RESEARCH ARTICLE

COMPARISON OF SYMPTOMS, SIGNS AND HAEMATOLOGICAL PARAMETERS IN DENGUE PATIENTS ADMITTED IN A TERTIARY CARE CENTERS IN KOLKATA, 2014 AND 2012 EPIDEMIC

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ABSTRACT

Dengue fever may present as subclinical infections, mild uncomplicated dengue fever or complicated dengue fever in the form of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). On and from the first incidence of dengue fever in 1824, six epidemics occurred in 1836, 1906, 1911, 1923, 2005 and 2012 in West Bengal. Our aim was to compare clinical and hematological profile between males and females as well as to compare the data with that of patients admitted in a tertiary care center in Kolkata throughout their hospital stay. Total 404 patients having either non structural (NS_1) antigen positive and/or immunoglobulin M dengue antibody positive were admitted in our hospital. Just after admission, proper history and examinations were performed, this was followed by drawing of blood for hematological and biochemical examinations. Within 24 hours, imaging studies in the form of ultrasound of upper abdomen and chest x-ray were performed. Above hematological and biochemical tests were repeated after 48 hours. After collection of all the data, we made comparisons of these collected data between males and females. Number of DHF and DF patients was 295 and 109 respectively having following significant symptoms, like, fever, nausea/vomiting, headache and backache and evidence of plasma leakage (in DHF patients). Females were anemic with low hematocrit value. 69.05% patients were leucopenic. During admission, 201 dengue patients (49.75%) were thrombocytopenic, but the number was increased to 295 (73%) during the course of illness. Male to female ratio was 1.34:1. Of 404 patients, 73% patients suffered from DHF. Commonest presentations in this study were fever, nausea/vomiting, backache and headache. Females were mainly anemic with low hematocrit value. Significant number of patients was leucopenic. Small number of patients showed evidence of plasma leakage.

INTRODUCTION

Dengue fever is an arthropod borne disease, results from the bite of aedes mosquito in the afternoon. The etiological agent is dengue virus, a member of flaviviridae family. The virus consists of four types, DNEV 1 to 4. The presentation of dengue fever is wide, it may be subclinical, mildly clinical, uncomplicated form or severe in the form of dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS)[1, 2]. According to WHO, this fever has been classified into undifferentiated fever, dengue fever and dengue hemorrhagic fever. In 1780, first clinical recognized dengue fever occurred in Asia, Africa and North America, but first case report of 1780's epidemic in Philadelphia was reported in 1789. In 1944, virus responsible for dengue fever was isolated in Kolkata from the serum of US soldiers[3]. In 1780, first epidemic of dengue fever was restricted in Madras (now called Chennai), whereas, virologically proved dengue was first recorded in Kolkata and in whole Eastern coast of India[4, 5]. First major epidemic of dengue fever was recorded in Philippines, then it spreaded to countries surrounding India despite the presence of all the risk factors. Ultimately ice broke the stones, this epidemic entered India in 1988[6, 7]. In Kolkata, dengue fever was first recorded in 1824 followed by several outbreaks in 1836, 1906, 1911, 1923, 2005 and 2012[8,9,10]. In 2014, also large number of patients was admitted in different tertiary hospitals in Kolkata. Male-female distinction is an important factor in Public Health Programs as regards to the rate of infection and severity of the disease. Low incidence of dengue fever in females in many Asian countries may be due to statistical artifact, like, low incidence of reporting, low-care seeking from the general population, less exposure due to home staying during the most of the day. Our aim was to correlate clinical and hematological profile of dengue patients between males and females and to compare this small epidemic with large epidemic in 2012 in sane tertiary care centre, Kolkata throughout the hospital stay.

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MATERIALS AND METHODS

We started our original and honest study only after getting permission from our Ethical Committee. Total 404 (four hundred four) patients were admitted in Kalipada Chowdhury Medical College and Hospital, Kolkata from the month of October to December, 2014. Immediately after admission, informed consent was taken from the patients' parties, and the blood was drawn for testing of NS_1 antigen, immunoglobulin M (IgM) antibody by Mac ELISA manufactured by Panibo diagnostics. No patients were died in this epidemic. So, all the 404 patients were included in our study. Thorough history taking was performed which included pain abdomen, nausea-vomiting, headache, Bachache, rash, heamatemesis/melena, cough, retrobulbar pain, urinary tract infection. Thorough general survey and related systemic examination revealed Hepatomegaly, body rash, ascites and pleural effusion in variable number of patients. After examination, blood was drawn and sent for hematological and biochemical estimation instantaneously and again after 48 hours. Imaging studies like, Ultrasonography and chest X-ray were performed to detect peritoneal and pleural involvement respectively. Then following data were compared between males and females, like, presenting symptoms, peritoneal and pleural involvement in the form of pleural effusions and ascites respectively, hemoglobin concentration, total white blood cell count, hematocrit level, platelet count.

All the patients recovered within two weeks by conservative management, like, intravenous fluid, antipyretics and occasionally antibiotics. Patients with platelet count of less than 20000/cc with or without any evidence of bleeding were provided with platelet concentrates. Patients with platelet count of more than 20000/cc didn't show any evidence of bleeding, so, no transfusion was given to those patients. Now we compared different items at selected confidence level of 95% between males and females, and 'p' value were extracted.

Statistical method used

1. 95% confidence interval for different percentage:
2. $(p_1—p_2) \pm 1.6SE\ (p_1—p_2)$, where SE $(p_1—p_2) = \quad [\{p_1 (1—p_1)/n_1\} + \{p_2\ (1—p_2)/n_2\}]$
3. Chi-square test with three degrees of freedom was used to show the significance of symptoms, signs and hematological investigations.
4. 'p' values showed maximum probability for a given level of significance.

RESULTS

Among 404 patients, 232 patients were males, 172 were females. All patients were included in our study. Total number of patients with DHF were 295(males =183, female=112) and DF patients were 109 (males = 49, females=60). Here most common symptoms were fever (94.80%), followed by nausea/vomiting (49.75%), headache (48.51%) and Bachache (47.47.27%). According to the table [table I]: Significant number of male patients showed pain abdomen, >9 gm% haemoglobin, high hematocrit (>40) as compared to females

(p=0.00), whereas, significantly low hemoglobin and low hematocrit were observed in females as compared to males (p=00). Again, significant number of females showed platelet count of more than 100000/cc.

DISCUSSION

According to the definition of WHO, 295 cases were DHF and 109 cases were uncomplicated dengue fever. In the study of Karoli *et al.*[11] common symptoms were headache (71%), followed by abdominal pain (63%), nausea with vomiting (58%) and rash (26%). But in our study, most common symptoms were fever (94.80%), nausea with vomiting (48.75%), headache (48.51%), and backache (47.27%). This is similar to that found in the study done by Ashis Saha et al.[10] In this study, incidence of headache, backaches, nausea with vomiting were 41.68%, 43.06% and 43.06% respectively. But the difference in our study is that the incidence of fever is 94%, which was not present in the study of 2012 epidemic in Kolkata.

In few studies done in Singapore and India, male to female ratio were 2:1[12, 13]. Male: female ratio was recorded as 2.5:1 in a hospital based study in Delhi in the year 1996[14]. Similarly, in one study in Bangladesh, the ratio was 1.5:1 in 1997 epidemic, but in the study of 2000, there was no sex prediliction[15]. Again, in the study of South Africa, this ratio was 0.65:1[16]. Study of Ashis Kumar Saha *et al.* demoed male: female ratio as 1:1.08, with little edging towards female. In the present study, this male: female ratio is 1.34:1.

Though dengue fever was known as childhood disease as described in South-East Asia, but there was gradual inclination of DHF patients towards higher age group since early 1980s as demoed in the studies done in Latin America and South –East Asia by Guzman *et al.* in Cuba and Rigau-Perez in Puerto-Rico respectively[17,18]. 2000 epidemic in Bangladesh demonstrated the incidence of DHF in adult age group as 82%[19]. Our study showed the incidence of DHF highest in 18-40 years age group followed by >40-60 years group, which is similar to the study done in 2012 epidemic[10].

Usually, the incidence of dengue fever is high in the rainy season, and EI Nino phenomenon has been incriminated in the increase in vector-borne diseases[20]. But weak relationship was demonstrated between the mean temperature and the incidence of dengue fever in study in Puerto-Rico from 1988 to 1992[21]. Our study showed the incidence of dengue occurred fever between September to December, which was similar to the previous study done during previous epidemic in 2012 in Kolkata[10]. This may be due to factors related to hard immunity, or demographic transition influencing transmission.

Usually, anemia does not occur in DHF due to transient decrease in maturation of erythrocyte precursors and longer half life of red blood cells[22]. Our present study showed anemia in 6.39% of females, on the contrary, 14.3% female patients showed anemia in last 2012 dengue epidemic[10]. The anemia may be due to nutritional deficiency as well as secondary

infection from different serotype of dengue virus or menstrual problems.

demoed ascites and pleural effusion in 7.92% and 9.90% respectively, it was similar to the study of 2012 epidemic, where the number of patients with ascites and pleural effusion

Comparison of symptoms & hematological parameters in male and female dengue patients

ITEM	MALE 232	%	FEMALE 172	%	P VALUE	Total cases	%
Pain abdomen	54	23.27	20	11.62	0.00	64	15.84
Nausea/vomiting	113	48.7	88	51.16	0.562	201	49.75
Retrobulbar pain	93	40.08	48	27.90	0.011	141	34.90
Diarrhea	51	21.98	33	19.18	0.493	84	20.79
Backache	118	50.86	72	41.86	0.073	190	47.27
Headache	114	49.13	82	47.67	0.773	196	48.51
Cough	27	11.63	16	9.30	0.453	43	10.64
Fever	221	95.25	162	94.18	0.632	383	94.80
Hematemesis/melena	4	1.72	0	0	0.847	4	0.99
Uti	0	0	0	0	0	0	0
Rash	78	33.62	68	39.53	0.222	146	36.13
Hemoglobin							
>7-9 gm%	3	1.29	11	6.39	0.005	14	3.46
>9 gm%	229	98.7	161	93.60	0.005	390	96.53
Total count							
<1000-3000/cc	47	20.25	48	27.90	0.073	95	23.51
>3000-5000/cc	117	50.43	67	38.95	0.022	184	45.54
>5000/cc	68	29.31	57	33.13	0.411	125	30.94
Hematocrit							
20-30	3	1.29	18	10.46	0.00	21	5.19
>30 – 35	10	4.31	57	33.14	0.00	67	16.58
>35 – 40	79	34.05	70	40.69	0.172	149	36.88
>40	140	60.34	27	15.69	0.00	167	41.33
Platelet							
<20000 /cc	7	3.01	3	1.74	0.416	10	2.47
20000 – 30000/cc	19	8.18	7	4.069	0.09	26	6.43
>30000 – 50000/cc	69	29.74	37	21.51	0.063	106	26.23
>50000 – 100000/cc	88	37.93	65	37.79	0.977	153	37.87
>100000/cc	49	21.12	60	34.88	0.002	109	26.98
Signs							
Ascites	12	2.97	20	11.62	0.017	32	7.92
Pleural effusion	18	4.45	22	12.79	0.094	40	9.90

Our present study recorded leucopenia (<5000/cc) in 69.05% patients, whereas, only 21% of patients showed leucopenia in the study by Ratgiri *et a*l[23]. Again, no evidence of leucopenia was demonstrated in the study of Banerjee *et al.*[24]. In 2012 epidemic study of Ashis Kumar Saha *et al.* showed leucopenia in 79.52% of dengue patients. This leucopenia may be due to infection by different virus serotype.

In our study, during admission 201 (49.75%) patients were thrombocytopenic, but within 48 hours, another 94 (total 73%) patients entered into a state of thrombocytopenia. In the study done by Ratagiri *et al.* and Banerjee *et al.* thrombocytopenic patients were 82% and 96% respectively[23, 24]. In the study of 2012 epidemic in Kolkata[10], 86.13% suffered from thrombocytopenia. But, in our present study, less number of patients was thrombocytopenic (73%). The thrombocytopenia may be due to decreased production of platelets due to bone marrow suppression[21] or due3 to immune –mediated dest5ruction due to production of antigen-antibody complexes[18]. Other factors responsible for thrombocytopenia are release of high of high level of plasma activating factors by monocytes as a consequence of secondary infection inducing platelet consumption and increased adhesiveness to vascular endothelium[27].

In the study done by Molta *et al.* evidence of right sided or bilateral pleural effusion and ascites were demonstrated in 28%, 11.2% and 74.6% respectively[28], whereas, our study

were 7.8% and 7.9% 12 respectively. Ascites and pleural effusion are mostly due to plasma leakage. According to different observations, in DHF, production of cytokines due to T cell activation, infected cell lysis by CD4+ and CD8+ dengue specific lymphocytes are mainly causative factors for development of plasma leakage. Protein of 22-25 kDa may also be responsible this plasma leakage in DHF patients as evidenced from some observations.

CONCLUSIONS

In our study, 295 (73.05%) patients suffered from DHF. Predominant symptoms were fever (94.80%), nausea/vomiting (49.75%), headache (48.51%), backache (47.27%). Females were mainly anemic (6.39%), having low hematocrit value (10.46% patient). Male to female ratio was 1.34:1. Infection occurred mainly in autumn season. Evidence of plasma leakage in the form of ascites and pleural effusion were 7.92% and 9.9% patients respectively. Leucopenia was seen in 69.5% of patients.

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