A STUDY OF DEMOGRAPHIC PROFILE ASSOCIATION WITH SEROPOSITIVE CASES OF DENGUE VIRUS INFECTION IN LAHORE

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ABSTRACT
Introduction: Dengue fever is caused by a flavivirus, called dengue virus. Aedes Egypti and Aedes Albopictus transmit this virus. Diagnosis is through direct i.e. virus isolation, genome detection and antigen detection and indirect i.e. serology IgG and IgM detection methods.

Objective: The objective of the study was to study the association of different epidemiological factors with dengue fever in Lahore.

Material and Methods: 300 suspected dengue cases presenting in Emergency, Dengue isolation ward, different wards and OPD’s of Mayo Hospital, Sir Ganga Ram Hospital and Jinnah Hospital Lahore were obtained.

Sampling: Convenience purposive sampling was opted.

Study Design: It was analytical cross sectional.

The different demographic and epidemiological factors were noted to see their association with dengue fever.

Results: 90 patients (30% of total) were positive for IgM and 210 (70% of total) were negative for IgM. 108 patients (36% of total) were positive for IgG and 192 (64% of total) were negative for IgG. 54 (18%) were positive for IgM and 63 (21%) males were positive for IgG. 36 females (12%) were positive for IgM and 45 (15%) females were positive for IgG. Simultaneous positivity of both IgG and IgM was in 18 male patients (6%) and in 21 female patients (7%). IgM positivity was more in age group 11-20 (9%) and least in age group 71-80. IgG positivity was more in age group 11-20 (12%) and least in age groups 0-11 and 71-80 (2% each). Their mean age were 29.14 + 17.03 (SD) years ranging from 9 months to 90 years? Maximum positivity of IgM and IgG both was observed in Northern Lahore i.e. 48 (19 %). Minimum positivity of both IgM and IgG was observed in Eastern Lahore i.e. 3 (3 %) respectively.

Key Words: Dengue fever, Antibodies, Demographic profile, Epidemiology, Immunoglobulins.

INTRODUCTION
Dengue virus is a flavivirus. Since last 20 years there is global increase in the disease caused by this virus. 2.5-3 billion people worldwide at risk by this virus(1). Along with Aedes Egypti, the other fellow mosquito Aedes Albopictus is also known to transmit this virus with varying distribution in the world(2). For diagnosis direct i.e. virus isolation, genome detection and antigen detection while indirect i.e. serology IgG and IgM methods are used(3). Various studies outside Pakistan have been done to review and assess the factors influencing the epidemiology of the dengue infection(4). In contrast to nine reporting countries in the 1950s, today the dengue viral infection distribution includes more than 100 countries worldwide. Most of these had not reported dengue for 20 or have no known history of the disease.(5,6). The pathogenesis of dengue viral syndrome i.e. DHF/DSS is believed to be antibody-dependent, exaggerated by in secondary infection with a virus of different serotype. Many studies inclusive of Cuban epidemics of 1981 and 1997 and a five-year study of Yangon (Myanmar) confirm this finding. (7,8). Changing patterns of rural epidemics have been reported in Indonesia, in Laos, Thailand and India. Investigations depicted distribution of Aedes aegypti, both in rural and urban areas.(9,10,11). In a research carried out in Lahore, total 930 (82.37%) were found infected with DENV. Out of the 930 DENV RNA positive samples, 893 (96.02%) had DEN-2 and 37 (3.97%) sample had concurrent infection with serotypes 2 and 3 (12). At least seven dengue epidemics have been reported from Pakistan in last 20 years (13, 14, 15, 16, 17, 18, 19).

Dengue epidemic is a comparatively new problem in Pakistan especially Lahore with such magnitude. The approach toward this calamity has been abrupt in initial
days while later days showed multiple hypothesis and ideas about this infection. The mortality rate as claimed in literature is 0.5-1% but on ground the daily mortality averaged 6-8 in Lahore depicting some mutant or new strain of this virus or pointing towards low immunological response by the affected population. Though the epidemic had subsided at the time of this research but the coming months onwards might be showing the positive cases due to variation in temperature. The patients presenting with fever, myalgias, backache and headache for more than 5 days were screened for Dengue IgG and IgM antibodies in this study. A Performa recording the area of residence, age and gender of patient was maintained and then results inferred.

The objectives of the study were
1. To detect the seropositivity of dengue fever by detecting antibodies in the patient serum.
2. To ascertain the association of different demographic factors with the seropositive cases of dengue fever.

MATERIAL AND METHODS
300 suspected dengue cases presenting in Emergency, Dengue isolation ward, different wards and OPD’s of Mayo Hospital, Sir Ganga Ram Hospital and Jinnah Hospital Lahore were obtained. The specimens were stored keeping all safety measures and guidelines and processed later. Convenience purposive sampling was opted. The type of study was analytical cross sectional. The residential status, gender, age of the patients were noted and an evaluation was made to ascertain which areas, age groups and genders are most frequently susceptible to this infection. Correspondingly other related suspicions and phenomenon i.e. role of any biological maneuver, external intervention in this epidemic was assessed. ELISA kit by NovaLisa™ was used for assessing the IgG and IgM antibodies with negative, positive controls applied. The results were processed and categorized according to the plan opted.

RESULTS
90 patients (30% of total) were positive for IgM and 210(70% of total) were negative for IgM. 108 patients (36% of total) were positive for IgG and 192 (64% of total) were negative for IgG (Table 1). 24 males(18%) were positive for IgM and 63 (21%) males were positive for IgG. 36 females (12%) were positive for IgM and 45 (15%) females were positive for IgG. IgM positivity was more in males -18% vs. 12 % in females while IgG positivity was also more in males than in females – 21% vs. 15% - p value < 0.5 (Table 2). Simultaneous positivity of both IgG and IgM was in 18 male patients (6%) and in 21 (7%) female patients (Table 3). 6 patients (2%) in the age group 0-10 years were positive for IgM and 3 (1%) patients were positive for IgG. 24 patients (8%) in the age group 11-20 years were positive for IgM and 33 (11%) patients were positive for IgG. 9 patients (3%) in the age group 21-30 years were positive for IgM and 12 (4%) patients were positive for IgG. 18 patients (6%) in the age group 31-40 years were positive for IgM and 18 (6%) patients were positive for IgG. 3 (1%) patients in the age group 41-50 years was positive for IgM and 6 (2%) patients were positive for IgG. 6 (2%) patient in the age group 51-60 years was positive for IgM and 9 (3%) patients were positive for IgG. 6 (2%) patient in the age group 61-70 years were positive for IgM and 9 (3%) patients were positive for IgG. 3 (1%) patient in the age group 71-80 years was positive for IgM and no patient was positive for IgG. No positivity for either IgM or IgG was detected in ages beyond 80 years. IgM positivity was more in age group 11-20(9%) and least in age group 71-80. IgG positivity was more in age group 11-20(12%) and least in age groups 0-11 and 71-80(2% each) (Table 4). Concerning IgG and IgM positivity in different corners of Lahore, 3 patients(1%)were positive for IgM and 9 patients(3 %) were positive for IgG in Eastern Lahore, 27 patient(9%) were positive for IgM and 30 patients(10 %) were positive for IgG in Western Lahore, 48 patients(16%) were positive for IgM and 57 patients(19 %) were positive for IgG in Northern Lahore, 12 patients(4%) were positive for both IgM and IgG in Northern Lahore. Maximum positivity of IgM and IgG both was observed in Northern Lahore i.e. 16 vs. 19 %. Minimum positivity of both IgM and IgG was observed in Eastern Lahore i.e. one and 3 % respectively (Table 5).

| Table 1: Positivity of IgG and IgM values in total number of patients: (300) |
|-----------------------------|----------------|----------------|
| IgM | % age | IgG | % age |
| +ve 90 | 30 | +ve 108 | 36 |
| -ve 210 | 70 | -ve 192 | 64 |
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Table 2: IgG and IgM positivity in genders. Total suspected cases: 300

<table>
<thead>
<tr>
<th>Gender</th>
<th>IgM+ve</th>
<th>%age</th>
<th>IgG+ve</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>54</td>
<td>18</td>
<td>63</td>
<td>21</td>
</tr>
<tr>
<td>Female</td>
<td>36</td>
<td>12</td>
<td>45</td>
<td>15</td>
</tr>
</tbody>
</table>

Table 3: Simultaneous positivity of both IgG and IgM in genders. Total suspected cases: 300

Gender Distribution in seropositive cases of dengue for IgM & IgG separately

Total

Gender Distribution in seropositive cases of dengue for both IgM & IgG

Total
Table 4: IgG and IgM positivity in different ages. Total suspected cases: 300

<table>
<thead>
<tr>
<th>Age in years</th>
<th>IgM +ve</th>
<th>%age</th>
<th>IgG+ve</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10 years</td>
<td>6</td>
<td>2</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>11-20 years</td>
<td>27</td>
<td>9</td>
<td>36</td>
<td>12</td>
</tr>
<tr>
<td>21-30 years</td>
<td>15</td>
<td>5</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>31-40 years</td>
<td>24</td>
<td>8</td>
<td>27</td>
<td>9</td>
</tr>
<tr>
<td>41-50 years</td>
<td>3</td>
<td>1</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>51-60 years</td>
<td>9</td>
<td>3</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>61-70 years</td>
<td>6</td>
<td>2</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>71-80 years</td>
<td>3</td>
<td>1</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 5: IgG and IgM positivity in different corners of Lahore.

<table>
<thead>
<tr>
<th>Area distribution of Lahore:</th>
<th>IgM</th>
<th>% (of total positive)</th>
<th>IgG</th>
<th>% (of total positive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>East: Cantt, Airport, Fortress, Saddar and nearby areas.</td>
<td>3</td>
<td>1</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>West: Mall Road, Iqbal Town, Mozang, Samanabad and nearby areas.</td>
<td>27</td>
<td>9</td>
<td>30</td>
<td>10</td>
</tr>
<tr>
<td>North: Azadi Chowk, GT Road, Badami Bagh, Mughalpura and nearby areas</td>
<td>48</td>
<td>16</td>
<td>57</td>
<td>19</td>
</tr>
<tr>
<td>South: Model Town, Liberty, Gulberg, Defence and nearby areas.</td>
<td>12</td>
<td>4</td>
<td>12</td>
<td>4</td>
</tr>
</tbody>
</table>

DISCUSSION

Viral infections are becoming a serious global threat to human life\(^{20}\). Viral epidemics are continuously increasing from a last decade in Asian countries especially in Pakistan. Among these epidemics, dengue is the most commonly occurring mosquito-borne viral disease affecting a large number of humans in the Punjab province of Pakistan and especially in Lahore. According to WHO Dengue infection is the most commonly spreading, vector borne disease in the globe \(^{21}\) and is now endemic in Pakistan. It is present throughout the year with epidemics in the post monsoon period as a serious outbreak. The number of dengue fever cases is continuously rising in Pakistan especially in Lahore since 2006. In 2006 the reported cases in Lahore were 309 whereas in 2007, 107 cases were detected in Lahore city. In 2008 the reported cases rose up to 1766. This number was continuously rising till 2011 when a major epidemic hit the province of Punjab especially Lahore. According to reports, the total number of patients was 14,077 in the entire province out of which 12,216 were in Lahore only. The total number of casualties from dengue in 2011 was 155 in Lahore while 172 in Punjab. As of November 2011, it has killed over 300 people in the last several months and over 14,000 are infected by this mosquito-borne disease. Majority of the people infected are from the Lahore area in Punjab, Pakistan.\(^{26}\)

This number declined in 2012 due to some strict measures adapted by the government. The number of dengue cases declined to 143 in Lahore in 2012. Present study attempts to evaluate, any relation between the area of residence and dengue infection, any link between ages of dengue patient and infection and any relation of dengue infection with the gender/sex of patients in the Lahore city.

The dengue fever cases were identified from all the towns of Lahore city. These cases were more concentrated in areas like Mozang, Mughalpura, Badami Bagh and Samanabad. One reason may be these areas are heavily populated. Congested residential style predispose a large number of humans to the bites of Aedes aegypti which bites several people in a short period \(^{22, 23}\). Uncontrolled population growth produces water and sewage problem. It also upsets waste management system creating ideal conditions for vector and water born infections\(^{24}\). The seropositivity of IgG and IgM does not necessarily depict the RNA presence in patients as reported in unpublished reports by Mayo Hospital main clinical laboratory research. The seropositivity in various areas of Lahore, ages and genders is not corresponding with the almost non significant incidence Dengue fever reported in Lahore. This could be due to more preventive and precautionary measures and hectic efforts by Punjab Health Department and Government of Punjab this year. This was also depicted by a survey done in Lahore\(^{25}\) as 60% people perceived that clean stagnant Water and mosquito (59%) is the main cause, while Dirty Water (28%), Garbage/Pollution (22%) and others such as hot weather, Rains, Sewerage system (17%).

If we analyze dengue viral antibodies in different age groups we come to know that it is more in young adults and adults i.e. between 11-40 years. In our study
mean age was 29.14 + 17.03 (SD) years ranging from 9 months to 90 years while in this Lahore study the mean age group were 31.14 + 16.03 (SD) years ranging from 9 months to 90 years (p value < 0.05)12. This is probably due to the fact that this age group is more mobile and active in their daily life.

If we analyze our results according to gender groups we found that males were more affected by the dengue fever. We evaluated the antibodies against IgM and IgG in genders and our findings showed 18 and 12% positivity for IgM in males vs. females while positivity for IgG in males and females was 21% vs. 15% respectively. Our results are closer to the results of Idrees et al (12) conducted in Lahore i.e. Male female ratio of the suspected dengue patients was 2.4:1 (p value< 0.05). One reason may be that females are fully dressed and covered while males are more exposed. Though Use of serological methods by detecting viral anti-IgM anti-IgG can give false positive results due to extensive antigenic cross-reactivity among flavivirus as well as between different dengue virus serotypes but financial constraints did not make it possible to assess the antigen(27).

CONCLUSION
This study will be helpful to the physicians in diagnosing outcome of this disease beforehand and will also guide them in controlling this menace. Family doctors in primary health care setting have an opportunity not only to give the best possible supportive care to their patients but also educate them regarding the spread of Dengue fever and vector control.

The demographic profile showed variable association of different factors with dengue fever. Younger, male adults were more frequently involved than the elderly and females according to the study. Areas of Lahore showing high rates of dengue viral antibodies seem to be mostly open areas having large vegetation. These areas need additional attention for control and eradication. Biological control or "biocntrol" is the use of natural enemies to manage mosquito populations with a minimum risk to humans, wildlife and the environment. Any of the feasible methods can help a lot in controlling/eradicating dengue outbreaks without heavy costs.

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