MEDICAL CHANNEL

Original Article

FREQUENCY OF THROMBOCYTOPENIA IN DIAGNOSED CASES OF DENGUE FEVER

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ABSTRACT

Introduction: Dengue infection is the most common mosquito born viral disease and is a major public health problem.

Objective: To determine the frequency of thrombocytopenia in diagnosed cases of dengue fever.

Study design: Cross Sectional study.

Setting: The study was conducted at the Department of Medicine Lyari General Hospital Karachi.

Duration of study: One year from 01-09-13 to 30-09-14.

Subjects and methods: one hundred and seventeen patients were included who fulfilled the selection criteria after taking the informed consent. The SPSS version 15 was applied to analyze.

Results: There were 82 (70.1%) male patients as compared to this the frequency of female patients was much lower 35(29.9%).

The mean ± standard deviation age of study population was 31.28 ± 14.3 years and the mean platelet counts were 81350.42 ± 80601.3. Among 101 (86.3%) patients had thrombocytopenia as compared to this only 16 (13.7%) patients did not have thrombocytopenia.

On further analysis of age and platelet count among the gender it was observed that the mean age of male patients was 30.09 ± 12.05 years as compared to this the mean age of female patients was 34.09 ± 18.34 years (p=0.289) and the mean platelet count of male study population was 74.97.56 ± 62369.19 as compared to this the female study population had mean platelet count of 98342.85 ± 111684.94 (p=0.059).

On analysis of mean age and platelet count in relation to frequency of thrombocytopenia we concluded that the mean age of study population having thrombocytopenia was 30.29 ± 12.58 years (p=0.111) and the mean platelet count was 56811.88 ± 39510.18 (p=0.011).

Conclusion: It is concluded that continuous surveillance and education of clinicians is essential for the recognition of risk factors of DHF for early diagnosis and management. In elderly patients, blood group and cross matching should be

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carried out as a routine precaution which may be helpful in emergency.

Key words: Dengue fever, Thrombocytopenia, VHF.

INTRODUCTION

Dengue fever (DF) has developed into one of the world's major emerging infectious diseases[1]. DF is a mosquito-borne illness[2]caused by the dengue viruses, a Flavivirus that is transmitted principally by the Aedes aegypti mosquito, and has emerged as the most common arboviral disease in the world[3]. The virus has four antigenically similar but immunologically distinct serotypes.

There is an annual incidence of 100 million cases of dengue fever, 250,000 cases of dengue hemorrhagic fever and mortality of 25,000 per year globally[4]. The disease is endemic in the tropical and sub-tropical areas of the world with about 2.5 billion people (40% of the world's population) at risk in these regions[5]. In Pakistan the first outbreak of Dengue fever was reported in 1994[6]. With no mandatory reporting system in the early days of emerging of this disease but recent data shows the high prevalence of this disease nationaly.[7]

DF caused by dengue viruses, presents classic dengue fever, dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS)[8]. DF should be suspected if patient presents with bleeding manifestations, retrobulbar headache, severe myelgias and/or thrombocytopenia. Dengue IgM antibodies ELISA appear in 50% of patients with primary infection in the febrile period 4-5 days after onset of fever[9]. In a local study by Shahid et al. dengue IgM antibodies were detected in 73% of patients and 83% had thrombocytopenia. If not properly managed, the mortality of dengue hemorrhagic fever can be as high as 30%[10]. Thrombocytopenia may be occasionally observed in DF but is a constant feature and one of the diagnostic criteria of DHF. In cases of DHF thrombocytopenia was observed in 8.6–96%, plasma leakage in 6–95% and haemorrhagic manifestations in 22–93%.[11] There was no association between the presence of active bleeding and the degree of thrombocytopenia on admission. Patients with DHF had lower platelet counts than patients with DF. Clinical manifestations of thrombocytopenia are not related only to the number of peripheral platelets in dengue infection, but its recovery is associated with clinical improvement. There was no statistical difference in the incidence of bleeding manifestations between thrombocytopenic and non-thrombocytopenic individuals highlighting poor association of thrombocytopenia with bleeding manifestations[12].

High prevalence of dengue fever and life threatening complications caused by this in an endemic area emphasizes the need for adoption of strict measures for prevention, detection and early treatment. Latest reports shown that intravenous Anti-D immunoglobulin is effective in increasing platelate counts[13]. Management of complications imposes a significant economic burden on the state and the individual. Epidemiological surveys are most crucial in planning and allocating resources as they provide critical information for good policy formulation in a resource poor country. Data regarding thrombocytopenia in dengue is scanty. Thus this study is designed to determine the frequency of thrombocytopenia in dengue fever locally.

THE STUDY

Title of Study: Frequency of thrombocytopenia in diagnosed cases of dengue fever in patients.

Objective: To determine the frequency of thrombocytopenia in diagnosed cases of dengue fever.

Operational Definition:

Thrombocytopenia: It is defined as a platelets count less than 150,000/microl.

Typical clinical features of dengue fever were defined as any patient having a body temperature higher than 38°C and headache, retro-orbital pain, myalgia, arthralgia, rash and pruritus.

Diagnosis of acute dengue fever was labeled on detection of dengue virus specific IgM antibody.

METHODOLOGY

Study design: Cross sectional study.

Setting: The study performed at the Department of Medicine Lyari General Hospital Karachi.

Duration of study: One year. From 01-09-13 to 30-09-14

Sample size: Taking confidence interval (1-α) of 95%, anticipated population proportion (P) of 83% and absolute precision (d) of 0.07 the sample size was calculated as 117.

Sample technique: Non-probability purposive.

Inclusion criteria:

- All patients with age above14 years of either gender with typical clinical features of Dengue fever i.e. high grade fever, headache, retroorbital pain, skin rash, mucosal bleeding, petechie and supported by positive serology of dengue specific IgM included.

Exclusion Criteria:

Following patients excluded from the study

- Co-infection of Malarial parasite detected
- Patients taking medications known to cause thrombocytopenia e.g. Heparin, Cephalosporins, Sulfamethoxazole, NSAID, Digoxin, Ranitidine, etc.
- All other causes of thrombocytopenia excluded e.g. malaria, bacterial infection, chronic liver disease and disseminated intravascular coagulation.

Data collection procedure: The patients were registered from Department of Medicine, Lyari General Hospital Karachi. The patient who fulfilled the selection criteria were enrolled in the study. Informed consent was obtained from all the patients after explanation of the study protocol. The

data was collected on the approved proforma, which included age, gender, and platelet count.

Data Analysis: The data was analyzed on SPSS version 15.0. The frequency and percentage were calculated for qualitative variable like gender and thrombocytopenia. Mean ± SD was computed for quantitative variables like age. P value ≤ 0.05 was taken as significant. Stratification was done with regards to age and gender to see the effect of these on outcome.

RESULTS

One hundred and seventeen patients admitted in medical ward of LGH Hospital Karachi from 01-09-13 to 30-09-14 were initially evaluated by brief History, examination and

TABLE I:
ANALYSIS OF AGE AND PLATELET COUNT OF THE STUDY POPULATION
n = 117

Descriptive Statistics	Minimum	Maximum	Mean	Std. Deviation
Age/years	14	80	31.28	14.263
Platelet count	9000	465000	81350.43	80601.33

TABLE II:
ANALYSIS OF AGE AND PLATELET COUNT AMONG THE GENDER
n = 117

Gender	Age	Platelet count
Male	30.09 ± 12.05	74097.56 ± 62369.19
Female	34.09 ± 18.34	98342.86 ± 111684.94
p value	0.289	0.059

TABLE III:
ANALYSIS OF FREQUENCY OF THROMBOCYTOPENIA IN RELATION TO PATIEN'S MEAN AGE AND PALTELET COUNT
n = 117

Thrombocytopenia	Age	Platelet count
Yes	30.29 ± 12.59	56811.88 ± 39510.18
No	37.56 ± 21.65	236250 ± 100922.08
p value	0.111	0.011

FIGURE I:
GENDER ANALYSIS
n = 117

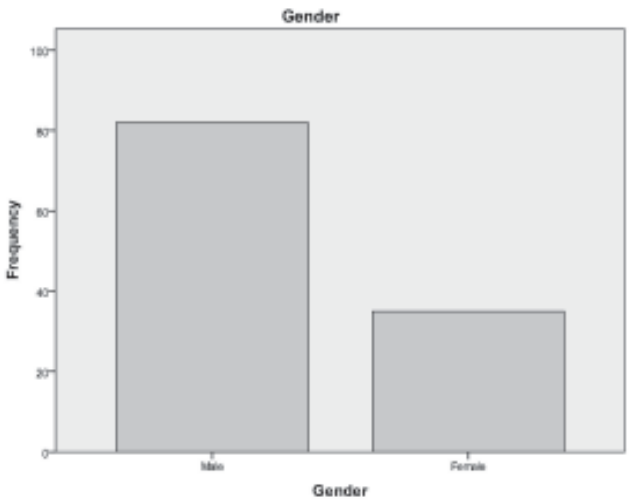
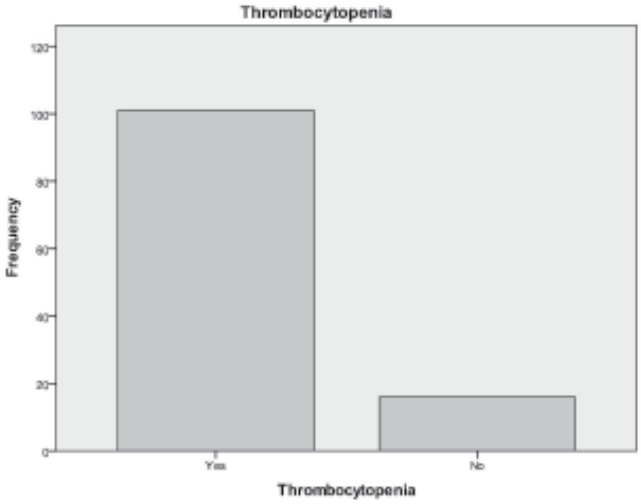


FIGURE II:
THROMBOCYTOPENIA FREQUENCY
n = 117



followed by baseline investigation i.e Blood CP, LFT, Giemsa staining, PT, INR, and Dengue serology.

Patients having dengue serology (IgM) positive and after excluding co-infection of malaria parasite, bacterial infection and other causes of thrombocytopenia as described in exclusion criteria were enrolled.

Out of 117 patients, there were 82 (70.1%) male patients as compared to this the frequency of female patients was much lower 35 (29.9%) (Figure I).

According to the analysis of the age and platelet count in the study population we observed that the mean ± standard deviation age of study population was 31.28 ± 14.3 years (Table I) and the mean platelet counts were 81350.42 ± 80601.3 (Table I).

In this study on data analysis it was observed that 101 (86.3%) patients had thrombocytopenia as compared to this only 16 (13.7%) patients did not have thrombocytopenia (Figure II).

On further analysis of age and platelet count among the gender observed that the mean age of male patients was 30.09 ± 12.05 years as compared to this the mean age of female patients was 34.09 ± 18.34 years (p=0.289) (Table II) and the mean platelet count of male study population was 74.97.56 ± 62369.19 as compared to this the female study population had mean platelet count of 98342.85 ± 111684.94 (p=0.059) (Table II).

On analysis of mean age and platelet count in relation to frequency of thrombocytopenia we concluded that the mean age of study population having thrombocytopenia was 30.29 ± 12.58 years (p=0.111) and the mean platelet count was 56811.88 ± 39510.18 (p=0.011) (Table III).

DISCUSSION

Dengue fever and dengue hemorrhagic fever are caused by one of four closely related, but antigenically distinct, virus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4) of the genus *Flavivirus*[14]. Infection with one of these serotypes does not provide cross-protective immunity, so persons living in a dengue-endemic area can have four different dengue infections during their lifetime[15]. Although dengue fever is a self-limited febrile illness, dengue hemorrhagic fever is characterized by prominent hemorrhagic manifestations associated with thrombocytopenia[16] and an increased vascular permeability[17]. Secondary infections, commonly observed in the dengue-endemic areas, are more likely to constitute a risk factor for DHF. Although dengue virus-induced bone marrow suppression[18] decreases platelet synthesis, an immune mechanism of thrombocytopenia caused by increased platelet destruction appears to be operative in patients with DHF. An increased level of platelet-associated IgG (PAIgG) is observed frequently in patients with chronic idiopathic thrombocytopenic purpura (ITP) but is also found in a variety of diseases[19]. The major pathophysiologic hallmarks that determine disease severity and distinguish DHF from DF and other viral hemorrhagic fevers are plasma leakage due to increased vascular permeability and abnormal hemostasis. Hypovolemic shock occurs as a consequence of, and subsequent to, critical plasma volume loss. Abnormal hemostasis including increased capillary fragility (positive tourniquet test and easy bruising at the site of venepuncture), thrombocytopenia, impaired platelet function, and consumptive coagulopathy in the most severe form disseminated intravascular coagulation (DIC) contribute to varying degrees of hemorrhagic manifestations. The role of platelets in restoring normal capillary integrity or limiting massive bleeding with DHF has not been adequately described.

Severe thrombocytopenia and increased vascular permeability are two major characteristics of dengue hemorrhagic fever (DHF). An immune mechanism of thrombocytopenia due to increased platelet destruction appears to be operative in patients with DHF[20].

Thrombocytopenia may be occasionally observed in dengue fever but is a constant feature[21] and one of the diagnostic criteria of dengue hemorrhagic fever. Its clinical presentation and relevance is still poorly described in the literature.

Mourão MP, et al.[22] in their study reported that patients with DHF had lower platelet counts than patients with DF ($P < 0.001$). Clinical manifestations of thrombocytopenia are not related only to the number of peripheral platelets in dengue infection, but its recovery is associated with clinical improvement.

Murillo-Llanes J, et al.[23] reported that average age was 34.5 ± 15 years. 61.7% of DF cases were women, while 77.3% of DHF cases were men. DF cases showed hemorrhagic manifestations (24.8%); plasma leakage (6.7%) and thrombocytopenia (34.4%); petequiae, gingival bleeding and epistaxis were associated to thrombocytopenia below 39 000/mm ($p < 0.05$).

CONCLUSION

It is concluded that continuous surveillance and education of clinicians is essential for the recognition of risk factors of DHF for early diagnosis and management. In elderly patients, blood group and cross matching should be carried out as a routine precaution which may be helpful in emergency.

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