ORIGINAL ARTICLE

SEASONAL VARIATION AND SEROPREVALENCE OF DENGUE FEVER IN KARACHI, PAKISTAN

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ABSTRACT

Background:
Dengue fever is a rapidly emerging arthropod born viral disease becoming an international public health problem. Approximately 500,000 people suffer from dengue hemorrhagic fever and dengue shock syndrome with 20,000 deaths annually.

Objective:
To identify seasonal variation and seroprevalence of dengue fever for primary and secondary dengue infection.

Materials and Methods:
The study was conducted on 4900 plus subjects with mean age of 30 years, admitted to Dow University Hospital, Karachi. Reported cases were diagnosed by immuno-chromatography kit, used to measure the presence of IgG and IgM antibodies against dengue virus.

Results:
Seasonal variation of seropositive dengue patient from 2010 to 2013 showed most prominent dengue fever disease onset found in the month of October whereas least seen in the months from Jan to April. Age wise younger subjects were more prone to the infection with mean age of 21 to 30 years. 64% of the total febrile seropositive cases were male as compare to female patients noted 36%.

Conclusion:
Dengue disease is a threat to Pakistani population, being a developing country there should be more focus in eradicating this debilitating diseases, to reduce the economic burden. Through adapting vaccination strategies, proper sanitation and awareness programs. Special campaign for sprays and dengue control measures prior to month of October and fall season should be adopted essentially on regular basis.

Keywords:
Dengue fever, hemorrhagic fever, dengue virus, dengue Prevalence, IgG

Introduction:
Inappropriate water draining system and lack of public awareness about sanitation may create more chances of breeding mosquitoes, especially in any locality having standing sanitary water, all these preceding may provoke the dengue endemics.[1] The clinical manifestation of dengue virus infection is varied ranging from subclinical to fatal. Most adult patient in countries where dengue is endemic usually develop secondary dengue infection which is difficult to treat. Dengue fever (DF), an arthropod-borne viral disease, which becoming a major public health issue, both in the tropical and subtropical countries of the world.[2] Currently there are four antigenically distinct serotypes: DENV-1,

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DENV-2, DENV-3 and DENV-4 belong to family Flaviviridae; being transmitted to humans principally by mosquito bite. There is no cross protection between serotype Infection. Only with IgG serotype, one of these provides lifelong immunity to that serotypes.[3] In 1906, it was recognized that dengue fever is transmitted by *Aedes* mosquitoes predominantly by *Aedes aegypti*, less commonly by other species like *Aedes albopictus*, *Aedes polynesiensis* and several *Aedes scutellaris* can also spread the disease. Dengue infection may also get transmitted by blood products, during pregnancy and delivery, bone marrow transplants, and needle-stick injuries.[2,4] The incubation period of the virus in the mosquito is 8-10 days. The virus is then transmitted to a human host where it resides in the blood for 2-7 days. It is the period when there is an onset of fever, and the time when the virus can be acquired by the mosquito by sucking the blood of the host.[2]

Clinically Dengue fever is a severe, flu-like infection that affects infants, young children and adults, but rarely causes death. The clinical presentation varies with the age group. Infants and young children showed non-specific febrile illness with rash. Children and adults developed either a mild febrile disease or the classical debilitating disease with sudden onset of high grade fever, severe headache, retro-orbicular pain, photophobia, muscle and joint pains, and rash.[5] High grade fever may be continued for 5-6 days. Additional signs and symptoms include a generalized maculopapular rash, lymph node enlargement, hepatosplenomegaly, a positive tourniquet test, petechiae. Complication is hemorrhagic diathesis, like epistaxis and gastrointestinal bleeding. In some cases, symptoms started as common cold and flu. In general, recovery occurs spontaneously and rapidly, but it might be prolonged, sometimes taking several weeks and patient developed prominent asthenia and depression.[6] Clinical presentation may vary from undifferentiated sign and symptoms to classic DF, dengue

hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[7]

The first ever isolation of the dengue virus was carried out at the hands of Hotta in Japan in 1942.[8] There has been a striking rise in the cases of Dengue viral disease in South Pacific and America, and South-East Asia during the previous 2.5 decades.[2] The global epidemiology of DF and DHF is continuously changing because dengue is one of the rapidly spreading mosquito-borne viral diseases throughout the world. In the last 50years, incidence has been increased 30-fold with geographic expansion to new countries. At present decade, an estimated 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic region of the world.[9] Geographical distribution and genetic diversity of dengue virus suggests that it is originated from Asia. So as far as Asia is concerned, Philippines was the first country to have notified a DHF epidemic in 1953.[8] Then, the first case at Cuba was reported in 1981.[10] Pakistan has episode of dengue fever outbreaks since 1992. In 2005 first dengue outbreak occurs at Karachi in which 4,500 patients were registered. This epidemic was continued to affect many people in Azad Jammu & Kashmir in 2006 but were for the most part unreported. But in 2010 approximately 21,204 diagnosed patients of dengue were registered throughout Pakistan.[10] In the same year the massive outbreak in Punjab give alarming situation to the Government of Pakistan, particularly the Punjab Government. This resulted in 18,000 cases nationwide. Punjab has bears the brunt of the 16,000 cases and 350 deaths out of which 14,000cases and 300 deaths from Lahore alone. Still these figures are not representative of actual disease burden due to missing cases of private sectors.[8] DHF was initially brought to notice in Karachi in the year 1994, the second case being reported in Baluchistan in 1995. Subsequently, 10 confirmed cases resulting in 4 deaths were reported in Haripur in 2003.[11] WHO Statistics of cases of Dengue Fever in Pakistan revealed that the death

toll is gradually increasing as 17, 13, 40 and 219 deaths were reported in 2008 to 2011 respectively.[12]

Materails And Methods:

The Study was performed in the Department of Microbiology, Dow Diagnostic Research and Reference Laboratory, DUHS, Karachi, Pakistan, from 2010 to 2013. Total 4923 febrile cases were included in the study. All cases were collected per inclusion criteria for the presence of sign and symptoms of dengue fever or rash and then blood samples were collected for tests. The serological test was performed on sera of the patients for presence of dengue specific IgM and IgG antibodies, using nitrocellulose strips (ICT kit Pan-bio). The reaction tray was divided into 3 columns marked as G, M and control. The 45 µL of sample diluent was dispensed in the sample well and after that 45 µL of buffer was added. The results were read and interpreted after 15 minutes.

Results:

To rule out the primary and secondary infection the assay kit is designed as to determine the as IgM and IgG positive antibodies respectively. Among patients, Seropositive indicated that most of the patients were suffering from acute dengue infection. Positivity pattern of IgG and IgM among patients in different months was analyzed from January 2010 to December 2013 and cumulative results were presented. Higher frequency of positive cases was seen during the month of September, October and November. However, month of August and December also have detectable number of cases (Fig. 1). So, we can assume that the whole period of winter in critical for the breeding and spread of dengue virus.

Based on immune-chromato-graph test for IgM and IgG antibodies against *Dengue,* results showed that out of 4000 febrile cases, about 64% were male positive patients and 36% were female positive. In addition, when IgG and IgM antibodies against dengue were separately analyzed than it was found that incidences as

primary infection (IgM positive) were only slightly higher as compare to secondary infection (IgG positive). Figure 1 so the detection of both antibodies found to be critical for the proper diagnosis, timely treatment and management of the disease.

The negative indicate the total number of febrile (Male + Female) cases with no active disease and positive indicate presence of either IgG or IgM antibodies against dengue (Fig. 2).

Result showing the mean age for positive febrile cases diagnosed with active dengue disease. In this study, when positive cases were analyzed per different age groups it was found that the highest number of the patients belong to age group 21-30 years. However, 1-20 and, 30-50 years were also affected moderately (Fig. 3).
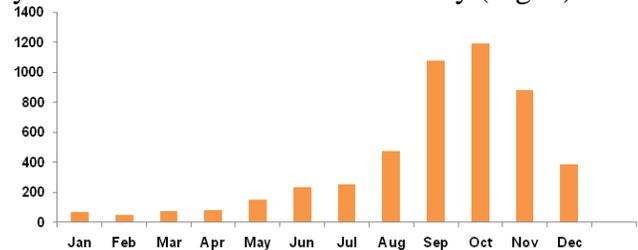

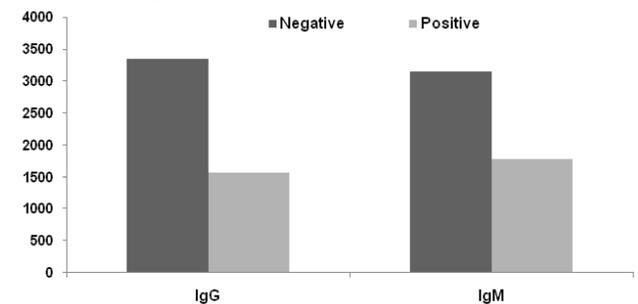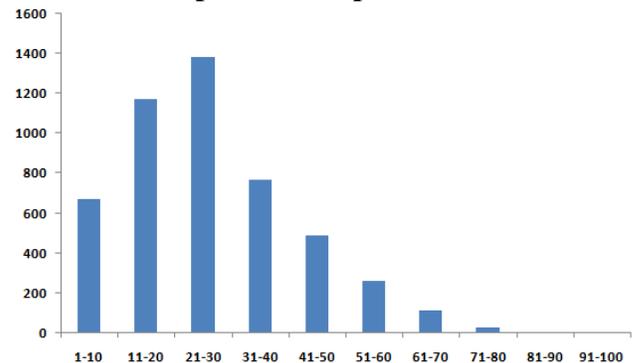**Fig. 1: 4972 cases seasonal variation in onset of the dengue infection in Karachi**

Fig. 2: Frequency of Dengue IgG and IgM antibodies in patient samples

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Years
Fig. 3: Distribution of seropositive findings by age group

Discussion:
Standing sanitary water, improper water draining system and lack of public awareness about hygiene may create more chances of breeding mosquitoes in any locality.[13] The clinical manifestation of dengue virus infection is varied ranging from subclinical to fatal. Most adult patient in countries where dengue is endemic usually develops secondary dengue infection which is difficult to treat. In our study, overall dengue seroprevalence which includes primary, secondary dengue infections were 51%. On the contrary, similar studies conducted by numerous authors and observed prevalence of dengue based on serology, recently 71 % cases documented by Malaysian hospital in year 2012.[14] In respect to age group the prevalence of dengue was higher in younger age group peoples, the higher prevalence of dengue in the age group of around 30 might be due to more outdoor activities allowing them to be exposed to Aedes mosquitoes. Similar results were obtained from another study.[15] Whereas in terms of genders, infection was more common in male patients as compare to females, epidemic intensity of the dengue infection in different months during study period starting from January to December, revealed that the highest infection recorded in the month of October and lowest in the months from January to April. The present data showed that male and female were 64% and 36%, respectively. It may be due to that males have the tendency to travel and do more outside works than the female also reported higher seropositive of dengue in men compared to women by Goh.[16]
Epidemiological data in terms of different months during study period, it was observed (Fig.2) that the highest number of cases was in October then September (1188) and November (878). The lowest numbers of cases were observed in months of Jan to April may be due to

unfavorable breeding environments as Dengue infection is related to season's due to higher activity after monsoon and the monsoon in Pakistan is getting shifting from June July to September and October.[17] Dengue is still an important public health problem in Pakistan like other countries in this region. In this study, it is observed that children, younger an adult population were at the high risk to infection. Strengthening of present dengue control program, improving local sanitation and proper drainage of stationary water around the roads, in addition to development of suitable tetravalent vaccines against 4 circulating serotypes of dengue virus could solve the prevailing problem.

Conclusion:
Still the dengue disease is a threat to Pakistani population as the new acute cases are arising at higher level. Being a developing country there should be more focus in eradicating the debilitating diseases like dengue fever, to reduce the economic burden through adapting vaccination strategies, proper sanitation and awareness programs. Special campaign for sprays and dengue control measures prior to month of October and fall season should be adopted essentially.

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