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Research Article

Seroprevalence of Dengue IgG Antibodies among Healthy Adult Population in Lahore, Pakistan

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Background. Dengue is a mosquito-borne flavivirus infection prevalent in tropical and subtropical regions around the world. Aim of this study was to determine seroprevalence of anti-dengue IgG antibodies in healthy adult population of Lahore and also describe risk factors in relation to dengue seropositivity. Methods. In this cross-sectional study, 274 healthy adult individuals aged 15 years and above were randomly selected using multistage sampling technique. These individuals were interviewed between July–September 2012, using a semistructured questionnaire, followed by drawing 3 mL of their venous blood for dengue IgG test. Nova Tech ELISA kit with sensitivity and specificity of 96.5% and 97.5%, respectively, was used for serology. Results. Out of 274 participants, 184 (67.2%) were found to be positive for dengue IgG antibodies. Seroprevalence was higher among individuals with poor awareness about potential breeding sites for dengue mosquito (63.6%), followed by the subjects who had poor knowledge about dengue signs/symptoms and complications (52.2% and 68.5%, resp.). Conclusion. About two-third of healthy population of Lahore was also seropositive for anti-dengue IgG during July–September 2012, indicating a considerable burden of subclinical dengue infection in the city. Males were predominantly affected than the females. We found no statistical association between dengue IgG seropositivity and socioeconomic status, occupation, and knowledge about the disease.

1. Background

Dengue is a mosquito-borne flavivirus infection prevalent in tropical and subtropical regions around the world, and it has emerged as an important global public health challenge. In recent years, disease transmission has increased predominantly in urban and semiurban areas owing to economic reasons and migration. There are four distinct but closely related serotypes (DEN-1, DEN-2, DEN-3, and DEN-4) of the dengue virus known; however, DEN-2 infection is more prevalent in South Asian region including Pakistan [1, 2]. Recovery from one type of virus infection, though, provides lifelong immunity against that particular serotype, but there is a strong evidence suggesting the occurrence of severe clinical manifestations of dengue fever in subsequent infection from other serotypes [3]. Infective female *Aedes*

aegypti mosquito species is the primary vector for dengue which transmits the virus through biting humans. On the other hand, Aedes albopictus is responsible for maintaining the endemicity in the population [4]. Absence of an effective vaccine, vector control measures, and personal protection represent the only available mitigation strategies against dengue outbreaks.

The first record of dengue fever like condition is mentioned in Chinese medical encyclopedia during Jin Dynasty (265–420 AD), which referred this as "water poison" associated with flying insects. The first recognized dengue epidemics occurred almost simultaneously in Asia, Africa, and North America in the 1780s, shortly after the identification and naming of the disease in 1779 [5]. The first confirmed case report dates from 1789 and was by Benjamin Rush, who coined the term "break bone fever" because of the

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symptoms of Myalgia and Arthralgia. The viral etiology and the transmission by mosquitoes were only deciphered in the 20th century. The socioeconomic impact of World War II resulted in increased spread globally [5]. In Pakistan, first dengue patient was diagnosed in Karachi during June–September, 1994. Economic and security related migration to Lahore (central Punjab, Pakistan) around 2007 introduced the virus here in this population, resulting in sporadic disease transmission from 2008 to 2010; however, a huge outbreak from September to December 2011 paralyzed whole city of Lahore and put immense pressure on public health system. In spite of increased number of dengue, there has not been any attempt to measure the burden of this disease [6].

According to an estimate of World Health Organization, 2.5 billion people live in regions potentially at risk of dengue infection. Every year approximately 100 million cases of dengue fever and 500,000 cases of dengue hemorrhagic fever occur, whereas about 25000 die from dengue related clinical manifestations [7]. A massive dengue outbreak (590339 suspected cases) in Lahore, Pakistan, during the last quarter of 2011 killed 335 people, in addition to 21685 serologically confirmed cases; majority (68%) of the cases were males in age group of 15-45 years [6]. In addition to climate change in last few decades, population growth, accelerated urbanization, increased international travelling, weakened public health infrastructure, lack of effective vector control, and disease surveillance have been reported as the major determinants of frequent dengue outbreaks [7–9]. The speed of spread has been in pace with urbanization and industrialization in these dengue endemic regions.

Currently, Vietnam, Thailand, Sri-Lanka, Indonesia, Pakistan, some parts of India, and Malaysia are exhibiting dengue hyperendemicity [10]. In India, 19.7% of clinical febrile episodes among admitted patients for five-year study period were positive for dengue virus infection. Majority of cases were from age group of 0-15 years followed by 16-30 years with 2:1 male to female ratio among them. Most (92%) of these infections were secondary [11, 12]. Similarly, a cross-sectional study in Sri-Lanka among pediatric population reported that nearly 34.1% of studied children had anti-dengue IgG antibodies on ELISA [13, 14]. In Pakistan, it has been reported that, out of 96 subjects from rural areas of Rawalpindi, 12 (13.5%) were found positive for IgG antibodies. Neither the sample size of 96 in the said study was sufficient enough for population generalization nor was its sampling technique rigorous enough for external validity. There is a need to conduct a study with larger sample size and with more population representation [15].

Dengue is an emerging disease in Lahore. Health department has accumulated a large amount of data about dengue in recent years; however, seroprevalence of dengue in healthy population in still unknown. The purpose of this was to determine seroprevalence of dengue IgG in adult population of Lahore as well as describe risk factors related to seropositivity. Information not only helps to establish the magnitude of this problem in Lahore but also provides a baseline for dengue subclinical cases in this area.

2. Methods

This cross-sectional comparative study was conducted from July-September 2012 in district Lahore covering all administrative towns. Total of 274 individuals aged 15 years and above were included in this study using multistage sampling technique. In first stage, three union councils were randomly selected from each town using lists of union councils obtained from city district government Lahore. From each union council, seven males and three females were randomly recruited using family registers of communitybased lady health workers. Difference based on gender is due to the observation that dengue is more pronounced among males. Out of 300 individuals initially recruited for the study, twenty-six did not give consent to draw blood for serological examination. These individuals were excluded from final analysis. After interviewing the eligible individuals about dengue awareness, 3 mL of venous blood was drawn by trained phlebotomist observing strict aseptic precautions. Clotted samples were centrifuged at 3000 rpm for 5 minutes to separate serum and stored in properly labeled and sealed plastic vials. These samples were stored in Pathology Department of Sir Ganga Ram Hospital, Lahore. Dengue serological test was performed in Institute of Public health, Lahore, using Nova Tech ELISA kit for qualitative immunoenzymatic determination of IgG-class antibodies against dengue virus in human serum. Sensitivity and specificity of the kit were 96.5% and 97.5,% respectively. Sample was considered positive if the absorbance value is higher than 10% over the cut-off. SPSS version 18 was used for data management and analysis. Data were compiled and analyzed. Continuous data was analyzed using mean and standard deviation, whereas categorical data was presented in the form of numbers and percentages. Difference of means was compared using *t*-test after checking assumptions, whereas categorical data was compared using chi-square test and Fisher exact test (where appropriate). A *P* value < 0.05 was considered statistically significant. Ethical approval for this study was obtained from institutional research committee of Sir Ganga Ram Hospital, Lahore.

3. Results

Out of 274 participants tested for dengue anti-IgG, 184 (67.2%) were found to be positive. Of these, majority 34 (18.5%) belonged to cantonment area followed by Samanabad 29 (15.8%), Shalimar town 22 (12%), and Nishtar town 22 (12%), respectively. All these towns consist of urban and semiurban areas. On the other hand, low prevalence was observed in Wagha towns (3.8%) and Aziz Bhatti town (2.2%) having predominantly rural areas. Last two towns are situated adjacent to international border with India. Seroprevalence among males was higher (68.9%) than females (63.7%), whereas, with increasing age, seropositivity was also found to rise (59.2% among those of 15-24 years as compared to 75.6% in 35-44-year-old participants). Regarding socioeconomic status of the individuals, dengue anti-IgG positivity was comparatively higher among subjects of low socioeconomic class (73% versus 59.6%), and this difference was also observed in relation to their educational status (76.1% among those

Table 1: Seroprevalence of dengue IgG among healthy subjects in Lahore based on their sociodemographic characteristics (n = 274).

Characteristics	N	IgG positive N (%)	IgG negative N (%)	Adjusted odds ratio	95% CI.	P
Age (years)						
15-24	76	45 (59.2)	31 (40.8)	1	Reference	
25-34	88	56 (63.6)	32 (36.4)	1.12	0.56-2.21	0.73
35-44	45	34 (75.6)	11 (24.4)	1.98	0.81 - 4.83	0.12
45-54	27	19 (70.4)	08 (29.6)	1.68	0.63-4.50	0.29
55+	38	30 (78.9)	08 (21.1)	2.48	0.95-6.47	0.06
Sex						
Female	91	58 (63.7)	33 (36.3)	1	Reference	
Male	183	126 (68.9)	57 (31.1)	1.31	0.66-2.63	0.43
Educational status						
No schooling	67	51 (76.1)	16 (23.9)	1	Reference	
Less than 10 years	65	43 (66.2)	22 (33.8)	0.67	0.30-1.49	0.32
10-12 years	88	60 (68.2)	28 (31.8)	0.75	0.34-1.65	0.47
More than 12 years	54	30 (55.6)	24 (44.4)	0.41	0.16-1.06	0.06
Monthly income (Pakistani Ru	pees)					
Low income	204	139 (68.1)	65 (31.9)	1	Reference	
Middle income	44	33 (75.0)	11 (25.0)	2.22	0.87-5.64	0.09
Higher income	26	12 (46.2)	14 (53.8)	0.62	0.22 - 1.74	0.36
Occupation						
Unemployed	94	60 (63.8)	34 (36.2)	1	Reference	
Unskilled workers	82	58 (70.7)	24 (29.3)	1.01	0.45 - 2.28	0.96
Skilled workers	56	37 (66.1)	19 (33.9)	1.00	0.41 - 2.39	0.99
Professional	10	05 (50.0)	05 (50.0)	0.76	0.18-3.13	0.71
Business/trade	32	24 (75.0)	08 (25.0)	1.71	0.57-5.10	0.33
Socioeconomic status*						
Low SES	87	64 (73.6)	23 (26.4)	1	Reference	
Middle SES	130	86 (66.2)	44 (33.8)	0.37	0.12-1.15	0.08
Upper SES	57	34 (59.6)	23 (40.4)	0.21	0.02-1.54	0.12

Low income: less than Rs.25000; middle income: Rs.25000-50000; higher income: >Rs.50000.

with no schooling compared to 55.6% with more than 12 years of education). Although age was found to be strongly associated with dengue anti-IgG seropositivity, in terms of odds (adjusted OR 1.98; 95% CI. 0.81-4.83; P = 0.12 for age group of 35-44 years), wide confidence intervals at 95% indicate low precision in estimation (Table 1). Similarly, no statistical association was observed with socioeconomic status (adjusted OR 0.21. 95% CI. 0.02–1.54; P = 0.08for higher socioeconomic status putting low socioeconomic status as reference). When seroprevalence of anti-dengue IgG among healthy adult population in Lahore was analyzed in relation to their level of awareness about dengue, it was found that most of these individuals had poor knowledge about dengue infection transmission 173 (63.1%), potential breeding sites for mosquito 143 (52.3%), dengue symptoms and signs 144 (52.6%), and dengue complications 182 (66.4%). Although seroprevalence was also higher among individuals with poor awareness about dengue potential breeding sites

(63.6%) and poor knowledge about dengue signs/symptoms and complications (52.2% and 68.5% resp.), Table 2 shows that no statistically significant difference was observed in relation to good, satisfactory, or poor level of awareness about dengue transmission (P = 0.56), complications (P = 0.53), potential breeding sites (P = 0.30), and preventive measures (P = 0.64).

4. Discussion

Dengue virus infection has emerged in recent years as an important public health problem in Pakistan. Being localized in port city of Karachi at the start of this millennium, health care institutions in Lahore began reporting sporadic cases in Lahore during 2009 onward till a huge outbreak surrounded this city in September 2011. Transmission of dengue infection to thousands of people and resultant death of more than three hundred patients demonstrated the fatal nature of

^{*}Socioeconomic status (SES) is based on combined score computed from education, income, and occupation.

Table 2: Seroprevalence of dengue IgG among healthy subjects in Lahore in relation to their level of awareness about dengue and its prevention (n = 274).

Characteristics	N (%)	IgG positive N (%)	IgG negative N (%)	$\chi^2_{ m trend}$	Р
Dengue infection transmission				0.33	0.56
Good	24 (8.8)	14 (7.6)	10 (11.1)		
Satisfactory	77 (28.1)	53 (28.8)	24 (26.7)		
Poor	173 (63.1)	117 (63.6)	56 (62.2)		
Potential breeding sites knowledge					0.30
Good	29 (10.6)	18 (9.8)	11 (12.2)		
Satisfactory	102 (37.2)	66 (35.9)	36 (40.0)		
Poor	143 (52.2)	100 (54.3)	43 (47.8)		
Dengue signs and symptoms				0.06	0.79
Good	20 (7.3)	14 (7.6)	06 (6.7)		
Satisfactory	110 (40.1)	74 (40.2)	36 (40.0)		
Poor	144 (52.6)	96 (52.2)	48 (53.3)		
Dengue complications knowledge				0.38	0.53
Good	15 (5.5)	11 (6.0)	04 (4.4)		
Satisfactory	77 (28.1)	47 (25.5)	30 (33.3)		
Poor	182 (66.4)	126 (68.5)	56 (62.2)		
Preventive measures knowledge				0.21	0.64
Good	23 (8.4)	14 (7.6)	09 (10.0)		
Satisfactory	87 (31.8)	59 (32.1)	28 (31.1)		
Poor	164 (59.9)	111 (60.3)	53 (58.9)		
Using bed nets				0.56	0.45
No	167 (60.9)	115 (62.5)	52 (57.8)		
Yes	107 (39.1)	69 (37.5)	38 (42.2)		
Frequency of anti-mosquito spray				3.0	0.08
Once a year	35 (12.8)	23 (12.5)	12 (13.3)		
Twice a year	116 (42.3)	71 (38.6)	45 (50.0)		
Never	123 (44.9)	90 (48.9)	33 (36.6)		

^{*} χ^2_{trend} used for ordered categories.

this infection in a relatively nascent population. According to department of health Punjab, the laboratory confirmed cases were around 32000; however it was suspected that approximately 200,000 individuals were exposed to dengue virus in Lahore during August to December 2011, yet no study estimated the exposure among those individuals who did not develop clinical manifestations of the disease. Aim of existing study was to bridge this gap. We report that 67.2% of the healthy population in Lahore is seropositive for dengue IgG which indicates the unprecedented extent of exposure to dengue virus. Large number of individuals with IgG positivity in Lahore would be at alarming risk of developing dengue hemorrhagic fever (DHF) with introduction of other serotypes owing to cross-reactivity. Therefore, early disease warning system for dengue should be introduced to fight against this menace. Globally, higher dengue IgG seroprevalence has also been reported in communities with similar sociodemographic backgrounds and economic status.

In 2010, seroprevalence of dengue IgG in American Samoa was found to be 95.6 (CI: 93.9%–96.8%). On the other hand, it was 31.3% in central part of India and 45% in Nigeria, respectively. Similarly, Sultana et al. found that 42.9% of suspected cases of dengue fever in Chittagong, Bangladesh, had anti-dengue IgG in their serums [12]. Differences in disease frequency can be explained on the basis of level of urbanization, deterioration of environment, and awareness about dengue in population [13].

Dengue virus infection has always been reported as the disease of urban areas; however, results of Ukey et al. [14] in India and Zafar et al. [15] in Rawalpindi, Pakistan, suggested its extent to rural population as well. For instance, sero-prevalence of anti-dengue IgG antibodies in tehsil kahuta, district Rawalpindi, among healthy rural population during 2010 was 13.5% and that in rural India was 31.3%. In contrast, our study did not demonstrate higher dengue prevalence in rural communities. In addition, the seroprevalence in rural

areas near border with India was the lowest (2.2%) rejecting the misconception that dengue virus infection was imported from Indian Punjab through adjacent border.

In many parts of the world, dengue infection is predominantly a childhood disease; however, it affects adult population primarily during first few years of its emergence. Results of current study also confirmed this notion. Adults aged 30 and above showed higher IgG positivity, and we observed upward trend with increasing age. Similar findings were also reported by Ukey et al. [14] in India where most affected population stratum in age range of 15-30 years (29.27) and that of Sri Lankans was between in age range of 26-40 years [16]. Although, males in Lahore were infected more than female population, yet this difference was not observed in other studies elsewhere except in India. This variation can be explained on the basis of differences in population selection in these investigations. Furthermore, there is a paradoxical relationship of dengue vector habitat and its biting nature. Since Aedes Mosquito mainly lives indoor where there are more chances of exposure to females in our settings, yet prevalence among females is on the lower side. There may be differences in biting nature of Aedes Mosquito in this part of globe or females might be protected owing to some hormones which repel the vector. These questions need to be explored more.

Dengue virus infection is the most underrecognized and underreported disease especially in developing countries. This is due to low level of awareness not only among general public but also lack of training to manage dengue among treating physicians, which might result in higher mortality associated with it. In addition, febrile illness is usually confused with other viral diseases and malaria. Level of awareness about dengue signs and symptoms and protective measure was found unsatisfactory among studies population, yet no statistical association observed between anti-dengue IgG seropositivity and knowledge about disease transmission, potential breeding sites, complications, and preventive measures. There were obvious differences in seroprevalence among studied individuals based on their educational status, monthly income, and occupation; however, when the relationship of these influences in the form of socioeconomic status score was statistically measured, the observed differences were not found statistically significant. These findings were in contrary to the studies by Duncombe at al. [17] and Amarasinghe et al. [18], where it was reported that dengue is related to poor socioeconomic conditions and poor knowledge. Similarly, Braga et al. [19] in Brazil found an inverse relationship between socioeconomic status and seroprevalence. Magnitude of dengue burden was higher (91.1%) in socioeconomically deprived areas compared to intermediate (87.4%) and high status regions (74.3%). Lack of association as regard to socioeconomic status in our study may be due to difference in methodology of computing socioeconomic status score. Other studies could have given different weights to educational status, monthly income, and occupation.

The results of this study should be interpreted in light of the consideration that study participants were limited to adult healthy population, excluding children for not granting ethical approval and using relatively small sample size for prevalence estimation; however, results are significant enough and providing evidence in order to devise a surveillance system for detecting dengue outbreaks in an early stage for preventive actions.

5. Conclusion

Seroprevalence of anti-dengue IgG in healthy population of Lahore during July–September 2012 was 67.2% with males being more affected than the females. Dengue was predominantly affecting individuals in age group of 35 years and above. We found no statistical association between IgG seropositivity and socioeconomic status, occupation, and level of awareness about the disease.

Conflict of Interests

Authors declare no conflict of interests regarding conduct of this study. No external funding was involved in this study.

Author's Contribution

Shahid Mahmood participated in study conception, design, data analysis and interpretation, and drafting the paper. Hibah Nabeel participated in data collection, data management and analysis, and drafting tables. Saadia Hafeez helped in data collection, and drafting the paper. Urooj Zahra helped in data collection, paper revision, and final drafting. Hammad Nazeer helped in study design, interpretation of results, and revision of paper. All the authors read and approved the final paper for publication.

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