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Original Research Article

Study of nutritional status, comorbidities and other risk factors associated with dengue fever: data from a tertiary hospital in North India

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ABSTRACT

Background: Dengue is a major health problem in India. The understanding of the factors which predispose to the infection and which are involved in its progression is fundamental for improved clinical outcomes. This study was initiated with the aim of identifying the patient population at risk and comorbidities involved in the development of complications.
Methods: This was an observational and case control study in which 130 cases and controls taken from the healthy population were evaluated with respect to data regarding demographics, complications and co morbid metabolic diseases.
Results: There was a predominance of males in cases as compared to controls especially between ages of 21-30 years . There was a significantly higher rate of comorbidities in cases as compared to controls and constituted 62.3% of the total cases. Obese /overweight cases were 60.8 %, fatty liver -30.76%, diabetics- 15.4 %, hypertensives 15.4%, cases of hypothyroidism 2.3 %, renal diseases 5.38% and ischemic heart disease 6.92%, 18.50% cases developed complications and severe disease (SD). There was a significant association of pleural effusion/ascites and gall bladder edema with SD. Association of comorbidities with SD was however not significant. Such cases tended to develop complications like heart failure, angina, renal failure and multiorgan failure and were difficult to treat. 5 (3.84%) patients died. 4 had associated comorbidities.
Conclusions: Comorbidities like obesity predispose to dengue infection and are liable to cause serious complications knowledge of which can prompt early clinical intervention and reduction of mortality.

Keywords: Comorbidities, Complications, Dengue

INTRODUCTION

In recent years, dengue has become a major public health concern. Recurrent outbreaks have been reported in India especially during the months of July to November which coincide with the rainy season, water stagnation and mosquito breeding. Dengue virus causes a disease which varies in severity. It was initially classified as Dengue fever (DF) and dengue hemorrhagic fever (DHF).[1] It was categorized into four grades, from less severe (grade 1) to severe (grade 4). Grades 3 and 4 in which plasma leakage is so profound so as to cause circulatory failure are also referred to as dengue shock syndrome (DSS). In 2009, the World Health Organization (WHO) released a new classification of dengue infections.[2] The cases are divided in to two groups: non-severe and severe dengue (SD) cases. Those who improve after defervescence are said to have non-severe dengue. Thrombocytopenia is a well-known marker of dengue severity.

Severe disease is marked by the problems of capillary permeability. It is defined as having at least one of the

following criteria: severe plasma leakage into the pleural and abdominal cavities leading to shock (DSS), fluid accumulation with respiratory distress, severe bleeding as evaluated by clinician, severe organ involvement, liver: AST or ALT ≥ 1000, impaired consciousness, failure of heart and other organs. Delayed or untreated shock can lead to complications of hepatic, renal or multiple organ failure (MOF) and death. Massive bleeding due to disseminated intravascular coagulation (DIC) after prolonged shock is another characteristic of severe and complicated disease.[3] The development from non-severe to severe dengue could be unpredictable.

Dengue disease continues to involve newer areas and newer populations with increasing intensity epidemic after epidemic. It is important to recognize the clinical pattern, patient population at risk, individuals who are more likely to develop complications and who need special intensive care. Several factors including nutritional status have been studied .Results from previous studies failed to show any solid consistency regarding the association between the nutritional status and dengue infection.

Certain epidemiological studies have focused on the patient factors in the past and have shown that females, children below 15 years and those above the age of 65 years were more prone to DHF.[4,5] However the mean age of acute dengue has undergone a shift change towards older ages. This fact points towards the relevance of assessing the influence of age-related comorbidities, such as diabetes on the clinical presentation of dengue episodes. Co-morbidities were shown to be associated with several other infectious diseases such as influenza, tuberculosis and hepatitis C.

It has been postulated that certain comorbid conditions like obesity, diabetes mellitus, hypertension and chronic renal failure make the patients susceptible to dengue infection. It was noted during the earlier epidemics that patients with comorbidities like diabetes and hypertension had a more aggressive course and needed intensive care. However, due to heterogeneity in studies, the effect of comorbidities as modifiers of dengue severity could not be established. Identification of comorbidities associated with dengue fever and factors associated with a severe presentation can lead to early diagnosis and timely medical intervention which can prevent complications and death.

This study was initiated keeping in view the possibility of identifying the patient population prone to develop dengue and to study the role of comorbidities like obesity, diabetes, hypertension and renal disease in making the individual vulnerable to the infection and also to investigate their influence on the development severe disease and other complications. It also aimed to study any other helpful warning signs associated with the severe disease.

METHODS

This was an observational and case control study in which 130 patients suffering from dengue fever in the study period from September to November 2016 admitted to the SGRD Medical College Amritsar were evaluated. All the patients, who presented with fever and found positive for NSI antigen and dengue IgM and IgG antibodies (MAC-ELISA) were included in the study.

Dengue infection was diagnosed according to case definition provided by WHO (2009). Those with incomplete record and suffering from co infections like malaria were excluded from the study. Data regarding demographics, related complications and comorbid metabolic diseases was collected. BMI of all patients was analyzed. Patients of diabetes mellitus, hypertension, heart, renal disease, hypothyroidism and rheumatoid arthritis were diagnosed from the history, patient record and by other relevant investigations. 130 healthy controls were also studied and the data was analyzed by excel and SPSS 20.0 software.

RESULTS

A total of 130 dengue cases were studied. (69.2%) were males and 40 (30.8%) were females. There was a clear predominance of males in cases as compared to that in controls (x^2 = 19.100; df = 1. p <0.001). (Table 1) Age and sex distribution is shown in Figure 1.The maximum number of patients were young adults were between 21-30 years with another peak between 40-50 years because of associated comorbidities in this age group. Most of the comorbidities were above the age of 40 years. However obesity was present across all age groups.

Table 1: Incidence of males and females in cases and controls.

Sex	Cases		Controls	
	No.	%	No.	%
Male	90	69.20	55	42.30
Female	40	30.80	75	57.70
Total	130	100.00	130	100.00

x^2 = 19.100; df = 1; p <0.001; Highly significant

Fever and myalgia were present uniformly in all patients. The important clinical presentations were epigastric pain in 24.6% cases, minor bleeding and eccymosis in 41.5% cases and hepatomegaly in 25.3 % cases.

The prominent sonographic features were pleural effusion/ ascites in 43.8% cases, gall bladder edema in 27.6 % and Fatty liver in 30.8% cases. Platelet count ranged between 10000 - 30000 mm^3 in 47.6 % cases and from 30000-60000 mm 3 in 34.6 % cases. There was a significant association between pleural effusion and gall bladder edema (seen on ultrasound) and severe disease (p = 0.013) and (p <0.001**) respectively (Table 2).

Table 2: Association between pleural effusion/ascites and gall bladder oedema with severe and complicated disease.

		Severe disease				Total	x^2 value	P value
		Absent		Present				
		No.	percentage	No.	percentage			
Pleural effusion/Ascitis	Absent	65	89.00	8	11.00	73	6.226	0.013*
	Present	41	71.90	16	28.10	57		
Gall bladder oedema	Absent	87	93.50	6	6.50	93	31.309	<0.001**
	Present	19	51.40	18	48.60	37		

Table 3: Complications of dengue fever and associated comorbidities and mortality.

	Case	Obese/ overweight	Diabetes	Hypertension	Rheumatoid arthritis	Mortality	No comorbidity
Dengue Shock syndrome	1	0	0	0	0	0	1
MOF	2	2	1	0	0	2	1
Severe bleeding	7	3	1	0	0	1	4
Encephalitis	2	0	0	0	0	1	1
Pancreatitis	2	0	0	0	0	0	2
Renal failure	3	3	2	1	1	1	0
CAD	1	0	0	0	0	0	
Heart Failure	6	6	6	3		0	0
Moderate degree of fluid overload /stable angina	9	9	9	5	0	0	0

Table 4: Incidence of obesity (including over weight individuals) in cases as compared to that in controls.

Obese /overweight	Cases	Controls	x^2	df	P value
	No. (%)	No (%)			
Total	130 (100.00%)	130 (100.00%)	33.190	1	<0.001; highly significant
Non-obese	51 (39.20%)	97 (74.60%)			
Obese /overweight	79 (60.80%)	33 (25.40%)			
Comorbidity absent	49 (37.70%)	91 (70.00%)	27.300	1	<0.001; highly significant
Comorbidity present	81 (62.30%)	39 (30.00%)			
Diabetes absent	110 (84.60%)	120 (92.30%)	3.768		p =0.052 Not significant
Diabetes present	20 (15.40%)	10 (7.70%)			

24 (18.50%) cases had complications and severe disease with 1 case having DSS, 2 each having MOF, pancreatitis and encephalitis, 3 had renal failure, 6 had fluid overload/heart failure, 1had unstable angina and another 7 had severe bleeding including pulmonary, GIT and intracranial bleeding. One case of rectus sheath bleeding was seen in a hypertensive patient. 6 cases needed ventilatory support and 5 cases died (Table 3).

Patients with all comorbidities including obese/overweight cases constituted 81 (62.3%), of the total cases. Obese/overweight cases were 79 (60.8%), fatty liver 40 (30.76%), diabetes 20 (15.4%), hypertension 20 (15.4%), hypothyroidism 3 (2.3%), renal disease 7 (5.38%), ischemic heart disease (IHD) 9 (6.93%) and rheumatoid arthritis 1 (0.77%) (Figure 2). Some cases had more than 1 comorbidity. On analysis it was found that there was a significantly higher rate of obesity and all comorbidities (including obesity) in cases as compared to that in controls ($p < 0.001$) (Table 4). Incidence of diabetics and hypertensive in cases was not significantly different than that in controls ($p > 0.05$) when taken alone. However the association of comorbidities with severe disease was not significant statistically. (Table 5) The complications are shown in Table 3.

Table 5: Association between comorbidities including obesity with severe and complicated disease.

Co-morbidity including obesity	Severe disease				Total
	Absent		Present		
	No.	Percentage	No.	Percentage	
Absent	39	79.60	10	20.40	49
Present	67	82.70	14	17.30	81
Total	**106**	**81.50**	**24**	**18.50**	**130**

$x^2 = 0.198$, df = 1, OR, 0.815 (95% CI : 0.331 - 2.009); p =0.656; Not significant

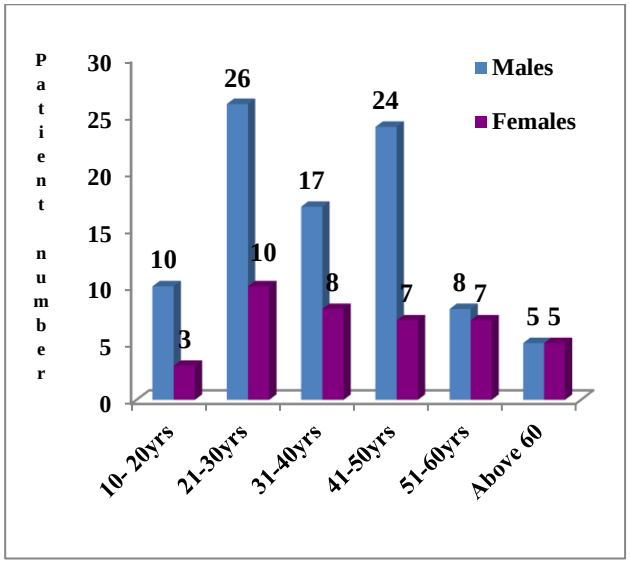

Figure 1: Age and sex distribution.

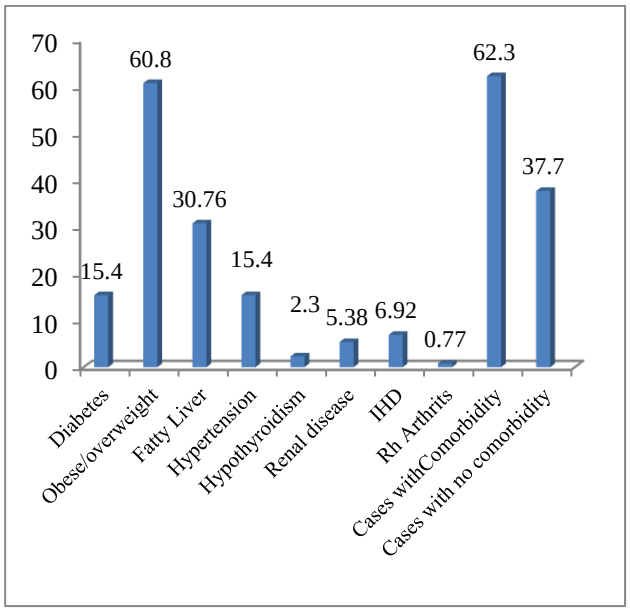

Figure2: Percentage of associated comorbidities.

DISCUSSION

In our study, there were significantly more number of males in cases as compared to that in controls ($p < 0.001$) showing male predominance. This was supported by another study by Antony in which 60.70% were males and 39.29% were females and 42.02% males were in the age group of 20 to 39 years.[6] The reason is not apparent. The maximum number of patient in our study were young adults between 21-30 years with another peak between 40-50 years possibly because of associated comorbidities like diabetes and hypertension which are prevalent in this age group. Obesity has aroused considerable medical and public health concerns worldwide. The effects of nutritional status on dengue disease outcome has been controversial in previous studies.[7-10] Some studies found that patients with excessive body weight were at increased risk for more severe disease, while malnutrition is a protective factor in malnourished children.[11-14] In our study there was significantly higher number of obese/overweight individuals in cases as compared to that in controls ($p < 0.001$). Obesity is characterized by a state of low-grade inflammation. Excess adiposity deranges immune function and host defence making an individual prone to infections like dengue.[15] In dengue cytokines cause vasculopathy with disruption of vessel integrity and increased capillary permeability.[16,17] This vasculopathy is thought to be enhanced in pro inflammatory states like diabetes mellitus and obesity due the activated immune response and enhanced cytokine release.[18]

According to some studies metabolic factors especially diabetes with and without hypertension, are important risk factors for development of DHF.[19-21] A metaanalysis of 5 case controlled studies which collected information towards WHO 1997 classification system a diagnosis of diabetes was associated with an increased risk for a severe clinical presentation of dengue.[22] The study by Shahid et al, failed to show any statistical association between these co morbidities like diabetes and DHF.[23] A study by Perez et al showed relation between comorbidities and dengue-related deaths.[24]

Present study shows that the association of cases having comorbidities (including obesity) with severe and complicated disease was not significant statistically. This difference could be because of the small sample size or some other factors like the difference in the classification that was used in earlier studies. However it was importantly observed that patients with comorbidities required longer stay and more medical attention in the hospital compared to others. Complications of fluid overload were found more in obese patients as has also been observed in another study 10 cases who developed

heart failure, (moderate to severe degree) angina, renal failure and multiorgan failure had associated comorbidities like diabetes, hypertension and obesity. 1 patient who had MOF was a patient of rheumatoid arthritis. In our study 4 patients out of 5 who died had related comorbidities. Patients who developed encephalitis, pancreatitis, dengue shock syndrome and 4 patients of severe bleeding (including pulmonary, GIT and intracranial bleeding) had no comorbidities. In such cases warning signs like pleural effusion, ascites and gall bladder odema on ultrasound could be could be helpful. Larger studies are desirable to confirm these findings.

CONCLUSION

Obese /overweight persons especially young males and persons with other comorbidities are susceptible to dengue infection. The importance of comorbidities in dengue cases cannot be overlooked. Though their relationship with severe and complicated disease was not statistically significant in our study it is important to note that such cases developed complications like fluid overload, heart failure, renal failure, MOF and angina and were important contributors of mortality. Though the sample size was very small it provides preliminary evidence that dengue patient with diabetes, hypertension and obesity need extra medical care to avoid the above complications but larger studies are needed in this regard. Pleural effusion /ascites and gall bladder oedema may portend further complications and severe disease and may serve as useful warning signs.

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