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A STUDY ON DEMOGRAPHIC, CLINICAL AND HAEMATOLOGICAL PROFILE OF DENGUE FEVER IN A TERTIARY CARE HOSPITAL, TELANGANA REGION- A PROSPECTIVE STUDY

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ABSTRACT

Introduction: Dengue is one of the most important viral diseases especially in the tropical regions. This disease increases in incidence in the immediate post monsoon period coinciding with the breeding of mosquitoes in the stagnant water. It has varied clinical presentation and more or less consistent abnormal laboratory values on complete blood count test. Aim of the study: The aim of the study was to determine the clinical and haematological profile in patients with Dengue fever. Materials and methods: This was a prospective study done in the department of Microbiology at Osmania Medical College Hospital, Hyderabad, Telangana, over duration of 8 months (From March 2015 to October 2015). The study included 420 patients admitted in the hospital and all the cases were IgM dengue positive. Results: In the present study, total samples 426, among them 147 were seropositive cases. The present study showed more seropositives cases (36%) were identified in 20-29 yrs age group. There were 246 (57.7%) male and 180 (42.3 %%) female patients. Out of 426 patients, 144 (34.2%) were in age group of 20 to 39 years. Most of the cases were found in post monsoon period in September and October. More no. of males (39.4%) was affected than females (27.7%) with ratio of 1.36:1 that belonged to age group 20-29 yrs. In the present study highest no. of cases were recorded from Hyderabad compared with other districts in the state. DF was noticed in higher no. of patients (95.3%) than DHF which was observed in only 4.7 % of cases. Fever is the most common clinical feature observed (100%). The most common clinical manifestation observed in the study population were fever (100%) followed by Headache (66%) and vomiting In our study out of 426 cases of dengue fever, raised hematocrit (>47%) was noted in 10 (16.6%) of patients at presentation and 50 (83.3 %) cases had thrombocytopenia, in which 8 (13.3%) cases had < 20,000/cumm with bleeding manifestations. In this category of patients evidently symptoms like fever and bleeding manifestations were recorded in 100% of cases with raised HCT in 5 patients(71.4%) followed by Mild hepatomegaly in 2 (28.5%) cases. In the present study, Leucopaenia seen in 3.5% cases. Normal TLC was observed in 28.4%. The present study revealed that, raised PCV seen in 50% of cases, none of the Seropositive female patients showed raised HCT. In our study, Platelet count < 1 lac /cumm is considered as Thrombocytopaenia, which was seen in 87% of seropositive cases. Mild TCP observed in 29.6 % of seropositives**.** Conclusion: Most common clinical presentation of Dengue fever is of fever with or without myalgia and presence of hepatospleenomegaly. Young adult males are more commonly affected. The most common laboratory abnormalities are of an increase in hematocrit, low total leucocyte count and low platelet count.

Key words: Haematocrit, Leucocytes, Hepatospleenomegaly, Platelates.

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INTRODUCTION

The incidence of dengue fever (DF) has increased manifold in last four decades. In developing nations like India, unplanned urbanisation and migration of population from rural to urban areas with complete lack of proper sanitation facilities are important factors resulting in this situation. The situation in India is reflected by the occurrence of major disease outbreaks in recent times [1]. Dengue fever is caused by a flavivirus and transmitted by mosquitoes of genus Aedes aegypti. In the last 50 years, an incidence has increased 30-fold with increasing geographic expansion to new countries and in the present decade from urban to rural settings. About 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries. In addition, the impact of dengue illness on the health sector leads to considerable global economic burden in India endemic countries, most of which are developing nation [2, 3]. Dengue is caused by dengue virus (DEN) and is transmitted to humans by the bite of *Aedes aegypti* mosquito.

The Incidence of dengue has grown dramatically around the world in recent decades [**3-5]**.In india, the risk of dengue has increased in recent years due to rapid urbanization, and deficient water management including improper water storage practices in urban, peri-urban and rural areas, leading to proliferation of mosquito breeding Sites [**7].** Presently, there is no specific anti viral drug or vaccine against dengue infection [**2,7].** For, early recognition of dengue cases, pathophysiology of haematological profile is useful and support early clinical diagnosis & prompt management.

We have undertaken retrospective analysis of clinical and laboratory features of patients admitted at Osmania medical college hospital, Hyderabad, from March 2015 to Dec. 2015.

STUDY DESIGN

It is Prospective cross sectional study and total size of the population is 426 and duration of this study is 8 months.

Nature of Study population:

All Dengue fever suspicious cases defined according to WHO suggested case classification as Dengue fever, Dengue Hemorrhagic fever & Dengue shock syndrome were enrolled into the study.

The serum samples comprised of both acute and early convalescent phase depending on the reporting time of the patients. Acute phase serum samples were collected from patients who reported < 5 days of fever in whom NS1 ag assay was done and early convalescent phase serum were collected from patients who came with history of fever for > 5 days in whom both NS1 ag assay and MAC-ELISA were done.

Inclusion criteria

Febrile patients admitted in medical and pediatric wards of Osmania Hospital. Patients of all age groups clinically diagnosed as having DF.

Exclusion criteria

Febrile cases with definite source of infection (eg.respiratory, UTI, Meningitis) as per available clinical and Laboratory data. The following patients were excluded, History of bleeding tendency since birth, Patients with thrombocytopenia and no fever, patients with fever of more than 2 weeks duration and other conditions that cause TCP like Autoimmune connective tissue disorders , ITP, Malignancy.

Data collection

Approval of the Institute's Ethics Committee was obtained to carry out the study. Informed consent was obtained from each patient. Information on demographic features and symptoms of the patients were collected by a structured questionnaire.

Sample collection and storage

2-3 ml of venous blood was collected under aseptic precautions in vaccutainers with no additives and kept at room temperature for 30 min to clot. Serum was separated by Centrifugation and transferred to aliquots and stored at -20 until tested.

Laboratory methods

Evaluation of hematological parameters was done by collecting 2 ml samples in EDTA containers which were examined for Haemoglobin count, Haematocrit, Platelet count, Total leucocyte count, Differential leucocyte count. The analysis was done by the automated analyzer SYSMEX XT 1800i (3-part differential). All the acute phase serum samples were detected for NS1 ag using the Commercially available kit (Panbio Dengue Early Elisa Kit and for Ig M kit obtained fron NIV Pune).

Dengue Day1 test kit was used to detect NS1 antigen and IgM and IgG antibodies. The test results were expressed as positives/negatives for antigen and both antibodies. All the relevant clinical details such as presenting complaints, duration of symptoms, length of hospital stay, presence or absence of purpuric rash, leucopenia, thrombocytopenia, and hematocrit were analyzed with the help of STAT A software version 2.0.

RESULTS

A total of 426 clinically suspected Dengue cases were screened for Serological markers NS1 ag and IgM ab at Osmania General Hospital, Hyderabad during the period March –October 2015.

Table 1. Distribution of study population

Total no.of samples	No. of Seropositives	Percentage
426	147	34.5 %

In the present study, total samples 426, among them 147 were seropositive cases.

Table 2. Age profile of study population (n= 426)

Age (yrs)	No. of cases	Percentage %
0-19	112	26%
20-29	144	34.2%
30-39	67	15.4%
40-49	49	11.5%
50-59	27	6.3%
>60yrs	27	6.3%

In the present study, A total of 144 patients belonged to age group 20-29 out of 426 patients reported.

Table 3. Age groups of seropositive Dengue cases n= 147

Age groups (yrs)	No. of positives	percentage (%)
0-19	41	27.8
20-29	53	36.05
30-39	24	16.3
40-49	16	10.8
50-59	8	5.44
>60	5	3.4

In the present study, more seropositives cases (36%) were identified in 20-29 yrs agegroup (Table 3)

Table 4. Total Sex wise distribution of study population.

Males	Females	Total
246(57.7%)	180(42.3%)	426

Males are more commonly affected compared to females. (Table 4)

Table 5. Age with Sex wise distribution of Seropositives.

Age gp (yrs)	Total males	Serppositives(%)	Total Females	Serppositives(%)
0-19	61	29 (47.5%)	51	12(23.5%)
20-29	85	36(42.3)	59	17 (28.8%)
30-39	44	15 (34)	23	9(39.1%)
40-49	27	9(33)	22	7(31.8%)
50-59	15	4(26.6%)	12	4(33.3%)
>60	14	4(28.5)	13	1(7.7%)
TOTAL	246	97(39.4)	180	50(27.7%)

More no. of males (39.4%) were affected than females (27.7%) with ratio of 1.36:1 that belonged to age group 20-29 yrs. (Table 5)

Table 6. Month-wise total distribution.

Month	Total no. of cases	Seropositives
March	18	2(11.1%)
April	16	3(18.75%)
May	22	9(40.9%)
June	15	1(6.66%)
July	28	8(28.5%)
August	79	26(32.9%)
September	118	40(33.8%)
October	130	58(44.6%)

Chi square test = 7.2, p value <0.05 .

Highest no. of cases were recorded during August to October. (Table 6)

Table 7. Area wise distribution of Dengue virus infection

District	Total cases	Seropositives %
Hyderabad	181	59(13.8)
Rangareddy	113	42(9.8)
Mahabubnagar	46	16(3.7)
Nalgonda	25	8(1.8)
Medak	19	8(1.8)
Nizamabad	12	3(0.7)
Warangal	9	2(0.4)
Karimnagar	5	2(0.4)
Adilabad	3	2(0.4)
Others	13	1(0.2)

In the present study highest no. of cases were recorded from Hyderabad compared with other districts in the state.. (Table 07)

Table 8. Dengue category classification of study population

Category	Total cases	Seropositives(%)
DF	410	140 (95.3)
DHF/DSS	16	7(4.7%)

DF was noticed in higher no. of patients (95.3%) than DHF which was observed in only 4.7 % of cases. (Table 8)

Table 9. Clinical features of suspected DF/DHF/DSS cases n=426

S.no	symptoms	Number	%
1	Fever	426	100
2	Headache	283	66.4
3	Nausea & Vomiting	225	52.8
4	rash	181	42.4
5	Pain abdomin	160	37.5
6	Gingival Bleeding	09	2.1
7.	Arthalagia	210	49.2
8	GI bleeding	08	1.8
9	Retro orbital pain	11	2.5

The most common clinical manifestation observed in the study population were fever (100%) followed by Headache (66%) and vomiting (52%).

Table 10. Clinical manifestations of patients with Dengue fever n=140

Characteristic	Numbers	Percentage%
Mild febrile illness	140	100
Severe headache	96	68.5
Vomiting	65	46.4
Myalgia	62	44.2
Rash	113	80.7
Pain abdomen	59	42.1
Gingival bleeding	4	2.8
Arthralgia	13	9.1
GI bleed	3	2.1
Fever was the most common clinical	feature observed	(100 %).(Table 13)

The most common symptoms observed were fever (100%) followed by Rash (80.7%) and Headache (68.5%). (Table 10)

Table 11. Clinical manifestations of patients with DHF/DSS n=7

S.NO.	Symptoms	Numbers	Percentage%
1.	High fever of abrupt onset	7	100
2.	Mild Hepatomegaly	2	28.5
3.	Capillary plasma leakage	5	71.43
4.	Bleeding tendencies	7	100

5.	Thrombocytopaenia	7	100
The most common clinical manifestation observed		was Fever (100%) ,	

bleeding tendency (100 %) and Thrombocytopaenia (100%) (Table 11).

In this category of patients evidently symptoms like fever and bleeding manifestations were recorded in 100% of cases with raised Hct in 5 patients(71.4%) followed by Mild hepatomegaly in 2 (28.5%) cases.

Table 12. Distribution of Serological markers.

Serological marker	Duaration of fever	No .of samples screened	No.of positives
Only NS1ag	<5 days	132	35(26.5%)
NS1 & IgM	6-9 days	106	44(41.4%)
Only IgM ab	>10 days	188	68(36.1%)

More no . Seropositives 44 (41.4%) were noticed when 106 serum samples were tested using both NS1 Elisa and MAC Elisa. (Table 12). Out of 132 samples that reported with fever < 5 days duration NS1 Ag ELISA was done and 35 samples were seropositive accounting to 26.5%. Out of 106 samples with fever between 6-9 days, both assays were performed and 44 (41.4%) were seropositive .Out of 188 samples received with >10 days of fever, only MAC Elisa was done and 68 showed seropositivity rate of 36.1 %.

Table 13. Total Leucocyte count of patients

TLC(/cumm)	No of Patients	No of positives
<4000	21	15 (3.5%)
4000-11,000	370	121(28.4%)
> 11,000	35	11 (2.5%)

Leucopaenia seen in 3.5% cases. Normal TLC was observed in 28.4%. (Table 13)

Table 14. Cut off value for Hematocrit

Category	Normal Range	Cut-off value
Males	39-49%	51%
Females	35-45%	48%

Cut off value for males was 51 % and females 48% (Table 14)

Table 15. Haematocrit of study population in DHF (Males)

Total no. of DHF	Patients with normal HCT	Patients with raised HCT>20% base line	No. of seropositive
16	8	8(50%)	5

Raised PCV seen in 50% of cases (Table 15)

None of the Seropositive female patients showed raised HCT

Table 16. Platelet count (per mm^3) in seropositives (n=147)

Range	Positive cases	%
< or equal to 20,000	10	7.80
21,000-40,000	28	21.8
41,000-60,000	29	22.6
61,000- 80,000	23	17.9
81,000-1,00,000	38	29.6
Total	128	87.07

Platelet count < 1 lac /cumm is considered as Thrombocytopaenia, which was seen in 87% of seropositive cases. Mild TCP observed in 29.6 % of seropositives**.**

DISCUSSION

Dengue fever is the one of the most important arboviral infection. It has become a major global public health problem in India. Epidemics are becoming more frequent now days. Classical dengue fever is an acute febrile illness but in a small percentage of dengue infection, a more severe form of disease known as DHF occurs. Early recognition and meticulous management are very important to save precious lives from this killer disease.

In the present study majority of patients i.e., 34.2% were in the age group of 20-29 years. It was more common in younger population. Observations made by Farhan F et al

showed that majority of patients i.e., 30% were in age group of 21-30 years which is almost similar to the present study [6]. Singh NP et al also showed mean age of 26±10 years in their study [7-10]. This may be due to young adults are being more active outside from the home.

The present study showed 37 (37%) were female and 63 (63%) were male patients. In the present study about 36% of cases were affected with dengue fever who mostly belonged to age group 20-29 yrs which is in correlation with other studies done by Ektha Guptha et al., [11].

It may be due to shift of mosquito population towards non residential areas and there by infecting working population. The monthly distribution of dengue seropositives illustrated in Table -10 that more number of cases were received in August (32.9%) September (33.8%) October (44.6%) as compared to March (11.1%) and June (6.6%) where in least number of cases were recorded which might be correlating with breeding time of mosquitoes in the environment. This pattern was recorded in most of the studies in India , illustrating seasonal incidence relating to climate.

Our results correlated with other studies done by Mohammed Murtuza Kauser et al, noticed that maximum number of patients admitted in the rainy season(August to October) which is clearly evident in this study also[12]. Similarly Ekta Gupta et al., also analysed outbreaks of Dengue infection in Delhi reported that there was a consistent increase in the Dengue incidence in the post monsoon period with peak in second and third week of October .Further our study also evidently showing similar results that in October highest cases were received[11].

Data on temperature and relative humidity also indicate that both might have favoured the survival of adult mosquitoes beyond their extrinsic incubation period, thereby increasing viral transmission throughout the year. Chouhan et al., reported on outbreak occurred at unusual season of dry summer (April – May) in Rajasthan and was contended that it was due to an increase in breeding of vectors in stored water in the houses, which is a common practice of the local population during summer on account of irregular water supply [13].

Since Osmaina General Hospital is situated in the Telangana region, most of the patients included in this study were referred from the surrounding districts with highest number of reported and seropositive cases were from Malapert, Rajendranagar,Jiyaguda, Afzalgunj areas of Hyderabad city (40%) as illustrated in Table 11, followed by Rangareddy (28.5%) Mahabubnagar (10.8 %), and Nalgonda (5.4%).

The reason observed was Hyderabad being highly urbanized area having substantial proportions of population living in crowded impoverished areas with poor sanitation that pose a major challenge to vector control activities [14].

DF was found to be the most common presentation which was similar to studies conducted by P.V. Barde et al.,[15]. No cases with Dengue shock syndrome were noticed and no mortality was reported. Saraswathy MP et al., has suggested that continuous scrutiny of warning signs can prevent development of DSS [16].

Our findings differ from other studies conducted by Muhammad Arif Munnir et al . who reported DF in 78% and DHF in 22% of cases [17].

Clinical features of different Serotypes of Dengue fever

The clinical features of patients with suspected DF/ DHF / DSS are presented in the Table- 13, where fever was the major presenting feature, followed by severe headache and vomiting, accounting for 100, 66.4 and 52.8 percent respectively. Further other symptoms like arthralgia, rash and pain abdomen were in 49.2%, 42.4%, and 37.5 % respectively. The symptoms like retro-orbital pain, gingival bleeding, and GI bleeding were observed in less no of cases.

The present study showed distribution of symptoms among patients similar to study conducted by Seema Awasthi et al., where Fever was the most common clinical presentation 100% which was mild to moderate degree with no specific pattern [18]. The next common manifestation was vomiting, rash, itching, myalgia which accounted for 73, 69, 24, 22 percent of patients respectively. Headache was noticed in only 9% and spontaneous bleeding in 8% of total study population.

In the present study, Fever is the most common manifestation (100%) followed by Rash (80.7%) Headache (68.5%), vomiting (46.4%), Myalgia (44.2%), Pain abdomen (42.1), bleeding tendency (15%). Gingival bleeding and GI bleeding seen in least no of patients accounting to 2.8 % and 2.1% respectively.

Our results showed concordance with a study of 62 patients in Japan, by Itoda et al where rash were more frequent in 82% cases [19]. Rahim MA et al [103] also found rash in high frequency of 78.5% in a Bangladesh based study [20]. Sanjay Kumar Mandal et al observed Thrombocytopenia as one of the important causes of developing petechial rash in their study from Kolkata [21].

Nadia A Malik et al in their study on cutaneous manifestations in DF noticed that other mechanism like immunologic cause may be an explanation for developing these rashes. Dengue virus when interacts with host cells, there occurs release of cytokines and stimulation of immunologic mechanism by which vascular endothelial changes, infiltration of mono-nuclear cells and perivascular edema occurs [22].

Headache and retro-orbital pain mostly from systemic inflammatory mediators, are well known features in dengue fever. In our study we found 68.5% patients presented with headache that is similar (61.6%) to the study by Singh NP et al[23]. But in some studies like by Itoda I et al in Japan, headache was present in 90% cases[19]. On the other hand the north Indian study by

Seema A et al reported headache in only 9% of cases [18]. Deviation from our results was observed in a study done by P.V. Barde et al in which they reported Fever in only 52.6% and rash in 2.8% of cases [15].

In the present study as illustrated in Table 12, out of 426 patients 16 (3.75%) cases were classified as DHF according to WHO criteria of which 7 (4.76%) cases were seropositive for either one or both serological markers. The most common clinical features were fever, haemorrhagic manifestations reported in 100% followed by raised PCV in 71.4% Hepatomegaly, petechiae malena, hematemesis in 28.5% of seropositive DHF cases. Thrombocytopaenia was noticed in 85.7% of cases. Only males were affected in this study belonging to age group 20-29 yrs. No mortality was encountered in this study, as most of the patients had classical DF, which is a self- limiting illness if diagnosed and treated early. The distribution of serological markers in DHF seropositive cases were only IgM (71.4%) followed by only NS1 and both in 14.2%.

C.V . Prathyusha et al observed 68.5 % DHF cases mostly belonging to 9-12yrs age group where in the common symptoms reported were fever 100%, pain abdomen (57.5%), bleeding (36.2%) [24].

Saraswathy M.P et al reported 61% cases with DHF mostly of age group 1-5 yrs which they attributed to be due to increase in capillary fragility in children which leads to increase in bleeding tendency. The increases of bleeding is higher with increasing severity of TCP [16].

Nazish Butt et al reported the cause of bleeding in DHF is multifactorial including coagulation factor deficiencies, hyperfibrinolysis, hepatic insufficiency and platelet dysfunction and the primary patho-physiologic abnormality seen in DHF and DSS is an acute increase in vascular permeability, resulting in hemoconcentration and decreased blood pressure [25].

In the present study, TLC < 4000/cumm was observed in 3.5 % of seropositive cases as represented in table -21, that showed association with only NS1 ag in 13.3%, only IgM ab in 60% and both NS1and IgM in 26.6 % of positive cases.

However studies conducted by Itoda et al showed higher percentage of Leucopaenia in 90% and 71% cases respectively. Sanjay kumar mandal et al has suggested that Leucopaenia in DF may be due to myelosuppression [19,21].

Hematocrit

In the present study, increased hematocrit of >51% was observed in 50% of male patients. The cut off value for raised PCV in females was >48% but none of the seropositive female showed hemoconcentration. Similar results were observed by Singh N P et al and Muhamed Murtuza Kauser et al who reported raised PCV in 52% and 57% of cases [12, 23]. Studies that observed separately in DF and DHF were M Basu et al and Muhammad Arif Munir et al who noted in 35%(DF) 39.7 (DHF) and 46.7%(DF) 31.7%(DHF) [26,17].

In the study conducted by C. Panduranga et al observed raised HCT in 25% children in contrast to 3% adult males, 2% of adult females and suggested to be due to increased micro vascular permeability in children which causes them to loose more fluid which reflect as increase in HCT also due to this reason children are more prone to DHF. However in Hyderabad based study by Khan AH et al did not find any hemoconcentration in any case, rather a fall in haematocrit was noticed during hospital stay once patients were a febrile and rehydrated adequately [27].

CONCLUSION

Most common clinical presentation of Dengue fever is of fever with or without myalgia and presence of hepatosplenomegaly. It is more common in immediate post-monsoon months and affects young adult males more commonly. The most common laboratory abnormalities are of an increase in hematocrit, low total leucocyte count and low platelet count. Thrombocytopenia was universal finding in our study validating the results of previous studies. With increasing severity of thrombocytopenia there is increasing incidence of bleeding manifestation.

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