



A study on the epidemiological, clinical and laboratory profile of patients admitted with Dengue fever at a tertiary medical centre in South Kerala

Authors

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Background of the Study

Globally 50 million dengue infections are reported annually^[1]. In recent years Dengue has become one of the most important mosquito borne viral disease around the world. Female mosquitoes mainly of the species *Aedes aegypti* and, to a lesser extent, *Aedes Albopictus* transmits Dengue. Chikungunya, yellow fever and Zika infection are also transmitted by this mosquito. Due to local variations in risk influenced by rainfall, temperature and unplanned rapid urbanization dengue is widespread throughout the tropics^[1].

Dengue haemorrhagic fever was first recognized in the Philippines and Thailand in the 1950s during dengue epidemics. Today, severe dengue affects most Asian and Latin American countries and has become a leading cause of hospitalization and death^[2]. The annual incidence is estimated to be 7.5 to 32.5 million in India^[3]. Dengue viruses (DV) belong to the family Flaviviridae. There are four serotypes of the virus DV-1, DV-2, DV-3, and DV-4^[2]. It is a positive-stranded encapsulated RNA virus. DV is composed of three structural protein genes. These structural protein genes encode the nucleocapsid or core(C) protein, a membrane-associated (M) protein, an enveloped (E) glycoprotein, and seven non-structural (NS) proteins. Infection with one dengue serotype

provides lifelong homotypic immunity to that serotype. It also confers a very brief period of partial heterotypic immunity to other serotypes. But a person can eventually be infected by all 4 serotypes^[4].

The disease spectrum may vary with asymptomatic illness to life threatening diseases like dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS).

The diagnosis can be made by IgM ELISA during recovery or by antigen-detection ELISA or RT-PCR during the acute phase^[14]. There are no specific management of dengue, other than supportive care.

Indian Scenario

Dengue fever (DF) probably was reported in India from Calcutta (now Kolkata), West Bengal in 1872. An epidemic of dengue hemorrhagic fever (DHF) was reported in Kolkata in July 1963. Around 0.1 million people were affected, mostly children with 40% case fatality rate in hospital admitted DHF cases. The first dengue haemorrhagic fever occurred in Calcutta during that epidemic. Since then several outbreaks have been reported in various states in India both the urban and rural areas.

Scenario in Kerala

As early as 1979 dengue antibodies had been detected in human sera from Kozhikode, Kannur, Palakkad, Thrissur, Kottayam and Thiruvananthapuram districts. Sporadic occurrence of DF cases has been reported in Kerala since 1997 when 116 suspected cases with 4 deaths were reported from Kottayam. In 2001, a total of 877 suspected cases with one death were reported from four districts, viz. Kottayam, Idukki, Ernakulam and Thiruvananthapuram. Since then dengue fever has been regularly reported from Kerala. Dengue cases reported are higher during the months from June to October. The seasonality pattern has been maintained from the beginning of the epidemic throughout the years. In Kerala the highest number of cases are reported from Thiruvananthapuram. According to the data published by DHS the number of cases of dengue reported from Kerala are 2575 in 2014 and 4114 in 2015 out of which Kollam reported 73 and 245 cases respectively. Our study aims to study the clinical and laboratory profile of the patients admitted with dengue fever in Government Medical College Kollam.

Objectives

To study the clinical features and laboratory profile of patients with serologically confirmed dengue fever.

Methods

The study was a prospective observational study done in government medical college from September 2017 to September 2018. The study was conducted among all cases of confirmed dengue cases above the age of 12 years admitted in the department of medicine between September 2017 and September 2018. Approval was obtained from the intuitional ethical committee. Informed consent was obtained from all patients included in the study.

Definition of Confirmed Case of Dengue Fever

Clinical features of dengue with dengue NS 1 Ag positive and/or IgM dengue positive using ELISA

Detailed history and careful clinical examination was performed on each patient. Laboratory investigations done were haemoglobin, total and differential leucocyte counts, platelet count, haematocrit, liver function tests, blood urea and serum creatinine, serum electrolytes and ECG. Serum lipase and amylase were done in indicated patients. Chest x ray and ultra sound abdomen were done in selected cases as indicated. Blood counts and LFT were monitored periodically as and when required till resolution. Other differential diagnosis were excluded by appropriate tests.

Statistical analysis was made using SPSS software.

Inclusion Criteria

All patients above the age of 12 years with confirmed dengue fever admitted in the department of medicine during the study period were including in the study.

Exclusion Criteria

Those with concomitant malaria, leptospirosis, typhoid etc.

Results

The study included 175 patients above the age of 12 years admitted with dengue fever in the department of medicine from September 2017 to September 2018.

Majority of patients belonged to the 20 to 50 age group (60.5%). among males the most common age group affected was 21-40 ages while among females the 31-50 age group was commonly infected.

There was only a slight male preponderance with 53.7 % males and 46.3 % females. It was notable that a significant 36% of the affected were homemakers suggesting that major source of breeding of Aedes mosquito was in the household itself. Manual labourers and students formed the next significant group affected.

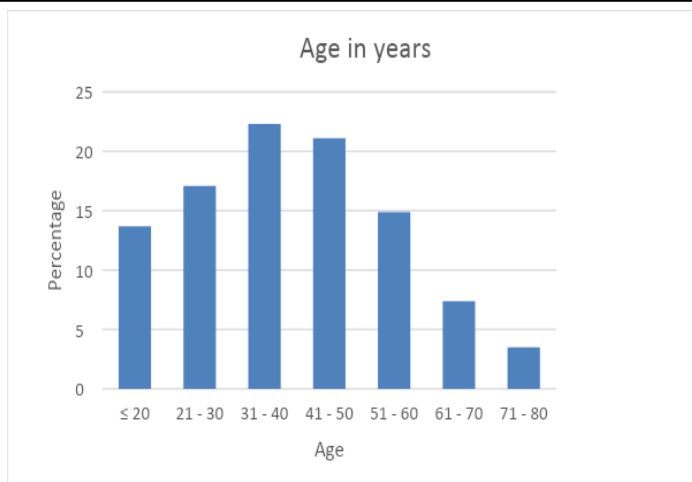


Figure 1 Age distribution of study population

Table 1 Sex distribution of the study population

sex	Frequency	Percent
Male	94	53.7
Female	81	46.3
Total	175	100

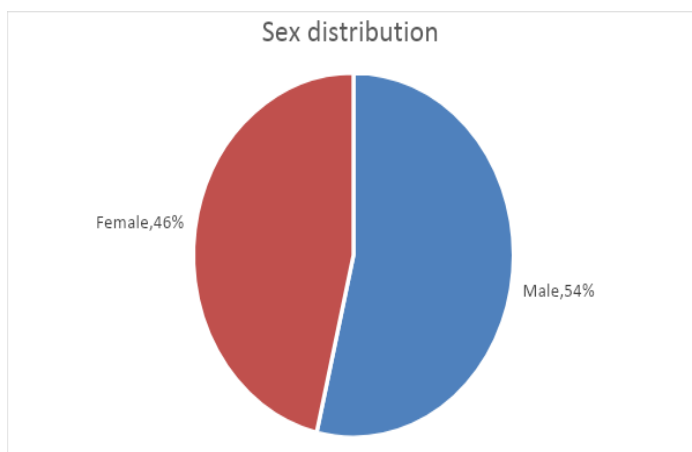


Fig 2 Sex distribution of the study population

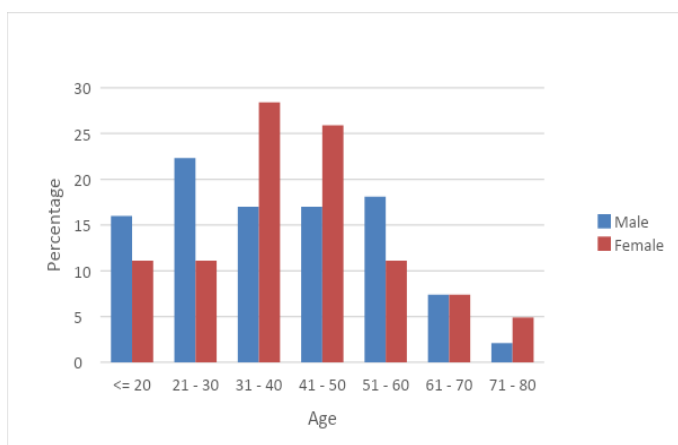


Fig 3 Age –sex distribution of the study population

Table 2 Occupation of the study population

Occupation	Frequency	Percent
Student	31	17.7
Professional	1	0.6
Manual Labourer	42	24
Office work	13	7.4
Housewife	63	36
fisherman	3	1.7
Factory work	3	1.7
Others	19	10.9
Total	175	100

Mosquito Control Practices and Waste Disposal Measures among Study Population

A meagre 4% of the study population conducted dry days once a week in their premises. The major method of waste disposal was burning of wastes in the premises of the house but a significant 41% of the study population admitted to open dumping of wastes. Only 11.4 % of them had the facility of collection of wastes by agencies. Only 75 patients give a history of using mosquito control measures with 25.7% using measures like mosquito coils and aerosols. None of them were using the biological measures or window meshes as preventive measures. 20.6% patients considered using long sleeved dresses as an effective preventive measures for preventing mosquito bites. Only 3 % were using mosquito nets prior to infection but all of them used mosquito nets after the infection.

Table 3 Mosquito control measures used by the study population

Mosquito control measures	Frequency	Percent
Mosquito coil	24	13.7
Liquids	7	4
Aerosols	14	8
Mosquito bats	7	4
bed net	3	1.7
Windows	0	0
Repellents	1	0.6
Long sleeved dress	36	20.6
Herbal measure	19	10.9
Biological measures	0	0

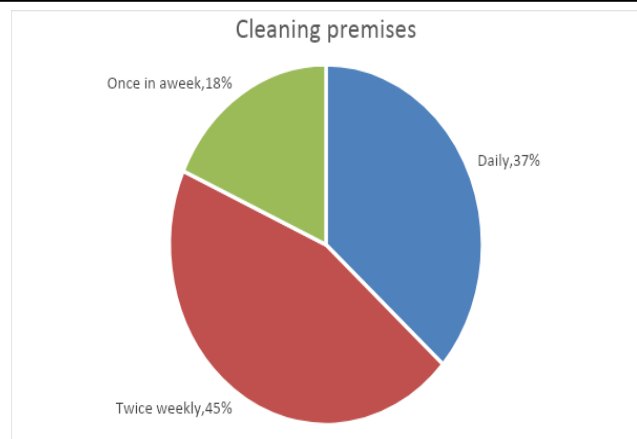


Fig 4 Cleaning practices among the study subjects

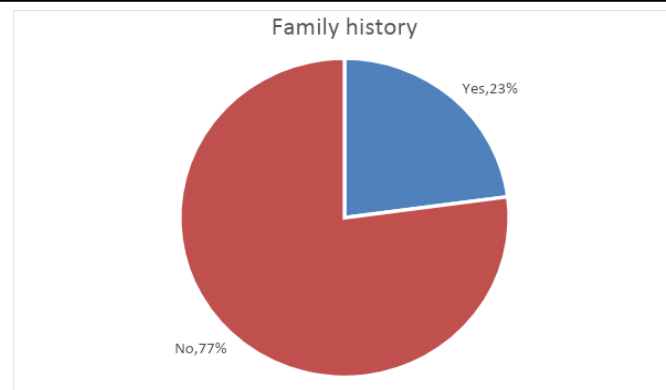


Fig 6 Family history of dengue fever in the study population

Table 4 Waste disposal measures used by the study population

Methods of waste disposal	Frequency	Percent
Composting	7	4
Open dumping	72	41.1
Collection by other agencies	20	11.4
Burning	112	64

Clinical features

Fever was the most common presenting feature with 93.7% patient giving a history of high grade fever. Most of the patients were admitted between the 4th and 7th day of fever probably coinciding with onset of thrombocytopenia.

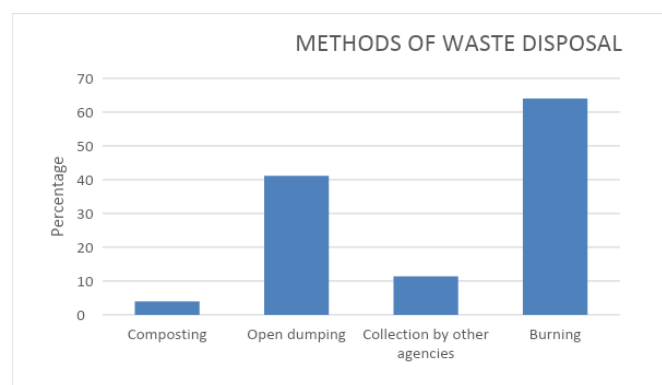


Fig 5 Waste disposal measures used by the study population

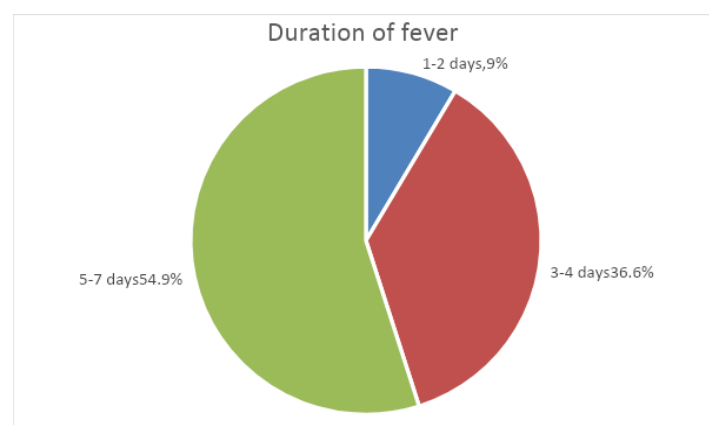


Fig 7 Duration of fever at the time of admission

Majority of the cases did not have a previous history of dengue infection and the family history of dengue infection was elicited only in 40 (22.3%) patients.

Majority of the patients (54.9) were admitted 5-7 days after the onset of fever which usually corresponded to the development of thrombocytopenia which was also the most common indication for admission.

Table 5 Family history of dengue fever in the study population

Family history	Frequency	Percent
Yes	40	22.9
No	135	77.1
Total	175	100

Table 6 Frequency of different symptoms among the study population

Symptoms	Frequency	Percent
Myalgia	169	96.6
Retro orbital pain	61	34.9
Headache	132	75.4
Arthralgia	44	25.1
Sore throat	43	24.6
Rhinorrhoea	54	30.9
Cough	90	51.4

Breathing difficulty	19	10.9
Calf pain	11	6.3
Low back ache	151	86.3
Nausea	153	87.4
Abdominal pain	75	42.9
Loose stools	55	31.4
Jaundice	1	0.6
Rashes	28	16
Pruritus	68	38.9
Clouding	12	6.9
Conjunctival congestion	48	27.4
Oliguria	1	0.6
Seizures	2	1.1

loose stools were present in 31.4% patients. Jaundice was an extremely rare symptom. Abdominal pain was a significant symptom seen in 75(42.9%) patients.

Rashes, which were maculopapular were seen only in 16% patients but pruritis was a common symptom seen in 38.9% patients. 17.7% of patients showed bleeding manifestations with melena (29%) and superficial skin bleeding and oral bleeding as the most common bleeding sites. Among females menorrhagia was the most common bleeding manifestation.

Table 8 Examination findings in the study population

General examination	Frequency	Percent
Warmth of the extremities	170	97.1
Pallor	7	4
Conjunctival congestion	63	36
Icterus	2	1.1
Lymphadenopathy	41	23.4
Odema	50	28.6
JVP - Elevated	20	11.4

Lymphadenopathy, conjunctival congestion and edema were the most common signs. Bradycardia was seen in 24(13.7%) patients. 18 (10.3%) patients had features of lower respiratory tract infection. Epigastric tenderness was seen in 25(14.3%) patients. Hepatomegaly was clinically detected in 7 (4%) patients. 2 patients had seizures but they were patients with seizure disorder that drug default and had no features of CNS involvement.

Laboratory Parameters

Table 9 Laboratory parameters among the study population

		Frequency	Percentage
Hemoglobin	≤ 11g%	45	25.7
PCV	>45%	32	18.3
Total Count	<4000	60	34.3
	4000-10000	99	56.6
	>10000	10	5.7
Platelet	<20000	16	9.1
	20000-50000	71	40.6
	50000-100000	66	37.7
	100001-150000	12	6.9
	>150000	6	3.4
ESR	Elevated >22	43	24.6
	Normal	127	72.6

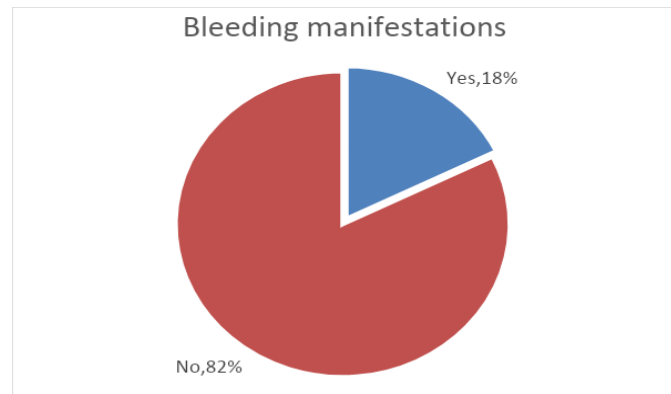


Fig 8 Frequency of bleeding manifestations in study population

Table 7 Bleeding manifestations seen among the study group

Bleeding manifestations	Frequency	Percent
Oral/ gum bleeding	9	29.0
Skin bleed	9	29.0
Hemarthroses		0.0
Epistaxis	3	9.7
Hematuria	7	22.6
Melena	14	45.2
Hematemesis	1	3.2
Menorrhagia	10	32.3

Myalgia (96.6%) and low back ache (86.3%) were very common symptoms. Majority of patients head ache (75.4%) though the classically described retro orbital pain was present only in 34.9% of the study population. Arthralgia was seen in 25.1% of the patients. Upper respiratory symptoms were common with rhinorrhoea seen in 30.9% and sore throat in 24.6 %. 51.4% of patient had cough but dyspnoea was present only in 10.9%.

Among the gastrointestinal symptoms nausea was the most common symptom seen in 87.4% and

Blood Urea	<= 20	103	58.9
	21 - 40	59	33.7
	41+	4	2.3
	>1.2	16	9.1
sodium	<135	91	52.0
	136-145	73	41.7
	>145	1	0.6
Potassium	<3.5	19	10.9
	3.5-5.0	146	83.4
	>5.0	1	0.6
Bilirubin	>2	28	16.0
SGOT	>40IU/L	147	84.0
PT	>40IU/L	115	65.7
ALP	126+	11	6.3
Albumin	<= 3.5	103	58.9
amylase	>140	5	2.9

Haematological Parameters

Anemia was seen in 45 (25.6%) patients which was present at the time of admission. Hematocrit

of >45% was seen in 32 (18.3%) patients. 60(34.3%) had leucopenia while only 5.7% had WBC count >10,000/cmm.ESR was normal in majority of patients.

153 patients had platelet count less than 1,00,000/cmm. 71(40.6%) patients had platelet count between 50,000/cmm and 20,000/cmm. 16(19.3%) patients had platelet less than 20,000/cmm. Bleeding manifestation and platelet count did not correlate as only 4 patients with platelet less than 20,000/cmm had bleeding. Bleeding manifestations were maximum when the platelet count was between 20,000/cmm and 50,000/cmm. 17 patients had bleeding manifestation when their platelet was in this range.

Table 10: Relation between platelet count and bleeding manifestation

Platelet count	Bleeding Manifestation				Total		χ^2	df	p
	Yes		No		N	%			
	N	%	N	%					
<20000	4	25.0	12	75.0	16	100.0	5.947	4	.203
20000-50000	17	23.9	54	76.1	71	100.0			
50000-100000	8	12.1	58	87.9	66	100.0			
100001-150000	1	8.3	11	91.7	12	100.0			
>150000	0	0.0	6	100.0	6	100.0			
Total	30	17.5	141	82.5	171	100.0			

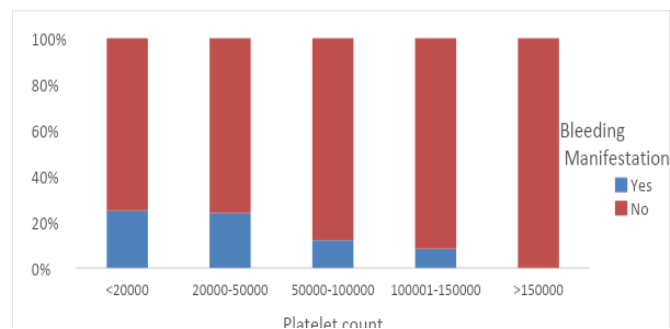


Fig 9: Relation between platelet count and bleeding manifestation

Biochemical parameters

Renal function tests were normal in majority of patients.

Bilirubin >2mg% was seen in 28 patients but only 2 of them had value >5 mg%. The major abnormality in LFT was a raised liver transaminases. AST (SGOT) >40IU/l were seen in 147(84%) patients and elevated ALT (SGPT) in

115(65.7%) patients. ALP >126IU/L was seen only in 11(6.3%) patients.

Amylase was done in 18 patients with abdominal pain but was only mildly elevated in 5 patients which were not significant. S. lipase was normal in these patients.

Other Investigations

Dengue NS1 Ag test was positive in 115 patients (65.7%) and IgM Dengue antibody test by ELISA was positive in 60 patients(34.3%).

Chest X-ray was done in 10 patients, 3 patients had mild bilateral pleural effusion and 2 had pneumonia.

USG abdomen was done in 12 patients, out of which 2 patients had acalculous cholecystitis., 8 (4.5%) had ascites and 9(5.1%) had hepatomegaly. 5 patients had pleural effusion

detected sonologically. 5 patients had polyserositis.

Duration of Hospital Stay

Average duration of hospital stay was 5.36±1.36 days an ranging from 2 to 12 days

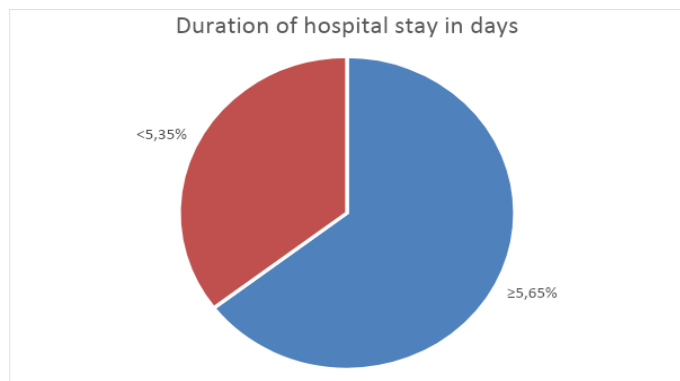


Fig 10 Duration of Hospital Stay

Transfusion Trends

21 (12%) patients had platelet transfusion. The most common indication was bleeding manifestation .5 patients had transfusion when platelet count was less than 15,000/cmm even without bleeding.

On Follow up of 154 patients who turned up for review in OPD at first week and 2nd week the major complaint was fatigue followed by persistent myalgia .Insomnia was an important symptom especially in the middle aged .

Table 11: Follow up evaluation in patients

Symptoms on follow up	Frequency	Percent
Fatigue	144	88
Myalgia	90	51.4
Arthralgia	22	12.6
Insomnia	40	22.9

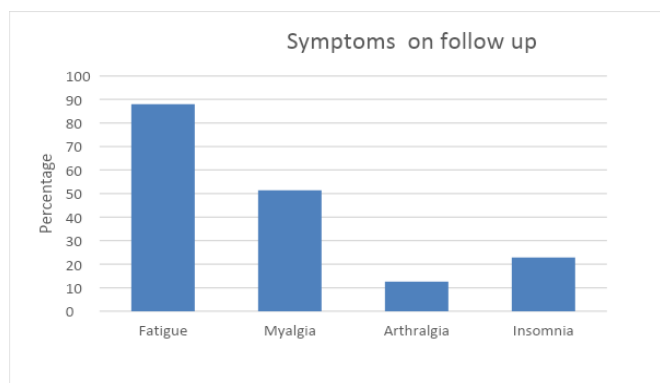


Fig 11: Follow up evaluation in patients

Outcome in the Study Populations

There was no mortality reported in the present study probably due to admission bias from the emergency room as patients with multi organ dysfunction like renal or hepatic failure were referred to the nearest MCH with super speciality facilities like dialysis .This could also reflect the increased awareness among health care workers and the availability of rapid diagnostic tests that can be positive from the 2nd day of fever itself resulting in prompt diagnosis and effective management.

Limitation of the Study

Single centre study

No mortality was reported probably hence mortality predictors of dengue could not be analysed.

Discussion

This study describes the clinical profile, laboratory features and outcome of DF in adult patients admitted in GMC kollam.83.3% were classified as dengue fever and 18.7% were DHF/DSS. Majority of DF cases were in the productive age group between 21 – 50 years underlying the public health and financial impact of dengue. Men were more frequently affected than women but among the 30 – 50 year age group females were more commonly infected. A significant proportion of the females affected were homemakers underlying the fact that domestic premises were the most common source for breeding of A.aegypti.

Majority of the patients had disabling myalgia, low backache and headache. Deshwal et al in their study noted myalgia and headache in more than 90/ of their study population^[8]. Low backache independent of myalgia was a significant symptom seen in 80.6% patients which was not mentioned in any of the previous studies in India. Retro-orbital pain as a cardinal feature of dengue fever was seen in few (34.9%) of our patients.

A significant finding was the increased prevalence of upper respiratory symptoms like sore throat

(24.6%), rhinorrhoea (30.4%) and cough (51.4%) in the study population. In a similar study by Rachel Daniel et al. Sore throat was seen only in 5.2% of patients^[6]. Ramesan K et al. studied the profile of dengue cases in north Kerala and reported the prevalence of cough as only 15%^[5]. In a study from Nimmannitya et al. around 96% of patients had congested pharynx, and rhinitis was reported in 13% of the patients^[10]. These symptoms were predominantly seen in the first few days of fever and thus symptoms can mimic influenza at their initial presentation in the present epidemic.

Gastrointestinal symptoms were also significantly higher compared to previous studies. Diarrhoea (31.4%) and abdominal pain (42.9%) were two important GI manifestations. All the previous studies in India (Ramesan et al, Varsha et al, Rajesh et al) reported the incidence of diarrhoea as less than 20%. Thus other infections that cause fever and gastrointestinal symptoms such as typhoid, and enteroviral infections that are common in India may often lead to a delay in the diagnosis of dengue.

Another significant finding was pruritis seen in 38.9% of patients even in the absence of rashes and features of cholestasis. Presence of rashes (16%) was lower in the present study compared to studies from other parts of the country but comparable to the study by Rachel et al in the same geographical area (33 patients)^[6].

Thus a combination of fever severe myalgia, low backache with diarrhoea and upper respiratory symptoms should raise the possibility of dengue in a patient.

Bleeding manifestations were significantly lower compared to the previous studies and the most common were bleeding from GI sites. An increase in menstrual bleeding was a significant finding in women. Thrombocytopenia was a common finding as it was the common indication for admission in our centre. However there was poor correlation between thrombocytopenia and bleeding tendencies, an observation similar to the one made by Sharma et al^[11] and Rachel et al. The

study by Rajesh D et al, from Agra showed 14.8% patients had hepatomegaly which was significantly higher in patients with DHF and DSS. Generally, it was reported that more than 90% of Asian subjects with DHF have hepatomegaly. Thus the lower incidence of hepatomegaly could be attribute to the less number of DHF cases. Liver function abnormalities, especially elevated transaminases, were noted in this study. 84% had SGOT >40IU/L. Three fold elevation of SGOT was seen in 40.5% patients. Dengue virus-induced damage to the hepatocytes, hypoxia, shock or associated liver disease have all been postulated to be the pathogenic mechanisms for the occurrence of transaminitis. No case of fulminant hepatic failure was noted in our study though 2 patients had SGOT >1000 IU/L. The series from Sharma et al. from India reported elevated transaminases in 90% of patients^[11]. In study by Kularatne et al, 88% patients showed elevated ALT and AST, with 122 of them having a two fold increase^[12]. Mandal et al documented elevated transaminases in 83.78% of cases^[7]. Liver enzyme elevation, a common feature in dengue infection was also apparent in a study done by Mohan et al^[9]. No mortality were reported in our study similar to the study by. Md. Yousuf Khan et al which indicate prompt diagnosis by health community due to availability of early antigen detection tests and increased awareness about dengue^[13].

An important aspect of the study was to assess the awareness of mosquito control measures among the study populations. Only 4% of the study population practised dry day at homes and open dumping of wastes were practised by 41% of the study population. Mosquito net use was prevalent only in 1.7% but *A.egypti* being predominantly day time biter its impact on dengue spread cannot be ascertained.

Conclusion

This study has revealed a varied clinical profile of dengue fever which is of important diagnostic value. In the recent few years, the world has seen

varied clinical presentation of the dengue fever in different epidemics, in the same regions. Some of the classical findings are still manifesting but their frequency is variable between epidemics. Few atypical features are also reported from different parts of the world like the higher incidence of upper respiratory symptoms and diarrhoea in the present study. Continuous seroepidemiological surveillance and clinical profile studies are needed for the early detection of cases with atypical features. This study also stresses on the lack of awareness for the mosquito control measures among public and need for more interventions in the vector control.

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