

# **Clinical Research in Infectious Diseases**

#### Research Article

# Clinical Manifestations and Biological Markers Noted in Adults Infected by Dengue Virus in Najran Region: Study of 60 Cases

Naoufel Kaabia<sup>1\*</sup>, Farhat Chelbi<sup>1</sup>, Muhammad Ilyas<sup>1</sup>, Imed Harabi<sup>2</sup>, Mohamed Ahmed Adam<sup>1</sup>, Dalinda Arfaoui<sup>1</sup>, and Saad AlGhamdi<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, Najran Armed Forces Hospital, Saudi Arabia

#### **Abstract**

**Aim:** Aim of this study was to determine clinical manifestations and describe hematological and biochemical markers in adult patients admitted for dengue fever.

**Methods:** It was a retrospective, descriptive study including adult patients with confirmed DF, admitted in Internal Medicine Department at Armed Forces Hospital during September to December 2013. Aaccording to 2009-WHO dengue classification, our population was dived in Group A (30 patients): patients without warning signs. Group B (30 patients): patients with warning signs (presence of one or more of these manifestations: abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, liver enlargement, increasing hematocrit with decreasing platelets).

**Results:** Among 112 patients suspected to have DF, 63 cases were confirmed by dengue RT-PCR, and 60 were enrolled in our study, 36 males and 24 females, their mean age were 35.9 years. The mean duration of hospitalization was 3.6 days (1 to 9 days). Fever and body ache were the most common symptoms present in 90% and 81.7% of patients. 8 patients presented mucosal bleeding; it was microscopic hematuria in all cases, associated with vaginal bleeding in one patient and epistaxis in two cases. Leucopenia and thrombocytopenia were noted in 90% and 61.6% respectively. 44.8% of patients had prolonged APTT. The most frequent biochemical abnormalities were high ALT, AST and CPK in 61%, 83.3% and 58.4% respectively. No case of severe DF was noted in our study. All patients received symptomatic treatment and recovered. Comparison of Group A and Group B showed that average WBC count was lower in Group B.

**Conclusion:** Non-severe dengue infection dominated the clinical picture in our study and none of the patients developed sever dengue (DHF or DSS). Although this disease is not common in Najran, surveillance should be attentive.

# INTRODUCTION

Dengue fever (DF), and its more severe forms, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), is the most important arthropod-transmitted viral disease affecting humans in the world today.50–100 million cases of DF and several hundred thousand cases of DHF occur [1] each year.

#### \*Corresponding author

Naoufel Kaabia, Department of Internal Medicine, Najran Armed Forces Hospital, Saudi Arabia, Tel: 966567849808; Email: naoufelkaabia2001@yahoo.fr

Submitted: 13 May 2016 Accepted: 06 June 2016 Published: 15 June 2016

ISSN: 2379-0636 Copyright

© 2016 Kaabia et al.

#### OPEN ACCESS

#### Keywords

- Dengue fever
- Adults
- Clinical Manifestations
- Dengue virus
- Saudi Arabia

Dengue fever is caused by the dengue viruses which belong to the genus flavivirus, family Flaviviridae. There are 4 antigenically related but distinct dengue virus serotypes, DEN- I, DEN-II, DEN-III, and DEN-IV, all of which can cause DF-DHF. These viruses are transmitted to humans by female mosquitoes mainly of species *Aedes aegypti* and, to a lesser extent, *Aedes albopictus* [2].

<sup>&</sup>lt;sup>2</sup>Department of Family Medicine, Najran Armed Forces Hospital, Saudi Arabia

Infection with one of serotypes of dengue virus is a systemic and dynamic disease, and cause a wide spectrum of clinical manifestations, with severity ranging from asymptomatic infection to a flue like state (DF) to a hemorrhagic form (DHF), characterized by plasma leakage and bleeding, representing a life-threatening complication [3]. After the incubation period the illness begins abruptly and is followed by three phases: febrile, critical and recovery [4] Therefore, the main problem for physicians during the initial days of illness is to discriminate, first between dengue and other febrile illnesses and second, among dengue cases, between non complicated cases and those evolving into DHF or DSS. However, clinical dengue diagnosis remains difficult.

In 1994, dengue virus was isolated in Jeddah, Saudi Arabia, for the first time from a fatal case of dengue hemorrhagic fever and from another nonfatal case [5]. Since that time, three serotypes (DENV-1, DENV-2and DENV-3) were found to circulate, often with more than one serotype in each outbreak. There was a major outbreak caused by DENV-1 and DENV-2 in 1994 while DENV-3 emerged in 1997. In the summer of 2004, all three serotypes were isolated and this gave way to an extended outbreak of DENV-1 that stretched from the summer of 2005 through early 2006 [6]. Most of the cases were dengue fever, with fewer cases of DHF, DSS and death. Dengue fever continues to be a significant health problem in the western region of Saudi Arabia and usually linked to the proliferation of the mosquito vector populations following the rain season [7].

Najran city in Southern Saudi Arabia is on the border with Yemen. It is the capital of Najran region and has a population of ≈250,000. It is an agricultural city in which residents commonly raise domestic animals in their backyards. This region was known to be endemic for brucellosis and Alkhurma hemorrhagic fever [8]. According to Najran Preventive Medicine Department few imported cases of DF were notified every year [unpublished results] but there was no data about clinical and laboratory profile of patients with DF in this region. During the last term of 2013,there was an outbreak of Dengue fever in this region and patients admitted to Najran Armed Forces Hospitalwith dengue fever were studied to determine clinical, hematological and biochemical manifestations.

# **MATERIALS AND METHODS**

# Study design

It was a descriptive study among patients with confirmed dengue virus infection in Najran Area-KSA during 2013 (September-December)

#### **Patients**

All adult patients admitted in Internal Medicine Department at Najran Armed Forces Hospital, with confirmed DF were included in our study.

#### **Methods**

On admission all patient were evaluated by a complete history, physical exam, two sets of blood culture, Brucella serology, urine analysis, CBC, coagulation profile, liver enzymes, renal function tests, serum electrolytes, CRP, LDH and CK. Early serum and plasma samples were also taken and sent to Virology PCR Department at Riyadh Regional Laboratory where Dengue RNA (RT-PCR), Alkhurma RNA (RT-PCR), Alkhurma serology, RVF RT-PCR and RVF serology were tested. In each patient, demographic, epidemiological, clinical, and laboratory findings were recorded from the medical charts. During hospitalization, some investigations were repeated according to the course of the disease. Convalescence sample was not done.

# **Definitions and Diagnostic Criteria**

Dengue infection was defined as a febrile illness associated with positive dengue RT-PCR. Aaccording to 2009-WHO [9] dengue classification, our population was dived in 3 groups:

**Group A**: patients without warning signs

**Group B**: patients with warning signs (presence of one or more of these manifestations: abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, liver enlargement, increasing hematocrit with decreasing platelets)

**Group C**: patients with severe dengue (dengue with severe plasma leakage, severe bleeding, or organ failure).

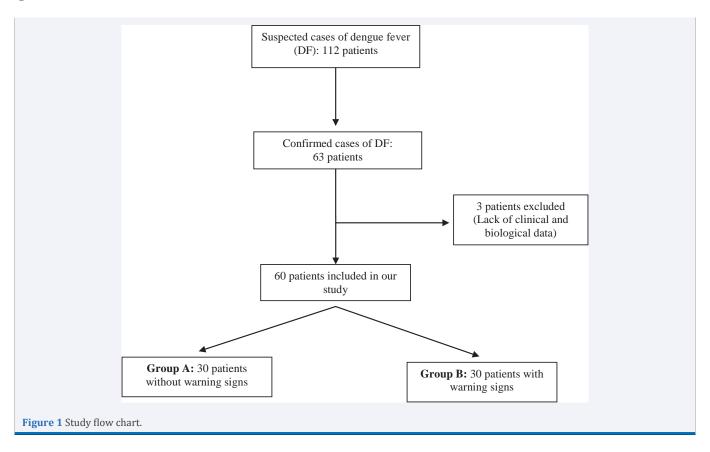
Cutoff values of white bloodcell count ( $<4000/\mu L$ ), neutrophil count (<1500/ $\mu$ L), lymphocyte count (<1000/ $\mu$ L), count (<500/ μL) were used to define leucopenia, neutropenia, lymphopenia, and marked lymphopenia, respectively. A cutoff value for platelets (<100,000/µL) was used to define thrombocytopenia [10]. Complete Blood Count (CBC) was done more than two times during the illness. We considered the lowest WBC count to determine the extent of leucopenia. We also compared the extent of leucopenia in the initial phase of illness in the individual patients and between the two groups (Group A and Group B). If the decrease in WBC count was more than 30% during the period of illness, it was considered as significant decrease in WBCs. For Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), LDH, CK, Serum Electrolytes and Coagulation Profile reference ranges given by the laboratory were considered as cut off values. All data was collected on structured forms and was analyzed thoroughly.

# Statistical analysis

Data was coded, validated, and analyzed using SPSS for Windows Version 17.0. Descriptive statistics were used to analyze the study variables. Chi-square and t-test were used respectively to compare percentages and means. P-value < 0.05 was considered significant.

# **RESULTS**

During the study period 112 patients were admitted for suspicion of dengue infection. Diagnosis was confirmed by positive dengue virus RT-PCR in 63 patients.3 cases were excluded due to lack of clinical and laboratory data. 60 patients were included in our study. All patients were infected by serotype 2 (DEN-II). Keeping in view the recent WHO classification criteria, 30 (50%) cases were without warning signs (Group A), 30 (50%) patients had warning signs (Group B), and none had severe signs of dengue infection(Group C), probably it was first outbreak of dengue fever (primary infection with DEN-II) in Najran Figure (1). There were 36 (60%) males and 24 (40%) females, their



**Table 1:** Clinical symptoms seen in adult patients with confirmed dengue fever infection (N=60).

Clinical manifestations	n	Percentage %
Fever	54	90
Skin rash	15	25
Mucosal bleeding	8	13.3
Vomiting	21	35
Body ache	49	81.7
Headache	16	26.7
Non bloody diarrhea	23	38.3
Abdominal pain	17	28.3
Cough	7	11.7
Sore throat	3	5

mean age was 35.9 years, and ranged between 16 to 82 years. The mean duration of hospital stay was 3.6 days (1 to 9 days). No patient was admitted in ICU. All patients recovered completely and were discharged.

Fever and body ache were the most common symptoms seen in 90% and 81.7% patients respectively. Others common clinical features were diarrhea without blood in 23 (38.3%) cases, persistent vomiting in 21 (35%), abdominal pain in 17 (28.3%) and headache in16 (26.7%).15 patients (25%) developed erythematous maculopapular skin rash. 8 (13.3%) patients presented mucosal bleeding with microscopic hematuria in all cases, associated with epistaxis in two and vaginal bleeding in

one case. These clinical features are summarized in Table (1).

Leucopenia (90%), lymphopenia (69.7%), thrombocytopenia (61.6%), rapid decrease in WBC (66.6%) and prolonged APTT (44.8%) were the most frequent hematological findings. High AST, ALT and CK were noted in 83.3%, 61% and 58.4% respectively. Tables (2 & 3) summarized all hematological and chemical abnormalities observed in our study.

The comparative study between Group A and Group B showed that the average number of white blood cells (WBC) was lower in group B, and significant decrease in WBC was more frequent in this group of patient with warning signs (Table 4).

# **DISCUSSION**

Typically, people infected with dengue virus are asymptomatic (80%) or have only mild symptoms such as an uncomplicated fever [11,12]. Others have more severe illness (5%), and in a small proportion it is life-threatening [11]. The more severe manifestations, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) occur in less than 1 percent of dengue virus infections [13]. In our study, keeping in view WHO classification of severity for dengue virus infection, out of total 60 patients who were studied, 30 (50%) patients were with mild infection and not having warning symptoms and signs (Group A) and 30 (50%) patients were with moderately severe infection and had warning symptoms and signs(Group B). During the study period no patient was admitted with sever dengue virus infection (Group C- DHF, DSS).Our study revealed that dengue virus infections in adults in Najran were mostly uncomplicated DF and cases with warning signs (Group B) and without warning

signs (Group A) being in equal ratio i.e. 50% each. This finding is different than previous reports that demonstrate severe cases are more predominant [14,15].

In fact, DHF can occur during infection with any of the four dengue serotypes. A fifth type has been reported in 2013 [16]. Several prospective studies have suggested that the risk is highest in secondary infection with dengue-2 viruses (DENV-II) [17]. Indeed, an outbreak of dengue-2 virus infections in Cuba in 1981 followed an outbreak of dengue 1 virus infections in 1977 that involved 45 percent of the island's population; 98 percent of cases of DHF/DSS in children and adults were associated with secondary infections [18]. The increased risk of DHF in

**Table 2:** CBC and coagulation profile data noted in adults with confirmed dengue infection.

CBC and coagulation profile abnormalities		Percentage %
Leucopenia (<4000 cells/ml), N=60		90
Neutropenia (<1500 cells/ml), N=56		75
Mild (1000-1500)	11	19.6
Moderate (500-1000)	18	32.2
Severe (<500)	13	23.2
Lymphopenia (<1000 cells/ml), N=56	39	69.7
Moderate (500-1000)	32	57.1
Marked (<500)	7	12.5
Thrombopenia (<150x10 <sup>3</sup> ), N=60	37	61.6
Mild (100- 150 x10 <sup>3</sup> )	20	33.4
Moderate (50-100 x10 <sup>3</sup> )	15	25
Severe (<50 x10 <sup>3</sup> )	2	3.2
Anemia (Hemoglobin <12 g/dl), N=60	5	8
Prolonged INR (>1.2), N=59	14	23.7
Prolonged APTT (>36 seconds), N=58	26	44.8
Significant decrease in WBCs, N=60		66.6
Rapid decrease in platelets, N=60	37	61.6

N: number of patients tested/ n: number of patient with abnormalities

**Table 3**: Chemical abnormalities noted in adults with confirmed dengue infection.

Chemicals abnormalities	n	Percentage %
ALT>40, N=59	36	61
AST>40, N=24	20	83.3
Hyponatremia (sodium <135), N=59	19	32.2
Hypokalemia (potassium>3.4), N=59	7	11.8
High LDH (>390), N=50	9	18
High CPK (>195), N=53	31	58.4
High GGT, N=59	26	44
Hypoalbuminemia (<40g/l)	10	16.7
High CRP (>10mg/l), N=56	19	33.9
Renal impairment*, N=60	1	1.6
Proteinuria in urine analysis, N=56	20	35.7

\*Renal impairment: creatinine>1.3 mg/dl, N: number of patients tested, n: number of patient with abnormalities test, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, LDH: Lactate Dehydrogenase, CPK: Creatine Phosphokinase, GGT: Gamma-Glutamyltranspeptidase, CRP: C-reactive protein

**Table 4:** Comparison between patients with and without warning signs.

Variables	Patients without warning signs Group A (N=30)	Patients with warning signs Group B (N=30)	р
Gender			
Male	18	18	NS
Female	12	12	
Age (mean± SD)	40.7±16	31.1±16.8	NS
Presence of skin rash, N=60	6	9	NS
Presence of Body ache, N=60	29	20	0.03
Significant decrease in WBCs, N=60	17	23	0.03
WBC (mean± SD), N=56	2.89±1.3	2.01±0.7	0.002
Lymphocytes (mean± SD) N=56	0.92±0.4	0.83± 0.34	NS
Platelets (mean± SD), N=60	153.2±69	120.7± 48.03	0.04
APTT (mean± SD), N=58	35.8±5.01	36.94±6.2	NS

secondary dengue virus infections is felt to reflect the differences in immune responses between primary and secondary dengue virus infections: antibody-dependent enhancement of infection, enhanced immune complex formation, and/or accelerated T lymphocyte responses. In our study although all patient were infected by serotype 2, no severe case was noted. Probably it was primary infection with dengue virus-2since it was the first outbreak of dengue fever in Najran.

Regarding the influence of age on the severity of infection, the risk for DHF appears to decline with age, especially after age 11 years. During the 1981 epidemic of DHF in Cuba, the modal age of DHF cases and deaths was four years, although the frequency of secondary dengue-2 infections was similar in those 4 to 40 years of age [19]. A specific population at higher risk for DHF in endemic areas is infants, particularly those between 6 and 12 months of age. These children acquire dengue virus–specific antibodies through placenta and become susceptible to primary dengue virus infection when antibody levels decline below the neutralization threshold [20,21].

In our study population all dengue virus infections were mostly uncomplicated DF, with no case of severe dengue (DHF, DSS). This fact can be explained by sample characteristics like: a) the relatively small size (n=60) of sample, b) all patients were adult, c) no previous exposure to dengue virus since it was the first outbreak of dengue in the region, d) our study took place during the dengue season when the prior probability of dengue was high and patients were given appropriate medical care promptly decreasing the chance of developing complications. e) we may have under-estimated the number of severe cases of dengue infection because we relied heavily on serial hematocrit results which may be influenced by intravenous fluid therapy and abdominal ultrasound was not done systematically for all patients to look for as cites as plasma leakage sign.

Most dengue virus infections in adults are reported to be symptomatic [22,23]. For example, in a survey of 41 military personnel with serologic evidence of dengue virus, approximately

86 percent of infections were symptomatic [24]. In contrast, most infections among children under age 15 years are asymptomatic or minimally symptomatic. In one study of schoolchildren in rural Thailand, 53 percent of dengue virus infections were not associated with a recognized febrile illness despite intense active surveillance [25]. Several clinical manifestations: headache, retro orbital pain, arthralgia, myalgia, vomiting, petechiae and melena are more observed in adults with dengue infection than in pediatric population. However, epistaxis, oliguria and hepatomegaly are more frequent in children [26]. Frequency of clinical manifestation in adults with dengue infection varied according to various series. Common dengue-induced laboratory changes include thrombocytopenia, leukopenia, atypical lymphocytes, immature neutrophils, raised hematocrit (Hct) and liver enzymes, mild increases in prothrombin time (PT) and activated partial thromboplastin time (aPTT), and increased fibrinolysis. Alanine transaminase (ALT)/AST increase tend to be mild to moderate (2.5-5 + upper limit of normal, but acute liver failure with severe bleeding may occur [14,15].

In our study most common symptoms were fever 90% and body aches 81.7%, while diarrhea 38.3%, vomiting 35%, abdominal pain 28.3%, headache 26.7%, skin rash 25% were present in more than one fourth of the patients. Mucosal bleeding, cough and sore throat were uncommon symptoms and were present in less than 13% of patients. Elevated liver enzymes (AST 83.3%, ALT 61%, GGT 44%) followed by CPK 58.4% were the most common chemical abnormalities. There was Hyponatremia (sodium <135) in 32.2%, Proteinuria in 35.7%, High CRP (>10mg/l) 33.9%, Hypoalbuminemia (<40g/l) 16.7%.

A similar study of 143 confirmed adult dengue cases in 2008 from Hanoi, Vietnam has shown fever (100%), headache (92.2%), myalgia (76.8%). rash (51%), vomiting (46.1%), cough (44.9%), eye pain (40%), bleeding (36.2%), diarrhea (34.5%), and itching (28.4%)as more frequent symptoms while abdominal pain (28.1%) was in same frequency [27].

In a prospective cohort study of 268 confirmed cases with dengue infection in West Java, Indonesia, symptoms and signs that were frequently reported included myalgia(91.3%), headache (90.9%), arthralgia (63.8%), and nausea (59.6%). Leukopenia (<4000/mm³) was detected in 29% of patients and thrombocytopenia (<150,000/mm³) was detected in 34% of patients. The majority of DF cases presented with an undifferentiated fever 38.6% (81/210) also presented with hemorrhagic signs or mild thrombocytopenia. There were no cases with complications such as organ impairment [28].

In order to look for other clinical and biological warning signs of dengue infection in our population, we compared patients with and without warning signs (Group B, Group A). Despite our small number of patients, our study showed that significant leucopenia was more frequent in group B. More prospective studies with large number of patients are needed to confirm this data.

# **CONCLUSION**

To conclude, non-severe dengue dominated the clinical picture in our study and none of the patients developed severe dengue infection. In our study epidemiological, clinical and laboratory parameters proved similar to features of adult dengue

infections in other parts of the word. More research is needed in community and hospital settings to broaden our knowledge of dengue epidemiology and various aspects of dengue infection. It will help in devising effective public health strategies and assess their preparedness for epidemics.

# **REFERENCES**

- Gubler DJ, Clark GG. Dengue/dengue hemorrhagic fever: the emergence of a global health problem. Emerg Infect Dis. 1995; 1: 55-57.
- 2. WHO: Media Centre; Dengue and severe dengue, Fact sheet. 2016.
- 3. Martina BE, Koraka P, Osterhaus AD. Dengue virus pathogenesis: an integrated view. Clin Microbiol Rev. 2009; 22: 564-581.
- Rigau-Pérez JG, Clark GG, Gubler DJ, Reiter P, Sanders EJ, Vorndam AV. Dengue and dengue haemorrhagic fever. Lancet. 1998; 352: 971-977.
- Fakeeh M, Zaki AM. Virologic and serologic surveillance for dengue fever in Jeddah, Saudi Arabia, 1994-1999. Am J Trop Med Hyg. 2001; 65: 764-767.
- Alhaeli A, Bahkali S, Ali A, Househ MS, El-Metwally AA. The epidemiology of Dengue fever in Saudi Arabia: A systematic review. J Infect Public Health. 2016; 9: 117-124.
- Aziz AT, A-Shami SA, Mahyoub JA, Hatabbi M, Ahmad AH, Rawi CS. An update on the incidence of dengue gaining strength in Saudi Arabia and current control approaches for its vector mosquito. Parasit Vectors. 2014; 3: 258.
- 8. Alzahrani AG, A Shaiban HM, A Mazroa MA, A-Hayani O, Macneil A, Rollin PE, et al. Alkhurma hemorrhagic fever in humans, Najran, Saudi Arabia. Emerg Infect Dis. 2010; 16: 1882-1888.
- Fruth U. Considerations regarding efficacy endpoints in HIV vaccine trials: executive summary and recommendations of an expert consultation jointly organized by WHO, UNAIDS and ANRS in support of the Global HIV Vaccine Enterprise. Vaccine. 2009; 27: 1989-1996.
- 10.WHO. Dengue Haemorrhagic Fever: Diagnosis, Treatment, Prevention and Control, 2nd Edition. Geneva, World Health Orgnization. 1997.
- 11. Whitehorn J, Farrar J. Dengue. Br Med Bull. 2010; 95: 161-173.
- Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. Nature. 2013; 496: 504-507.
- 13. Díaz A, Kourí G, Guzmán MG, Lobaina L, Bravo J, Ruiz A, et al. Description of the clinical picture of dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS) in adults. Bull Pan Am Health Organ. 1988; 22: 133-144.
- 14. Corwin AL, Larasati RP, Bangs MJ, Wuryadi S, Arjoso S, Sukri N, et al. Epidemic dengue transmission in southern Sumatra, Indonesia. Trans R Soc Trop Med Hyg. 2001; 95: 257-265.
- 15. Suwandono A, Kosasih H, Nurhayati, Kusriastuti R, Harun S, Ma'roef C, et al. Four dengue virus serotypes found circulating during an outbreak of dengue fever and dengue haemorrhagic fever in Jakarta, Indonesia, during 2004. Trans R Soc Trop Med Hyg. 2006; 100: 855-862
- 16. Normile D. Tropical medicine. Surprising new dengue virus throws a spanner in disease control efforts. Science. 2013; 342: 415.
- 17. Sangkawibha N, Rojanasuphot S, Ahandrik S, Viriyapongse S, Jatanasen S, Salitul V, et al. Risk factors in dengue shock syndrome: a prospective epidemiologic study in Rayong, Thailand. I. The 1980 outbreak. Am J Epidemiol. 1984; 120: 653-669.
- 18. Guzmán MG, Kourí G, Martínez E, Bravo J, Riverón R, Soler M, et



- al. Clinical and serologic study of Cuban children with dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS). Bull Pan Am Health Organ. 1987; 21: 270-279
- 19. Guzmán MG, Kouri GP, Bravo J, Soler M, Vazquez S, Morier L. Dengue hemorrhagic fever in Cuba, 1981: a retrospective seroepidemiologic study. Am J Trop Med Hyg. 1990; 42: 179-184.
- 20. Kliks SC, Nimmanitya S, Nisalak A, Burke DS. Evidence that maternal dengue antibodies are important in the development of dengue hemorrhagic fever in infants. Am J Trop Med Hyg. 1988; 38: 411-419.
- 21. Simmons CP, Chau TN, Thuy TT, Tuan NM, Hoang DM, Thien NT, et al. Maternal antibody and viral factors in the pathogenesis of dengue virus in infants. J Infect Dis. 2007; 196: 416-424.
- 22.Tantawichien T. DENGUE FEVER AND DENGUE HEMORRHAGIC FEVER IN ADULTS. Southeast Asian J Trop Med Public Health. 2015; 46: 79-98.
- 23. Sharp TW, Wallace MR, Hayes CG, Sanchez JL, DeFraites RF, Arthur RR, et al. Dengue fever in U.S. troops during Operation Restore Hope, Somalia, 1992-1993. Am J Trop Med Hyg. 1995; 53: 89-94.

- 24.SABIN AB. Research on dengue during World War II. Am J Trop Med Hyg. 1952; 1: 30-50.
- 25. Endy TP, Chunsuttiwat S, Nisalak A, Libraty DH, GreenS, Rothman AL, et al. Epidemiology of in apparent and symptomatic acute dengue virus infection: a prospective study of primary school children in Kamphaeng Phet, Thailand. Am J Epidemiol. 2002; 156: 40-51.
- 26.Kittigul L, Pitakarnjanakul P, Sujirarat D, Siripanichgon K. The differences of clinical manifestations and laboratory findings in children and adults with dengue virus infection. J Clin Virol. 2007; 39: 76-81.
- 27. Taylor WR, Fox A, Pham KT, Le HN, Tran NT, Tran GV, et al. Dengue in adults admitted to a referral hospital in Hanoi, Vietnam. Am J Trop Med Hyg. 2015; 92: 1141-1149.
- 28. Kosasih H, Alisjahbana B, Nurhayati, de Mast Q, Rudiman IF, Widjaja S, et al. The Epidemiology, Virology and Clinical Findings of Dengue Virus Infections in a Cohort of Indonesian Adults in Western Java. PLoS Negl Trop Dis. 2016; 10: 0004390.

# Cite this article

Kaabia N, Chelbi F, Ilyas M, Harabi I, Adam MA, et al. (2016) Clinical Manifestations and Biological Markers Noted in Adults Infected by Dengue Virus in Najran Region: Study of 60 Cases. Clin Res Infect Dis 3(1): 1024.