Patterns and Trends in Atypical Manifestations of Dengue among Inpatient Adults in Tertiary Care Teaching Institute of South India

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ABSTRACT

Introduction: Global impact of dengue fever is more likely in under developed and developing countries like India. Around 50% of the population all over world is prone to this disease. Spreading of this disease is due to mosquitoes with environmental nonhygienic conditions. Living area, age group, gender etc are some demographical factors along with atypical manifestations of dengue. This study intends to search the prevalence of dengue and its different atypical manifestations.

Material and Methods: This study deals around 385 dengue patients visited to Pondicherry Institute of Medical sciences (PIMS) as inpatient of general medicine department during the reference period 1st January 2011 to 31st December 2016. A structured statistical study tool with all types scaling measures is considered. Statistical reports are extracted for the study variables using SPSS. The test hypotheses related to intra and inter association among the disease manifestations are verified through chi-square statistic.

Results: It is observed that there is a statistical evidence on the association between febrile diarrhea and abdominal pain ($p < 0.001$); between febrile diarrhea and myositis ($p < 0.001$); between abdominal pain and myositis ($p < 0.001$).

Conclusion: As the spread of dengue and dengue haemorrhagic fever is increasing causing significant mortality and mortality, it is extremely important to consider atypical manifestations of dengue for appropriate diagnosis, treatment and notification.

Keywords: Atypical Manifestations, Dengue Fever

INTRODUCTION

Dengue is a tropical disease affected by single stranded RNA flavivirus spread by the bite of female Aedes aegypti and Aedes albopictus mosquitoes.[1,2] Dengue fever is usually a non-specific and self-limiting biphasic febrile illness. Clinical presentation of Dengue fever varies with a wide spectrum of signs and symptoms. Infection can be asymptomatic or cause a range of severity from mild dengue fever to dengue hemorrhagic fever, which can then progress to dengue shock syndrome and death.[3] Headache and abdominal pain are more common manifestations among the major warning signs associated with dengue.[4,5] Atypical manifestations are rare and include encephalopathy, encephalitis, seizures, hepatocellular damage, acalculous cholecystitis, myocarditis, pericardial effusion, severe gastrointestinal hemorrhage, Guillain-Barre syndrome and rhabomyolysis.[6,7] Climatic conditions are also more responsible factor for increasing the incidence and morbidity of dengue illness.[8]

In the recent years, the incidence of dengue is increasing in developing countries and increased mortality is not exceptional to this. Globally, almost 50% of the population is estimated to be under risk resulting in 390 million new dengue infections in each year.[9] Under integrated disease surveillance project in India, weekly dengue cases are reported regularly from all registered health facilities through symptom based screening followed by laboratory confirmation. New onset of dengue cases in a dengue free area, clustering of cases, cases with atypical manifestation are made mandatory to get include under notifiable diseases. As per the recent WHO guidelines 2011, there are three categories of clinical features in typical dengue manifestation such as (i) dengue fever without warning signs, (ii) dengue fever with warning signs and (iii) severe dengue fever. Symptoms apart from the mentioned features are often co-existing. Many health care providers had expressed the need for expanding the list of symptoms to be included under typical dengue. Study aimed to search the prevalence of dengue and its different atypical manifestations.

MATERIAL AND METHODS

The hospital record based study is carried out with 385 samples in Pondicherry Institute of Medical sciences (PIMS) Tertiary Care Teaching Institute. The target population for the present study includes adults admitted for dengue under general medicine department during the reference period 1st January 2011 to 31st December 2016 (for duration of six years). The average number of dengue admitted patients in PIMS is ranging from 80 to 100 per year. Hence, this study was planned as retrospective cohort from 2011-2016. Adults who were admitted in general medicine wards with confirmed diagnosis of dengue either by NS-I antigen or IgM ELISA or four fold rise in titres of IgG antibody are considered on inclusion criteria. Dengue patients with pregnancy, bleeding diathesis, co-infection with other infections such as scrub typhus, leptospirosis, parvovirus,

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malaria, sepsis, decompensated alcoholic liver disease, hepatitis, on treatment with thrombocytopenic drugs are excluded from the study. A detailed clinical history, physical examination and baseline investigations were undertaken and followed up till the patient got discharged from hospital. All clinical and laboratory details were carefully reviewed with daily assessment during hospital stay as per pre-tested questionnaire. The study includes demographic variables age, sex and area of living; and clinical diagnosis variables namely febrile diarrhea, gall bladder edema, IC bleed, petechiea, hematuria, gum bleed, melena, days of complication, rash, abdominal pain, encephalitis, DIC, acute pancreatitis, myositis, rhabdomyolysis, HGE and shock, amount of urea, creatinine, platelets, SGOT, SGPT, PT, INR, etc. Out of above clinical diagnosis, only atypical manifestations of dengue such as febrile diarrhea, gall bladder edema, acute pancreatitis, abdominal pain, myositis, rhabdomyolysis, urea, creatinine, platelets, ECG, SGOT and SGPT are considered for further study.

STATISTICAL ANALYSIS

The data was collected from the patients and with retrospective medical records using structured questionnaire. This statistical study tool consists of data with nominal scale, ordinal scale and also with continuous scale. A consolidated and summarized master spread sheet of subjects (rows) and study variables (columns) was prepared for data processing and extraction of results through statistical software SPSS. In order to obtain various indicators on the study variables various descriptive statistics were explored with supporting devices such as Univariate and Bivariate frequency tables. Further, the test hypotheses related to intra and inter association among the study variables were verified through standard operating procedures of statistical data analysis such as chi-square statistic.

RESULTS

It is observed that in a sample of 385 patients, 289 patients (75.1%) were of urban residence and 96 patients (24.9%) of rural residential area. This hospital consists around 3/4th of urban and 1/4th of rural patients as depicted in figure 1. Highest prevalence age group (41.6%) to the dengue fever is 21-30 years. The second most prevalence group (20.3%) is 31 to 40 years. Prevalence of dengue fever with respect to age distribution of the patients is depicted in figure 2. Frequencies and percentages of age group distribution with sex are shown in figure 3. The distribution of age group and area of living depicted in figure 4. Atypical manifestations of dengue summarized in Table 1. 85.5 % of dengue patients are having febrile diarrhea, 28.3% patients have gall bladder edema, and 90.9% of patients have abdominal pain. Abnormal as acute pancreatitis is observed with 1.8% of dengue patient, 77.9% patient have myositis and 3.6 % patients have rhabdomyolysis. Out of 385 patients, it consists of 16.9% of normal levels of SGOT and 83.1% of abnormal SGOT. Regarding SGPT, it is observed that 69.1% of patients have abnormal SGPT.

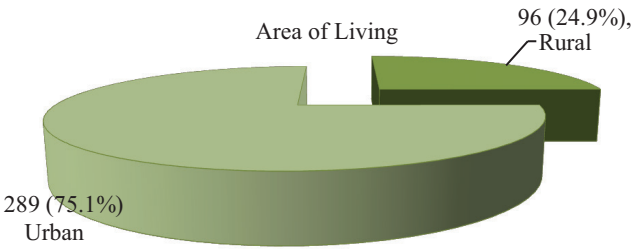

Figure-1: Prevalence of dengue fever with respect to the living area of the patient:

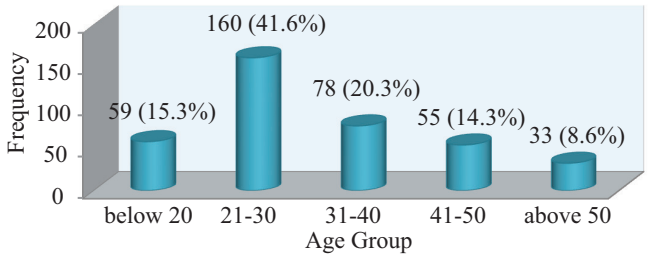

Figure-2: Distribution of Dengue patients with respect to their age

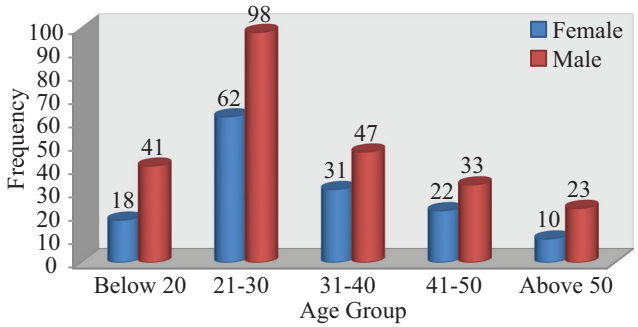

Figure-3: The Comparative Analysis of Age Group and Sex:

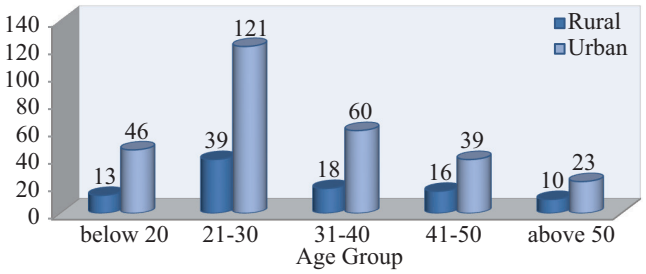

Figure-4: Distribution of Age groups with respect to their living place

In order to carry out meaningful inferences on findings of the study, statistical hypotheses were formulated for identified research objectives. The objectives include the following (i) To test the significance of the association among the demographical variables say age, gender and area of living; (ii) To verify the statistical significance and validity on the association between the demographical variables and the case study variables, more specifically atypical manifestations of dengue fever; (iii) to test the significant association between different atypical manifestations of dengue fever.

The statistical reports in tables and figures were presented in this section based on

(a) The categories of frequency tables of the patient with

respect to living area, gender, and age.

(b) Cross frequency tables for Age and Sex; Age and Living Area.

Variable name	Variable Group	Frequency
Febrile Diarrhoea	Absent	56 (14.5%)
	Present	329(85.5%)
Gall Bladder Edema	Absent	276(71.7%)
	Present	109(28.3%)
Abdominal Pain	Absent	35(9.1%)
	Present	350(90.9%)
Myositis	Absent	85(22.1%)
	Present	300(77.9%)
Rhabdomyolysis	Absent	371(96.4%)
	Present	14(3.6%)
Acute Pancreatitis	Normal	378 (98.2%)
	Abnormal	7(1.8%)
Platelets	Abnormal	332(86.2%)
	Normal	53(13.8%)
SGPT	Normal	119(30.9%)
	Abnormal	266(69.1%)
SGOT	Normal	65(16.9%)
	Abnormal	320(83.1%)

Table-1: Frequency tables of clinical diagnosis of atypical manifestation of Dengue

(c) Frequencies on Prevalence of different atypical manifestations of dengue.

(d) 2x2 contingency tables along with chi-square statistic for testing the significance of association among the atypical manifestations such that one with the remaining among (i) Febrile Diarrhoea, (ii) Gall Bladder edema, (iii) Acute pancreatitis, (iv) Abdominal Pain, (v) Myositis, (vi) Rhabdomyolysis depicted in table 2, table 3, table 4 and table 5.

DISCUSSION

In comparison of association between febrile diarrhea and gall bladder edema among 385 subjects, it is observed that there are 230 subjects having febrile diarrhea without gall bladder edema. It counts 59.7% of the total studied population. It is also observed that there are 99 cases that are having both febrile diarrhea and gall bladder edema which counts 25.7% of the total patient's population. The above table shows that 46 cases have no evidence of febrile diarrhea and gall bladder edema and its share is 11.95% of the total population. Least contribution is observed with 10 patients belong to patients who have gall bladder edema and the absence of febrile diarrhea and the percentage of their share is 2.59% of total population. It is also observed that there

		Febrile Diarrhoea		Chi-Sq Value	p value
		Absent	Present		
Gall Bladder	Absent	46 (11.95%)	230 (59.74%)	3.529	0.60
	Present	10 (2.59%)	99 (25.71%)		
Acute Pancreatis	Normal	56 (14.54%)	322 (83.64%)	1.214	0.271
	Abnormal	0	7 (1.82%)		
Abdominal Pain	Absent	21 (5.45%)	14 (3.64%)	63.996	0.000*
	Present	35 (9.09%)	315 (81.81%)		
Myositis	Absent	27 (7.01%)	58 (15.06%)	26.021	0.000*
	Present	29 (7.53%)	271 (70.36%)		
Rhabdomylosis	Absent	55 (14.28%)	316 (82.07%)	0.641	0.424
	Present	1 (0.25%)	13 (3.37%)		

Table-2: Statistical analysis for atypical manifestations of dengue fever

		Acute Pancreatis		Chi-Sq Value	P value
		Normal	Abnormal		
Abdominal Pain	Absent	35 (9.09%)	0	0.713	0.398
	Present	343 (89.09%)	7 (1.82%)		
Myositis	Absent	85 (22.08%)	0	2.02	0.155
	Present	293 (76.10%)	7 (1.82%)		
Rhabdomyolysis	Absent	364 (94.54%)	7 (1.82%)	0.269	0.604
	Present	14 (3.64%)	0		

Table-3: Statistical analysis for abdominal pain, myositis, rhabdomyolysis in patients presenting with acute pancreatitis

		Abdominal Pain		Chi-Sq Value	P value
		Absent	Present		
Myositis	Absent	20 (5.20%)	65 (16.88%)	27.516	0.000*
	Present	15 (3.9%)	285 (74.02%)		
Rhabdomyolysis	Absent	34 (8.83%)	337 (87.53%)	0.067	0.796
	Present	1 (0.26%)	13 (3.38%)		

Table-4: Statistical analysis for myositis, rhabdomyolysis in patients presenting with abdominal pain

		Myositis		Chi-Sq Value	p value
		Absent	Present		
Rhabdomyolysis	Absent	85 (22.08%)	286 (74.28%)	4.116	0.042*
	Present	0	14 (3.64%)		

Table-5: Statistical analysis for rhabdomyolysis in patients with myositis

is no statistical evidence on the association between febrile diarrhea and gall bladder edema as chi- square statistic value is 3.529 and its p-value is 0.60(>0.001).

In comparison of association between febrile diarrhea and acute pancreatitis among 385 subjects, the above table shows that there are 322 subjects having febrile diarrhea with normal acute pancreatis. It counts 83.64% of the total studied population. It is also observed that there are 56 cases having febrile diarrhea and normal pancreas which counts 14.54% of the total patient's population. It shows that 7 cases have evidence of febrile diarrhea and abnormal acute pancreatis and its share is 1.82% of the total population. There is no evidence of patients having absence of febrile diarrhea and abnormal acute pancreatitis. The association table above shows that there is no statistical evidence on the association between febrile diarrhea and acute pancreatis as chi- square statistic value is 1.214 and its p-value is 0.271(>0.001).

On comparing the association between the condition of febrile diarrhea and abdominal pains among 385 dengue affected subjects, it is observed that there are 315 subjects having febrile diarrhea and abdominal pain. It counts 81.81% of the total studied population. The above table shows that there are 35 patients having abdominal pain and absence of febrile diarrhea which counts 9.09% of the total patient's population. It shows that 21 cases are not having both the evidence of febrile diarrhea and abdominal pain and its share is 5.45% of the total population. The remaining 14 patients are having febrile diarrhea and absence of abdominal pain and its count is observed as 3.64%. The association table above shows that there is statistical evidence on the association between febrile diarrhea and abdominal pain as chi- square statistic value is 63.996 and its p-value is 0.000(<0.001).[3-5]

The above table-1 shows the comparison of association between febrile diarrhea and myositis among 385 dengue subjects, it is observed that there are 271 subjects having both febrile diarrhea and myositis. It counts 70.38% of the total studied population. It is also observed that there are 58 cases that are having febrile diarrhea and absence of myositis which counts 15.06% of the total patient's population. 29 cases of the above table shows there is a evidence of febrile diarrhea and absence of myositis in dengue patients and its share is 7.53% of the total population. Least contribution is observed with 27 patients belong to patients who are not having both myositis and the febrile diarrhea and the percentage of their share is 7.01% of total population. It is also observed that there is statistical evidence on the association between febrile diarrhea and myositis as chi- square statistic value is 26.021 and its p-value is 0.000(<0.001).

In comparison of association between febrile diarrhea and rhabdomyolysis among 385 dengue subjects, it is observed that there are 316 subjects having febrile diarrhea without rhabdomyolysis. It counts 82.07%% of the total studied population. It is also observed that there are 55 cases that are not having both febrile diarrhea and rhabdomyolysis which counts 14.28% of the total patient's population. The above table shows that 13 cases have both febrile diarrhea and rhabdomyolysis and its share is 3.37% of the total population. Least contribution is observed with only one patient who have rhabdomyolysis and the absence of febrile diarrhea and the percentage of their share is 0.25% of total population. It is also observed that there is no statistical evidence on the association between febrile diarrhea and gall bladder edema as chi- square statistic value is 0.649 and its p-value is 0.424(>0.001).

On comparing the association between the condition of acute pancreatitis and abdominal pains among 385 dengue affected subjects, it is observed that there are 343 subjects having normal pancreas and abdominal pain. It counts 89.09% of the total studied population. The above table shows that there are 35 patients having normal pancreas and absence of abdominal pain which counts 9.09% of the total patient's population. It shows that 7 cases have abnormal acute pancreatic and its share is 1.82% of the total population. There is no evidence of abnormal acute pancreatis and abdominal pain. The association table above shows that there is no statistical evidence on the association between abdominal pain and acute pancreatitis as chi- square statistic value is 0.713 and its p-value is 0.398(>0.001).

The above table shows the comparison of association between acute pancreatitis and myositis among 385 dengue subjects, it is observed that there are 293 subjects having both normal acute pancreatitis and myositis. It counts 76.10% of the total studied population. It is also observed that there are 85 cases that are having normal pancreas and absence of myositis which counts 22.08% of the total patient's population. 7 cases of the above table shows there is an evidence of abnormal acute pancreatitis and the presence of myositis in dengue patients and its share is 1.82% of the total population. There is no patient who has abnormal acute pancreatitis and absence of myositis. It is also observed that there is no statistical evidence on the association between acute pancreatis and myositis as chi- square statistic value is 2.02 and its p-value is 0.155(>0.001).

On comparing the association between the condition of acute pancreatitis and rhabdomyolysis among 385 dengue affected subjects, it is observed that there are 364 subjects having normal pancreas and absence of rhabdomylosis. It counts 94.54% of the total studied population. The above table shows that there are 14 patients having rhabdomyolysis and normal pancreas which counts 3.64% of the total patient's

population. It shows that 7 cases having abnormal acute pancreatitis and absence of rhabdomyolysisand its share is 1.82% of the total population. There is no patient who has abnormal acute pancreatitis and rhabdomyolysis. The association table above shows that there is no statistical evidence on the association between acute pancreatitis and rhabdomyolysis as chi- square statistic value is 0.269 and its p-value is 0.604(>0.001).

In comparison of association between abdominal pain and myositis among 385 subjects, the above table shows that there are 285 subjects are having both abdominal pain and myositis. It counts 74.02% of the total studied population. It is also observed that there are 65 cases having abdominal pain and myositis which counts 16.88% of the total patient's population. It shows that 20 cases have evidence of absence of both abdominal pain and myositis and its share is 5.20% of the total population. Least contribution is 15 cases and its share is 3.9%. The association table above shows that there is statistical evidence on the association between abdominal pain and myositis as chi- square statistic value is 27.516 and its p-value is 0.000(<0.001).

The above table shows the comparison of association between abdominal pain and rhabdomyolysis among 385 dengue subjects, it is observed that there are 337 subjects having abdominal pain and absence of rhabdomyolysis. It counts 87.53% of the total studied population. It is also observed that there are 34 cases that are having absence of both abdominal pain and rhabdomylosis which counts 8.83% of the total patient's population. 13 cases of the above table shows there is a evidence of abdominal pain and rhabdomyolysispresence in dengue patients and its share is 3.38% of the total population. Only one case is observed belongs to patients who are not having abdominal pain and having rhabdomyolysis and the percentage of their share is 0.26% of total population. It is also observed that there is no statistical evidence on the association between abdominal pain and rhabdomyolysis among dengue patients as chi- square statistic value is 0.067 and its p-value is 0.796(>0.001).[6-9]

On comparing the association between the condition of myositis and rhabdomyolysis among 385 dengue affected subjects, it is observed that there are 286 subjects having myositis and absence of rhabdomyolysis. It counts 74.28% of the total studied population. The above table shows that there are 85 patients are not having both rhabdomyolysis and myositis which counts 22.08% of the total patient's population. It shows that 14 cases having both rhabdomyolysis and myositis and its share is 3.64% of the total population. There is no patient who has rhabdomyolysis and myositis. The association table above shows that there is no statistical evidence on the association between myositis and rhabdomyolysis as chi- square statistic value is 4.116 and its p-value is 0.042(>0.001).

CONCLUSION

In this study 75.1% of patients were of urban residence. Highest prevalence (41.6%) age group to the dengue fever is 21 – 30 years. Males (62.9%) were predominantly affected than females. Among the atypical manifestations, febrile diarrhea (85.5%), gall bladder edema (28.3%), abdominal pain (90.9%), myositis (77.9%), rhabdomyolysis (3.6%) (urine myogloin present) were observed. Acute liver injury with elevated SGOT (83%) and SGPT (69%) were significant. Other atypical manifestations like encephalitis, acute pancreatitis, acute renal failure, disseminated intravascular coagulation, cardiac conduction disturbances and ischaemic heart disease were insignificant in the present study. As the spread of dengue and dengue haemorrhagic fever is increasing causing significant mortality and mortality, it is extremely important to consider atypical manifestations of dengue for appropriate diagnosis, treatment and notification.

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