Clinico-Epidemiological Study of Dengue Fever in Nishtar Medical University Hospital Multan, Pakistan

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Abstract

Introduction: Dengue fever is a common vector borne disease caused by dengue virus. In developing tropical countries, it is considered as one of the major public health problems. Consequently, this disease is highly associated with increased morbidity, mortality and economic burden to poorly resourced health system of less privileged countries.

Aim and objectives: The current work is intended to assess the incidence, signs, symptoms, and epidemiological characteristics of cases of Dengue fever presenting in Nishtar Medical University Hospital Multan Pakistan.

Study design:
Descriptive cross-sectional study

Place and duration of study:
Department of Infectious Diseases, Nishtar Medical University Hospital Multan Pakistan. The time span of study was from January 01, 2016 to December 31, 2017.

Method:
The present work was a prospective cross –sectional study conducted in our centre. A total 876 fever cases, fulfilling WHO criteria for dengue suspicion were included as target population of the study. For each individual case, detailed history and thorough physical examination was performed. In addition to routine baseline investigations, the disease-specific investigations such as rapid immuno chromatographic card test were also performed to confirm the diagnosis. A specifically predesigned proforma was used to collect socio- demographic profile, signs and symptoms of serologically diagnosed cases. The data were analyzed by using computer program SPSS 21.

Results: The results of our study exposed that out of 576 suspected cases, 254 patients were serologically positive for Dengue fever. The highest number of cases (110 cases) was reported in the 3rd week of September. Maximum number of dengue cases reported were males belonging to 31-40 years age group from urban area. Fever was the main complaint in all the cases followed by vomiting, headache, and abdominal pain.

Conclusion: Dengue is one of the major public health problems in developing countries like India. A large number of cases are reported in the monsoon and post-monsoon period in the month of September and October. Measures can be taken both at personal and government level to reduce morbidity and mortality from dengue.

Keywords: Dengue, Epidemiology, Fever, Signs, Symptoms

INTRODUCTION

Man is living in a quite hostile environment, and badly vulnerable to internal and external enemies. Of these numerous enemies, various kinds of microbial infections are of supreme importance. These microbial infections can be further sub-categorized on the basis of their etiological organisms, mode of transmission and organ system which is mainly affected by the injurious effects of microbial invasion. Dengue fever, also known as "break-bone fever", is one of these lethal microbial infections. Dengue fever is caused by Dengue virus which belongs to the Flavivirus group. Up till now, the researchers have discovered its four serotypes i.e. serotype 1-4. Usually, the virus is transmitted to the human through the bite of Aedes aegyypti mosquitoes (1). This viral infection badly impairs the human life and result in catastrophic presentations. Dengue is a systemic disease and exhibits dynamic nature. The full spectrum of disease varies from a subclinical infection to a mild self-limiting disease, the Dengue fever. On the other hand, Dengue hemorrhagic fever (DHF)/dengue shock syndrome are proven to be very severe diseases that may be fatal.

Dengue fever is an ancient disease and many centuries ago its very first case was recorded in a Chinese medical encyclopedia in 992 (2). In the past dengue fever was considered as a tropical disease which was confined to a specific geographical area and was uncommon in temperate countries. But the increased global shipping industry, rapid urbanization, and development of new port cities created ideal conditions for the extensive dispersal of this mosquito-borne disease (3). Thus, the mosquitoes and the viruses disseminated widely across the globe. This "neo-colonization" of Aedes aegypti mosquito resulted in major epidemics of Dengue fever (4). The first major epidemic of the severe and fatal form of the disease, known as dengue hemorrhagic fever, occurred in Southeast Asia 1950's. In 1980's a dramatic expansion of epidemic of Dengue fever and Dengue hemorrhagic fever occurred around the globe (5). Even, in the 21st century, the epidemic of Dengue fever (DF) and Dengue hemorrhagic fever (DHF) is the leading infectious diseases affecting tropical urban areas.

It is estimated that incidence of DF and DHF is ranging from 50 million to 528 million per year (6). A study by WHO states that the actual statistics of Dengue cases are underreported and many cases are misdiagnosed. The recent medical literature estimates that 390 million dengue infections occur every year (with a 95% confidence interval 284–528 million) (7). Another study which was conducted to determine the prevalence of Dengue fever reports that up to 3.9 billion people of 128 countries are prone to the infection with dengue virus (8). Dengue is one of the major public health problems in Pakistan. However, during the last decade more frequent and severe epidemics of dengue have been reported in several Pakistani cities. A study on the recent Dengue outbreak in Pakistan states that Pakistan has become endemic for Dengue fever (9). A total of 24,807 laboratory confirmed cases with 69 associated deaths were so far reported in 2017 (10, 11). Hence, it is crystal clear that epidemics of dengue fever and dengue hemorrhagic fever are causing increased morbidity, mortality and economic burden to the poorly resourced health systems of Pakistan. Therefore, the authors intended to assess the incidence, signs, symptoms, and epidemiological characteristics of cases of Dengue fever presenting in Nishtar Medical University Hospital Multan, Pakistan.

MATERIALS AND METHODS
It was a descriptive cross-sectional study conducted at Department of Infectious Diseases, Nishtar Medical University Hospital, Multan. The time span of study was from January 01, 2016 to December 31, 2017. The due approval was taken from the Institutional Ethical Review Board of Nishtar Medical University. All the new fever cases, fulfilling WHO criteria for dengue suspicion were included as target population of the study. The inclusion criteria were the presence of fever (or history of fever) plus two or more of the following: nausea/vomiting, rash, aches and pains, leukopenia, positive tourniquet test (petechia $\geq$20 per inch^2) and any warning sign (abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy/restlessness, liver enlargement >2 cm, or increase in hematocrit concurrent with rapid decrease in platelet count (12). Furthermore, the study population was not restricted to the gender, age and residential area of the patients. However, all the follow up cases were excluded from the study. For each individual case, detailed history and thorough physical examination was performed. In addition to routine baseline investigations, the disease-specific investigations such as rapid immuno chromatographic card test was also performed to detect for the dengue NS1 antigen and dengue immunoglobulin M and immunoglobulin G (IgM and IgG antibodies) for the confirmation of the diagnosis. A specifically predesigned proforma was used to collect socio- demographic profile, signs and symptoms of serologically diagnosed cases. The data were analyzed by using computer program SPSS 21. The descriptive statistics were used to calculate mean $\pm$ SD for the age of the patients. Frequencies and percentages were calculated for all the variables included in the study.

RESULTS
A total of 576 patients visited in Nishtar Medical University Hospital, Mulatn with the complaint of fever and other dengue like symptoms. Out of 576 patients from target study population, 254 patients were tested serologically positive for DF. Of these 254 patients, 188 (74%) were males and 66 (26%) were females. The median age of the patients was 26 years and age ranged from 3 to 64 years. The children below 16 years of age accounted for 33 (13%) of the study population while there were 221 adults patients (87%). Amazingly, seven cases were below five years of age. The highest prevalence of dengue patients was observed between 16 to 30 years. The highest number of cases (110 cases) was reported in the 3rd week of September from September. Table 2 describes the clinical features of patients of Dengue fever. Fever was the most frequent symptoms which was noticed in 254 (100%) patients, followed by headache (n= 221, 87%) , myalgia/arthralgia (n= 232, 91.3%), Vomiting (n=168, 66.14%), Nausea (n=125, 49.2%), Abdominal Pain (n=109, 42.9%), Retro-orbital pain (n=59, 23.2%), Rash (n=27, 10.6%), and diarrhea (n=22, 8.7%).

Table 1. Demographic Features of patients with dengue Fever

Variable	N (%)
Age	
01-15 years	33 (13%)
15-30 years	121 (47.6%)
31-45 years	71 (28%)
46-60 years	19 (7.5%)
Greater than 60 years	10 (3.9)
Gender	
Male	188 (76%)
Female	66 (24%)
Residential Area	
Urban	83 (32.7%)
Rural	171 (67.3%)

Table 2. Clinical features of patients suffering from Dengue fever

Variable	N (%)
Symptoms	
Fever	254 (100%)
Headache	221 (87%)
Myalgia/arthralgia	232 (91.3%)
Vomiting	168 (66.14%)
Nausea	125 (49.2%)
Abdominal Pain	109 (42.9%)
Retro-orbital pain	59 (23.2%)
Rash	27 (10.6%)
Diarrhea	22 (8.7%)
Anorexia	19 (7.5%)
Sore throat	17 (6.7%)
Restlessness	18 (7.1%)
Cough	16 (6.3%)
Periorbital puffiness	15 (5.90%)
Cold skin/clammy skin	5 (1.9%)
Hemorrhages	
Petechiae	23 (9.1%)
Epistaxis	21 (8.27%)
Bleeding gums	15 (5.9%)
Melena	13 (5.1%)
Hematuria	11 (4.3%)
Hemetemesis	9 (3.54%)
Clinical Signs	
Elevated temperature	254 (100%)
Abdominal tenderness	14 (5.5%)
Spleenomegaly	11 (4.3%)
Hepatomegaly	9 (3.5%)

Table 3. Distribution of dengue cases as per laboratory findings

Variable	N (%)
Thrombocytopenia	237 (93.3%)
NS1 Antigen	231 (90.9%)
Anemia	204 (80.3%)
Leukopenia	154 (60.6%)
IG M Antibody	74 (29.1%)
IG G Antibody	67 (26.4%)
Both NS1 Ag and IGM	59 (23.2%)
Increased ALT and AST	53 (20.9%)
Both IGM and IGG Antibodies	13 (5.1%)

Table 4. Stratification of Dengue cases on the basis of diagnosis

Diagnosis	Number of cases (N)	% of cases
Dengue fever	89	70.07 %
DHF	30	23.63
DHF with shock	2	1.57

DISCUSSION

Despite the years of scientific efforts and research, the exact etiology and the pathogenesis of dengue hemorrhagic fever and dengue shock syndrome is still unclear (6). Currently, there is neither an FDA approved vaccines or any antiviral drug available for dengue viruses (8.9). The only effective way to prevent epidemic DF/DHF is to control the mosquito vector (16). So we need to focus towards the epidemiology and clinical presentation of this overwhelming global health problem. Consequently, approximately 18000 scientific articles and nearly 350 kinetic studies (These findings are based on PubMed comprehensive search) explored the various aspects of this morbific and fatal disease. However, all the kinetic studies have used two systems for reporting the timing of different phases of dengue. One system utilizes the day of onset or the day in which fever appears for the very first time as the criterion, and declares it as the day one[6]. In contrast to it, the second system use defervescence day as day zero, the day before this day is the day -1, one day after it is +1 day (17). The researchers use this system to study the pathogenesis with an aim to evaluate the evens that exist during the critical phase of disease during which the shock develops. In fact, the researchers sometimes alter the way of setting day zero. That day will be considered as the day of the shock for shock patients while defervescence day is used for non-shock patients (18). However, there arises a problem, as the defervescence and shock day are not the same and identical. This confusion leads to the wrong setting of time as day zero for studies. Currently, there is no available systemic review to address this problem. Therefore, a systemic review and meta-analysis of the available medical literature are vitally important to provide the best evidence-based answer to this burning question.

In the present study, out of all reported cases of Dengue fever 188 (76%) were male and 66 (24%) female. Nasreen et al., in her study in Faisalabad, Pakistan also reported similar finding (17). In the present study 83 (32.7%) of dengue cases belonged to urban area while 171 (67.3%) belonged to rural area. These findings of our study are not coherent with the results of study conducted by Nasreen et al., in which most of the patient belonged to urban areas (17). In an Indian study, the highest number of cases (110 cases) was reported in 3rd week of September from September. Another similar study also showed that a maximum number of cases are reported from 1st week of September to almost mid- October (18). This may be attributed to increased vector transmission in the monsoon period. A Pakistani study conducted by Nasreen et al., revealed that relative incidence was the highest (43%) in the month of October (17). In our study the highest number of dengue cases was reported in 16-30 years age group. It is in contrast to a western study in which Dengue fever was more prevalent in old age population. While another study by Pardeshi et al., revealed that maximum number of dengue cases were in the age group of 21-30 years (19). This evidence supports our findings. Nasreen et al., also reported maximum cases in 21-30 years group in Faisalabad, Pakistan (17). A previous study showed that there is an association between platelet count and disease prognosis (18). The more severe signs and symptoms result in serious complications and death in dengue cases. The findings related with clinical presentations of Dengue fever are very close to the results reported by Turkish and Iranian studies in which fever was the presenting symptom in all the cases followed by vomiting and headache. Hepatomegaly, myalgia, bleeding manifestations was reported in 27.70%, 27.33% and 20.55% cases, respectively (19, 20). Generalized weakness, cough, and splenomegaly were reported in 17.79%, 16.88%, and 10.45% cases, respectively (20, 21). Rashes and diarrhea were the least common complaint reported in 5.32% and 2.01% cases, respectively (22).

CONCLUSION

Dengue is one of the major public health problems in Pakistan. A large number of cases are reported in the monsoon and post-monsoon period. The young males belonging to 16-30 years of age are more prone to infection. Fever, vomiting, headache, and abdominal pain are the most common clinical manifestation of Dengue fever.

References

1. Gubler DJ, editor Dengue/dengue haemorrhagic fever: history and current status. Novartis foundation symposium; 2006: Chichester; New York; John Wiley; 1999.
2. Stanaway JD, Shepard DS, Undurraga EA, Halasa YA, Coffeng LE, Brady OJ, et al. The global burden of dengue: an analysis from the Global Burden of Disease Study 2013. The Lancet infectious diseases. 2016;16(6):712-23.
3. Messina JP, Brady OJ, Pigott DM, Brownstein JS, Hoen AG, Hay SI. The global distribution and burden of dengue. Nature. 2013;1:140004.
4. . !!! INVALID CITATION !!! {}.
5. Dick OB, San Martín JL, Montoya RH, del Diego J, Zambrano B, Dayan GH. The history of dengue outbreaks in the Americas. The American journal of tropical medicine and hygiene. 2012;87(4):584-93.
6. Crane G. Dengue haemorrhagic fever: diagnosis, treatment, prevention and control. Pathology. 1999;31(1):75.
7. Ben-Shachar R, Koelle K. Minimal within-host dengue models highlight the specific roles of the immune response in primary and secondary dengue infections. Journal of the Royal Society Interface. 2015;12(103):20140886.
8. Organization WH. Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever. 2011.
9. Khanani MR, Arif A, Shaikh R. Dengue in Pakistan: Journey from a disease free to a hyper endemic nation. Editorial Board. 2011;5:81.
10. Mahmood S, Hafeez S, Nabeel H, Zahra U, Nazeer H. Corrigendum to "Does Comorbidity Increase the Risk of Dengue Hemorrhagic Fever and Dengue Shock Syndrome?". International Scholarly Research Notices. 2017;2017.
11. Naveed M, Chaudhry Z, Bukhari SA, Awan I, Khalid N. Dengue death tolls: A nightmare for Khyber Pakhtunkhwa, Pakistan. Journal of infection and public health. 2017.
12. Organization WH, Research SPf, Diseases TiT, Diseases WHODoCoNT, Epidemic WHO, Alert P. Dengue: guidelines for diagnosis, treatment, prevention and control: World Health Organization; 2009.
13. Dick OB, San Martín JL, Montoya RH, del Diego J, Zambrano B, Dayan GH. The history of dengue outbreaks in the Americas. *The American journal of tropical medicine and hygiene.* 2012;87(4):584-593.
14. Gubler DJ. Dengue/dengue haemorrhagic fever: history and current status. Paper presented at: Novartis foundation symposium2006.
15. Stanaway JD, Shepard DS, Undurraga EA, et al. The global burden of dengue: an analysis from the Global Burden of Disease Study 2013. *The Lancet infectious diseases.* 2016;16(6):712-723.
16. Messina JP, Brady OJ, Pigott DM, Brownstein JS, Hoen AG, Hay SI. The global distribution and burden of dengue. *Nature.* 2013;1:140004.
17. Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. *Nature.* 2013;496(7446):504.
18. Moulton SL, Mulligan J, Srikiatkhachorn A, et al. State-of-the-art monitoring in treatment of dengue shock syndrome: a case series. *Journal of medical case reports.* 2016;10(1):233.
19. Nasreen S, Arshad M, Ashraf M, Raza A, Bahar-e-Mustafa. The epidemiology of Dengue fever in district Faisalabad, Pakistan. Int J Sci Res Publications 2015;5(3):1-6.
20. Gubler DJ. Dengue and dengue hemorrhagic fever. Clin Microbiol Rev 1998;11(3):480-96.
21. Carey DE, Myers RM, Reuben R, Rodrigues FM. Studies on dengue in Vellore, South India. Am J Trop Med Hyg 1966;15(4):580-7.
22. Bandyopadhyay B, Bhattacharyya I, Adhikary S, Konar J, Dawar N, Sarkar J, et al. A comprehensive study on the 2012 dengue fever outbreak in Kolkata, India. ISRN Virol 2013;2013:Article ID: 207580, 5.