

The epidemiology of dengue fever in district Faisalabad, Pakistan

Sadia Nasreen,* Muhammad Arshad,* Muhammad Ashraf,* Ahmad Raza** and Bahar-e-Mustafa*

*Institute of Microbiology, University of Agriculture, Faisalabad-38040, Pakistan.

** Institute of Pharmacy, Physiology and Pharmacology, University of Agriculture, Faisalabad-38040, Pakistan.

Abstract Dengue fever (DF) is globally emerging mosquito born viral disease. Pakistan is at high risk of dengue fever due to unavailability of vaccine, crowded cities, inadequate sanitation, unsafe water and large number of refugees. The present study was intended to investigate the epidemiology of DF in Faisalabad, Pakistan. This was a retrospective study to measure the frequency and distribution of the disease. Total 1509 cases of Dengue fever were admitted in Allied Hospital, Faisalabad during 6 months. Case-control epidemiological study was also conducted to identify some of the risk factors of the disease. For this purpose cases (n = 200) and control (n = 200) were confirmed through identification of antibodies against Dengue virus (immunoglobulin G) in the serum. The pre-tested questionnaires were used to collect the data on various factors. The results showed that the relative incidence of DF was significantly higher ($p < 0.05$) in males (71%) than in females (29%). The most susceptible age group was 21-30 years with relative incidence of 34%. Relative incidence was highest (43%) in the month of October. Various factors which were found associated with the disease were People working in Lahore, people visiting Lahore during epidemic, excessive travelling, presence of disease in the family or neighboring houses, people living near watery areas, immunocompromised persons and low level of awareness. Further epidemiological studies are needed to establish the effect of risk factor on population.

Index Terms- Antibodies, Dengue fever, Epidemiology, Immunoglobulin G

I. INTRODUCTION

Dengue fever is globally emerging mosquito born viral disease [1-7]. The causative agent of dengue fever is dengue virus of family Flaviviridae. There are four distinct serotypes of dengue virus DEN1, DEN2, DEN3 and DEN4 [8-12]. The virus has seven non structural proteins (NS1, NS2a, NS2b, NS3, NS4, NS4b, and NS5) and three core or structural proteins. There is no cross protective immunity but Lifelong immunity develops with infection of one type of dengue virus [12]. It is a confirm fact that the more severe signs were develop in patients infected with DEN-2 as compare DEN-1, DEN-3 and DEN-4 [9]. DEN-2 and DEN-3 have been mostly linked with dengue hemorrhagic fever although the exact mechanism is not still implicit [11].

The *Aedes aegypti* is a highly domesticated mosquito. It is small and black and white in color and prefers to feed blood on humans during the daytime. Its peak biting activity reaches during dawn and dusk [12]. The origin of *Aedes aegypti* is considered to be from tropical forests of Africa. *Aedes albopictus* is indigenous to South East Asia. It supposed to spread globally through import and export of tyres [10]. The most important and suitable arthropod vector for the dengue virus is *Aedes* (*Ae.*) *aegypti* due to its social behavior and frequent biting habit before breeding which belongs to the native African *Aedes aegypti* mosquito species which is considered as the dengue vector of urban areas. The recent urban *Ae. aegypti* domesticated from sub-saharan sylvatic *Ae. aegypti formosus*, which is an ancestral species. This urban *Ae. aegypti* dispersed to the many areas of the world especially tropical and subtropical countries of the world and involves in many outbreaks. The urbanization of *Ae. aegypti* occurred due to biodiversity, increase in population, global warming and climate change [13-14].

The residents at risk of dengue are 2500 million makes 2/5th of the population worldwide. The annually reported cases of dengue and dengue hemorrhagic fever are 50-100 million and 500,000 respectively leading to 24,000 deaths [10, 14]. Dengue fever incidence increase 30 times from 1960 to 2010 [15].

In Asia, epidemic of DHF was first documented in 1553 from Phillipine [10]. In 1942 dengue virus was isolated from Japan [16]. Dengue hemorrhagic fever disseminated to Singapore, Indonesia, Vietnam, Sri Lanka and Malaysia in 1960. The disease epidemiology expands and DHF outbreaks documented from India, French Polynesia, Pakistan and Bangladesh in 1988, 1990, 1992 and 2000 respectively [10]. During last thirty years DF budded as a pandemic disease. The occurrence of DF in Asia and pacific is more than 70% and remaining from Africa, America and Middle East [9].

In last twenty years the numbers of epidemics reported from Pakistan are seven. A number of dengue fever epidemics have occurred after the period of two to three years following the previous outbreak [9, 11]. Pakistan is at high risk of dengue fever due to unavailability of vaccine, crowded cities, inadequate sanitation, unsafe water and large number of refugees. Dengue virus is supposed to come in Pakistan with tyres at Karachi sea port having eggs of infected mosquitoes. There was no official data available about dengue fever in Pakistan until 1994 [16]. Dengue fever (Anti-D3) was first reported in 1982 from Central Province of Pakistan (Punjab) according to world health organization, 12 patients out of a sample of 174 were documented [17]. In 1985, 50-60% population of Karachi was founded heamagglutination inhibition (HI) positive for flavivirus, West Nile, Japanese encephalitis. The

first epidemic of dengue hemorrhagic fever was reported in Karachi 1994 [15-17]. DEN-1 and DEN-2 serotypes were found in the blood of patients infected during the epidemic of 1994. Next epidemic occurred in Baluchistan with approximately eighteen hundred reported cases in the following year. In 1997 confirmed one hundred and forty five dengue fever cases were reported from Aga Khan University Karachi out of which 45% patients had dengue hemorrhagic fever and one died [17].

In 2005 dengue fever again hit Karachi and four thousand five hundred confirmed cases were reported [10]. First confirmed outbreak of dengue fever due to DEN-3 was reported in 2005 [18]. In 2006 Azad Jammu & Kashmir became victim of dengue fever but went chiefly undocumented [10]. Again in 2006, dengue fever became epidemic in Karachi and travelling of employees to their destinations for the Eid vacations inoculated dengue virus to other cities of Pakistan. In the same year a lot of cases of DF and DHF (approximately 220 cases) reported from the general hospital Rawalpindi during the months of October and December [19]. DEN-2 and DEN-4 were found in the serum samples of the patients infected during epidemic of dengue hemorrhagic fever in the year 2008. Dengue surveillance cell reported eight hundred and eighty one confirm cases out of one thousand eight hundred and nine susceptible individuals and five deaths from Sindh till October 2010. In the same year sixteen confirm cases of dengue fever and zero mortality reported from capital city of Pakistan and five hundred and sixty three cases reported from Aga Khan University Karachi. Most of the cases had DHF manifested with secondary disease while mild to moderate sign in the patients were present at primary health care centre [6]. Once again in the descend of 2011, Dengue fever epidemic occurred in Pakistan with fifteen thousand cases from Lahore and above two hundred cases from Khyber Pakhtoonkhawa and Peshawar [11, 15, 20]. In February 2012, 73 cases of dengue fever in Lahore and 13 other areas of Punjab were reported. The year 2007 and 2011 has been worst years in regard of dengue virus infection in Pakistan. Dengue virus circulates in Pakistan throughout the year with a peak incidence in the post monsoon period. Recent flood in Pakistan made the situation worse [16].

Population density, water, sanitation, level of literacy, poor socioeconomical stresses and climate variation deliberated as reasons of dengue fever occurrence in the South East Asian. DF is endemically present in Asia but epidemic of DHF repeat cyclically after three to five years [10].

II. MATERIAL AND METHOD

Descriptive epidemiological Study

Epidemiological data for retrospective descriptive studies were collected from allied hospital Faisalabad. A total of number cases reported during 6 months epidemic of DF during 2011 were selected. Epidemiological data were collected on a predesigned Performa which included name of patient, age, sex, complete residential address, contact no, sign and symptoms, date of admission and date of discharge.

Area based distribution of dengue fever

The prevalence of disease in urban and rural areas of Faisalabad was checked through distribution of cases in these areas. The most prevalent area was also found through this study.

Age based distribution of dengue fever

To check the age wise distribution of disease 9 groups was formed from <10 to >80 years and distribution of cases were found in these different groups to determine the prevalence in different age groups.

Sex based distribution

Male and female two groups were formed to check the sex wise prevalence of disease.

Month based distribution

The distribution of cases in different month of epidemic of disease was used to check the pattern of disease.

Case-Control Analytical Study

Blood collection

Case-control was done on individuals of two groups diseased and non diseased. All individuals were further confirmed through detection IgG antibodies. The blood samples of 200 healthy individuals and 200 infected individuals were collected. The blood samples were collected in sterilized syringes. The serum from blood was collected through centrifuging the samples at 2500 rpm for 5 minutes. The serum samples were store at -20 degree Celsius for detection of immunoglobulin. The immunoglobulin G (IgG) was determined through IgG capture enzyme linked immunosorbent assay ELISA. SD dengue capture ELISA was used for this purpose.

Statistical analysis

The obtained data was analyzed by measuring odds ratio of each factor and through Chi square test.

III. RESULTS

Results of descriptive epidemiological study

Age based distribution of dengue fever

To check the age wise distribution of disease 9 groups was formed from upto10 years, 11-20 years, 21-30 years, 31- 40 years, 41-50 years, 51-60 years, 61-70 years, 71-80 years, >80 years. The distributions of cases were found in these different groups to determine the prevalence in different age groups. Distributions of cases were 7%, 17%, 38%, 19%, 9%, 8%, 2%, 0.5% and 0% in upto10 years, 11-20 years, 21-30 years, 31- 40 years, 41-50 years, 51-60 years, 61-70 years, 71-80 years, >80 years respectively. The highest relative percentage was found in group at age of 21-30 years as presented in Table 1.

Table 1: Age wise distribution of dengue fever

Sr. No.	Age	Relative % age
1.	Up to 10 years	7%
2.	10-20 years	17%
3.	21-30 years	38%
4.	31-40 years	19%
5.	41-50 years	9%
6.	51-60 years	8%
7.	61-70 years	2%
8.	71-80 years	0.5%
9.	Above 80	0%

Sex based distribution

Male and female two groups were form to check the sex wise prevalence of disease. Relative percentage of cases in males and females were 71.1% and 28.9% respectively. Highest relative percentage was found in males as compare to females as presented in Figure 1.

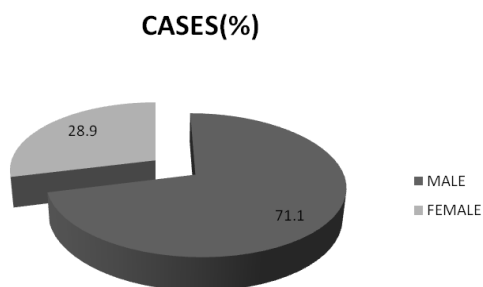


Figure 1: Sex based distribution

Area wise distribution of dengue fever

The prevalence of disease in urban and rural areas of Faisalabad was checked through distribution of cases in these areas. The relative percentage of cases was 62% and 38% in urban and rural areas respectively. Highest relative percentage was found in urban areas as compare to rural areas as presented in Figure 2.

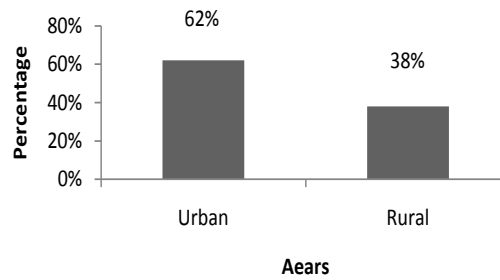


Figure 2: Area wise distribution of dengue fever

Month wise distribution of dengue fever

The distribution of cases in different month of epidemic of disease were use to check the pattern of disease. Relative percentage of cases was 1.5%, 35.5%, 43%, 17%, 2% and 0.19% in August, September, October, November, December and January respectively. Highest percentages of cases were found during month of October as presented in Figure 3.

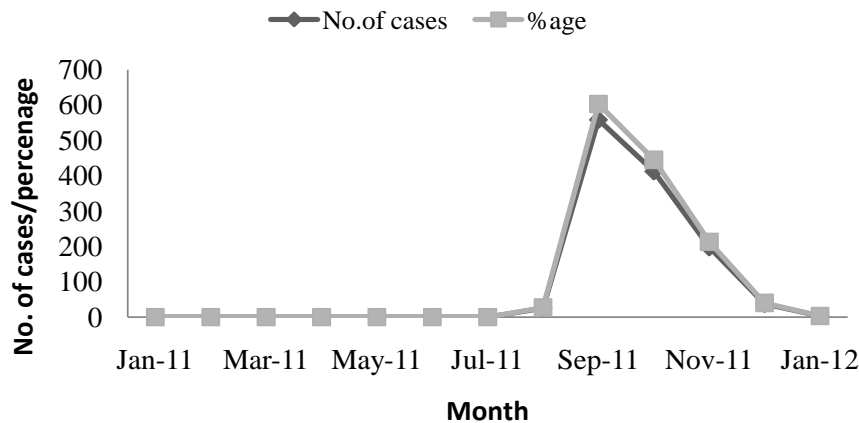


Figure 3: Month wise distribution of dengue fever

Case-Control Analytical Study

Case control analytical study determined the different risk factors associated with the disease. The associated risk factor were people work and visit to Lahore, watery areas near house, Immunocompromised individuals, dengue patients in family and neighbor, travelling, socioeconomical variables and awareness. Odds ratio for different risk factors presented in Table 2.

Table 2: Risk factors for dengue fever

Sr. No.	Risk factors	Diseased	Non diseased	Odds ratio
1	People work & visit to Lahore	102	22	2.6
2	Watery areas near house	81	21	2.05
3	Immunocompromised	65	18	1.88
4	Dengue patient in family and neighbour	40	12	1.68
5	Travelling	42	15	1.39
6	Socioeconomical variables	43	21	0.99
7	Awareness	35	89	0.11

IV. Discussion

This study describes the epidemiology of dengue fever in Faisalabad. Until now this type of study has not been described. The prospective epidemiological study showed that the ratio of incidence of dengue fever in male and female was 2.4:1. The ratio of male was > 2 as compare to females and this fact is supported by another study conducted in India which showed the male to female ratio was 2:1 in one of the retrospective study [4].

The most effected age was 21-30 years and number of cases gradually decreases up to age of 80 years, it showed that the epidemiology of dengue fever changed during recent epidemic of dengue fever 2011 because one of the studies conducted in India

showed the most effected age was 0-15 years. A short report on epidemiology of dengue fever in Pakistan supports this study because it showed that the mean age detected is 32 years [4, 6].

The epidemic of dengue fever started post monsoon in August when the mosquito population was high. Highest number of cases reported during the month of October. This is supported by another study which describes that dengue fever is endemic in Pakistan with maximum incidence during post monsoon period. Another five years Indian study showed the gradual increase in cases post monsoon from August, obtain peak in October and then gradually decrease [4, 6].

Dengue fever and dengue hemorrhagic fever has been reported as occur dominantly in urban population where density of dwelling create the favorable conditions for the transmission of disease. However some studies show that in some cases, outbreaks also reported in rural areas of Asia and America [21]. This study measure the incidence of dengue fever in rural and urban areas of Faisalabad. The maximum cases was reported from city area as compare to rural areas because of short flying distance of vector and congested construction which promote the rapid spread of disease leads to epidemic. The global case fatality rate has been decreasing in many of the endemic countries according to government statistics. The overall case fatality ratio in the Southeast Asia region is now less than 1%. The case fatality rate was 0.86% during epidemic of 2011 which also shows the declining trend of the case fatality ratio [21].

The case control analytical studies which are used to detect the level of IgG through IgG capture ELISA showed that patient with severe clinical sign were positive for IgG. In another study it is a well known fact that the severe form of dengue fever like dengue hemorrhagic fever and dengue shock syndrome occur in the patient having secondary infection due to antibody enhancement mediated by activated T cell response with TH-2 lineage cell activation and stimulation of other soluble factor [22]. It means out of total 30% which showed positive result remain at high risk of dengue hemorrhagic fever and dengue shock syndrome.

Acknowledgements

Authors really acknowledge the hospital staff for helping to collect data for completion of this study.

V. CONCLUSION

Various factors which were found associated with the disease were People working in Lahore, people visiting Lahore during epidemic, excessive travelling, presence of disease in the family or neighboring houses, people living near watery areas, immunocompromised persons and low level of awareness. Further epidemiological studies are needed to establish the effect of risk factor on population.

ACKNOWLEDGMENT

Authors really acknowledge the hospital staff for helping to collect data for completion of this study.

REFERENCES

1. Phuonga HL, et al. Dengue Virus Infections in Viet Nam: Tip of the Iceberg. *Dengue Bulletin*; 2006; 30: 15-25.
2. Egger JR, et al. Reconstructing historical changes in the force of infection of dengue fever in Singapore: implications for surveillance and control. *Bulletin of the World Health Organization*; 2008; 86: 187-196.
3. Siddiqui FJ, Haider SR, Bhutta ZA, Endemic Dengue fever: a seldom recognized hazard for Pakistani children. *Journal of Infection in Developing Countries*; 2009; 3: 306-312.
4. Garg A, et al. Prevalence of dengue among clinically suspected febrile episodes at a teaching hospital in North India. *Journal of Infectious Diseases and Immunity*; 2011; 3: 85-89.
5. Gharbi M, et al. Time series analysis of dengue incidence in Guadeloupe, French West Indies: Forecasting models using climate variables as predictors. *BMC Infectious Diseases*; 2011; 11: 166.
6. Jahan F, et al. Clinical and biochemical characteristics of suspected dengue fever in an ambulatory care family medical clinic, Aga Khan University, Karachi, Pakistan. *Dengue Bulletin*; 2011; 35: 59-64.
7. Wang Z, et al. Delayed effects of weather variables on incidence of Dengue fever in Singapore from 2000-2010. *International Journal of Environmental Science and Development*; 2012; 3: 195-198.
8. Ilyas M, et al. Bioinformatics analysis of envelope glycoprotein e epitopes of Dengue virus type 3. *African Journal of Biotechnology*; 2011; 10: 3528-35.
9. Idrees M, et al. Dengue virus serotype 2 (DEN-2): the causative agent of 2011-Dengue epidemic in Pakistan. *American Journal of Biomedical Sciences*; 2012; 4: 307-315.
10. Khan AH, et al. Frequency and clinical presentation of dengue fever at tertiary care Hospital of Hyderabad/Jamshoro. *Journal of Liaquat University of Medical and Health Sciences*; 2010; 09: 88-94.
11. Nieto CN, et al. The emergence and maintenance of vector-borne diseases in the Khyber Pakhtunkhwa Province, and the Federally Administered Tribal Areas of Pakistan. *Frontier in Physiology*, 2012; 3: 250.
12. Sulehri MA, Hussain R, Gill NI, Dengue fever its diagnosis, treatment, prevention and control. *Gomal Journal of Medical Science*; 2012; 6: 22-27.
13. Mukhtar M, et al. Entomological investigations of Dengue vectors in epidemic-prone districts of Pakistan during 2006-2010. *Dengue Bulletin*; 2011; 35: 99-115.
14. Sajid A, Ikram A, Ahmed M, Dengue fever outbreak 2011: clinical profile of children presenting at madina teaching Hospital Faisalabad. *Journal of University of Medical and Dental Collage*; 2012; 3: 42-47.
15. Alam S, et al. Dengue fever outbreak: a clinical management experience. *Journal of the College of Physicians and Surgeons Pakistan*; 2012; 18: 8-12.
16. Idrees S, Ashfaq UA, A brief review on dengue molecular virology, diagnosis, treatment and prevalence in Pakistan. *Genetic Vaccines and Therapy*; 2012; 10: 6 1-10.
17. Wasay M, et al. Changing patterns and outcome of Dengue infection; report from a tertiary care hospital in Pakistan. *Journal of Pakistan medical association*; 2008; 58: 488.
18. Fatima Z, et al. Serotype and genotype analysis of dengue virus by sequencing followed by phylogenetic analysis using samples from three mini outbreaks-2007-2009 in Pakistan. *BMC Microbiology*; 2011; 11: 200.
19. Ahmed SI, et al. Dengue fever in northern Pakistan: The Hepatic Implications. *Journal of Rawalpindi Medical College*; 2009; 13: 56-59.
20. Azfar NA, et al. Cutaneous manifestations in patients of dengue Fever. *Journal of Pakistan Association of Dermatologists*; 2012; 22: 320-324.

21. Sapir DG, Schimmer B, Dengue fever: new paradigms for a changing epidemiology. *Emerging Themes in Epidemiology*; 2005; 2: 1-10.
22. Martina BE, Koraka P, Osterhaus A, Dengue virus pathogenesis, an integrated view. *Clinical Microbiology*; 2009; 22: 564–581.

AUTHORS

First Author – Sadia Nasreen, M.Phil, Institute of Microbiology, University of Agriculture, Faisalabad-38040, Pakistan and sadianasreen3@gmail.com.

Second Author – Muhammad Arshad, PhD, Institute of Microbiology, University of Agriculture, Faisalabad-38040, Pakistan and drarshaduaf@gmail.com.

Third Author – Muhammad Ashraf, PhD, Institute of Microbiology, University of Agriculture, Faisalabad-38040, Pakistan and mashraf@uaf.edu.pk.

Fourth Author– Ahmad Raza, M.Phil, Institute of Pharmacy, Physiology and Pharmacology, University of Agriculture, Faisalabad-38040, Pakistan and ahmed.uaf@hotmail.com

Fifth Author– Bahar-e-Mustafa, M.Phil, Institute of Microbiology, University of Agriculture, Faisalabad-38040, Pakistan and bharmf@yahoo.com.

Correspondence Author – Muhammad Ashraf, Institute of Microbiology, University of Agriculture, Faisalabad-38040, Pakistan. Tel: 03336625110. E-mail: mashraf@uaf.edu.pk