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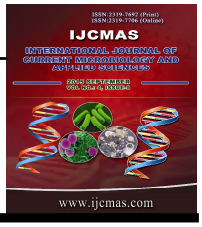

Original Research Article

Evaluation of Recent WHO Classification (2009) for Assessment of Dengue Disease Severity

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Keywords

Clinical and hematological parameters, Dengue, Dengue with warning signs, Severe dengue, Severity markers, Thrombo-cytopenia, WHO classification 2009

A B S T R A C T

Four antigenically distinct dengue virus serotypes cause most important arboviral diseases in humans. To compare Clinical And Hematological Profiles Of Dengue Cases as per WHO Classification(2009). An observational cross-sectional study was done from 1st June 2013 to 30th November 2014 at tertiary care hospital. 8364 serum samples were collected from clinically suspected cases of dengue patients. Samples were tested for Dengue NS-1 antigen before 5 days of onset of illness and for Dengue IgM after 5 days of onset of illness. All demographic, clinical, hematological and other laboratory parameter data were collected and analyzed. Out of 859 Dengue positive cases included in study50.6% (435) are of Dengue without warning signs (D), 37.6% (323) are of Dengue with warning signs (DW) and 11.8% (101) cases are of Severe Dengue (SD). As per traditional (1997) WHO classification out of 859 Dengue positive cases 72.75%(625) cases are of Dengue Fever (DF), 25.49%(219) are of Dengue Hemorrhagic Fever (DHF) and 1.7%(15) cases are of Dengue Shock Syndrome (DSS). Hemoglobin, RBC count, MCHC decreases, Platelet count serum bilirubin, SGPT, blood urea and serum creatinine increases as severity of dengue rise as severity of dengue increases. 59.6%(512) cases normocytic hypochromic RBCs. Thrmbocytopenia was observed in 59.95%(515) cases. Atypical lymphocytes were seen in 6.75% (58) dengue cases. Recent (2009) WHO classification of dengue is more competent in diagnosing severe cases which were missed earlier if classified using traditional (1997) classification. In addition to Hematocrit and platelet count suggested in traditional 1997 classification, as per our study Hemoglobin, RBC count, MCHC, Differential leucocyte counts, Blood urea, Serum creatinine, Serum Billirubin and SGPT can be used as severity markers for dengue cases as per recent 2009 classification.

Introduction

Dengue is the most rapidly spreading mosquito-borne viral disease in the world. In the last 50 years, incidence has increased 30-fold with increasing geographic expansion to new countries and, in the present decade, from urban to rural settings. An estimated 50

million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries. Dengue is widely prevalent in India, and all the 4 serotypes are found in the country.[1-4]

The aim of this study includes to evaluate traditional (1997) and recent (2009) WHO classification for assessment of dengue disease severity. And also to establish new laboratory parameters as severity markers in recent (2009) WHO classification of Dengue.

Material and Methods

An observational cross-sectional study was done from 1st June 2013 to 30th November 2014at tertiary Care Hospital. Total 8364 serum samples were collected from clinically suspected cases of dengue patients as per WHO case definition of dengue (2009) (Table 1)[4,21]. Adequate amount of non-hemolysed, non-lipemic serum without precipitate or particulate matter is collected from patients and tested for Dengue NS-1 antigen ELISA/immunochromatography before 5 days of onset of illness and for Dengue IgM Capture ELISA after 5 days of onset of illness. All demographic, clinical, hematological and other laboratory parameter data were collected using data collection form.

Data were analyzed by using SPSS 21.0 demo version. Pearson's chi square test was used for sets of categorical data to evaluate how likely it is that any observed difference between the sets arose by chance Fisher's exact test was used for analysis of contingency tables between 2 groups. ANOVA (Analysis of variance) test was used to analyze the differences between group means. Statistically significant P value is considered below 0.05.

Results and Discussion

Out of total 8364 Samples 859 serologically positive dengue cases from actual study site was considered for further discussion and statistical calculation.

As per recent (2009) WHO classification out of 859 Dengue positive cases 50.6% (435) are of Dengue without warning signs (D), 37.6% (323) are of Dengue with warning signs (DW) and 11.8% (101) cases are of Severe Dengue (SD). As per traditional (1997) WHO classification out of 859 Dengue positive cases 72.75%(625) cases are of Dengue Fever (DF), 25.49%(219) are of Dengue Hemorrhagic Fever (DHF) and 1.7%(15) cases are of Dengue Shock Syndrome (DSS). Comparison of both these classification system is depicted in figure 1.

Dengue cases are positive more in Male patients (58.54%) compared to female (41.55%) in each clinical type. Most common age group affected by dengue was 21 to 30 years. Minimum age affected is 5 days and maximum age affected is 75 years. Maximum cases were noted between August to November in both the years (91.89%).Majority of the dengue patients in each clinical type is presented commonly within or at 5 days of onset of illness. Demographics and clinical presentation of all three types of dengue cases are depicted in Table 2.

Decreased hemoglobin< 11 gm/dl is noted in 59.59% of dengue cases. RBC count in 62.4% female was within normal range of 4-5.1 per cm. The same for the male patients was seen below minimal normal value of 4.5 percmm in 55.38% (278) dengue cases. Most of the female patients (62.18%) showed normal PCV range of 35.9 to 44.6 %.

The same for the male patients was below minimum normal value of 41.5% in 64.54% (324) dengue cases.61.7% (530) of total dengue, 65.06% (283) of D, 56.97%(184) of DW and 62.38% (63) of SD patients showed MCV within normal range of 80 to 90 fl . 77.88% (669) of total dengue, 79.31% (345) of D, 76.78% (248) of DW, 75.25% (76) of SD patients showed decreased MCH value of less than 27.5 pg . Lowered MCHC value below 33.4 g/dl is observed in 87.9% (755) dengue cases. (Table 3)

Most common group for total WBC count was in normal range of 4400 to 11000 per cmm in 49.94% (429) of total cases. Atypical lymphocytes were seen in 6.75% (58) dengue cases. Maximum cases with atypical lymphocytes were noted in DW patients 9% (29). Detailed total differential count distribution is depicted in table 4.

Thrombocytopenia (Platelet count below 1,50,000 per cmm) is noted in 60%(517) dengue cases. While D cases showed low platelet count between 1,00,000 to 1,49,999 per cmm, DW and SD cases showed platelet count <1,00,000 per cmm. For detailed distribution of platelet count see table 5.

Raised serum bilirubin levels (>1.2 mg/dl) and SGPT (>55 U/L) were noted 15.48% (134) and 32.48% (279) cases. Raised blood urea (>45 mg/dl) and serum creatinine (>1.5 mg/dl) were noted in 9.42% (81) and 5.59 % (48) cases. Such cases were increased as dengue cases increased in severity as depicted in table 6.

In Present study the incidence of dengue was 12.24%. This is comparable to the study conducted by Mehta et al in 2012 at Ahmedabad [5.] High incidence was recorded byPatankaret al[6] in 2012 at Ahmedabad and by Durani et al[7] in 2011 to 2013 at Jamnagar. Lowered incidence of dengue in present study compared to past years 16.36% in 2011 and 16.87% in 2012 in same study location, indicate improved prevention and control strategies.

Male preponderance (58.44%) was noted compared to females (41.55%) in present study. This is comparable to studies by Patankar et al[6], Durani et al[7]& Jain et al [8] showing incidence in male patients of 65%, 70.79% and 60% respectively. Though with pearson chi square test this gender preponderance is not statistically significant (p=0.463) in present study, it may beat tributed to more exposure of the males to the bite of vector *Aedes aegypti*, due to their clothing habits or outdoor activities.

The most common age group affected in present study was 21 to 30 years (30.96%). This is comparable to studies by Patankaret al[6], Durani et al [7]&Goyal et al [9] noting most common age group affected as 18-35 years (58%), 16-20 years (92%) and 21-30 years (99%) respectively. DW and SD commonly affected younger age group of 11 to 20 years of age group. SD affected older patients compared to DW. This finding is very statistically significant (P=0.012). High Numbers of cases in young age groups implies that disease is endemic in this region. Less incidence of sever dengue forms in >20 years indicates immunity against virus. 10-30 years of age group is more exposed to external environment and mosquito vectors. Affection of young also results in economic non-productivity.

Seasonal distribution was observed in present study with maximum cases from July to November (91.89%). This comparable to study done by Durani et al[7]&Mehta et al[5]. July to November months corresponded to the monsoon and post - monsoon season providing an environment

favorable for the breeding of the vector *Aedes aegypti*.

As per WHO classification 2009 present study noted incidence of Dengue (D) 50.6%, Dengue with warning signs (DW) 37.6% and Severe dengue (SD) 11.8%.This is comparable to study done by Pongpan et al [10]. Study by Abhinav Jain et al [8] showed less cases in DW (20%) and SD (3%). As shown in Figure 1 by comparing it with traditional (1997) classification scheme 38.69% (125) DW & 64.35 %(65) SD cases were misdiagnosed as mild Dengue fever (DF) cases and 21.72%(22) SD cases were misdiagnosed as DHF cases. So the sensitivity and specificity of recent(2009) classification is more in diagnosing severe cases which were missed earlier. This can lead to better management and outcome in dengue patients.

Most common presenting feature in present study was fever with chills and rigors (100%) Muscle pain (53.2%) and Headache (48.2%) which is comparable to studies by Patankar et al[6], Singh et al[11], Khan et al [12], Dutta et al[13] and Low et al[14]. In our study incidence of vomiting (5.59%) and abdominal pain (3.03%) were less compared to these studies. Joint pain (20.95%) is more in present study compared to Patankar et al[6], but less compared to Low et al[14].In present study hemorrhagic manifestations (15%) are comparable to study by Khan et al[12].While Singh et al[11] noted a high incidence(22.1%), Patankar et al[6] noted a low incidence (1%) of the same.

The fever and influenza- like symptoms that typify dengue probably reflect patients' cytokine response. However, myalgia, a cardinal feature of the illness, may also indicate pathologic changes in muscle, typified by a moderate perivascular mononuclear infiltrate with lipid accumulation.

In present study cases of Dengue without warning signs had fever (100%), Chills & rigors (100%), Muscle pain (50.57%), headache (42.53%) and joint pain (19.08%) as principal clinical manifestations, which is comparable to study by Jain et al[8]. Study by Pongpanetal[10]noted high rate of vomiting (62.4%), Skin rash (42.5%) and headache (58.3%), but low incidence of muscle pain (21.5%). Dengue with warning signs presented mainly, in addition to above, with jaundice 54.48% (176), skin rash 52.32 % (169), Hepatomegaly 12.07 % (39) and hemorrhagic manifestations 15% (48) in present study. Jain etal[8]and Pongpan et al[10]noted the same as 9 % and 27% respectively. Present study noted high incidence of Hemorrhagic manifestation (63%) compared to Jain etal[8](50%) and Pongpan et al[10](57%) in severe dengue cases. Elevated hepatic transaminase concentrations have been reported in most cases of dengue and viral antigen has been demonstrated in hepatocytes, Kupffer cells and endothelia. Histopathologic examination of skin from patients with rash discloses a minor degree of lymphocytic dermal vasculitis and, variably, viral antigen. The hemorrhagic diathesis is complex and not well understood, reflecting a combination of cytokine action and vascular injury, viral antibodies binding to platelets or cross-reacting with plasminogen and other clotting factors, reduced platelet function and survival, and a mild consumptive coagulopathy.

60% of dengue cases were having normocytic hypochromic anemia and Thrombocytopenia. Incidence of both were increased as severity of dengue increased. Similar findings has been noted in study done by Azinet al[15.] Study by Maimoona M. Ahmed[16] showed no hemoglobin change in dengue patients but thrombocytopenia was noted in 87% of cases. Other significant

findings noted in present study are described as follows. 67% of D, 52% of DW and 51% SD patient showed low hemoglobin of <11 gm/dl. This finding is highly statistically significant for D (P < 0.0001) and DW (P = 0.0002). Male patients showed RBC count below minimal normal value of 4.5 per cmm in 62.35% (164) of D, 49.17 % (89) of DW and 25 43.1% (25) of SD patients. This finding is statistically significant for D (P < 0.0001) and DW (P = 0.0015) and SD (P = 0.0354). PCV of male patients was below minimum normal value of 41.5% in 69.96% (184) of D, 57.46% (104) of DW and 62.07% (36) of SD patients. This finding is highly statistically significant for D (P=0.0042) and DW (P = 0.006). 82.76% of D, 93.19% of DW and 93.07% of SD patients showed MCHC level below 33.4 g/dl. This finding is highly statistically significant for D (P<0.0001) and DW (P<0.0001). MCHC values decrease more in SD patients compared to D patients. This finding is very statistically significant (P=0.012).

In D group no patient showed platelet count below 1,00,000 per cmm (P<0.0001). Thromobocytopenia in D group is seen within range of 1,00,000 to1,49,999 per cmm (P<0.0001). In DW and SD group most of the patient showed platelet count was below 1,00,000 per cmm (P<0.0001). DW group showed decrease in platelet count compared to D and SD group (P<0.0001).Local suppression of erythrocytic, myelocytic, and thrombocyticpoiesis within 4 to 5 days is reflected in peripheral cytopenia. Shock in dengue shock syndrome (DSS) occurs after the sudden extra vasation of plasma into extravascular sites, including the pleural and abdominal cavities, usually with the defervescence of fever. The extensive increase in vascular permeability is associated with immune activation.

Table.1 Recent WHO Case definitions of Dengue (2009)

Dengue without Warning Signs(D): Fever and two of the following: • Nausea, vomiting • Rash • Aches and pains • Leukopenia • Positive tourniquet test	**Dengue with Warning Signs (DW):** requires strict observation and medical intervention. It is defined as above with any of the following: 1. Abdominal pain or tenderness 2. Persistent vomiting 3. Clinical fluid accumulation (ascites, pleural effusion) 4. Mucosal bleeding 5. Lethargy, restlessness 6. Liver enlargement >2 cm 7. Laboratory: increase in HCT concurrent with rapid decrease in platelet count	**Severe Dengue (SD):** Dengue with at least one of the following criteria: 1. Severe Plasma Leakage leading to: 2. Shock (DSS) 3. Fluid accumulation with respiratory distress 4. Severe Bleeding as evaluated by clinician 5. Severe organ involvement 6. Liver: AST or ALT ≥ 1000 7. CNS: impaired consciousness 8. Failure of heart and other organs

Table.2 Demographics and Clinical features of Dengue cases

	D	DW	SD	Total
Gender distribution				
Female	172 (39.54%)	142 (43.96%)	43(42.57%)	357(41.55%)
Male	263 (60.54%)	181 (56.03%)	58 (57.42%)	502(58.44%)
Age group (in years)				
Mean ± SD	21.6 ± 12.95	20.46 ± 12.53	24.2 ± 15.51	21.48 ± 13.15
0 to 10	102 (23.44%)	73 (22.60%)	18 (17.82%)	193 (22.46%)
11 to20	97 (22.29%)	103 (31.88%)	31 (30.69%)	231 (26.89%)
21 to30	151 (34.71%)	92 (28.48%)	23 (22.77%)	266 (30.96%)
31 to 40	56 (12.87%)	38 (11.76%)	14 (13.86%)	108 (12.57%)
41to 50	14 (3.21%)	9 (2.78%)	9 (8.91%)	32 (3.72%)
51 to 60	11 (2.52%)	3 (0.92%)	3 (2.97%)	17 (1.97%)
>60	4 (0.91%)	5 (1.54%)	3 (2.97%)	12 (1.39%)
Duration of onset of illness				
Mean ± SD	5.17 ± 5.71	5.41 ± 3.92	5.53 ± 3.96	5.3 ± 4.91
5 days or less	259(59.50%)	174(53.90%)	54(53.50%)	487(56.70%)
More than 5 days	176(40.50%)	149(46.10%)	47(46.60%)	372(43.30%)
Fever	435(100%)	323(100%)	101(100%)	859(100%)
Chills with rigor	366(84.13%)	219(67.8%)	69(68.31%)	654(76.13%)
Nausea and Vomiting	5(1.14%)	20(6.19%)	23(22.77%)	48(5.58%)
Skin Rash	26(5.97%)	35(10.83%)	20(19.8%)	81(9.42%)
Muscle Pain	220(50.57%)	176(54.48%)	61(60.39%)	457(53.2%)
Headache	185(42.52%)	169(52.32%)	60(59.4%)	414(48.19%)
Joint pain	83(19.08%)	61(18.88%)	36(35.64%)	180(20.95%)
Positive torniquet test	3(0.68%)	8(2.47%)	30(29.7%)	41(4.77%)
Abdominal pain	1(0.22%)	7(2.15%)	24(3.76%)	32(3.71%)
Persistent vomiting	0(0%)	0(0%)	12(11.88%)	12(1.39%)
Jaundice	32(7.35%)	64(19.81%)	38(37.62%)	134(15.59%)
Hepatomegaly (> 2 cm)	0(0%)	39(12.07%)	27(26.73%)	66(7.68%)
Petechiae	8(1.83%)	41(12.69%)	46(45.54%)	95(11.05%)
Purpura	8(1.83%)	32(9.9%)	48(47.52%)	88(10.24%)
Ecchymosis	5(1.14%)	21(6.5%)	47(46.53%)	73(8.49%)
Epistaxis	0(0%)	15(4.64%)	52(51.48%)	67(7.79%)
Gum bleeding	0(0%)	9(2.78%)	51(50.49%)	60(6.98%)
Hemetemesis	0(0%)	0(0%)	49(48.51%)	49(5.7%)
Malena	0(0%)	0(0%)	51(50.49%)	51(5.93%)
Fluid accumulation in body cavities	0(0%)	0(0%)	36(35.64%)	36(4.19%)
Shock	0(0%)	1(0.3%)	48(47.52%)	49(5.7%)
Neurological involvement	0(0%)	0(0%)	8(7.92%)	8(0.93%)
Multiorgan failure and Death	0(0%)	0(0%)	14(13.86%)	14(1.62%)

Table.3 Iron indices dengue cases

	D	DW	SD	Total	P
Hemoglobin (gm/dl) (Normal : 11-17 gm/dl)					
Mean ± Std.Deviation	10.26 ± 2.01	10.84 ± 2.52	10.70 ± 2.82	10.53 ± 2.33	0.002
< 11	293 (67%)*	167 (52%)*	52 (51%)*	512 (59.59%)*	
> 11	142 (33%)	156 (48%)	49 (49%)	347 (40.4%)	
RBC Count (per cmm)					
Mean ± Std.Deviation	4.29 ± 0.74	4.43 ± 0.97	4.44 ± 1	4.36 ± 0.86	0.063
RBC count in Female (Normal: 4.5-5.1 milion/cmm)					
<4	43(25%)	35(24.65%)	16(37.21%)	94(26.33%)	
4-5.1	115(66.86%)*	87(61.27%)*	21(48.84%)*	223(62.46%)*	
>5.1	14(8.14%)	20(14.08%)	6(13.95%)	40(11.2%)	
RBC count in Male (Normal: 4.5-5.9 million/cmm)					
<4.5	164(62.35%)	89(49.17%)	25(43.1%)	278(55.38%)	
4.5-5.9	96(36.5%)*	80(44.2%)*	27(46.55%)*	203(40.44%)	
>5.9	3(1.14%)	12(6.63%)	6(10.34%)	21(4.18%)	
PCV (%)					
Mean ± Std.Deviation	37.94 ± 5.53	38.1 ± 7.13	38.01± 7.58	38.01 ± 6.42	0.948
PCV in Female (Normal: 35.9-44.6%)					
<35.9	56(32.56%)	43(30.28%)	17(39.54%)	116(32.49)	
35.9-44.6	109(63.37%)*	90(63.38%)*	23(53.49%)*	222(62.18%)	
>44.6	7(4.07%)	9(6.34%)	3(6.98%)	19(5.32%)	
PCV in Male (Normal: 41.5-50.4)					
<41.5	184(69.96%)	104(57.46%)	36(62.07%)	324(64.54)	
41.5-50.4	78(29.66%)*	72(39.78%)*	17(29.31%)*	167(33.27%)	
>50.4	1(0.38%)	5(2.76%)	5(8.62%)	11(2.19%)	
MCV (fl) (Normal :80-90 fl)					
Mean ± Std.Deviation	82.02± 8.94	82.43 ± 8.69	82.83 ± 9.79	82.27 ± 8.94	0.652
<80	119 (27.36%)	106(32.82%)	24(23.76%)	249(28.99%)	
80 to 90	283 (65.06%)*	184 (56.97%)*	63 (62.38%)*	530 (61.70%)	
>90	33 (7.59%)	33 (10.22%)	14 (13.86%)	80 (9.31%)	
MCH pg (Normal: 27.5-33.2 pg)					
Mean ± Std.Deviation	25.53± 4.87	26.5 ± 19.05	25.27 ± 3.77	25.86 ± 12.25	0.491
<27.5	345(79.31%)	248(76.78%)	76(75.25%)	669(77.88%)	
27.5to 33.2	81(18.62%)	71(21.98%)	24(23.76%)	176(20.49%)	
>33.2	9(2.07%)	4(1.24%)	1(0.99%)	14(1.63%)	
MCHC g/dl (Normal: 33.4-35.5 g/dl)					
Mean ± Std.Deviation	30.98 ± 2.26	30.76 ± 1.71	30.41 ± 2.08	30.83 ± 2.05	0.032
<33.4 g/dl	360 (82.76%)*	301 (93.19%)*	94 (93.07%)*	755 (87.9%)	
>33.4 g/dl	75 (17.24%)	22 (6.81%)	7 (6.93%)	104 (12.11%)	

Table.4 WBC counts in Dengue cases

	D	DW	SD	Total	P
Total WBC count (per cmm) (Normal: 4400-11000/cmm)					
Mean ± Std.Deviation	6799.18 ± 5579	6163.94 ± 4466	7199.99 ± 5818.95	6607.45 ± 5255.87	0.122
< 4400	158(36.32%)	127(39.32%)	35(34.65%)	320(37.25%)	
4400 to 11000	221(50.80%)	161(49.85%)	47(46.53%)	429(49.94%)	
> 11000	56(12.87%)	35(10.84%)	19(18.81%)	110(12.81%)	
Neutrophils (%) (Normal: 50-70%)					
Mean ± Std.Deviation	59.13 ± 12.88	56.43 ± 15.3	61.48 ± 13.38	58.39 ± 13.98	0.002
<50	57(13.10%)	58(17.96%)	9(8.91%)	127(14.78%)	
50 to 70	326(74.94%)	228(70.59%)	73(72.28%)	627(72.99%)	
>70	52(11.95%)	37(11.46%)	19(18.81%)	108(12.57%)	
Lymphocytes (%) (Normal: 20-40%)					
Mean ± Std.Deviation	33.76 ± 10.72	35.39 ± 12.29	31.89 ± 11.59	34.16 ± 11.48	0.016
<20	29(6.67%)	26(8.05%)	14(13.86%)	69(8.03%)	
20 to 40	323(74.25%)	214(66.25%)	69(68.32%)	606(70.55%)	
>40	83(19.08%)	83(25.70%)	18(17.82%)	184(21.42%)	
Monocytes (%) (Normal: 2-6%)					
Mean ± Std.Deviation	4.92 ± 3.55	6.58 ± 7.67	4.48 ± 3.43	5.49 ± 5.52	0
2 to 6	395(90.80%)	269(83.28%)	95(94.06%)	759(88.36%)	
>6	40(9.20%)	54(16.72%)	6(5.94%)	100 (11.64%)	
Eosinophils (%) (Normal: 1-6%)					
Mean ± Std.Deviation	2.2 ± 2.17	1.98 ± 1.83	2.01± 1.69	2.09 ± 2	0.288
1 to 6	424(97.47%)	317(98.14%)	99(98.02%)	840(97.79%)	
>6	11(2.53%)	6(1.86%)	2(1.98%)	19(2.21%)	
Basophils (%) (Normal: 0-2%)					
Mean ± Std.Deviation	0.13 ± 0.37	0.2 ± 0.73	0.15± 0.68	0.16 ± 0.57	0.192
≤2	435(100%)	319(98.76%)	100(99.01%)	854(99.42%)	
>2	0(0%)	4(1.24%)	1(0.99%)	5(0.58%)	
Peripheral Smear findings					
Atypical lymphocytes	23(5.29%)	29(8.98%)*	6(5.94%)	58(6.75%)	

Table.5 Platelet counts in Dengue cases

	D	DW	SD	Total	P
Platelet count (Normal: 50,00-4,50,000 per cmm)					
Mean ± Std.Deviation	200732.08 ± 8764.85	71534.41 ± 59033.72	115595.05 ± 104382.04	142141.05 ± 100735.11	0
<50,000	0 (0)	136 (42.1)*	37 (36.6)*	173 (20.13)	
50000 to 99,999	0 (0)	157 (48.6)*	25 (24.8)*	182 (21.18)	
1,00,000 to 1,49,999	143 (32.87)*	10 (3.1)	9 (8.91)	162 (18.86)	
1,50,000 to 4,50,000	292 (67.14)	22 (6.82)	30 (29.7)	344 (40.04)	

Table.6 Renal and Liver function tests in Dengue cases

	D	DW	SD	Total	P
Blood urea (mg/dl) (Normal: 15-45 mg/dl)					
Mean ± Std.Deviation	24.09 ± 23.34	23.39 ± 15.77	43.74 ± 53.05	26.14 ± 27.17	0
<15	129(29.66%)	92(28.48%)	19(18.81%)	240(27.94%)	
15-45	276(63.45%)	204(63.16%)	58(57.43%)	538(62.63%)	
>45	30(6.90%)	27(8.36%)	24(23.76%)	81(9.43%)	
Serum Creatinine (mg/dl) (Normal: 0.7-1.5 mg/dl)					
Mean ± Std.Deviation	0.78 ± 0.62	0.75 ± 0.37	1.38 ± 2.23	0.84 ± 0.93	0
<0.7	206(47.36%)	154(47.68%)	33(32.67%)	293(34.11%)	
0.7 -1.5	215(49.43%)	159(49.23%)	47(46.53%)	421(49.01%)	
>1.5	14(3.22%)	10(3.10%)	24(23.76%)	48(5.59%)	
Serum Billirubin (mg/dl) (Normal:0.2-1.2 mg/dl)					
Mean ± Std.Deviation	0.71 ± 0.44	1.31 ± 2.09	2.49 ± 3.68	1.15 ± 1.91	0
0.2-1.2	403(92.64%)	259(80.19%)	63(62.38%)	725(84.40%)	
>1.2	32(7.36%)	64(19.81%)	38(37.62%)	134(15.60%)	
SGPT (U/L) (Normal: 0-55 U/L)					
Mean ± Std.Deviation	55.63 ± 84.5	83.92 ± 164.71	188.5 ± 428.72	81.89 ± 192.11	0
<55	328(75.40%)	194(60.06%)	58(57.43%)	580(67.52%)	
>55	107(24.60%)	129(39.94%)	43(42.57%)	279(32.48%)	

Maximum Atypical lymphocytes were seen in DW cases 8.98% (29) patients compared to 5.29%(23) of D and 5.94% (6) of SD cases. This finding is statistically significant with Fisher's exact test (P=0.0495). Association of atypical lymphocytes was also noted in study by Jameelet al[17].

In present study jaundice was observed in 15.59% (134) cases. This is comparable to study by Singh et al[11]17.1%(24). Present study showed hepatomegaly in 7.68% (66) of total cases. Singh et al[11]observed a very high rate of 43.6% (61). Hepatomegaly in DW 2.1% (8) and SD 8.8% (26) patients in present study is also less compared to study done by Pongpan et al[10] which showed involvement for the same 12.07%(39) % and 26.73% (27) respectively. Raised bilirubin and SGPT in present study was 15.58% (134) & 32.48% (279) cases. Jain et al[20] noted the same in 15% and 68% cases. Present study also notes that none of the D patients showed billirubin level>5.2 mg/dl and 13.86% (14) SD patients showed billirubin level >5.2 mg/dl. Both these findings are highly significant (P<0.0001). Serum billirubin level increases as severity of dengue increases. This is highly statistically significant (P<0.0001). None of the patient in D group showed SGPT level >1055. 5.94% (6) SD patients showed SGPT level in that range. Both these findings are highly statistically significant having P values of <0.0001 and 0.0004 respectively. SGPT level increases as severity of dengue increases. This is highly statistically significant (P<0.0001). Altered liver function tests correlate with the clinical severity of the dengue cases.

In present study blood urea and serum creatinine levels increases as severity of patient increases in dengue infection. 23.76% of SD cases showed elevated renal function test levels. Jain et al[20] noted 61%

cases of elevated serum creatinine levels in hospitalized patients. In present study SD (23.76%) cases showed higher blood urea & serum creatinine levels compared to DW and D patients. This finding is highly statistically significant (P<0.0001). Renal failure is observed 15.84% (16) in SD patients in present study. Though overall mortality rate in Dengue patients is low 1.62%. Most common cause of death is hemorrhagic shock followed by Respiratory failure. 50% of patient who showed mortality were <15 years of age.

As per traditional (1997) classification Hematocrit and platelet count were used to monitor severity of dengue cases. But from our study we can conclude that in addition to that Hemoglobin, RBC count, MCHC, Differential leucocyte counts, Blood urea, Serum creatinine, Serum Billirubin and SGPT can be used as severity markers in dengue cases for better management of patients classified as per recent(2009) classification. These new marker changes can be used to track the progress of dengue case from Dengue cases without warning signs to Severe dengue cases.

Recent (2009) WHO classification of dengue is more competent in diagnosing severe cases which were missed earlier if classified using traditional (1997) classification. In addition to Hematocrit and platelet count as per our study Hemoglobin, RBC count, MCHC, Differential leucocyte counts, Blood urea, Serum creatinine, Serum Billirubin and SGPT can be used as severity markers for dengue cases in recent (2009) classification. This is of enormous importance in terms of better management and outcome in dengue patients.

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