

# Association of Seroprevalence with Demographic Characteristics of Dengue Viral Infection in a Megacity, Karachi, Pakistan

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## Abstract

**Objective:** To determine the association between demographic characteristics as risk factors for seroprevalence of dengue viral infection in an urban community of a megacity, Karachi, Pakistan.

**Methods:** A cross-sectional study was carried out in a dengue endemic area of a megacity, Karachi. Simple random sampling was used for selecting 378 research subjects. Gadap town consists of 13 union councils. Three union councils in the periurban area of Gadap Town, Karachi were randomly selected initially. A total of 200 houses (lady health worker had full data on each house) were observed. The inclusion criteria was active adult (18-55 years), both genders, resident of union council 1 and 3 in Gadap town, Karachi for at least 5 years. The exclusion criteria was severe comorbidities. The study was conducted in between January 2014 and January 2015.

The data included demographic characteristics and their association with seroprevalence by enzyme-linked immunosorbent assay (ELISA) to detect anti-dengue immunoglobulin G (IgG) and M (IgM) antibody. Initially patients presented with high fever, rashes, severe headache, joint pain, nausea, vomiting and thrombocytopenia. All patients were subjected to serological examination. The sociodemographic variables were analysed on SPSS version 15.

**Result:** A total of 378 cases were analysed. There were 126 (33.3%) cases positive for anti-dengue IgG and IgM antibody. Females were more affected, 266 (70.4%) and commonest age group affected in these adults was between 37-54 years, 143 (37.8%). A significant association at p-value<0.5 was found in gender, ethnicity, marital status, primary education and unemployed subjects with seropositive tests.

**Conclusion:** About one-third of the sample had an association between demographic characteristics as risk factors for seroprevalence of dengue viral infection in an urban community of the megacity, Karachi, which can be used for preventive strategies in future to control dengue fever in the community.

**Keyword:** Seroprevalence, demography, risk factors, dengue virus, urban health.

**IRB:** An ethical permission was obtained by the institute of environmental diseases, University of Karachi. **Dated:** 20th December 2013.

**Citation:** Quadri SMA, Khan M, Fatima G, Siddiqui NY. Association of Seroprevalence with Demographic Characteristics of Dengue Viral Infection in a Megacity, Karachi, Pakistan [Online]. *Annals ASH KM&DC* 2017;22:81-8. Available at: [www.annals-ashkmdc.org](http://www.annals-ashkmdc.org).

(ASH & KMDC 22(3):171;2017)

## Introduction

Currently re-emergence of dengue fever/dengue haemorrhagic fever has been observed globally

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Date of Submission: 22<sup>nd</sup> July 2017

Date of Acceptance: 7<sup>th</sup> September 2017

which is more fatal and is a cause of high morbidity in Asian countries<sup>1</sup>. Dengue fever is a major public health problem in the tropical and subtropical countries<sup>2</sup>. Non-availability of an effective tetravalent dengue vaccine and poor *Aedes aegypti* mosquito control, focuses on interventions for transmission of dengue fever<sup>3</sup>. Vector control is required to stop the disease from spreading at the household level in the low socioeconomic countries. Various dengue virus serotypes (DENV) are associated with variety of clinical pictures in low social groups in the community<sup>4</sup>. All the four serotypes (DENV) are not

found in the laboratory test performed in the community for diagnosing dengue fever. The seroprevalence with demographic characteristics of dengue viral infection in urban community varies including their immunity, environmental factors, behavioural factors regarding seeking care in the community. According to the environment and other characteristics of population the demographic characteristics appear to be different with DENV-2 and DENV-35<sup>6</sup>.

The prevalence of dengue infection was 37.3% in one year. The household surveys have confirmed low prevalence areas which have been converted to high-risk area in consecutive years<sup>7-8</sup>. Currently, the disease is endemic in more than 100 countries and all over the tropical and subtropical areas<sup>9</sup>. The suboptimal strategies for vector control, low literacy and poor behavioral factors leads to more positive cases in the communities<sup>10</sup>. Mostly dengue cases are underreported and misclassified globally. Accordingly, there has been an estimate of dengue infections occurring every year. The reported cases are undiagnosed because of lack of awareness and early diagnostic technologies in the under-privileged and poor societies. The vaccine is still under trial and vector control is not optimum. There is lack of political will and enforcement of strategies at ground root levels.

Since the vaccine is under trial and is still not available and morbidity/mortality in Pakistani urban slums is increasing, therefore, this cross-sectional study was conducted. The study aims to determine the association with demographic characteristics as risk factors for seroprevalence of dengue viral infection in an urban community of the megacity, Karachi. Dengue infection has become an endemic disease in urban communities. The study will help in prediction of dengue infections based on demographic characteristics in the community.

## Subjects and Methods

A cross-sectional study was carried out in a dengue endemic area of the megacity, Karachi. Simple random sampling was used for selecting

378 research subjects. The study was conducted during January 2014 to January 2015.

Based on previously published data<sup>7</sup>, sample size was calculated through OpenEpi.org (Version 3) and an open source calculator. The sample size was calculated using a proportion of dengue fever positive cases at 37%<sup>6</sup> with margin of error 5% and 95% confidence interval. The computed sample size was 359. Adding 5% non-response rate and incomplete data, the final sample size was 378. Simple random sampling was used to select 378 research subjects. Gadap town consists of 13 union councils. Three union councils in the periurban area of Gadap Town, Karachi were randomly selected initially. A total of 200 houses were observed. Lady health worker had full data on each house. The inclusion criteria were active adult (between 18 to 55 years of age), belonging to either gender, resident of union council 1 and 3 in Gadap town, Karachi for at least 5 years and willing to contribute in the study. The exclusion criteria were severe comorbidities diagnosed in last five years. An ethical permission was obtained by the institute of environmental diseases, University of Karachi.

A semi-structured questionnaire was developed and observations were recorded as a pilot study for the validation of the study tool. Later the study was conducted in the community of Gadap town with the same validated tool. The demographic, medical, surgical and clinical data were recorded. Early laboratory investigations were performed and cases were managed according to the diagnosis. Severe cases were referred to tertiary care hospitals in Karachi for further management. The data included demographic characteristics of all subjects and their association with seroprevalence by enzyme-linked immunosorbent assay (ELISA) to detect anti-dengue immunoglobulin G (IgG) and M (IgM) antibody. Initially patients presented with high fever, rashes, severe headache, joint pain, nausea, vomiting and thrombocytopenia. All patients were subjected to serological examination.

Each questionnaire was coded, and all data were accessible only to principal and co-investiga-

tors for data analysis. The analysis was performed with the assistance of Statistical Package for Social Sciences 15.0 (SPSS, Inc., Chicago, IL). Means with standard deviation for numerical variables and proportions for categorical variables including education, ethnicity, marital status and occupation were analysed. The association between variables was tested using the  $\chi^2$  test between dengue infection present and absent groups.

### Result

There were 378 cases observed in this study. The analysis confirmed 126 (33.3%) cases positive for anti-dengue IgG and IgM antibody and 252 (66.7%) were declared negative for dengue infection by laboratory tests. Females were 266 (70.4%) in number and the commonest age group affected in these adults were between 37-54 years; 143 (37.8%), as shown in Table 1. Most of the research subjects were 5 years educated; 176 (46.7 %), unmarried; 220 (66.9%), and 164 (65.1 %) from low socioeconomic conditions. The significant association at  $p$ -value  $\leq 0.5$  was found in gender, ethnicity, marital status, primary education and unemployed subjects.

### Discussion

Dengue has rigorously increased in the last two decades particularly in Asian communities and observed as fatal outbreaks after monsoon rains after which it has become an endemic disease<sup>8</sup>. The socio-demographic covariates were observed in this cross-sectional study for association of seroprevalence with different types of serotypes<sup>9</sup>.

Dengue virus is extending its range and prevalence because its mosquito vector breeds rapidly in the urban environment<sup>10</sup>. The result in this study has been consistent with previous studies which found that the majority of dengue cases occurred in months with higher rainfall in "dengue season". The risk of dengue was higher in urban areas due to overcrowding and behavioral factors associated with spread of dengue infections<sup>11</sup>.

Clinically, dengue resembles malaria, leptospirosis and typhoid, therefore, immediate laboratory investigations are required for diagnosis<sup>12</sup>. The clinical and haematological profiles showed 29% cases positive for DEN NS1 antigen and/or IgM antibodies 45% similar to this study where 33% were positive cases for dengue fever.

The study showed fever was the most common presenting symptom followed by myalgia/arthritis which is similar to studies in India. Majority of the patients had thrombocytopenia also initially, which turned out to be dengue fever later<sup>13</sup>. One study found 36% positive dengue test in age groups 15-24 years and 25-50 years, which is similar to our study. In this study about 63% were asymptomatic as per WHO guidelines. Therefore, in the com-

Table 1. Demographic characteristics of study sample n= 378

Characteristic of sample		No.	%
Gender	Male	112	29.6
	Female	266	70.4
Age Groups	Less or equal 36 years	133	35.2
	Between 37-54 years	143	37.8
	Above 54 years	102	27.0
Education	No education	70	18.5
	Less than 5 years	176	46.7
	5- 10 years	84	22.2
	10.1- 14 years	20	5.29
Ethnicity	14.1- 16 years	28	7.40
	Muhajir	32	8.5
	Sindhi	147	38.9
	Punjabi	99	26.2
Marital status	Pushto	44	11.6
	Baluchi	56	14.8
	Married	220	66.9
	Unmarried	114	14.3
Occupation	Divorced/widow	44	18.3
	Employee	84	22.2
	Un- employed	294	77.8
Family income	<6000/ Rs. Per month	253	66.9
	6000-10,000 Rs.per month	54	14.3
	10,001-20,000 Rs.per month	71	18.8

Rs: Pakistani Rupee

Table 2. Association of demographic characteristics and seroprevalence in dengue infection, n= 378

Demographic characteristics		Dengue fever infection n= 378				p-value
		Negative (n= 252)		Positive (n= 126)		
		No.	%	No.	%	
Age Group	Less or equal 36 years	84	33.3	49	38.9	0.56
	Between 37-54 years	98	38.9	45	35.7	
	Above 54 years	70	27.8	32	24.4	
Gender	Male	112	44.4	0	0	<0.01*
	female	140	55.6	126	0	
Marital Status	Married	112	44.4	108	85.7	<0.01*
	Unmarried	96	38.1	28	14.3	
	Divorced/widow	44	17.5	0	0	
Education	No education	56	22.2	14	11.1	<0.01*
	Less than 5 years	84	33.3	92	73	
	5- 10 years	70	27.8	14	11.1	
	10.1- 14 years	14	5.6	6	4.8	
	14.1- 16 years	28	11.1	0	0	
Ethnicity	Muhajir	14	5.6	18	24.3	<0.01*
	Sindhi	122	48.4	25	19.8	
	Punjabi	32	12.7	67	53.2	
	Pushto	28	11.1	16	12.7	
	Baluchi	56	22.2	0	0	
occupation	Employee	0	0	84	66.7	<0.01*
	Un- employed	252	100	42	33.3	
Family income	< 6000/ Rs Per month	164	65.1	87	70.6	0.174
	6000-10,000 Rs Per month	42	16.7	12	9.5	
	10,001-20,000 Rs Per month	46	18.3	25	19.8	

\*P <0.05 considered significant

Pearson Chi Square test was used for categorical data

munity asymptomatic cases were found with positive laboratory tests. This may be due to subclinical cases that may be under-reported<sup>14</sup>.

These under-reported cases reduce an effective control of dengue transmission. These asymptomatic dengue infections later will become reservoir for dengue transmission and will worsen the attack rate as secondary dengue infection. The spectrum of clinical symptoms ranged from mild fever to severe clinical and haemorrhagic manifestations<sup>15</sup>. An effective vector surveillance and diagnostic virology laboratories work is required at community level. The exact burden of dengue remains unknown and this debilitating disease in the country has become endemic and sprouts as outbreaks after rain nationwide.

More research studies are required to determine laboratory test providing rapidity in result, simplicity, ease of interpretation and low cost. Dengue virus infection is a major cause of morbidity in the tropical and subtropical regions globally<sup>16</sup>.

There is no specific treatment for dengue/dengue haemorrhagic fever and dengue shock syndrome, therefore, an early and prompt detection is required to reduce fatality rate<sup>14</sup>. An effective vector control is lacking for dengue prevention and control in our urban community. Dengue virus is extending its range and prevalence because its mosquito vector breeds rapidly in the urban environment<sup>16</sup>.

This study showed that dengue in an endemic community requires active surveillance for detecting symptomatic infections at an early stage to reduce morbidity and mortality. A clinical-based surveillance

in the community will be useful for control of spread of disease before the out-break<sup>17,18</sup>.

The association of dengue fever with socioeconomic factors were significant in females with 5 years or less education, unmarried and self-employed. The urban environment has lack of space which was not associated with occurrence of the dengue disease dynamics<sup>19</sup>. There has been an increase in fever cases of unknown origin however, about 43.5% suspected cases were diagnosed as DENV infection based on a positive enzyme immunoassay or reverse transcriptase-polymerase chain reaction. The overall attack rate has been 9.4 cases/1000 population in different communities in India<sup>19</sup>.

In another study the clinical and epidemiological characteristics observed differences in age, gender and complications of dengue infections<sup>20</sup>. However, in this study the significance was seen more in females, unmarried and low socio-economic status. Currently, some of the studies have shown that platelet counts did not determine outcome in dengue patients. In the last decade platelet counts was one of the major predictor to monitor outcome of fever of unknown origin. However, in our study also platelet count was not the major risk factor to monitor the fate of dengue infection<sup>20</sup>. This study recommends timely referral an early access to healthcare system is mandatory in low income and underprivileged communities. The demographic, behavioural, environmental, climatic and clinical risk factors will be useful after confirmation in larger cohorts<sup>20</sup>. Community educational programs should target housewives/old peer women in the community looking after water storage and cleanliness in the house. There is a dire need of door-to-door information regarding prevention of vector breeding sites<sup>21</sup>.

The association of sero-prevalence with demographic characteristics of dengue viral infection in amegacity showed that affected females were 266 (70.4%) in number and commonest age group affected in these adults were between 37-54 years 143 (37.8%). These two demographic factors must

be considered in the slum areas with history of fever of unknown origin to be diagnosed as dengue viral infection at an early stage to avoid complications in future. The infection usually targets families and may affect children also<sup>22</sup>.

Most of the research subjects were 5 years educated; 176 (46.7%), in this study which points towards easy, understandable messages which can be practiced in the house by the natives to avoid vector breeding in the community collectively. Individual protection, water storage in house, use of preventive measures for all age groups to combat vector control is also necessary<sup>23</sup>.

Mostly unmarried; 220 (66.9%), and 164 (65.1%) subjects from low socioeconomic status were found positive for dengue fever infection in this study. Practically these demographic factors have also been shown in other studies. These subjects are exposed to environmental and individual risk factors as they work in the field starting early in the day and working till the end of the day. Therefore, vector control must be taken as the mandatory tool in order to reduce the occurrence of the dengue infection<sup>24</sup>. This study found a significant association at  $p\text{-value} < 0.5$  in female, unmarried, primary education and unemployed subjects. These demographic factors must be included in the major risk factors which may develop later dengue outbreaks in the community.

Currently, dengue is one of the most important mosquito-borne, fatal disease and a major health problem in the tropical countries. It has been estimated that 50 million infections per year occur across 100 countries globally<sup>25</sup>. The annual number of dengue fever cases are still under-reported globally and particularly in low social area where the health care system is not optimum at the community level<sup>25</sup>. In Pakistan, most of the public health sector institutes cater only 30% of the total population. The remaining 70% of the population in rural and peri-urban areas have a lack of healthcare facilities in the primary healthcare centers and at community levels. The lack of health care facilities, suboptimal community care and under-reporting re-

duces optimum strategies for decision making by the public health sector<sup>26</sup>. This study identified and confirmed that under-reporting leads to an impact on a national level. Therefore, major remedies are required to effectively address risk factors and its association with dengue fever bridging the gap between health institutional centers to the community level.

Dengue virus is a major public health problem in the low resource areas. Currently, frequent dengue outbreaks have been reported globally, in the developing countries<sup>27</sup>. The spread of dengue has been associated with frequent movements of population to endemic areas. Therefore, the vector control becomes difficult in some areas because of frequent daily and weekly movements for jobs and business<sup>28</sup>. The immunity of the particular community is not dependent on less acquiring the dengue infection. As one-third of the sample was found positive for dengue viral infection in this study because the natives frequently travel to other areas of the megacity in Karachi. This was also found in other studies from central India<sup>29</sup>.

The geographical and climatic conditions have been favourable in most of the thickly populated union councils of Gadap Town, Karachi. The breeding of dengue vectors has been enhanced due to multiple factors resulting in an increased seroprevalance of dengue fever. There is an alarming increase as some of the areas are now endemic for the dengue infection in this megacity including these union councils.

There is risk of an increase in the incidence of dengue and chikungunya associated with the huge amount of garbage in the urban communities along with lack of protective measures used by the entire community, urbanisation and for travelers<sup>30</sup>. Since mosquito control has not been optimum and no vaccine or antiviral treatment is available, therefore, new approaches are needed<sup>22,23</sup>. The molecular and cellular biology technologies of dengue virus will design efficient strategies for the control of dengue disease dynamics<sup>31</sup>.

This study confirmed an association between demographic characteristics as risk factors for seroprevalance of dengue viral infection in an urban community of a megacity which can be used for preventive strategies in future to control dengue fever in the community.

The study was conducted in only three union councils and was not logistically implemented in other towns of this megacity which was the limitation of this project. It is recommended that a passive continuous surveillance must be performed and demographic characteristics along with preliminary laboratory test performed for an early diagnosis to reduce morbidity and mortality. The serotype DNGV 3 has been found in 2015 outbreak in Khyber Pakhtunkhwa province<sup>27</sup>. The molecular epidemiology and phylogenetic analysis of dengue virus serotypes has been found useful for early diagnosis. This can be used at the community level to break the cycle for high morbidity and mortality at national level. However, the test is expensive and not available in low socioeconomic areas.

Suspected dengue, among fever of unknown origin required immediate laboratory investigation to reduce morbidity in the community. Dengue seroprevalance increased with age. Early suspicion, prompt and effective management will reduce morbidity. One of the important issue is a typical presentation due to varied serotypes. Knowledge of atypical presentations is necessary for early diagnosis and timely referrals to prevent severe morbidity at community levels. The demographic features in a community will be associated with the seroprevalance along with environmental, behavioural and clinical features. The clinical symptoms and signs may be mild to severe. A group of patients may be observed without clinical features and laboratory test of NS1 protein positive test along with ELISA positive results<sup>30</sup>. The level of education of heads of the house and women looking after water storage and cleanliness of each house is also an important factor.

Dengue fever is endemic and recurrences may occur. The spectrum of dengue fever varies there-

fore, WHO case definition has been used in the dengue outbreaks. A probable case is defined as acute febrile illness with two or more of any findings including headache, retro-orbital pain, myalgia, arthralgia, rash, haemorrhagic manifestations, leucopenia and serology according to the World Health Organization guidelines globally<sup>22</sup>.

Currently, the disease is endemic in more than 100 countries and all over the tropical and subtropical areas. The suboptimal strategies for vector control, low literacy and poor behavioral factors leads to more positive cases in the communities. As in this cross-sectional survey there were 126 (33.3%) positive cases.

Management of effective dengue prevention and vector control also requires control of ecological risk factors and demographic characteristics in reducing mortality and morbidity by dengue infections.

## Conclusion

About one-third of the sample had an association between demographic characteristics as risk factors for seroprevalence of dengue viral infection in an urban community of the megacity, Karachi, which can be used for preventive strategies in future to control dengue fever in the community.

## Conflict of interest

Authors have no conflict of interests and no grant/funding from any organisation for this study.

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