ORIGINAL ARTICLE

Seroprevalence of Dengue Virus by Detection of IgG Antibodies: A Tertiary Care Hospital Study in Rawalpindi

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ABSTRACT

Objective: To determine the seroprevalence of dengue virus infection by detecting IgG antibodies in a tertiary care hospital in Rawalpindi.

Study Design: Cross sectional study.

Place and Duration of Study: Virology department, Armed Forces Institute of Pathology Rawalpindi, July 2021 to December 2021.

Materials and Methods: A total of one hundred and fifty healthy general population of Rawalpindi aged 15 – 45 years were included in this study. Enzyme Linked Immunosorbent Assay (ELISA) was performed for the detection of dengue immunoglobulin G (IgG) antibody in serum samples of patients. Statistical Package for Social Sciences (SPSS) version 25 was used to analyze the data.

Results: Among 150 patients, 71 (47.3%) were males and 79 (52.7%) were females. Out of total patients, 50 (33.3%) were positive and 100 (67.7%) were negative for dengue IgG antibodies. Majority of dengue IgG positive patients were 25-40 years of age. Acute febrile illness was present among 37 (24.6%) patients and was absent in 113 (75.3%) patients. Participants provided history of presence of waste points and stagnant water in surrounding areas of 84 (56%) patients.

Conclusion: This study shows that there was a high exposure of dengue virus in Rawalpindi population. This can be problematic from public health point of view in future as sensitized population against dengue virus is more prone to dengue fever and serious effects of dengue virus reinfection.

Key Words: *Dengue Fever, Dengue Virus, Enzyme Linked Immunosorbent Assay, Immunoglobulin G, Seroprevalence.*

Introduction

Dengue fever (DF) is a significant public health issue worldwide, affecting millions of individuals annually including Pakistan.[1] In Pakistan last major outbreak occurred in 2019, resulting in 53000 cases and 95 reported deaths.[1] Outbreaks of DF in Rawalpindi region became more frequent after 2011 outbreak.[2]

The World Health Organization (WHO) classified DF in 1997 and revision of this classification was done in 2009 to make it more inclusive. DF was divided into three categories in 1997 as DF, undifferentiated fever, and Dengue hemorrhagic fever (DHF).[3] Dengue was categorized later in 2009 as with warning signs or without warning signs and severe dengue. Fever and at least two clinical symptoms or any warning signs are required for dengue diagnosis.[4] More than 350,000 people have been admitted to hospitals across Asia since 1956, with nearly 12000 reported deaths.[5] After 2006, epidemics of dengue occurred each year which has increased populations of infected people with this virus in different cities of Pakistan. In upcoming years, it is expected to become a health concern in Asia including Pakistan.[6]

DF spreads by mosquitos mainly in tropical and sub-tropical regions because of its peri-domestic breeding. Dengue virus is caused by the Aedes aegypti, which also causes yellow fever. The growth and reproduction of this vector is associated with freshwater reservoirs. International travelers were one of the main facilitators in the global spread of this disease.[7]

Dengue cases have increased up to 30 folds in past 50 years and approximately half of the world's population in over 100 countries is affected by this disease. The first confirmed and reported cases of dengue fever took place in Asia, North America, and Africa consecutively in 1779-1780. According to WHO, an expected 1.3 billion number of cases DF were reported between 1996 to 2005.[8] Global travel was mainly responsible for rapid spread of this

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disease. The total number of cases of dengue virus infection according to WHO gradually increased from 505,430 in 2000 to more than 2.4 million in 2010 and 5.2 million in 2019. This increase occurred during the previous 20 years and 960 fewer deaths were reported in 2000 as compared to 4032 in 2015.[9]

The basis for the laboratory diagnosis of dengue infection is by detection of glycoprotein dengue NS1 antigen, dengue anti-IgM, anti-IgG, and polymerase chain reaction (PCR) for the detection of DENV. The production of antibody against DENV infection depends on the immune status of the host. Patients with early-stage dengue infection have significant amounts of the nonstructural protein (NS1) in their sera, and this presence is persistent from day 1 to day 9 after the onset of symptoms. In cases of dengue infection, IgM may become detectable on days 4–5 of illness and last for 12 weeks, but IgG develops by day 14 and may last a lifetime. The IgG rises within 1 to 2 days following the development of symptoms in secondary dengue infection, along with the IgM antibodies.[10]

The four DENV serotypes are 1, 2, 3, and 4. Secondary infection caused by another serotype leads to increased chances of severe dengue due to antibody dependent enhancement.

Several studies have been conducted on dengue virus seroprevalence globally and locally, there is still a lack of data on the prevalence of the virus in the Rawalpindi region of Pakistan. This article aims to fill this research gap by conducting a study on the seroprevalence of dengue virus by detection of IgG antibodies in a tertiary care hospital in Rawalpindi.

Therefore, this study was conducted to establish the exposure of Rawalpindi population to previous dengue infection by detecting IgG. Previous exposure of dengue infection determines the seroprevalence and burden of the disease. Individual with positive IgG is more vulnerable for severe dengue reinfection due to antibody dependent enhancement. Reinfection with dengue should be prevented by prompt management.

Materials and Methods

This cross-sectional study was carried out in the Virology department of the Armed Forces Institute of Pathology Rawalpindi, Rawalpindi, from July 2021 to December 2021. Approval from Institutional Review Board (IRB) (BS AHS/VIR-2/READ-IRB/21/625) was taken. The sampling technique was non-probability consecutive sampling. Sample size was calculated by confidence interval of 95%, a margin of error of 5%, and a reported prevalence of dengue IgG of 18% from a prior local study of Pakistan.[11] The sample size of 150 was estimated by the WHO sample size calculator.

Patients of either gender, aged between 15 to 45 years and resident of Rawalpindi were included in this study. Patients with autoimmune diseases, acute febrile illness or those who were not willing were excluded. Patients were informed about the study's purpose and written consent was taken.

The demographics information of the participants included age, gender, and history of febrile illness during last one-year, previous history of dengue virus infection and environmental surroundings such as presence of waste points and stagnant water were recorded. Participants were selected from general population of Rawalpindi.

Blood specimen of participants was drawn at Armed Forces Institute of Pathology, Rawalpindi and was transported to Virology department. Specimen was centrifuged at 3500 rpm for 4 minutes to separate serum. Indirect manual ELISA with dengue ELISA IgG kit of Vircell Spain was used for the detection of IgG antibody against dengue virus and optical density was analyzed by ELISA plate reader.[12]

The Statistical Package for the Social Sciences (SPSS) version 25.00 was used to analyze the data. For continuous variables, mean and SD were determined. Categorical variables were calculated by using frequency and percentages. P-value of ≤ 0.05 considered statistically significant.

Results

Among total 150 patients, 71 (47.3%) were males and 79 (52.7%) females. Dengue IgG antibodies were detected in 50 (33.3%) patients. Patients of different age groups showed positive seroprevalence, however middle age group showed higher frequency of dengue IgG detection as shown in figure 1. Age group (26-35 years) showed the highest prevalence of 25 (59.5%) cases whereas age group (15-25 years) showed the least prevalence of 10 cases (37%). About 37 (24.7%) patients had a history of acute febrile illness during the last 1 year, whereas 113 (75.3%) had no such history. The presence of waste points and stagnant water within 400 meters among

seropositive individuals was observed in 84 (56%).

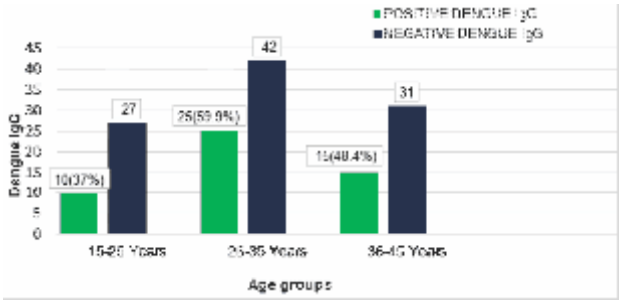

Fig. 1: IgG Seropositivity in Relation with Different Age Groups

Discussion

Dengue fever is a major public health concern worldwide, and seroprevalence studies are essential in understanding the spread and impact of the diseases.

Pakistan is one the countries with highest incidence of dengue fever according to WHO. Our study determined seroprevalence of dengue IgG in Rawalpindi. Dengue seroprevalence determine the percentage of individuals in population who have been infected with a dengue virus.

In our study, 150 samples were collected to determine the seroprevalence of dengue virus. There were 47.3% males and 52.7% females. The IgG antibody was detected using enzyme linked immunosorbent assay. Dengue IgG antibody was found in 33.3% patients. According to our results, out of 50 positive samples, 35.2% were males and 31.6% were females. This showed that prevalence of infection among males was approximately equal to females. Age group (26-35 years) showed the highest prevalence and 59.5% were positive for IgG antibodies against dengue virus. The age group (15-25 year) showed the least prevalence of 37%. In majority of cases waste points and stagnant water was present near the homes of people which also indicate to the problem of DF in urban and semi urban regions. These waste and stagnant water help in the propagation of mosquitoes which in turn help in spreading DENV. A study was conducted by Jyothi *et al* in India.[13] Five hundred and twenty serum samples were collected from clinically suspected dengue fever cases. A total of 11.9 % of the total tested serum samples were positive for one or more of the three serological markers (NS1, IgM, and IgG). Among 62 positive serum samples, 62.9% were positive for NS1, 11.3% were positive for dengue IgM, and 4.9% cases were positive for dengue IgG. This study shows low seroprevalence of Dengue IgG in comparison with our study.

A study was conducted by Eshetu D *et al* in 2016, in Ethiopia on dengue seropositivity and related risk factors.[14] In this study, risk factors associated with prevalence of DENV were evaluated. A total of 529 samples of patients having acute febrile illness were taken in 2016 and tested for dengue IgG and IgM antibodies. The prevalence of IgG and IgM antibody was 25.1% and 8.1% respectively which is lower in comparison with our study. Overall, people of age group 15-35 years accounted for 47.45 % of cases whereas 19.86% of cases were seen in age group 31-45 years. This showed that age group of young adults was more frequently infected by this virus as compared to other age groups.

A study conducted in Multan, Pakistan by Mukhtar et al, shows that out of 689 dengue suspected cases, 54.1% were positive for dengue IgG (27.6%) and IgM (54.7%). These results show high seroprevalence of dengue infection in comparison with our study.[15]

A study conducted in Lahore, found that seroprevalence of dengue IgG was 55.8% in the general population. This study also found that the prevalence was higher in males 62.2% than in females 49.3%. This study shows high seroprevalence of Dengue IgG in comparison with our study.[16]

In a study conducted in the district of Mardan in Khyber Pakhtunkhwa in 2017, a total number of 1978 patients were studied who were infected with DENV.[17] A total of 302 were positive (208 males and 94 females) for antibodies against DENV. Number of cases of dengue virus infection was higher in males 10.5% than in females 4.75%. The low prevalence in comparison with our study was found in this study of IgG and IgM antibodies was 23.84% and 53.9% respectively. The maximum amount of positivity of 47 % was in patients of age group 15 to 35 years.

There has been a variation in seroprevalence of dengue among different age groups and gender in previous studies. [18] Dengue viral infection prevalence is not similar but is different in various cities across Pakistan.[19] Our study showed that a considerable proportion of population of Rawalpindi might be exposed to DENV in the past which was detected by

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IgG antibodies. The population is especially at risk in future but to an outbreak by a different serotype of DENV. It is crucial to carry out extensive seroprevalence studies to ascertain the true scale of the issue. Timely identification can aid in reducing the morbidity and mortality rates. Neglecting the matter could result in significant dengue-related complications.

Limitations

The study was based on single center data in Virology department of the Armed Forces Institute of Pathology Rawalpindi. Sample size was small, and the duration of study was short which could have affected the results.

Conclusion

In this study it is concluded that there is a high exposure of DENV in Rawalpindi population. This can be problematic from public health point of view in future as sensitized population against dengue virus is more prone to serious effects of dengue virus reinfection with a different serotype.

Recommendations

Both large-scale epidemiological studies and vector control initiatives are urgently required. It is a concerning scenario, and if it is not handled by taking precautions, dengue will probably become a much bigger health issue in the years to come.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

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