

To study Clinical and Laboratory Characteristics and Risk Factors for Fatality in Geriatric Patients compared with Adult with Dengue Hemorrhagic Fever at tertiary hospital.

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ABSTRACT

Introduction: Dengue fever (DF) has been re-emerging over the last several decades. A large number of patients were adults in general and elderly individuals in particular which was in sharp contrast to the predominant pediatric patients seen in the dengue epidemics recently. Advanced age per se has been previously reported to be a high risk factor for mortality in dengue virus infection. There only few study in elderly patients, so this study was conducted to find risk factors for fatality in elderly.

Aim Of Study

1. To Compare clinical and Laboratory manifestations of DHF between elderly and adults.
2. To identify risk factors for fatality in the elderly population.

Materials And Methods: This was retrospective study conducted in patients with DHF admitted between January 2010 to December 2012 in Dr Prabhakar's KLE Hospital and research Center Belgaum, Karnataka India, a 2000 bed multispecialty hospital. Medical records were revived and detail data was collected for 154 patients.

Results: 21 elderly (age>60 years) and 132 adults (age 19–60 years) with DHF were retrospectively analyzed. Compared with adults, in elderly individuals there was no significant difference in symptoms' and signs seen. When compared with non-fatal elderly patients with DHF, a significant higher frequency in men ($P = 0.019$), those with hypertension ($P =$

0.018), those with dengue shock syndrome (DSS; $P < 0.001$), and those with acute renal failure ($P < 0.021$) was found in the Fatal elderly, with statically significant. Multivariate analysis showed that only DSS (odd ratio 3.81, $P = 0.036$) was an independent risk factor for fatality.

Conclusion: There were no differences in clinical manifestations and laboratory characteristics between the elderly and younger adults with DHF. Among adults with DHF, the elderly have a higher mortality rate compared with the younger ones. DSS is an independent risk factor for fatality in elderly patients with DHF.

INTRODUCTION

Dengue is endemic in India and has caused a large number of epidemics at different place and dengue fever (DF) has been re-emerging over the last several decades. Patients of first DHF was first noticed in Delhi in 1988 and then in madras in 1989. There was large epidemic outbreak in north India in 1996, there was case reported first from Delhi (Sharma 1997) and soon adjoining states (Kawar at ell 1997), there after disease is emerging and outbreak in different part of country¹. In this recent epidemic in Taiwan, a large number of patients were adults in general and elderly individuals in particular, which was in sharp contrast to the predominant pediatric patients seen in the dengue epidemics in southeast Asia. Advanced age per se has been previously reported to be a high risk factor for mortality in dengue virus infection. Garcia-Rivera and Rigau-Perez reported that the elderly seemed to be more likely than younger adults to develop severe illness when they were infected with DEN 2. There are very few studies conducted in this part of country to study clinical and risk factor profile in DHF, so this study was taken up.

MATERIALS AND METHODS

We conducted a retrospective study of adult patients with acute DHF admitted between January 2010 and December 31, 2012 at KLE Hospital and Research Center Belgaum, a 2,400-bed Multispecialty Hospital, tertiary Care referral center in North Karnataka. The medical Records of the included DHF patients were reviewed for collection of demographic, clinical, laboratory, and imaging information. The diagnosis of dengue

infection in a DEN-infected patient was based on one of the following criteria: 1) a positive NS 1 Antigen 2) a positive enzyme-linked immunosorbent assay result for specific immunoglobulin M antibody for DEN in acute phase serum, or 3) at least 4-fold increase in dengue-specific hemagglutination Ig G antibodies inhibition titers in convalescent serum compared with that in acute-phase serum. The patients were divided into two groups: Elderly (≥ 60 years of age) and adults (19–59 years of age). Patients in the elderly group were further divided into fatal and non-fatal subgroups. The severity of DHF was categorized into grades I–IV according to the World Health Organization (WHO) criteria.

Risk Factors of Fatality defined were

1. Gallbladder edema - (thickened gallbladder wall > 3.5 mm)
2. Concurrent bacteremia - (positive bacterial growth from blood that was sampled for culture within 72 hours after the patient was hospitalized for DHF)
3. Acute renal failure (ARF) – rapid increase in serum creatinine up to > 2 mg/dL in a patient with original normal kidney function.
4. Rhabdomyolysis was made in a patient with abnormally high serum creatine kinase (normal, < 120 U/L) coupled with the presence of myoglobin in blood and/or urine
5. Fatality referred to all-cause death within 1 week in patients with DHF.

Statistics

univariate analysis to compare the demographic, clinical, laboratory, and imaging characteristics of patients between the elderly and nonelderly groups and variables between the fatal and non-fatal elderly subgroups. In univariate analysis, Student t test used for comparison between continuous variables, whereas the 2 test or Fisher exact test was used to assess differences between dichotomous variables. Significant variables in univariate analyses between the fatal and non-fatal subgroups were entered into a multivariate logistic regression model to identify the risk factor(s) for fatality in the elderly patients with DHF. odd's ratio was calculated for hazard ratio.

RESULTS

Table 1: Showing Symptoms and signs of 153 adult patients with dengue hemorrhagic Fever.

S NO.	Symptoms/Signs	Elderly(>60Yrs)	Adults (19-59)	P Value
		(N = 21)	(N = 132)	
1	Fever	21(100%)	131(99.2%)	1
2	Abdominal Pain	5(23%)	47%(35.6%)	0.416
3	Retroribital Pain	0	0	0
4	Headache	1(4.7%)	16(12.12%)	0.47
5	Arthralgia	2(9.5%)	11(8.3%)	1
6	Cough	2(9.5%)	15(11.36%)	1
7	Myalgia	6(28.5%)	3(2.22%)	0.902
8	Rashes	3(14.28%)	33(25.0%)	0.408
9	Dizziness	1(4.7%)	8(6.06%)	1
10	Nausea/Vomiting	9(42.8%)	57(43.1%)	0.314
11	Diarrhea	2(9.5%)	33(25%)	0.613
12	Disorientation	1(4.7%)	0	0.137
13	petechiae	3(14.28%)	5(3.7%)	0.139
14	GI Bleed	6(28.5%)	30 (22.7%)	0.583
15	Gum Bleeding	0	11(8.3%)	0.32
16	Hematuria	2(9.5%)	8(6.6%)	0.904
17	Hemoptysis	4(19.4%)	2(1.5%)	1
18	Sub conjunctival Hemorrhage	0	5(3.7%)	1
19	Epistaxis	0	4(3.0%)	1
20	Menorrhagia	0	2(1.5%)	1

Table 2.

Co Morbid condition	Elderly >60 yrs	19 - 59yrs	P value
	(N = 21)	(N = 132)	
Diabetes Mellitus	3(14.8%)	2(1.5%)	0.018*
Hypertension	8(38.09%)	3(2.2%)	<0.001**
Previous stroke	0	0	0
COPD	1	0	0.317
CKD	0	0	0
Heart Disease(IHD)	3(14.28%)	0	<0.002**
Malignancy	0	0	0

Table 3: Laboratory data of patients with dengue hemorrhagic fever

S No	Variables	>60 yrs (N=21)	19-59 yrs(N= 132)	P Value
1	Leucopenia(< 4000 cells/L)	3(14.28%)	12(9.0%)	0.435
2	Leukocytosis (>11000 cells/L)	2(9.5%)	8(6.06%)	0.904
3	Thrombocytopenia (< 100000 cell/L) (%)	14(66.6 %)	34(25.7%)	0.001***
4	Prolongation of APTT, n/N (%)	2(9.95%)	7(5.3%)	0.792
5	Prolongation of PT, n/N (%)	1(4.7%)	8(6.0%)	0.594
8	SGPT (Reference value < 40 IU/L): Mean	12(57.1%): 268.0	75(56.6%): 71.15	0.834
7	SGOT (reference value < 40IU/L)	12(57.1%) : 115.2	75(56.6%) : 70.15	0.834
8	Sr Albumin (Reference 3.5mg - 5.5 mg / dl)	17(80.9%)	67(50.7)	0.019*

Table 4: Demographic and Imaging Characteristic patients with Dengue hemorrhagic fever

S No	Variables	Elderly (N = 21)	Non Elderly (N = 132)	P value
1	Age (years mean \pm SD)	63.3 \pm 3.66	29.9 \pm 9.59	
2	Male/ Female(%)	20(95.3)/1(4.7)	105(79.6)/ 27(20.4)	0.154
3	DSS (%)	6 (28.57)	13 (9.88)	0.026**
4	Length of fever	6.0 \pm 2.56	6.3 \pm 3.27	0.714
5	Acute Renal Failure (%)	12 (57.1)	23 (17.42)	0.0002**
6	Rhabdomyolysis (%)	0	0	0
7	Concurrent Infection (%)	0	0	0
8	Receiving Antibiotics (%)	3.9 \pm 1.84	2.9 \pm 2.76	0.118
9	Pleural Effusion (%)	10 (47.1)	7 (5.3)	0.001**
10	Gall Bladder (%)	2(9.52)	7 (5.3)	0.792
11	Ascites (%)	11 (52.1)	1 (0.75)	0.001**
12	Length of Hospital Stay (day Mean \pm SD)	5.1 \pm 3.41	5.1 \pm 2.35	0.98
13	Fatality (%)	7 (33.33)	13 (9.8)	0.008**

Table 5: Characteristics of the Fatal (N=7)and Non fatal(N=14) subgroups in elderly patients with DHF.

S No	Variables	Fatal (N=7)	Non Fatal (N= 14)	P Value
1	M/F Ratio	6/1	14/0	0.333
2	Co morbid conditions			
	Diabetes Mellitus	1(14%)	2(14.2%)	100.00%
	Hypertension	1(14%)	5(35.7%)	0.12
	COPD	0	1(7.1%)	1
	Heart Disease	0	3(21.4%)	0.521
	Malignancy	0	0	0
3	Leucopenia	2(28%)	1(7.1%)	0.247
4	Leukocytosis	0	2(14.2%)	0.533

5	Prolongation of APTT	0	2(14.2%)	0.533
6	Prolongation of PT	0	2(14.2%)	0.533
7	SGPT (>40 IU)	6(85%)	6(85%)	0.158
8	SGOT (>40IU)	6(85%)	6(85%)	0.158
9	Sr Albumin < 3.5mg / dl	6(85%)	11(78.5%)	1
10	Sr Creatinine > 1.4mg/dl	6(85%)	5(35.7%)	0.042*
11	Gall Bladder wall thickness	6(85%)	4(28.8%)	0.021*
12	CXR Pleural effusion	6(85%)	4(28.8%)	0.021*
13	MRI Brain (Bleed/Infarct)	4(57.1%)	0	0.006***
14	DSS	5(71.4%)	0	0.001***
15	GI Bleed	1(14%)	0	0.333

DISCUSSION

There are only a few studies on DHF involving in elderly patients have been reported. so this study was taken up to know the spectrum of clinical manifestation and risk factors for mortality in elderly patients in this part of our country. Physiological function declines with aging making elderly patients subjected to higher risk infection related to mortality and morbidity. In Southeast Asian countries DHF is primarily a disease of childhood, while in tropical Americans all the age groups are affected. Recently epidemic in Taiwan 2002 a large number of adults and elderly were affected with DHF, compared with children². Nowadays there is a shift in the age pattern of DHF and noted that advanced age is a high risk factor for mortality in DHF³.

In our study 21(13.3%) were elderly group and 132(86.6%) were in the adult group. Mean age of elderly group was 63.3 ± 3.66 and 29.9± 9.59, when compared with other studies (70.2 ± 4.5 and 48.8± 11.9).DHF was much more common in the early age group compared with other groups. Male were more commonly affected than females which were similar to other studies². Fever was the most common symptom seen in both the groups but Headache, Abdominal pain, Diarrhea was more common in non elderly group (Table 1). Myalgia was seen in both the groups, but arthralgia was more common in adults compared with elderly. Findings in study conducted in lucknow India were myalgia seen in (90%) patients and arthralgia in (9%) which is similar to our study (27% Vs 8.3% in adults and Elderly group was 28% vs 9.5%) were as study conducted 1.Bleeding manifestation in form GI bleed, Gum Bleeding, Rash ,Subconjunctival, Epistaxis was common in adult group ,Hemoptysis,petechiae,Hematuria was common in elderly compared with adult group these finding was similar to other study in Taiwan 2.but did not shown statically difference. Retrospective study conducted in Singapore showed in elderly patients less likely to present with headache, rash and mucosal bleeding which was similar to our study³. Elderly patients had atypical manifestation as defined by WHO criteria.

Diabetes, Hypertension, IHD were Co morbid conditions associated with DHF and when compared with the adult group there was statically significant (Table 2). Diabetes, Hypertension, IHD were Co morbid conditions associated with DHF and when compared with the adult group there was statically significant (Table 2). However our data showed that Diabetes was not a risk factor for fatality in elderly patients with DHF, which was similar to other studies done (table 5). When laboratory data was compared, Leukopenia and leukocytosis was more in elderly versus adults, but statistically no difference which was similar to other studies. In our study platelet count <100.000cu/mm elderly versus adults was (66.6% vs 25%).PT and APTT was prolonged in elderly compared with adults but statistically no difference which was similar to other studies. in elderly compared with adults mean SGOT (115 vs 70) and SGPT was (268 vs 71).Serum albumin level was low, which was statistically significant in our study compared to study conducted in taiwan².when we compared Demographic and imaging characteristics ,Male patients affected in both the groups.DSS was more common in elderly compared with adults (28.5% vs 9.88%) p= 0.02 which was statistically significant. and evidence of polyserositis, in form of pleural effusion and ascites and Gallbladder thickness was more in elderly versus adults patients was statistically significant (Table 4) but when compared with study conducted in Taiwan showed only pleural effusion was significant and ascites and gallbladder edema was not significant^{2,3}.Length of fever was slightly longer duration in our study elderly and adult was (6 days vs.6.3 days) compared with Taiwan study(4.4 vs 4.5). In our study ARF in elderly group compared with Non elderly (57.1% vs 17.4% p = 0.002) was very much stastically significant.ARF was more commonly found in elderly group was similar to study conducted in Taiwan (12.1%)².In our studies ARF in elderly was more compared to Taiwan group. Elderly Fatal (57.1% vs 12.1%) and Non Fatal group (85% vs. 35.5%)². DSS among elderly and Non elderly was (28.5% vs. 9.88%) and sub group among fatal elderly and non fatal elderly was (71.4% vs 0).when compared with other studies DSS was more in our studies (28.5% vs 10.%) and Non elderly

(9.88% vs 4.6%) 2. Antibiotics in elderly and adults received same duration and did not have any concurrent infection in both groups in our study. Length of Hospital stay in elderly and adult was (5.1 vs 5.1 days) and compared with other study was (7.9 vs 6.3 days) both the study did not have statistically significant. when compared with fatality in elderly and adults (33.33% vs 9.8%) there was statistically significant $p = 0.0008$ compared to other study (7.6% vs 0.8%)^{2,4}. Our study had more fatality rate compared to other study. Reason unknown, may be late recognition of symptoms, socioeconomic status. When we compared with characteristics between fatal and nonfatal subgroup among elderly patients (table 5), male were more commonly affected compared to females and there was no comorbid illness difference among both groups, laboratory parameters was not significant compared with other study. ARF was common among fatal versus nonfatal elderly group in our study which was similar compared with other study (85% vs 35.7%) and (80% vs 6.6%)². There are several factors responsible for severity of Dengue fever in elderly, First advancing age impairs physiology function and negatively impairs the function of the immune system. In elderly monocyte appears to have lower antioxidant response, against oxidation stress induced by dengue virus. T cell response to dengue virus infection have been observed impaired to dengue fever in elderly. Secondly probably of acquiring secondary dengue increase with age. Third increase prevalence of chronic disease and other comorbid disease in elderly. Renal failure was more common in both the studies. aging brings structural and functional change in the kidney render this organ susceptible to insult in elderly persons. Multifactorial cause may lead to renal failure in elderly DHF patients. Shock and kidney hypo perfusion resulting from plasma leakage in DHF/DSS may provoke in elderly as there was evidence in this study²³. elderly patients less likely to show less hemorrhagic manifestation and more likely to get hospitalization and serious illness compared to adults. But our study differ from the above study. 4. Mortality rate was higher in our study compared to previous study.

Limitations Of The Study

Its unicentric study. Suspicion of dengue patient was based on physician diagnosis, were mild cases can be missed. As this study was retrospective, some of the patient did not have given history in details and lab parameters were incomplete. In many patient blood culture was negative and some patient blood culture was not sent, so concurrent Bacteremia was not seen in our study.

CONCLUSION

There were no differences in clinical manifestations and laboratory characteristics between the elderly and younger

adults with DHF. DHF in elderly have a higher mortality rate compared with the adult ones. Age is an independent Risk factor for death in Dengue hemorrhagic fever. Risk factors associated were ARF and DSS. DSS is an independent risk factor for fatality in elderly patients with DHF

Aims and Objectives

1. To Compare clinical and Laboratory manifestations of DHF between elderly and adults.
2. To identify risk factors for fatality in the elderly population.

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