INNSPUB

International Journal of Biosciences | IJB |
ISSN: 2220-6655 (Print) 2222-5234 (Online)
http://www.innspub.net
Vol. 15, No. 1, p. 548-553, 2019

RESEARCH PAPER OPEN ACCESS

Evaluation of haematological parameters in dengue infection

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Key words: Dengue, Hematological parameters, Peshawar

http://dx.doi.org/10.12692/ijb/15.1.548-553 Article published on July 30, 2019

Abstract

Dengue cause high mortality and morbidity in developing countries due poor preventable management and un-hygienic condition. Early identification and diagnosis of dengue infection is important for provision of particular care and to reduce the fatality outcomes. The aim of this study was to determine the haematological parameter in dengue viral infected patients in Peshawar, Khyber Pakhtunkhwa province of Pakistan. Demographic, clinical, serological and hematological information from n=2189 patients were obtained in duration of January 2017-January 2018 in district Peshawar. Serological test were performed on Immunochromatography technique for detection of non-structural antibodies against dengue virus. All non-structural antibodies (positive) cases were confirmed by standard Enzyme Linked Immunosorbent Assay. Automated sysmax X-2100 were used for Haematological parameters (complete blood count). Statistical package for social sciences version 21 were used for data analysis. Out total 2189 patients, 59.06% were male and 40.94% were female. Burden of dengue infection was 25.94% (n=568) as examined positive. Majority dengue infected patients were diagnosed in age of 21-30 years with high male percentage (59.06%). Frequently affected hematological parameter was lymphocytes and mean cell hemoglobin concentration in numerous dengue viral infected patients while mean cell hemoglobin was observed decreased in all patients. Platelets were decreased in age group of ≥70 years. This study shows that the prevalence of dengue was high with significance impact on hematological parameters. There is need to initiate Public-awareness campaign and also educate them regarding the spread of dengue fever and vector control. These measures, eventually, will lead to implement community-friendly and sustainable disease management strategies in the country.

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Introduction

Dengue virus is the most common arbovirus in more than 100 countries located in tropical and sub-tropical region of the world due to environmental condition favors the growth and development of principal vector "Aedes mosquito" (Ekanayake, Perera, Ellepola, & Athauda, 2013). Dengue viruses (DENVs), is a single stranded RNA and capsulated virus which belongs to the family Flaviviridae, in the genus Flavivirus (Group B arboviruses) (Malathesha & Ashwini, 2014). According to immunological and biological criteria, Dengue virus have four distinct serologic and closely similar antigenically related sub-types; Dengue virus-1 (DV-1), DV-2, DV-3 and DV-4 (Ahmed *et al.*, 2008). Transmission to human of any these four serologic type virus DV 1-4 through bite of infected female Aedes aegypti and albopictus (arthropod borne virus) (Gitika and Gill). Humans to mosquito, period of transmission start one day earlier then fever up to the upcoming day of sickness related to the viremia phase. Female mosquito bites a viremia phase patients, extrinsic incubation (viral replication) start from 8 to 12 days in the mosquito while the incubation phase in humans ranges from 3 to 15 days with mean of 5 days (Patel, Patel, & Das, 2016).

Clinical manifestation of all these dengue virus serotypes range from asymptomatic infection to severe and may cause lethal infections. Sometimes from non-specific febrile fever, dengue fever (DF), Dengue Hemorrhagic Fever (DHF) and sometimes lead to hypovolumic shock known as Dengue Shock Syndrome (DSS) (Ahmed *et al.*, 2008). Dengue fever is defined by biphasic fever, headaches, retro-orbital pain, flushed faces, petechie, purpura, weakness, myalgia, sore throat, arthralgia, and vomiting, altered taste sensation and skin maculopapular rashes. Other associated severe and disseminated intravascular coagulation and bleeding tendency symptoms may detect in DHF (Pai Jakribettu *et al.*, 2015). Currently, no specific therapeutic vaccine or treatment is accessible for dengue viral infection and the most challenging task related to this infection is early diagnosis and patient management (Jampangern *et al.*, 2007).

Approximately 50-100 million cases of DF whereas 0.25-0.5 million cases of DHF occur annually and at least 12 thousand deaths occur globally (Ahmed *et al.*, 2008). Epidemic of dengue hemorrhagic fever occur in 1970 only in 9 countries then increased four times in 1995 and according to the WHO, about 2,500 million of individual are living in area at risk to dengue fever (Ekanayake *et al.*, 2013). Epidemic of dengue fever was frequently observed in Asia and Pacific throughout the 12th century. In South East Asia, the number of infected individual of DHF has increased from 10,000 to more than 200,000 from 1950s to 1990s annually (Khan *et al.*, 2010).

In Pakistan, DF first outbreak was reported in 1994 in Karachi due to serotypes DV-2. After that, sporadic cases of DHF were continuously reported from different region of the country (Khan *et al.*, 2010). Another outbreak was reported in 2003 at upper regions of Punjab and was also recorded in Mangla, Abbottabad, Rawalpindi, Peshawar and Haripur (Ahmed *et al.*, 2008). Moreover, Paul *et al.,* study revealed that in 1998 epidemic of DF in Baluchistan province was due to DV-1 and DV-2 (Paul, Patel, Mirza, Fisher-Hoch, & Luby, 1998). Abrupt increased in DHF cases in three major hospitals of Karachi due to DV-3 genotyping reported in 2005. Thereafter, Pakistan experience the severe epidemic of DHF in 2006, predominant serotypes were identify DV-2 and DV-3 (Ahmed *et al.*, 2008).

Hematological tests (complete blood count) provide important part of the therapy and prognosis especially in the limited resource areas (Joshi, Gayathri, & Muneer, 2018). Major variables in complete blood count (CBC) including the peripheral smear can help the clinician in better treatment of patients (Malathesha & Ashwini, 2014). Thrombocytopenia is frequently detect in Dengue infected patients and leucopenia were also observed in the these patients (Tsai *et al.*, 2017). Another study also reported that leucopenia and thrombocytopenia are the prominent hematological altered variables. In differential leucocytes count, lymphocytosis was observed with the presence of atypical lymphocytes. Platelets count tend to decrease with the course of illness and found to predict about the severity of the infection (Gitika & Gill, 2018).

Atypical lymphocytes with high percentages are detected in rapid and early diagnostic aid in secondary infection (Jampangern *et al.*, 2007). Only few studies have been discussed the changes in the differential leucocytes counts.

The aim of present study was to evaluate the complete blood count along with differential leucocytes count in dengue viral infected patients.

Materials and methodology

Study Design, Duration, Setting and Sample Size

This observational study was carried out on 2189 dengue patients at different district hospitals in Peshawar during the period of Jan 2017 to January 2018.

Study Population

Patients with episodic fever with at least 2 consecutive days, positive NS-1 ICT antibodies against dengue and presenting the typical clinical characteristic of dengue fever according to the WHO criteria were included in present study while NS-1 negative dengue patients, hematological abnormalities, septicemia, transfusion reaction, allergic and have other concomitant infections such as malaria, typhoid were excluded from current study.

Blood Sample Collection and Procedure

Two milliliters (ml) of venous blood in EDTA for Complete blood count and 3 ml of blood in sterile plain tube for serological examination were collected from 400 patients for blood parameter analysis. Complete blood count was performed on automated sysmax (X-2100) and DLC were performed from peripheral smear by hematologist within the 24 hours of blood collection. Geimsa stain were used for blood smear and studied for TLC and DLC. Dengue specific IgM/IgG was performed through commercial rapid diagnostic kit (Immunochromatography technique) for NS1 antigen and the positive cases were confirmed by standard Enzyme Linked Immunosorbent Assay (ELISA).

Ethical Consideration

The study protocol was approved by the ethical committee and relevant authorities of the hospitals and written consent form was obtained from each patients.

Statistical analysis

Statistical package for social science version 22 was used for data entry, processing, management and analysis. All the analyzed data were presented as mean± standard deviation. Less than 0.05 P-value were considered as significant.

Results

Out of total (2189) patients, 59.06% (n=1293) were male and 896 (40.93%) were female patients. Out of total, 25.94% (n=568) were found positive and 1621 (74.05%) patients were negative for Dengue NS1. In present study, out of total positive patients (n=568), 336 (59.15%) were male patients and 232 (40.85%) were female patients. Majority, uninfected and positive patients were frequently observed within age group of 21-30 years. Dengue infection was found more in male than female patients as shown in table No.1.

Out of total 2189 patients, 1293 (59.06%) were male patients and 896 (40.93%) were female patients while in total positive patients, 336 (59.1%) were male patients and 232(40.8%) were female patients. Abnormal MCHC and lymphocytes were frequently observed in dengue infected patients.

Table 1. Prevalence of dengue fever according to gender wise.

Age	≤-10	11-20	21-30	31-40	41-50	51-60	61-70	71≤	Total
Male	153	330	396	174	117	87	33	19	1293 (59.06%)
Female	96	223	266	143	89	44	27	08	896 (40.94%)
Total	249	543	662	317	206	131	60	27	2189

In this study, distribution of Dengue infection by age wise were distributed in eight groups (0-80 years), which describe the prevalence of Dengue in different groups as shown table No.2. Distribution of cases were 11.3%, 24.5%, 30.2%, 14.4%, 9.41%, 5.98%, 2.74% and 1.23% in ≤10 years, 11-20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years, 61-70 years and 71-80 years respectively. The present study describe that Dengue infection were more common in adults (21-30 years) as compared to the children age group (≤10 years) and the oldest age group (≥51 years). Dengue infection in adults was followed by 11-

20 years, 31-40 years, ≤--10 years, 41-50 years, 51-60 years, 61-70 and >70 years of age patients as given in the table No.2.

Table 2. Prevalence of dengue infected patients according to Age (year).

Age	Positive	Negative	Total
≤--10	47	202	249 (11.3%)
11—20	143	394	537 (24.5%)
21—30	171	491	662 (30.2%)
31—40	93	224	317 (14.4%)
41—50	56	150	206 (9.41%)
51—60	35	96	131 (5.98%)
61—70	16	44	60 (2.74%)
71—80	7	20	27 (1.23%)
Total	568 (25.95%)	1621 (74.05%)	2189

Frequently decline parameters of complete blood count in dengue infection were MCHC, MCH, Lymphocytes and Platelets. In Dengue positive patients MCHC were decrease 81.86% patients while MCH were decreased in 47.35%. Platelets were decreased in 36.61% positive patients. Abnormal lymphocytes count was observed in 50.70% patients. Both MCH and MCHC were obtained lower in present study with mean value of 26.54 (pg) and 31.19 (g/dl) as shown in table No.3.

Table 3. Various parametes of CBC withr normal and abnormal (↑/↓) values.

Parameters	Increased (↑)	Decreased (↓)	Abnormal (n)	Normal (n)
WBC (/cmm)	29	168	197	371
RBC (*10^9/L)	37	26	63	505
HGB (g/dL)	5	86	91	475
HCT (%)	2	61	63	505
MCV (FL)	24	66	90	477
MCH (PG)	6	266	272	293
MCHC (g/dL)	8	462	470	95
PLT (*10^3/Cmm)	6	206	212	354
Neut%	175	47	222	345
LYMP%	42	243	285	280
MONO%	152	14	166	400
EOS%	10	0	10	558

Lowest level of MCH was observed in 0-10 year of age group with mean of 24.14±3.74. MCHC level were declined in all age groups but lowest were found in 0-10 year age group. Platelets counts remain normal in children and adults but decline was observed in old age group such as 61-70 year and 71-80 year respectively.

Table 4. Complete Blood Count parameters with mean and S.D values.

AGE (Year)	0--10	11--20	21--30	31—40	41--50	51—60	61--70	71--80
WBC (/cmm)	8.3±4.3	6.0±2.3	5.2±2.4	5.3±2.5	6.0±2.5	5.3±2.7	5.2±3.0	5.5±2.5
RBC (*10^9/L)	4.7±0.5	4.8±0.6	5.1±0.7	5.1±0.7	5.1±0.8	4.8±0.7	4.5±0.8	5.2±0.6
HGB (g/dL)	11.3±1.9	14.0±9.1	13.5±2.0	13.4±0.1	13.6±1.9	13.5±1.3	12.5±2.2	14.0±1.6
HCT (%)	37.1±4.6	42.2±4.0	43.4±6.3	43.2±5.5	43.2±5.2	42.2±4.5	39.7±6.9	46.7±2.5
MCV (FL)	79.2±8.0	85.4±7.2	84.3±8.3	83.4±10.0	85.7±9.0	87.8±9.1	88.4±5.9	90.2±6.7
MCH (PG)	24.1±3.7	26.8±3.1	26.5±3.4	26.3±3.5	27.0±3.9	28.2±3.4	27.5±2.0	28.1±2.3
MCHC (g/dL)	30.3±2.6	31.2±2.0	31.3±2.2	31.0±2.1	31.4±2.1	32.1±1.4	31.2±1.4	31.2±0.7
PLT (*10^3/Cmm)	244.4±9	202.3±9	171.7±7	167.2±7	166.5±8	163.1±8	150.0±1	129.7±4
Neut %	58.8±19	67.7±15	62.2±18	65.4±15	69.0±13	62.2±15	65.2±11	68.3±13
LYMP %	29.5±18	21.1±12	25.8±14	23.8±12	21.4±11	22.7±14	23.7±1	21.7±12
MONO %	7.9±4.3	8.1±5.1	8.7±5.7	8.4±5.1	7.1±4.6	8.1±3.7	7.8±3.2	6.8±5.8
EOS %	2.4±2.0	2.0±1.6	2.2±1.9	1.9±1.3	2.2±1.8	2.7±1.6	2.8±1.8	3.1±1.4

Discussion

This study shows that the frequency of Dengue infection was 25.94% which is similar to the study conducted by Khan *et al.,* that show Dengue prevalence is 26.3% (Khan *et al.*, 2010). Dengue infections were found more common in males as compared to females because males were more susceptible to Dengue infection, predominantly belongs to worker population and *Aedes aegypti* mosquito were commonly found in outdoor environment. The outcome of present study is similar to the study conducted in Mumbai, India which shows that the *Aedes aegypti* mosquito were commonly found in outdoor population (Lounibos & Kramer, 2016).

Adults were more expose to the environmental conditions, causative agent, traveling to infected areas, constructors and laborer. The present study show that median age is decreases up to time because the old population produced immunity against Dengue serotypes earlier infection but adults were no active immune system against that serotypes thus the

adults were more susceptible to infection and the results is comparable to the study conducted by Gajera *et al.,* (Gajera, Sahu, & Dhar, 2016). Present study shows that Dengue infection is now found endemic and occurs throughout the year in Pakistan because increasing number of positive cases is collected in the months of October and November which shows a peak incidence rate because of a favorable condition to mosquito such as highly rainy season (Salam, 2018).

Tripathi *et al* and Erum *et al* reported in their studies that Dengue transmission peak incidence is observed in post monsoon season (Vasanthapuram *et al.*, 2019), (Khan *et al.*, 2010). The prevalence of this study is comparable with a study conducted in Pakistan in 2011 (Jahan, 2011). The current study revealed that MCH and MCHC level were decreased because in response to Dengue viral replication and immune cells cause increase production of cytokines. Cytokines decrease blood oncotic pressure leads to plasma leakage from circulation and leaks into body cavities. As a results of plasma leakage MCH, MCHC and other blood parameters were decreased (Butthep, Chunhakan, Yoksan, Tangnararatchakit, & Chuansumrit, 2012). The following study suggests about the adaptation of all the self-preventive measures in such conditions to avoid further spreading of the virus; otherwise, this situation could lead to considerable dengue complications in future.

Conclusion

The Dengue infection is endemic throughout year in Pakistan but the peak rate occurs in the months of October and November in post monsoon and high rainy season. Plasma leakage results decrease in the MCH, MCHC and Platelets which helps to diagnose Dengue fever and Dengue hemorrhagic fever along with other parameters. Most of the studies show greater prevalence of the Dengue infection in male while the death rate of patients due to dengue infection is higher in female than in male. It may be due to the fact that the male can seek health facilities than female. The present study doesn't describe the severe effect of dengue on blood parameters other than MCH and MCHC.

Conflict of Interest: Authors have no conflict of interest.

Funding Disclosure: Nil

Author's Contribution

All authors equally contribute in Study Concept and Design, Data Collection and interpretation, Statistical Analysis, Protocol Writing, Manuscript Writing, Critical Manuscript Review, Final approval of article.

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