Original article

A CLINICO-HEMATOLOGICAL PROFILE OF DENGUE OUTBREAK AMONG HEALTHCARE PROFESSIONALS IN A TERTIARY CARE HOSPITAL OF AHMEDABAD WITH ANALYSIS ON ECONOMIC IMPACT

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ABSTRACT

Introduction: There has been a recent surge of Dengue infections in India, with many outbreaks in urban areas. This study is the biggest documented in-hospital dengue fever outbreak among health care personnel in India.

Aims & objectives: To study the clinical and hematological profile of Dengue outbreak and its cost impact.

Materials & methods: 56 patients from medical, dental and nursing fraternity with Dengue were studied. The cost of indoor treatment, investigations and loss of work were calculated. The cases were classified using the *newer WHO Dengue classification (2009)*.

Results & discussion: The commonest symptom was fever followed by myalgia. The commonest sign was delayed capillary filling. The most common abnormalities that predict severity were raised hematocrit of >40% and a low platelet count of <50,000/mm3. The outbreak produced a huge financial loss of Rs 19,48,800 with a loss of 6300 man-hours of doctors. The mortality rate was 1.7%, lower than average.

Conclusion: Dengue has a huge economic impact and is largely preventable.

Keywords: Dengue, economic impact, haematology, outbreak

INTRODUCTION

Dengue fever is one of the most common arboviral infection in humans.[1] The epidemic trend of dengue, in India, is on the rise in recent years with 28,292 cases in 2010 and increasing mortality.[1] All four serotypes of dengue have been isolated in India.[1] Dengue shows a cyclical trend with a peak in September-October every year. It is spread by female aedes mosquito which breeds exclusively in domestic man made water receptacles. Clinical manifestations result from uncomplicated dengue fever to dengue hemorrhagic fever with/without shock. There is no specific antiviral treatment for dengue. Management includes supportive therapy and hydration and close monitoring for signs and symptoms suggestive of DHS/DSS.[1,2]

The study was conducted to explore the clinical and haematological profile of Dengue infection during its outbreak in the campus of Civil Hospital, Ahmedabad in from Aug 2011 to Dec 2011 and compare it amongst the three group of Dengue case as per the new WHO-TDR (Tropical Diseases Research) classification, and study its cost impact.

MATERIALS & METHODS

A total of 56 patients from medical, dental and nursing fraternity that were admitted to Civil Hospital, Ahmedabad from Aug 2011 to Dec 2011 were studied. Dengue was diagnosed by RT-PCR (Reverse Transcriptase-Polymerase Chain Reaction), IgM ELISA (Enzyme Linked Immunosorbent Assay) and NS1-Ag (Nonstructural protein-1 antigen) positivity. Patients co-infected with P. vivax, P. falciparum and Enteric fever were excluded from the study. All the patients were residing within the hospital campus.

Serial hemograms, RFT: Renal Function Tests, LFT: Liver Function Tests, Urinalysis and Chest roentgenogram were done in all patients. Ultrasound, PT: Prothrombin Time& aPTT: activated Partial Thromboplastin Time was done as and when indicated.

Patients were divided according to the new WHO-TDR (Tropical Diseases Research) classification (2009) into Dengue (D), Dengue with warning signs (DW), and Severe Dengue (SD) as follows:[2]

Dengue (D): A case of laboratory confirmed Dengue or a presumptive dengue based on clinical features with none of the following warning signs : Abdominal pain or tenderness, Persistent vomiting, Clinical fluid accumulation, Mucosal bleeding, Lethargy, restlessness, Liver enlarged > 2 cm, Increase in Hct (Hematocrit) with rapid fall in platelets.

Dengue with warning signs (DW): A case of laboratory confirmed Dengue or a presumptive dengue based on clinical features with any of the aforementioned warning signs.

Severe Dengue (SD): Severe plasma leakage with shock and/or fluid accumulation with respiratory distress, severe bleeding, severe organ impairment.

The economic impact was based on fairly good estimates of an individual patient. It include cost of the loss of productive workforce to the hospital; the cost of indoor treatment including the room charges, treatment and medications, investigations, diagnostic kits for serological studies; and the loss to the hospital from the 3-day strike that ensued during this period for the better facilities and cleanliness.

The man hours lost were calculated by estimating the average no. of hours of work multiplied by the average no. of days required for hospital admission + rest advice post discharge.

The SPSS software v 20 was used for statistical analysis. The statistical tests used were t-test, ANOVA, chi-square& Fisher's test wherever applicable.

Informed consent was taken from all the patients.

RESULTS

A total 58 patients were enrolled in our study comprising of 34 (60%) males and 22 (40%) females. The maximum numbers of patients were the resident doctors: 23 (41%) followed by Undergraduate medical students: 10 (18%) and the nursing students: 10 (18%).The mean duration of fever at the time of admission to the hospital was 2.1 days± 0.95 days.

Out of all cases, 43 (76%) were Dengue, 11 (20%) were Dengue with warning signs, and 2 (3%) were Severe Dengue.

The most common symptom was fever 56 (100%) with chills/rigors 49 (87%), followed by myalgia 31 (55%) and headache 25 (45%). The most common sign was decreased capillary filling time 30 (53%). Hypotension was not seen in the 'D' category, while one (9%) in 'DW' and two (100%) in 'SD' category had hypotension with systolic BP<100 mmHg (p=0.01). The tourniquet test has not been done as it is no longer required for diagnosis. The tourniquet test has been reported to have a low sensitivity. [5] [Ref: Table 1]

Our study has shown that the Hematocrit values across the groups does not show a statistically significant difference (p=0.18). Mean Hct rise in 'D','DW', and 'SD' were 8.73%, 11.17%, and 11.72% respectively (p=0.41). [Ref: Table 2]

The WBC trend shows leucopenia with lymphocytosis. The mean WBC count in 'D','DW', and 'SD' were 5074(±2274), 4474(±1895), and 3418(±1789). The difference was not statistically significant (p=0.456). [Ref: Table 2]

The more severe groups had higher level of thrombocytopenia. Positive predictive value of PC < 50,000 for severe group is 87.5% & a specificity of 97%. Positive predictive value of PC > 1,00,000 for mild group is 96% with a specificity of 92% [Ref: Table 3]. The mean platelet counts in 'D','DW', and 'SD' were 182,228 (±78,563), 132,090 (±89065), and 86,443 (±63537) (p=0.07). (Table 2)

Table 1: Frequency of symptoms and signs in various groups as per WHO-TDR classification

	Dengue (D) (n=43)	Dengue with warning (DW) (n=11)	Severe Dengue (SD) (n=2)	P-value (Fischer#)
Symptoms				
Fever	43 (100)	11 (100)	2 (100)	1
Chills/ rigors	37 (86)	10 (90)	2 (100)	1
Myalgia	24 (55)	7 (63)	1 (50)	0.76
Headache	19 (44)	5 (45)	1 (50)	1
Abdominal pain	2 (5)	3 (27)	1 (50)	**0.02**
Retro orbital pain	9 (21)	2 (18)	1 (50)	1
Arthralgia	6 (14)	2 (18)	1 (50)	0.42
Bleeding	0	1 (9)	1 (50)	**0.05**
Sore throat	8 (18)	1 (9)	0	0.66
Vomiting	8 (18)	6 (54)	2 (100)	**0.005**
Signs				
Hypotension (Sits BP<100 mmHg)	0	1 (9)	2 (100)	**0.01**
Blanching (decreased capillary filling time)	21 (49)	8 (72)	1 (50)	0.22
Rashes	6 (14)	1 (9)	0	1
Petechiae	2 (5)	3 (27)	1 (50)	**0.02**
Conjunctival suffusion	3 (7)	2 (18)	1 (50)	0.13

#Fischer test was used to calculate the p value; Figure in parenthesis indicates percentage.

Table 2: Haematological profile of patients in each group

	Dengue (D) (n=43)	Dengue with warning (DW) (n=11)	Severe Dengue (SD) (n=2)	P-value ANOVA@ Fischer#	Normal lab value
Hemogram					
Mean Haemoglobin (S.D.)@	12.88 (1.48)	12.80 (1.64)	11.9 (3.9)	0. 696	M:13.3-16.2 F:12-15.8
Mean hematocrit (S.D.)@	36.93 (4.12)	39 (3.16)	40.5 (5.86)	0.18	M:38.8-46.4 F:35.4-44.4
Mean hematocrit rise*	8.73%	11.17%	11.72%	0.41	
Hematocrit ≥ 40% (%)#	11 (25)	6 (54)	1 (50)	0.089	
Mean WBC† count (S.D.)@per cmm	5074 (2274)	4474 (1895)	3418 (1789)	0.456	4000-11,000
WBC < 4000/cmm (%)#	25 (58)	9 (82)	2 (100)	0.1	
Lymphocytes > 50%#	12 (28)	3 (27)	2 (100)	0.5	20-40%
PC‡< 50,000#	1 (2)	6 (54)	1 (50)	<0.01	
PC: 50,000-1,00,000#	10 (23)	4 (36)	1 (50)	0.3	
PC > 1,00,000#	32 (74)	1 (9)	0	<0.01	
Mean PC (S.D.)@@ per cmm	182228 (78563)	132090 (89,065)	86433 (63,537)	0.07	1.5 - 4.5 lac
ALT (Alanine Aminotransferase)					
ALT >35U/L (%)#	8 (18)	5 (45)	2 (100)	0.06	<35 U/L

* Mean haematocrit rise: The mean rise of haematocrit in percent in the group from the haematocrit on admission to the peak value; †White Blood Cells; ‡ Platelet Count; #Fischer test was used to calculate the p value. The data was analysed by clubbing the frequencies in 'DW' and 'SD' together and comparing against 'D'; @ANOVA test was applied; M=Male; F=Female.

An elevated ALT (>45 IU/ml) were found in eight (18%) of 'D' cases, five (45%) of 'DW' cases, and two (100%) of 'SD' cases. (p=0.06) (Table 2).

Calculation of economic impact:
(a) Loss of productive workforce: Rs 760/day
(b) Cost of indoor treatment

- Semi-special room charges: Rs 1200
- Treatment-Rs 1800
- Investigations-Rs 1000
- Total approx Rs 3900 per person for entire stay
- Dengue diagnosis(RT-PCR: Rs 7000,IgM ELISA: Rs 300)

(C) 3-day strike: Rs 11,40,000
Total: Rs 19,48,800

The man hours lost were calculated by estimating the average no. of hours of work multiplied

by the average no. of days required for hospital admission + rest advice post discharge.

For residents, an average of 16 hours/day * 10 days/patient * 23 patients= 3680 man hours

For nursing students, interns and undergraduate students an average of 8 hours/day * 10 days/patient * 33 patients = 2640 man hours

Total approx. 6300 man hours lost.

The mortality rate in our study was 1.7% with one death. The cause of death was DIC (Disseminated Intravascular Coagulation) with MODS (Multi-Organ Dysfunction Syndrome).

Table 3: Platelet count in different group

Platelet count	'D' group	'DW' & 'SD' group	Total
< 50,000	1	7	8
>1,00,000	32	1	33
Total	33	8	41

(Note: 9 patients had platelet count between 50,000 and 1,00,000)

DISCUSSION

In our study we are comparing various clinical as well as haematological parameters between the three groups classified as per WHO-TDR classification into Dengue, Dengue with warning signs and Severe Dengue. The old system which classified cases into Dengue Fever, Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) with DHF further classified in to four grades. The new system was developed by WHO as the older system was cumbersome and difficult to use, resulted in inability to classify some cases and inappropriate classification in some cases.[1,8] The new system is also better at detecting severe dengue infections. Considering that most of previous studies were

done on old WHO classification and that some studies were only in patients with hemorrhagic patients, and my study has taken the new WHO-TDR classification, direct comparisons with older studies are not possible as patients would fall in different categories in different classifications.

Dengue infection has the propensity to spread among urban places with poor hygiene and cause explosive outbreaks. Monsoon season, construction at multiple sites within campus and poor drainage gave ideal conditions for such an outbreak in Civil Hospital, Ahmedabad. This study is the biggest documented in-hospital dengue fever outbreak among health care personnel in India.

In our study, clinical features such as persistent vomiting, bleeding, severe abdominal pain, hypotension and petechiae were found to occur in a higher frequency in more severe groups like 'DW' and 'SD'. And so these features predict a more severe dengue infection. Altered sensorium, icterus and decreased urine output were seen exclusively in severe dengue patient only. The most common symptom observed was fever, vomiting and body acheas has been seen in previous studies.[3,4,5,7]

Higher haematocrit is related to increased severity and is explained by the increased plasma permeability which is the basic pathophysiological alteration in Dengue. In our study, higher haematocrit was related to more severe Dengue infection and the difference was statistically significant. A 20% rise in hematoritwas taken previously as a cut-off for diagnosis of DHF. It indicates that intensive fluid therapy is required. But in our study, it was found that the mean haematocrit rise by 20% was seen in very few cases even in the severe DW and SD groups. Thus a criteria based on cut-off increase in haematocrit would fail to recognise many patients. A lesser than expected rise in Hct has been found in other studies,[7,8] making it imperative to develop new recommendations for hemoconcentartion and its use in diagnosis and monitoring.[4,5,8] Various pitfalls of Hct are non availability of pre-illness hematocrit, High prevalence of anaemia in the Indian population,[4,5]blunting of hemoconcentration due to early institution of fluid therapy and a fall in hematocrit if there has been significant blood loss.[8]

Dengue causes leucopenia with lymphocytosis and thrombocytopenia. The causes include bone marrow suppression and binding of dengue antigens to platelets and antibody mediated immunological destruction of platelets. In our study we found that while the WBC changes are poor indicators of severity, the degree of thrombocytopenia is related to severity. Those with a platelet count of <50,000 were more likely to be in the 'DW' or 'SD' groups. The changes in WBC count is useful in differentiating dengue infections from other febrile illnesses.[8]

A rise in serum transaminases (ALT/AST > 35) has been reported in several studies.[7,8] But in our study there is no statistically significant difference in ALT levels among the subgroups, as also

found in few other studies.[7,10] This is contrary to findings in some studies where the difference has been significant.[9] The cause for such rise has been postulated to be due to ischemic hepatitis or virus induced liver damage.[3]One explanation could be the small sample size of our study.

The mortality rate in our study of 1.7% is less as compared to the rate of 3-5% on other Indian studies.[3,4,9,10] It may be related to the earlier presentation of patients due to increased awareness and easy access to healthcare.[4,6]The mean duration of fever at the time of admission to the hospital was 2.1 days (± 0.95 days) for our patients, which is less than that in other Indian studies (4.8-5.9 days).[6,7] This reinforces the need for early detection and treatment.

The financial burden of the outbreak was to the tune of Rs. 19,48,800 and nearly 6200 productive man-hours of the health personnel were lost.

CONCLUSION:

Most, if not all, deaths from Dengue are preventable with appropriate and timely medical attention. Attention to some key clinical features can give clue to the severity of the dengue infection and hence closer attention to those patients. The hemogram is the most important guide to therapy and prognosis. Dengue carries a huge economic cost which can be offset by simple preventive measures.

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