

ORIGINAL ARTICLE

A STUDY OF CLINICAL FEATURES AND LABORATORY PROFILE OF DENGUE FEVER IN OUTPATIENT SETTING

Reda Goweda^{1,3} and Ahmed Faisal²¹Department of Family Medicine, Faculty of Medicine, Suez Canal University, Egypt.²Department of Infectious and Endemic Diseases, Faculty of Medicine, Suez Canal University, Egypt.³Department of Community medicine, Faculty of Medicine, Umm Al-Qura University, Saudi Arabi.

Corresponding author: Reda Abdelmoaty Goweda

Email: redagoweda@yahoo.com

ABSTRACT

Dengue fever (DF) is one of the common mosquito-borne viral diseases. It is transmitted by *Aedes aegypti* and *Aedes albopictus*. The aim to study the clinical and laboratory manifestations of serologically confirmed cases of DF in outpatient clinics. This cross-sectional study was carried out in outpatient setting. According to WHO criteria all patients above 14 years old who were suspected to have DF were tested by IgM dengue antibody test. Additionally all patients underwent history, clinical examination and investigation including complete blood count, liver function test and abdominal ultrasound. Data was analyzed using SPSS version 20. Out of 126 patients presented with acute febrile illness, 71 (56.3%) had seroreactivity for dengue IgM antibodies. Fever, headache and musculoskeletal pain were the most common clinical presentation (100%). Decreased appetite (92.9%), retro-orbital pain (78.8%) and dizziness (64.7%) were the next common symptoms. 29 (40.8%) had hepatomegally, 11 (15.4%) had splenomegally. Elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were observed in 58 (81.6%) and 53 (74.6%) respectively. Lastly; Fever associated with headache, retro-orbital pain, along with thrombocytopenia and elevated liver transaminases should prompt a clinician on the possibility of DF. Increased community awareness and vector control measures need to be strengthened to reduce the burden of dengue cases.

Keywords: Dengue fever, Clinical, Laboratory.

INTRODUCTION

Dengue fever (DF) is an acute febrile illness transmitted by *Aedes aegypti* and *Aedes albopictus* and considered one of the most important mosquito-borne viral diseases¹. The World Health Organization (WHO) classified DF as one of the top 10 threats to global health in 2019². It was estimated that 390 million person infected by dengue virus per year, out of them 96 million can manifest clinically³.

In Saudi Arabia, isolation of the dengue virus was done for the first time during an outbreak, this was happened in 1994 in Jeddah, where 289 established cases were reported⁴. The ministry of health in Saudi Arabia recorded 3350 dengue cases in 2009⁵. Recent systematic review (2016) found that the studies done inside Saudi Arabia found that the prevalence of DF ranging from 31.7% to 56.9% among patients presented with acute febrile illness clinically suggesting dengue fever. Studies were done in Jizan (2013), Jeddah (2006) and Makkah (2004) found the prevalence of 31.7%, 48.75% and 56.9% respectively^{7,8}. DF is endemic only in certain cities in Saudi Arabia (Jeddah, Makkah, Madinah and Jizan), this may be due to high humidity and temperatures that may help worsen the condition^{10,11}.

The management of DF is usually asymptomatic by antipyretics and pain killer to alleviate muscle

and bone pain. Severe cases may need hospitalization and good hydration¹.

In 2019, Makkah received 7.5 million Umrah visa holding visitors from different countries worldwide so Makkah's community is different and endemic diseases should be controlled. This study was carried on the authors' place of work (Makkah) which serve the people belong to the university (students, administration staff and education staff and their families). So most of those people have high education which differs from the general population. In addition, the authors noticed that recording of dengue fever was increased in the last two years and there was monocytosis in most of dengue patients' profile which was not mentioned in the literature. So this study was done to confirm the authors' notices and to determine the patients' characteristics. Accordingly more prevention and control can be applied.

METHODS

This cross-sectional observational study was carried out in outpatient clinics of Um Alqura University medical Center, Saudi Arabia during period of July 2018 to November 2019. WHO classified dengue into dengue (with / without warning signs) and severe dengue according to the severity of the disease. Dengue can be clinically suspected when a patient presents with a high

fever ($40^{\circ}\text{C}/104^{\circ}\text{F}$) and has two of the following symptoms at the same time (severe headache, retro-orbital pain, muscular and joint pains, nausea, vomiting, enlarged glands and skin rash)¹.

Comprehensive sample of all patients ≥ 14 years old who attended to the clinics complaining of acute febrile illness at least 24 hours and were suspected to have DF according to the mentioned WHO criteria were included in the study without sampling technique during period of July 2018 to November 2019. Patients didn't met WHO criteria and patients with confounding factor such as co-infection, bone marrow diseases that may altered clinical and laboratory results were excluded from study. The target sample was 162 according to the equation $n = z^2 p(1-p)/d^2$. Where n is the sample size, Z is the statistic corresponding to level of confidence (1.96), P is the latest prevalence which was 12.8% of a study was done in Almadina in Saudi Arabia¹² and d was proportion of sampling error (5%).

All suspected patients underwent Dengue IgM antibody test depending on enzyme-linked immunosorbent assay (ELISA).

All such patients who were included in the study underwent detailed history, clinical examination and investigation. The history included age, gender, socioeconomic, and history of chronic diseases or medications. Clinical examination included blood pressure, pulse, body temperature, lymph node, skin rash, yellow sclera, abdominal and cardiac examination.

Laboratory investigations done were hemoglobin, total leucocyte count (TLC) and differential leucocyte count (DLC), platelet count, hematocrit (HCT), liver function tests (LFT), blood urea, serum creatinine, CPK, LDH and CRP. All patients exposed to abdominal ultrasound scan to detect organomegally, ascites, pleural effusion and enlarged lymph nodes. Other relevant investigations were performed according to the clinical conditions of the patients. Informed consent was taken from the patients and data collection and confidentiality were protected to the maximum possible standards.

Data was analyzed using SPSS version 20. Dependent variable was seroreactivity while independent variables were age of the patients, systolic BP, CBC parameter, LFT and CRP. Comparison between seropositive and seronegative cases was done by non-parametric t-test and P-value less than 0.05 was considered significant.

RESULTS

We recruited 126 patients who attended to the clinics with WHO suspected criteria during period of July 2018 to November 2019. We didn't reach the target sample size (162) because of the low rate due to the clinics received only the people belong to the university (students, administration staff and education staff and their families). Out of 126 patients presented with acute febrile illness, 71 (56.3%) had seroreactivity for dengue IgM antibodies. Out of those having DF, 44 (61.9%) were males and 27 (38.1%) were females with mean of the age was 31.30 ± 9.68 .

On analysis of patients had DF it was found that; Fever, headache and musculoskeletal pain were the most common clinical presentation and it was present in all the patients. Decreased appetite (92.9%), Retro-orbital pain (78.8%) and dizziness (64.7%) were the next common symptoms. Nausea and vomiting were present in 35 (49.2%) patients. 25 (35.2%) patients had diarrhea. Positive tourniquet test was observed in 7 (9.8%) of the patients while minor bleeding was noticed in 4 (5.6%) of the patients in the form of bleeding per gums and petechiae. No major bleeding in our population was recorded. 19 (26.7%) patients had skin rash. 17 (23.9%) of the patients had low systolic BP ($<90\text{mmHg}$). 8 (11.2%) had enlarged more than group of lymph nodes. (Table 1).

On ultrasound examination it was found that 34 (47.8%) had bright liver texture, 29 (40.8%) had hepatomegally, 11 (15.4%) had splenomegally, 6 (8.4%) had gall bladder edema and only 1 (1.4%) has pleural effusion. (Table 1).

Among haematological parameters, 53 patients (74.6%) had thrombocytopenia with platelet $<100000/\text{cc}$ while leucopenia ($<4000/\text{cc}$) was noticed in 33.8%. Elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were observed in 58 (81.6%) and 53 (74.6%) respectively. 7 (9.8%) of the patients had hyperbilirubinaemia. (Table 2).

On comparing DF patients with seronegative patients it was found that factors associated with seroreactivity; ALT, AST, CRP, low WBC count, low platelets count, high monocyte count and low neutrophils count with P-values of 0.014, 0.002, 0.020, 0.034, 0.000, 0.012 and 0.036 respectively. On the hand age, systolic BP, Hemoglobin level, Bilirubin, LDH, Lymphocytic count, Eosinophilic count and basophilic count didn't show significant analysis. (Table 3)

Table 1: Clinical features of patients with dengue fever

Symptoms and Clinical signs	N (%)
Fever	71(100%)
Headache	71(100%)
Abdominal pain	23(32.3%)
Bone ache	71(100%)
Muscle and joint pain	71(100%)
Retro-orbital pain	56(78.8%)
Blurring of vision	6(8.4%)
Decreased appetite	66(92.9%)
Nausea and or Vomiting	35(49.2%)
Diarrhea	25(35.2%)
Cough	10(14%)
Skin Rashes	19(26.7%)
Positive tourniquet test	7(9.8%)
Dizziness	46(64.7%)
Bleeding	4(5.6%)
Lymphadenopathy	8(11.2%)
Hypotension	17(23.9%)
Ultrasonography findings	
Splenomegally	11 (15.4%)
Hepatomegally	29(40.8%)
Bright liver texture	34(47.8%)
Gall bladder edema	6(8.4%)
Pleural effusion	1(1.4%)

Table 2: Laboratory parameters of dengue fever patients

Laboratory results	N (%) total 71
TLC (<4000/cc)	24(33.8%)
Platelets (<100000/cc)	53(74.6%)
AST(>40IU/L)	58(81.6%)
ALT(>45IU/L)	53(74.6%)
Total bilirubin (>1.2mg/dl)	7(9.8%)

Table 3: Comparison between seropositive with seronegative dengue IgM antibodies

	Positive dengue IgM antibodies		Negative dengue IgM antibodies		p
	Mean	SD	Mean	SD	
Age	31.30	9.68	32.94	11.85	0.396
systolic	111.40	10.15	109.24	12.34	0.291
Hemoglobin(gm/dl)	13.44	2.08	13.59	1.98	0.688
ALT(IU/ml)	83.47	56.27	57.09	61.68	0.014
AST(IU/ml)	96.81	51.51	61.12	76.00	0.002
Bilirubin(total)(mg/dl)	0.88	0.33	0.79	0.29	0.122
CRP	25.35	20.03	18.03	14.39	0.020
LDH	418.60	243.60	350.35	234.22	0.119
WBC	3.65	1.48	4.17	1.17	0.034
Neutorophils	41.71	13.71	46.90	13.52	0.036
Lymphocytes	45.12	12.16	42.69	12.52	0.274
Monocytes	8.64	5.15	6.50	4.08	0.012
Esonphils	1.92	1.83	1.55	1.12280	0.195
Basophils	2.45	2.19	2.59	2.06	0.711
Platelet count(/cmm)	135.09	56.95	186.36	63.20	0.000

DISCUSSION

In the current study out of 126 presenting with acute febrile illness, 71 (56.3%) showed seroreactivity for dengue IgM antibodies which is in unison with other similar studies in Makkah and Jeddah, Saudi Arabia that reported a seroprevalence of 56.25% and 48.75% respectively^{7,8}. Our study result was slightly higher than results observed by study done in Aseer and Jizan, Saudi Arabia which reported seropositivity in 31.7% of the suspected cases⁸. The higher prevalence in our study because the disease is endemic in Makkah due to its atmosphere and nature.

The current study has shown that DF is common in male gender and young age this may be due to males are more exposed to the virus because most of females in Makkah wear cloths and Nikab which cover the hole body including face . These findings are consistent with other studies^{13,16}. Without statistically significant relationships studies performed in Australia, France and Mexico, reported that DF was more common among female gender^{17,19}.

Headache, myalgia and retro-orbital pain are well-known symptoms of DF. As compared to similar studies^{13,14,20,21}, the main symptoms and clinical signs of our patients were headache, bone ache, myalgia, joint pain and retro-orbital pain.

All of our patients in the current study experienced headache. Most of the previous studies describe similar results, however lower incidence of headache (9 %) was reported by Awasthi et al.²² which is much less than our study patients. Myalgia was found in 100% of our patients which is comparable with previous studies²³, however study conducted by Mohamed et al., showed lower incidence (32.87%) (24). Retro-orbital pain was noticed in 78.8% of the patients in present study comparable to Deshwal et al., (18.3%) and Lepakshi et al., (14%)^{25,26}; however study done by Nandini Chatterjee et al., had 90%²¹.

In our study, abdominal pain was found in 32% of the patients which correlates with the previous studies, however studies conducted by Ragini Singh *et al.*, and Munde *et al.*, showed slightly lower incidence of 3.6% and 15% respectively^{27,28}. In our study, 49.2% of the patients presented with nausea/vomiting comparable to 25% in study conducted by Munde *et al.*, however Ragini Singh *et al.*, reported only 11.4%²⁸.

Skin rash was noticed in 26.7% of our patients, this was comparable to the prevalence of skin rash (26%) documented by Karoli et al.²⁹. This presentation is less in other studies by Itoda et al. in japan ,and Rahim et al. in a Bangladesh, showed higher incidence (82%,78.5% respectively)^{30,31}.

Hemorrhagic manifestation is one of the complications of DF due to low platelet count and increased capillaries permeability of blood vessels. Bleeding manifestations and a positive tourniquet test were relatively uncommon in our study. These findings are inconsistent with three studies performed in Saudi Arabia^{13,14,20}. Bleeding was seen in 5.43% of cases and positive tourniquet test was recorded in 16.50% of patients in a study by Rajesh Deshwal et al.²⁵, however other study recorded a higher incidence (40%)²⁸.

Abdominal ultrasound scan has an important role in DF for diagnosis of organomegally, ascites, gall bladder edema and pleural effusion. Only one patient among this study population, presented to us with pleural effusion but no patient with ascites. In a study by Mandal et al.³² ascites was present in 8.1% and pleural effusion in 18.9% of cases. In present study we found that 8.4% of the patients had gall bladder edema, it could be due to direct viral effect on the gall bladder wall leading to increased vascular permeability and edema. Hepatomegally was detected in 40.8% of our cases while Deshwal, R et al.,²⁵ reported 14.8%. the high incidence in our study may be due to pre existing fatty liver due to sedentary life and obesity. In the present study 15.4% of patients had splenomegally, this is consistent with Deshwal, R et al.²⁵ 13.2%.

The main hematological abnormalities were thrombocytopenia, low WBC count and elevated liver enzymes which are similar to previous studies in Saudi Arabia^{7,9,20}.

Thrombocytopenia (<100000/cc) documented in 74.6% of all dengue cases in our study. Rashmi et al.³³ have documented thrombocytopenia (<140000/cc) in all cases, but platelet count less than 100000 were reported in 89.4% cases. Mandal et al.³², in their series of patients have shown platelet count (<50000/cc) in 37.8%. A study conducted in 2014 found the common laboratory presentations of DF were thrombocytopenia (96%)³⁵.

Among the laboratory profile, leukopenia (<4000/cmm) was noticed in 33.8% of our patients. A study by Itoda³³ found that low WBC count was observed in 71% of cases. However studies done by Munde et al.,⁽³⁵⁾ and Karoli²⁹ reported leukopenia in 50% and 89% of their patients respectively. Ageep³⁶ detected leucopenia in 90% of cases while Mandal³² found leucopenia in 29.73% of cases.

Liver involvement is common in DF and its damage manifests as elevation of ALT and AST, hypoalbuminaemia, and prolonged of PT and PTT³⁷. Elevated liver transaminases were noted in the majority of the cases in this study (82%). In study by Deshwal²⁵ (88.54%) patients showed elevated ALT and AST. Kularatne et al documented elevated transaminases in 88% of

cases. Another study recorded that 57% of patients had elevated ALT and 49% had raised AST²². Previous studies in Saudi Arabia reported similar results⁷.

In our study there was significant difference in monocyte count being high in DF group. Additionally no case mortality was reported among our sample population, however previous studies observed mortality rate of 4%^{38,39}.

LIMITATION OF THE STUDY

This study is a single center outpatient clinic based study recruited small sample size. This small sample during this long time because of the low rate due to the clinics received only the people belong to the university (students, administration staff and education staff and their families) Also, there was lacking of information regarding if the infection is primary or secondary as well as dengue serotype. A multi-center and tertiary hospitals cross sectional study with larger sample size that include all general population would prove more useful conclusions.

CONCLUSION

Dengue is a challenging infectious disease with a major public health concern that can present with no symptoms to severe life threatening symptoms. Fever associated with headache, retro-orbital pain, thrombocytopenia and elevated liver transaminases show high susceptibility criteria for dengue diagnosis. Monocytosis was observed in our study in dengue fever group and further studies are needed to confirm this finding. Community awareness regarding prevention and control and mode of transmission more is needed. Additionally, continuous surveillance and mosquito control measures in Makkah are needed.

CONFLICT OF INTEREST: NO

FUNDING: No

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