low as 0.2% in hospitals with staff experienced in the disease. Warning signs that dengue shock syndrome is impending include sustained abdominal pain, persistent vomiting, change in level of consciousness (irritability or somnolence), a sudden change from fever to hypothermia, and a sudden decrease in platelet count. Rare presentations of infection include severe haemorrhage, jaundice, parotitis, and cardiomyopathy. Unusual neurological presentations include mononeuropathies, polyneuropathies, encephalitis, and transverse myelitis. Guillain-Barré syndrome has been associated with dengue. Encephalopathy occurs occasionally and may result from cerebral oedema, cerebral haemorrhage, liver failure, or electrolyte imbalances. Laboratory findings commonly associated with dengue include neutropenia, lymphocytosis, increased concentration of liver enzymes, and thrombocytopenia. Diagnosis can be confirmed with several laboratory tests; most often the haemagglutination inhibition test and IgG or IgM enzyme
immunoassays. The non-specific presentation and course of infection underscore the importance of laboratory testing for confirmation of cause. Several diseases should be considered in the differential diagnosis\textsuperscript{13}

**Dengue Shock Syndrome:**

Dengue shock syndrome is associated with very high mortality (around 9.3%, increasing to 47% in instances of profound shock). Severe plasma leakage leading to dengue shock syndrome is associated with cold blotchy skin, circumoral cyanosis, and circulatory disturbances. Acute abdominal pain and persisting vomiting are early warning signs of impending shock. Sudden hypotension may indicate the onset of profound shock. Prolonged shock is often accompanied by metabolic acidosis, which may precipitate disseminated intravascular coagulation or enhance ongoing disseminated intravascular coagulation, which in turn could lead to massive haemorrhage. Dengue shock syndrome may be accompanied by encephalopathy due to metabolic or electrolyte disturbances.\textsuperscript{4} Rhabdomyolysis is not well described as a complication of dengue virus infection and is probably underrecognized. All patients with
severe dengue virus infection should undergo urinalysis, and serum
creatinine kinase levels should be measured if urinalysis reveals
heme. Ocular complications associated with dengue fever are rare
but may result in permanent visual impairment.
Acute acalculous cholecystitis Found in a small proportion of patients
with DF.

**Dengue Fever in Pregnancy:**

More cases of dengue infection in pregnancy can be found
because of the increasing incidence of dengue infection among
adults. The infection should be suspected when a pregnant woman
presents with the similar pattern of symptoms and signs like in a non-
pregnant case. Conservative treatment should be given unless there
are complications.

**Mosquitoes Vectors in Dengue Infections:**

Mosquitoes belonging to the genus aedes (Aedes aegypti,
Aedes albopictus, and Aedes polynesiensis) play an important part in
transmission of dengue. The primary and most important vector is A.aegypti, but A albopictus and A polynesiensis may act as vectors
depending on the geographic location. For instance, A albopictus has been found to sometimes transmit dengue in Thailand, Samui island, India, Singapore, and Mexico. Aedes aegypti, a container breeding, day biting mosquito is found in tropical and subtropical areas. They rest indoors, mainly in living rooms and bedrooms. This maximises man-vector contact and minimises contact with insecticides sprayed out doors, hence contributing to difficulty in controlling this vector. Aedes aegypti can breed in polluted water or small collections of water such as flower vases or coconut shells. Eggs can survive for long periods, as they are capable of withstanding desiccation. ⁴ Humans and mosquitoes are the principal hosts of dengue virus; the mosquito remains infected for life, but the viruses are only known to cause illness in humans.⁸ Improper disposal of garbage or inadequate wastewater drainage facilitates, both consequences of unplanned urbanisation, may be responsible for high mosquito densities in endemic areas. Significant increases in the mosquito larval populations are seen during the rainy season. This may be a reason why epidemics of dengue tend to coincide with the rainy season. Furthermore, ambient temperature and relative humidity affect viral propagation in mosquitoes rates being highest in climates
resembling the rainy season. Environmental temperatures also affect the time to acute viraemia in female mosquitoes, being shorter with rises in temperature. After biting an infected human, dengue viruses enter an adult female mosquito. The virus first replicates in the midgut, reaches the haemocoel and haemolymph, and then gains access to different tissues of the insect. After viral replication in the salivary glands, the infected mosquito can transmit the virus to another human. Ultrastructural studies show viral particles within the nervous system, salivary glands, foregut, midgut, fat body, epidermal cells, ovary and internal body wall lining cells of the mosquito. In contrast, they are absent from muscle, the hindgut, and malphigian tubules. Compared with uninfected mosquitoes, infected ones take longer to complete a blood meal. This may contribute to the efficiency of *A aegypti* as a dengue viral vector. This increased time corresponds to dengue virus infection of organs known to control or influence activities associated with feeding.

Pathogenesis of Dengue Fever/ Dengue Haemorrhagic Fever:
Several studies suggest the existence of transovarial dengue virus transmission in aedes infected female mosquitoes, allowing propagation of virus to their progeny. Such a process would allow it to act as a reservoir for virus maintenance during interepidemic periods (without human or other vertebral host participation). Reports also suggest that dengue viruses may be transmitted sexually from the male to female mosquitoes, but not vice versa. Dengue haemorrhagic fever is distinguished from dengue by the presence of increased vascular permeability, not by the presence of haemorrhage. Patients with dengue may have severe haemorrhage without meeting WHO criteria for dengue haemorrhagic fever. In these cases the pathogenesis probably derives from thrombocytopenia or a consumptive coagulopathy, not from the vascular leak syndrome seen in dengue haemorrhagic fever. Dengue haemorrhagic fever may (grades III and IV) or may not (grades I and II) include clinical shock, referred to as dengue shock syndrome. Dengue virus antigen has been found in a variety of tissues, predominately the liver and reticuloendothelial system. Viral replication is thought to occur primarily in the macrophages, although dendritic cells (Langerhans cells) in the skin may be an early target of
infection. As with yellow fever, focal central necrosis has been found in the liver of patients who have died of dengue. Autopsies of patients who died of dengue haemorrhagic fever show diffuse petechial haemorrhages in most organs and serous effusions of pericardial, peritoneal, and pleural spaces. Dengue virus (by isolation and reverse transcription-polymerase chain reaction) and antibody (including IgM) have been identified in the cerebrospinal fluid, but direct involvement of dengue virus in neuronal damage is controversial. More studies on this are needed. All four serotypes have been associated with dengue haemorrhagic fever. Variations in virus strains within and between the four serotypes may influence disease severity. Secondary infections (particularly with serotype 2) are more likely to result in severe disease and dengue haemorrhagic fever. This is explained by the theory of antibody dependent enhancement, whereby cross reactive but non-neutralising antibodies from a previous infection bind to the new infecting serotype and facilitate virus entry into cells resulting in higher peak viral titres. In primary and secondary infections, higher viral titres are associated with more severe disease. Higher titres may result in an amplified cascade of cytokines and complement activation causing endothelial
dysfunction, platelet destruction, and consumption of coagulation factors, which result in plasma leakage and haemorrhagic manifestations. 13

Prognostic Indicators and Outcome:

The risk of infection was significantly associated with older age, low education and low income. Risk factors that influence disease severity include the strain of virus, and the age, immune status, and genetic background of the host, low education and low income. 3 When a person has been exposed to one flavivirus, cross-reacting antibodies may affect the outcome of infection with a second flavivirus. Thus, for patients with Japanese encephalitis, prior infection with dengue virus, which circulates through much of Asia, appears to protect against severe disease. In contrast, serial infection with different serotypes of dengue virus appears to be associated with more severe disease (e.g., dengue hemorrhagic fever), possibly because of an antibody-dependent enhancement of infection, though the strain of dengue virus may also be important. 18 DHF is also reported to be more severe among females. 4 DHF tends to be
commoner among patients suffering from other chronic illnesses (for example, diabetes mellitus or bronchial asthma.4

Case fatality and hospitalization rates due to DHF/dengue shock syndrome are highest in infants and the elderly.4 Predictive markers for DSS were younger age at onset, altered sensorium, paralytic ileus, and significantly deranged PT. Patients with DSS also had a longer recovery period and required more supportive management in the form of component therapy and ionotropic support.19

**Laboratory Diagnosis of Dengue Infections:**

In most cases of dengue fever, platelet counts and serum biochemistry are normal. However, leucopenia, thrombocytopenia, and raised liver enzymes may be seen. In contrast, DHF is always accompanied by a platelet count <100 x 10⁹/l, haemoconcentration (a rise in the packed cell volume >20% of basal levels), leucopenia, and raised liver enzymes. Elevation of both alanine and aspartate aminotransferase levels occur with plasma aspartate aminotransferase levels being higher in children who develop DHF than in those with dengue fever.4 A leucopenia of 5x10⁹/l has been
suggested to predict the onset of DHF. Initial leucopenia is followed by a relative lymphocytosis (with more than 15% atypical lymphocytes) towards the end of the febrile phase. Abnormal coagulation profiles (prolonged partial thromboplastin time and prothrombin time, raised fibrinogen degradation products), hypoalbuminaemia, and reduced serum complement levels are also seen. These coagulation abnormalities suggest that there is activation of both coagulation and fibrinolysis during acute infection and the degree of activation being greater in severe DHF and dengue shock syndrome. In numerous acute dengue fever patients an early diagnosis will be obtained only by combining IgM antibody detection with detection of virus or virus RNA using RT-PCR. The HFVs (including Rift Valley fever and the flaviviruses) are highly infectious in the laboratory setting and may be transmitted to laboratory personnel via small-particle aerosols. Designated laboratory workers should receive training in handling specimens from any suspected VHF patients in advance of such an event. Laboratory workers should wear personal protective equipment that ensures VHF-specific barrier and airborne precautions. At least 2 cases of nosocomial transmission of dengue (a flavivirus) have been reported in the
medical literature: one through a needlestick injury and the other through bone marrow transplantation. 21

Management of Dengue Infection:

The mainstay of treatment of VHF is supportive, with careful maintenance of fluid and electrolyte balance, circulatory volume, and blood pressure. Closely monitoring vital signs to avoid shock and correct thrombocytopenia to avoid bleeding could be adequate for most patients. In some cases, surgical treatment may be needed for DF fever patients with complications of diffuse peritonitis. 16 Because in some cases intravenous fluids have not reversed hypotension and may have contributed to pulmonary edema, consideration should be given to early vasopressor support with hemodynamic monitoring. Mechanical ventilation, renal dialysis, and antiseizure therapy may be required. Intramuscular injections, aspirin, nonsteroidal anti-inflammatory drugs, and anticoagulant therapies are contraindicated. Steroids are not indicated. 7

Prevention and Control of Dengue Haemorrhagic Fever:
Current procedures to control the disease usually include interrupting the breeding cycles of the mosquitos as well as the use of insecticides. Both are inadequate in the long term. Global warming is also increasing the necessity for prevention, according to World Wildlife Fund spokesman Dr Paul Epstein, from Harvard Medical School. He warned in a November 1998 report on climate change, which was submitted to the United Nations, that the warming of the earth will cause a rise in infectious diseases including dengue, malaria, cholera, yellow fever, and encephalitis.  

The Australian Foundation for the Peoples of Asia and the Pacific, an aid organisation, recently completed a three year programme using the mesocyclops crustacean, which is about 1 mm long and devours the larvae of the mosquitos that carry dengue fever. Researchers say that the results look promising.  

The actual changes in the incidence of malaria and dengue fever would, of course, depend on many factors, including future patterns of social development, land use and urban growth, and the effectiveness of preventive measures such as vector control and vaccination.  

Targeted community cleanup campaigns, particularly those directed at discarded tires and solid waste, are likely to have the greatest impact on reducing the risk
of dengue infection. They included a public education campaign (targeting reducing mosquito breeding habitats) and improved solid waste disposal. Control of dengue currently depends on controlling its mosquito vector. The actual changes in the incidence of malaria and dengue fever would, of course, depend on many factors, including future patterns of social development, land use and urban growth, and the effectiveness of preventive measures such as vector control and vaccination. N,N-diethyl-3-methylbenzamide (DEET) is the most effective, and best studied, insect repellent currently on the market. This substance has a remarkable safety profile after 40 years of worldwide use, but toxic reactions can occur (usually when the product is misused). When DEET-based repellents are applied in combination with permethrin-treated clothing, protection against bites of nearly 100% can be achieved. Plant-based repellents are generally less effective than DEET-based products. Ultrasonic devices, outdoor bug "zappers," and bat houses are not effective against mosquitoes. Highly sensitive persons may want to take oral antihistamines to minimize cutaneous reactions to mosquito bites. early detection and diagnosis of potential dengue fever outbreaks. Efforts to prevent transmission of infection must rely on the meticulous implementation
of and compliance with strict infection control measures. Filoviruses and arenaviruses are highly infectious after direct contact with infected blood and bodily secretions. Vertical transmission of dengue infection in a newborn from Bangladesh was reported.25

**Laboratory and Working Staff Infection Control:**

Given the lack of licensed or effective therapies and vaccines against the HFVs, efforts to prevent transmission of infection must rely on the meticulous implementation of and compliance with strict infection control measures. Filoviruses and arenaviruses are highly infectious after direct contact with infected blood and bodily secretions. A suspected case of VHF must be immediately reported to the hospital epidemiologist (or infection control professional) and to the local or state health department. The epidemiologist (or infection control professional) should, in turn, notify the clinical laboratory (so that additional precautions are put in place) as well as other clinicians and public health authorities. 3 Until the Aedes mosquito can be effectively controlled or a cost effective vaccine developed, dengue can be expected to continue to escalate. 13
Protective Measures against Nosocomial Transmission of HVF:

At least 2 cases of nosocomial transmission of dengue (a flavivirus) have been reported in the medical literature: one through a needlestick injury and the other through bone marrow transplantation. These events, although rare, suggest that nosocomial spread may also be possible for a more feared flavivirus—yellow fever. 26

Strict Adherence to Hand Hygiene:

Double gloves, Impermeable gowns N-95 masks or powered air-purifying respirators, and a negative isolation room with 6-12 air changes per hour, as required by Healthcare Infection Control Practices Advisory Committee standards for airborne precautions
Leg and shoe coverings Face shields Goggles for eye protection
Restricted access of nonessential staff and visitors to patient's room
Dedicated medical equipment, such as stethoscopes, glucose monitors, and, if available, point-of-care analyzers
Environmental disinfection with an Environmental Protection Agency–registered hospital disinfectant or a 1:100 dilution of household
bleach. If there are multiple patients with viral hemorrhagic fever in one health care facility, they should be cared for in the same part of the hospital to minimize exposures to other patients and health care workers. These resources may not be possible in many health care facilities or in a mass casualty situation. In this case, all other measures should be taken and would, in combination, be expected to substantially diminish the risk of nosocomial spread. 3

Postmortem Practices:

Contact with cadavers has been implicated as a source of transmission, trained personnel, using the same infection control precautions as those used to transport ill patients, handle the bodies of patients who die of VHF. Autopsies should be performed only by specially trained persons using VHF-specific barrier precautions. 3

Vaccine:

Much research has been carried out to develop a dengue vaccine that is safe and immunogenic against all four serotypes. Although many of the vaccines developed so far (live attenuated, chimeric, DNA, and subunit vaccines) show promising results, none
are sufficiently immunogenic for routine use. A live attenuated tetravalent vaccine was developed by serial passage of wild type viruses in primary dog kidney cells or other cell types. A randomised, double blind placebo controlled study showed all tetravalent vaccine recipients to have DEN-3 viraemia, and subsequently develop DEN-3 neutralising antibodies. Furthermore, all monovalent DEN-2, DEN-3, and DEN-4, and 60% of DEN-1 vaccine recipients developed neutralising and/or IgM antibodies. When seven formulations of tetravalent live attenuated dengue vaccine were evaluated, 58% of recipients seroconverted (neutralising antibody titre $\geq 1:10$) to three or more serotypes after the first dose, increasing to 76% after the second dose. Both monovalent DEN-2 and the tetravalent vaccines show T-cell responses against all dengue serotypes. However, proliferation responses are higher to DEN-1 and DEN-3 than to DEN-2 and DEN-4, whereas cytotoxic T-lymphocyte responses are higher to DEN-2 and DEN-3 than to DEN-1. It is reasoned, therefore, that any vaccine should induce solid immunity to all 4 serotypes. In neonates the antibodies to dengue virus disappeared in the first year of life. So the most appropriate age for vaccination with a live-attenuated dengue vaccine in an endemic area is one year of age.
Travelers:

The most common tropical infections in travellers who have returned from a tropical country include malaria, enteric fever, viral hepatitis, and dengue fever. Malaria is by far the single most important cause of fever in a recent traveller from the tropics. As falciparum malaria has the potential to be rapidly fatal and is curable with appropriate treatment, this diagnosis must be a primary consideration in such patients. Travellers may unwittingly be infected with dengue virus because transmission is maintained even between epidemics; malaria should be ruled out in those returning with symptoms from an endemic area. In Australia and Germany up to 8% of travellers returning with febrile illnesses were found to have dengue. Because the incubation period can vary from 3 to 14 days (typically between 5 and 7 days) and viraemia can persist up to 12 days (typically 4 to 5 days), dengue can be ruled out if symptoms begin more than 2 to 3 weeks after the patient has left an endemic area or if the fever lasts more than two weeks. Nevertheless, dengue haemorrhagic fever and dengue shock syndrome are rare in
travellers; those with a history of dengue should be advised to protect themselves well from mosquitoes when travelling to endemic areas.\textsuperscript{13}

OBJECTIVES OF THE STUDY

1.1. **General objective:**

To study the prevalence and clinical criteria predicting diagnosis and outcome of dengue viral infection among patients with acute febrile illnesses seeking healthcare in Sudan. The ultimate goal is to assist healthcare providers in the differential diagnosis of malaria and provide evidence in order to avoid over diagnosis of malaria in Sudan.

1.2. **Specific objective:**

1.2.1. To determine the prevalence of Dengue Fever among the acute febrile illnesses.
1.2.2. To identify the clinical criteria predicting diagnosis of Dengue Fever, particularly for the differential diagnosis from malaria. And the predictors of outcome will be studied.

1.2.3. To see if co-infection with other febrile illnesses (e.g. malaria) will affect the course of disease.

1.3. **Secondary objectives (optional):**

These are subsidiary objectives that could be studied during the course of the project but are not the main objectives of the study.
Chapter Two

2- MATERIALS AND METHODS

2.1. Study area:

This is a hospital-based study that will be carried out in Khartoum Teaching Hospital. This is the main and biggest hospital in Sudan and patients from all over the country use to come and treated there. Both outpatients and inpatients with acute febrile illnesses will be candidates for the study.

2.2. Study subjects:

This is a hospital based descriptive case-control study.

Inclusion criteria:

1) Acute fever of less than two weeks duration.
2) With or without encephalopathy or unrousable coma.

3) Age 15-60 years old.

**Exclusion criteria:**

4) Fever due to known underlying infection e.g. diabetic septic foot or a vascular lesion.

5) Comatose or drowsy patients following renal failure or there metabolic disease.

6) Patients on antiviral treatment.

7) Patients with chronic febrile illness > 2 weeks.

2.3. **Study design:**

This is an ambidirectional design (case-control) to allow for studying prevalence and determinants. All eligible patients (adults > 18 years) will be enrolled till completing the sample size. They will be subjected to clinical examinations, laboratory investigations, constituting the control group, regarding the clinical criteria predicting diagnosis and outcome.

2.4. **Data collection methods, instruments used, measurements:**

2.4.1. *The instruments used for data collection:*
A written consent will be obtained from all patients participating in the study. A detailed questionnaire (attached) will be filled for every patients in the study including data about the illness including the onset and symptomatology and detailed clinical examinations looking and recording all signs initially and during follow up. General investigations for acute febrile illnesses will be carried out including ICT for malaria. Serum of 3ml sample will be collected in blood collection tubes and will be screened for IgM and IgG antibodies of the dengue virus.

Student t test will be used to compare the study and the control groups.

**2.4.2. Techniques:**

History taking.

Physical examinations.

Rapid test for screening for IgM and IgG Antibodies for the dengue virus.

Using SD BIOLINE Dengue IgG/ IgM rapid test, this is a solid phase immunochromotographic assay for the rapid, qualitative and differential detection of IgG and IgM antibodies to Dengue virus in human serum, plasma or whole blood. This test is intended for
professional use as aid in the presumptive diagnosis between primary and secondary infection. This test can also detect all 4 Dengue serotypes by using a mixture of recombinant Dengue envelope proteins. Dengue IgG/ IgM test strip has 3 pre-coated line, "G" (Test line for Dengue IgG), "M" (Test line for Dengue IgM) and "C" (Control line) on the surface of the strip. All three lines in result window are not visible before applying any samples.

2.4.3. Study definitions:

Case definition:

2.4.4. Adult patients with acute febrile illness of less than two weeks duration.

2.5. Data management and statistical analysis:

After designing the master-sheet, all variables were introduced into the computer using D-base III for data entry. Consistency checks and analysis was carried out using Statistical Package for Social Sciences (SPSS).

2.6. Implications of study results on disease control:
2.6.1. Expected results and potential contribution of the project to the relevant control program viral infections are usually not looked for or investigated in patients with acute febrile illnesses or encephalitis and only considered by exclusion of other illnesses. There might be a reason for a lot of delay in treating infections resulting from these viral infections and therefore a lot of morbidity and mortality.

2.6.2. Mechanisms to ensure implementation of research results in the health policy of the concerned control program of the ministry of health. National endorsement will be obtained from the federal ministry of health. The results and the recommendations of the study will be presented to the health officials.

2.7. Areas of integration of research activities:

All these data and results will be available to the ministry of health for implementation.
Chapter Three

3- RESULTS

Patient Demographics:

Age and Sex distribution

The mean age of patients in the study group (Fig 1) and the control (Fig 2) was 32.49 and 29.54 years respectively. 57% of them were males and 43% were females (Fig 3) while all the control groups were males. The IgM antibody was detected in (81.8%) of the study
group between the age 15-45 years (Table 1), no sex difference regarding IgM positive group was detected (Table 2).

**Residence**

50.6% of the study group and 49.4% of the control resided in Khartoum area. While 48.3% and 51.7% for the study group and control resided outside Khartoum area respectively. Positive IgM patients were noticed to be from Khartoum area.

Housewives, and student had high positive results for IgM 45% and 36.4% respectively (Table 3).

**Headache:**

(88%) of the patients presented complaining of headache (Fig 4), 11 of them (100%) had positive IgM antibodies for dengue virus (Table 4).

**Bodyaches:**

85 (79.4%) patients of the study group complained of generalized body aches, 10 (11.8%) of them proved to be positive for IgM. This is consistent with (90.9%) of total positive IgM (Table 5).

**Neck pain:**
(43.9%) of the study group patients complained of neck pain, only 7 (63.6% of total positive IgM) of them discovered to have positive IgM antibodies (Table 6).

**Cough:**

Cough was not a common complain in this study group, but we noticed that all the study groups, that proved to be positive for IgM had complained of cough. (100% of IgM positive)

**Nausea and vomiting:**

Constituted complain of (48.6%) patients, with only 7 (63.6% total positive IgM) of them found to be positive for IgM (Table 7).

**Retro-orbital pain:**

Only 24 (22%) patients gave history of retro-orbital pain, 3 (27.3% of total positive IgM ) of them showed serological evidence of IgM antibodies (Table 8).

**Photophobia :**

Constituted complain of 27(25.2%) patients with only 3 (27.3% of total positive IgM) of them found to be positive for IgM (Table 9).
**Diarrhea:**

17 (15.9%) patients complained of diarrhea, only 3 of them (27.3% of total positive IgM) discovered to have positive IgM antibodies. (Table 10)

**Fever:**

(68.5%) of the patient their temperature ranges between (38-38.5°C), seropositive (IgM) patient temperature was between (37.7-38.7°C) (Fig 5).

**Lymphadenopathy:**

Enlarged lymphnodes, were detected in most of the patients (106). 11 (100% of total positive IgM) of them had positive IgM antibodies (Table 11).

**Total white blood count (TWBC):**

Most of the patients of the study group (81 pts) had their total white blood count less than 5.000 per micro liter, 8 of them had positive serology for IgM antibody (72.7% of total positive IgM),

**Immunoglobulin M:**
Only 11 (10.28%) of patients their serum showed a positive test for IgM (Fig 6).

**Immunoglobulin G:**

Was found to be negative for all patients and the control group in the study.

Table 1: Age distribution in relation to positive IgM antibody

<table>
<thead>
<tr>
<th>Years</th>
<th>IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve</td>
<td>-ve</td>
</tr>
<tr>
<td>15-30</td>
<td>6 (54.5%)</td>
<td>54 (56.3%)</td>
</tr>
<tr>
<td>31-45</td>
<td>3 (27.3%)</td>
<td>36 (37.5%)</td>
</tr>
<tr>
<td>46-60</td>
<td>2 (18.2%)</td>
<td>6 (6.3%)</td>
</tr>
</tbody>
</table>
Table 2: Sex distribution in the study and control group

<table>
<thead>
<tr>
<th></th>
<th>CASES</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Study group</td>
<td>Control</td>
</tr>
<tr>
<td>Male</td>
<td>61 (57.0%)</td>
<td>107 (100.0%)</td>
</tr>
<tr>
<td>Female</td>
<td>46 (43.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Residence distribution in the study and control group:

<table>
<thead>
<tr>
<th>Area</th>
<th>CASES</th>
<th>CONTROL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Khartoum</td>
<td>79 (50.6%)</td>
<td>77 (49.4%)</td>
<td>156 (100.0%)</td>
</tr>
<tr>
<td>Out Khartoum</td>
<td>28 (48.3%)</td>
<td>30 (51.7%)</td>
<td>58 (100.0%)</td>
</tr>
</tbody>
</table>
Table 4: Headache distribution in the study and control group

<table>
<thead>
<tr>
<th></th>
<th>IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve</td>
<td>-ve</td>
</tr>
<tr>
<td>Headache</td>
<td>11 (100.0%)</td>
<td>83 (86.5%)</td>
</tr>
<tr>
<td>No headache</td>
<td>13 (13.5%)</td>
<td>13 (12.1%)</td>
</tr>
</tbody>
</table>

Table 5: Bodyaches distribution in the study group with and without IgM

<table>
<thead>
<tr>
<th></th>
<th>IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve</td>
<td>-ve</td>
</tr>
<tr>
<td>Bodyaches</td>
<td>10 (90.9%)</td>
<td>75 (78.1%)</td>
</tr>
<tr>
<td>No bodyaches</td>
<td>1 (9.1%)</td>
<td>21 (21.9%)</td>
</tr>
</tbody>
</table>
Table 6: Neck pain distribution in the study group with and without IgM

<table>
<thead>
<tr>
<th></th>
<th>IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve</td>
<td>-ve</td>
</tr>
<tr>
<td>Neck pain</td>
<td>7 (63.6%)</td>
<td>40 (41.7%)</td>
</tr>
<tr>
<td>No neck pain</td>
<td>4 (36.4%)</td>
<td>56 (58.3%)</td>
</tr>
</tbody>
</table>

Table 7: Nausea and vomiting distribution in the study group with and without IgM

<table>
<thead>
<tr>
<th></th>
<th>IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve</td>
<td>-ve</td>
</tr>
<tr>
<td>Nausea / vomiting</td>
<td>7 (63.6%)</td>
<td>45 (46.9%)</td>
</tr>
<tr>
<td>No nausea / vomiting</td>
<td>4 (36.4%)</td>
<td>51 (53.1%)</td>
</tr>
</tbody>
</table>
Table 8: Retro-orbital pain distribution in the study group with and without IgM

<table>
<thead>
<tr>
<th></th>
<th>IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve</td>
<td>-ve</td>
</tr>
<tr>
<td>Retro-orbital pain</td>
<td>3 (27.3%)</td>
<td>21 (21.9%)</td>
</tr>
<tr>
<td>No retro-orbital pain</td>
<td>8 (72.7%)</td>
<td>75 (78.1%)</td>
</tr>
</tbody>
</table>

Table 9: Photophobia distribution in patient with & without IgM antibody

<table>
<thead>
<tr>
<th></th>
<th>IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve</td>
<td>-ve</td>
</tr>
<tr>
<td>Photophobia</td>
<td>3 (27.3%)</td>
<td>24 (25.0%)</td>
</tr>
<tr>
<td>No photophobia</td>
<td>8 (72.7%)</td>
<td>72 (75.0%)</td>
</tr>
</tbody>
</table>
Table 10: Diarrhea distribution in the study group with & without IgM antibody

<table>
<thead>
<tr>
<th></th>
<th>IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve</td>
<td>-ve</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3 (27.3%)</td>
<td>14 (14.6%)</td>
</tr>
<tr>
<td>No diarrhea</td>
<td>8 (72.7%)</td>
<td>82 (85.4%)</td>
</tr>
</tbody>
</table>

Table 11: Lymphadenopathy distribution in the study group with and without IgM antibody

<table>
<thead>
<tr>
<th></th>
<th>IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve</td>
<td>-ve</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>11 (100.0%)</td>
<td>95 (99.0%)</td>
</tr>
<tr>
<td>No lymphadenopathy</td>
<td></td>
<td>1 (1.0%)</td>
</tr>
</tbody>
</table>
FIG (1) AGE DISTRIBUTION FOR THE STUDY GROUP
FIG (2) AGE DISTRIBUTION FOR CONTROL GROUP
FIG (3) SEX DISTRIBUTION FOR THE STUDY GROUP

43% MALE

57% FEMALE
FIG (4) DISTRIBUTION OF HEADACHE AMONG THE STUDY GROUP
FIG (5) FEVER GRADES AMONG THE STUDY GROUP

<table>
<thead>
<tr>
<th>Temperature</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>37-37.5</td>
<td>2</td>
</tr>
<tr>
<td>37.6-37.9</td>
<td>10</td>
</tr>
<tr>
<td>38-38.5</td>
<td>84</td>
</tr>
<tr>
<td>38.6-38.9</td>
<td>8</td>
</tr>
<tr>
<td>&gt;39</td>
<td>14</td>
</tr>
</tbody>
</table>
FIG (6) IgM ANTIBODY RESULT AMONG STUDY GROUP

89.72%

10.28%

IGM +VE  IGM -VE
This is a prospective hospital-based case control study that was carried out in Khartoum Teaching Hospital in the period from February 2004 to August 2004.

In this study, the distribution of age of patients and control was between 15-60 years. The age group of 15-45 years was the most affected and had significant anti Dengue IgM antibodies in other studies children were reported to be the most affected group ⁹. This study was done in emergency and accident of Khartoum hospital
where most of patients were adult and children were excluded from this study which considered individuals older than 15 years.

Cough (100%), headache (87.9%), and myalgia (79.4%) remained the most complains of the febrile patients selected for this study. Interestingly these complain significantly coincided with the presence IgM antibody against Dengue antigens. These symptoms were common with other febrile illnesses that dominate the emergency and accident unit. The other symptoms were less frequently detected (nausea / vomiting 48.6%, neck pain 43%, photophobia 25.2%, retro-orbital pain 22.4%, diarrhea15.9%). In the study done in Egypt, the main complain of Dengue fever were headache myalgia and retro-orbital pain and they were difficult to differentiate from other febrile illnesses especially malaria and influenza¹.

The grades of Fever in the study group was ranged between 37-39.2 °C, most of patient (68.5%) their temperature range between 38-38.5 °C.

No sex difference was noticed regarding IgM positive group, indicating no gender preference for Dengue infection.
In this study no hemorrhagic features were observed, and this may augment the hypothesis that African ethnic group’s were more resistant to hemorrhagic fever. They may be immuned against severe hemorrhagic fever. In this study all patients recovered within 1-2 weeks with supportive treatment.

The clinical examination of the studied patient showed lymphadenopathy (cervical, submandibular), in 100% of the study group who had significant IgM titer against Dengue.

In other patients who did not react with Dengue antibody 99% also had lymphadenopathy. So other causes of lymph node enlargement are highly possible in the tropical areas.

Non of study group or the control group had IgG detected antibody against Dengue in this study this result disagree with previous study that done in Sudan during an outbreak of acute febrile illness occurred between August and September 1989 in the Northern Province of Sudan that coincided with a high phlebotomone density. In that study 185 febrile individuals studied were investigated and tested for IgG and IgM antibody against arboviruse using enzyme immunoassay (EIA). Prevalence of IgG antibody was 59% for West Nile (WN), 53% for Sandfly Fever Sicilia (SFS), 32% for Sandfly
Fever Naples (SFN), 39% for Yellow Fever (YF), 24% for dengue (DEN-2), 23% for Rift Valley Fever (RVF), 12 for Chikungunya (CHIK) and 5% for Crimean-Congo Hemorrhagic fever (CCH) viruses. The prevalence of IgM antibody to SFN was 24% while it was 5% for the other viruses. They use ELISA for detection, but in our study we use a new rapid test (SD BIOLINE Dengue IgG/ IgM), so we suggest to screen a larger sample number to assure validation of this new rapid test.

The prevalence of IgM in our study was 10.25%, while in that studies was only 5%, these slight differences could be attributed to the seasonal variation in the disease prevalence.

The frequency of recent infection (IgM) was estimated to be 9.8% in study done in Salvador 2000, which coincided with our study finding. But in the study done by joao Siqueira in central Brazil seroprevalence of dengue was 29.5%.

Another study in Sudan, that was carried out on patients with cerebral malaria concluded that a significant number of cerebral malaria patients had antibodies of IgM class to Dengue virus and West Nile virus that was more significant than in control group (normal individuals).
CONCLUSION

• This is a hospital-based prospective case control study that was carried out in Khartoum Teaching Hospital in the period (Feb 2004 - Aug 2004). Both outpatients and inpatients with acute febrile illnesses will be candidates for the study.

• This study aimed to determine prevalence of dengue infection, and pattern of clinical presentation, among febrile Sudanese persons who sought medical advice.

• The mean age of the study group and control was 32.49 and 29.4 years, 57% were male, and 43% of them were females, all
the control group were males. No significant sex difference between positive IgM group.

- The study showed that possible presentations of this virus are high grade fever (37-38.5 c°), cough (100%), headache (100%), myalgias (90.9%) and neck pain (63.3%), while diarrhoea retro-orbital, and photophobia constitutes only (27.3%) are less common presentations in this study. Lymphadenopathy (cervical and submandibular) was detected in most of the study group (99.1%) and all IgM positive group, raising the high possibility of other causes rather than dengue virus.

- No hemorrhagic manifestations among studied group were detected and all patients recovered spontaneously with in 1-2 week’s duration.

- IgM was detected in 10.28% of the study group, but no IgG was detected for both control and the study group, indicating primary infection is commoner than secondary infection in this study.
RECOMMENDATIONS

1. There might be a lot of delay in treating infections resulting from dengue viral infection and therefore a high morbidity and mortality. Dengue diagnosis should be considered in patient presented with febrile illness after exclusion of malaria.

2. Increasing the awareness of the public health and patients regarding these infections, and medications for viral disease will be availed and registered in the medical supplies to be affordable for these patients.

3. Facilities for diagnosis and control of viral infections should be established.
4. A large studies should be conducted to determine the extent of these viral infections.

REFERENCES

1. Jacobs M. Dengue: Emergence As A Global Public Health Problem And Prospects For Control Transactions Of The Royal Society Of Tropical Medicine And Hygiene Volume 94, Issue 1, January-February 2000, Pages 7-8


29. Watts Dm, El-Tigani A, Botors Ba, Salib AW. Arthropod-borne viral infections associated with a fever outbreak in the northern province of Sudan. MD Thesis. 1989; University of Khartoum; Sudan.

Questionnaire

The prevalence of viral infections (WNF, HSV, Dengue) among acute febrile ill

No:...

Personal Data:
Name…………………… Occupation…………………… Sex  M……F……
Residence……………….  Marital status…………………. Age………………
Address………………….. Tribe…………………………….. Tel………………

Symptoms: Yes
Headache…………………………………………………………………………
Body aches……………………………………………………………………
Photophobia……………………………………………………………………
Neck pain ………………………………………………………………………
Nausea & vomiting ……………………………………………………………
Retro-orbital pain ……………………………………………………………
Diarrhea ………………………………………………………………………
Cough ………………………………………………………………………
Convulsions……………………………………………………………………
Loss of consciousness…………………………………………………………
Unsteadiness……………………………………………………………………
Hallucination……………………………………………………………………
Others…………………………………………………………………………

Past History:
Hypertension……………………………………………………………………
Diabetes…………………………………………………………………………
Meningitis………………………………………………………………………
Encephalitis……………………………………………………………………
Malaria within the last three months…………………………………………
Trauma…………………………………………………………………………
Alcohol……………………………………………………………………… I
Others………………………………………………………………………...

