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Evaluation of world health organization grading system in estimating the severity of dengue in adults in a tertiary care centre

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Abstract: *Objectives:* (1) To study the profile of dengue fever in patients admitted to a tertiary care centre. (2)To assess the performance of WHO classification in estimating the severity of dengue (3) To know the outcome of patients according to WHO grading for dengue fever. *Background:* Dengue virus infection causes a spectrum of clinical manifestations, usually classified according to the World Health Organization (WHO) grading system. We aimed to evaluate the WHO grading system in estimating the severity of dengue in adults in a tertiary centre. *Methods:* Our study included 88 laboratory confirmed cases of dengue infection. WHO criteria were applied to classify patients into Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).Patients were followed up with clinical and laboratory monitoring until discharge or death. We also grouped patients on the basis of whether they received significant intervention based on fluid replacement or requirements for blood transfusion. *Results:* Out of 88 patients, 36.3% of patients were found to have dengue fever, 56.7% with DHF, 10.2% with DSS. Plasma leakage and thrombocytopenia were significant factors in differentiating dengue from DHF, DSS. Majority of patients with DHF, DSS required interventions like fluid resuscitation and blood transfusion. Mean duration of hospital stay was longer in DHF, DSS. *Conclusion:* In a tertiary care centre, WHO criteria for grading of dengue can estimate the severity of dengue, helps us to segregate the patients who need aggressive management.

Keywords: Dengue Fever, WHO classification and Grading, Severity

Introduction

Dengue has become a worldwide public health concern [1]. It is endemic in more than 100 countries with south-east Asia and western pacific regions more seriously effected [1]. In India, cyclic epidemics affect mostly the deciduous dry and wet climatic zones and infection with multiple serotypes has been observed [2]. Dengue can be a self limiting infection or can be associated with complications like hemorrhage, hypotension and shock which are life threatening. The mortality of dengue is as high as 20%, but if recognized early and managed properly mortality is less than 1% [2].

The WHO set up a classification system to differentiate between the self-limiting though debilitating dengue fever (DF) and the potentially lethal dengue hemorrhagic fever (DHF) [2]. According to these criteria, DHF is defined by the presence of fever, hemorrhagic tendency, thrombocytopenia and some evidence of plasma leakage due to increased vascular permeability. DHF is further subdivided, with most severe cases categorized as dengue shock syndrome (DSS) when circulatory failure is present [2]. This classification system was introduced so that it could be applied for diagnosis and management of dengue, early identification of patients at a major risk of dengue related complications. Several studies have evaluated the performance of WHO classification in estimating the disease severity of dengue. The WHO classification has aided in the assessment of global dengue disease burden and in the development of treatment algorithms, resulting in an improvement in the mortality rate of DHF [3]. Prospective study from Thailand involving 60 patients and including a comparison group, difficulties with classification were encountered in approximately 20% of the cases [4]. Several other studies also have reported difficulties with the WHO classification, found it necessary to define new categories to identify severe cases that do not meet the criteria of DHF or DSS [5-7]. We conducted a

prospective study in the adults to evaluate the performance of WHO classification in estimating the severity of dengue, assess the performance of its each component in the diagnosis of dengue.

Material and Methods

Study population included suspected dengue cases aged above 18 yrs admitted in wards and ICU of M.S.Ramaiah group of hospitals, Bangalore from February 2008 to August 2009. Patients with the following complaints – fever, myalgia, arthralgia, headache, retro orbital pain, rashes whose serology showed evidence of dengue disease were included in the study. A detailed history and physical examination was done at the time of admission .Informed consent was taken. Routine baseline laboratory investigations like complete blood count, liver function tests, renal function tests, chest X ray in lateral decubitus position for evidence of pleural effusion, ultrasonography of abdomen and pelvis for evidence of ascites were done at the time of admission. A tourniquet test was done at admission and in patients with features of shock.

A Blood sample for serological evidence of dengue was collected at the time of admission, repeated after 3 or 5 days after admission in high degree of suspicion. Dengue antibodies were demonstrated by a rapid test-Immunochromatog-raphic assay for the rapid qualitative detection of IgM and IgG antibodies to dengue virus in human serum, plasma, or whole blood. This test device has 3 pre coated lines G (dengue IgG line), M (dengue IgM), C (Control line).All the 3 lines are not visible before applying the blood sample. If the C and M line is visible then the test is positive for IgM antibodies to dengue virus. If the C and G line are visible then the test is positive for IgG antibodies. If the C, G, and M line are visible then the test is positive for both IgG and IgM antibodies. Platelet counts and hematocrit values were recorded at the time of admission and repeated at intervals depending on the clinical course. Patients were followed up through the entire course of hospitalization until discharge or death. Patients were assigned in to different grades according to WHO classification see table 1 below. Increased vascular permeability or plasma leakage was documented by the presence of atleast one of the following:

1. A rise in the haematocrit equal to or greater than 20% above average for age, sex and population
2. A drop in the haematocrit equal to or greater than 20% of baseline following volume replacement therapy
3. Signs of plasma leakage like pleural effusion, ascites and hypoproteinemia

Table-1: WHO grading of dengue

Sl. No.	Grades	Symptoms/Signs	Lab Investigations
1.	Dengue fever (classical)	Fever with 2 or more of the following headache, myalgia, retro orbital pain, Arthralgia	Leucopenia, thrombocytopenia (> 1 lakh) No plasma loss
2.	I (DHF)	Above+ positive tourniquet test	Thrombocytopenia (< 1 lakh) Hematocrit > 20%
3.	II (DHF)	Above+ spontaneous bleeding	Above + plasma loss
4.	III (DSS)	Above+ circulatory failure (weak pulse, Hypotension, restlessness)	"
5.	IV (DSS)	Above+ Profound shock (No BP/PR)	"

Patients who fell in to grade II DHF and DSS were admitted to ICU for further management and observation. Patients whose platelet count was less than 50,000 were admitted to ICU for platelet transfusions. Patients needing fluid resuscitation and blood transfusions were also recorded.

Statistical analysis: Comparisons of continuous variables were performed using the Student *t* test. The x2 test was used to evaluate statistical differences in categorical variables between groups. All statistical analyses were performed using SPSS statistical package, version 16.0.0 (SPSS).

Results

A total of 3000 patients were admitted to hospital with symptoms consistent with dengue out of which 88 patients were found to be positive for dengue fever. 32 patients were admitted to ICU and rest to the wards. Among 88 patients, majority of patients had fever in 90.9%(n-78), followed by myalgia 37.5%(n-33), arthralgia 17%(n-15), rashes 13%(n-12), bleeding 11%(n-10), retrorbital pain in one patient. Positive tourniquet test was seen in 44 patients (50%). Hepatomegaly and Splenomegaly was seen in minority patients.

Out of 88 patients who were serologically positive for dengue, 25(28.4%) were IgM positive, 63(71.6%) were IgG and IgM positive. We categorized the patients according to range of platelet count, majority of patients had thrombocytopenia less than 50000. We also found that there was an inverse relationship between bleeding tendencies and platelet count.

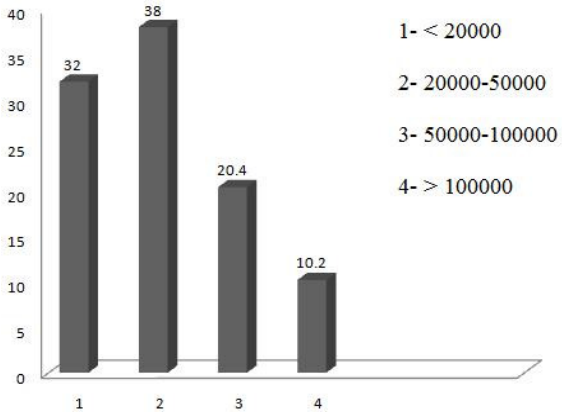

Figure-1: Bar diagram showing the percentage of patients with different Platelet count ranges

Bleeding manifestations were noted in 36 patients. 20 patients had petichiae, 6 had hemetemesis, melina in 6 patients and epistaxis in 1 patient. A combination of haemorrhagic manifestations was seen in 10 patients. None of the patients died due to bleeding manifestations.

Al Ameen Journal of Medical Sciences deeply mourned the demise of Nobel Laureate Prof. Sir. Andrew Huxley

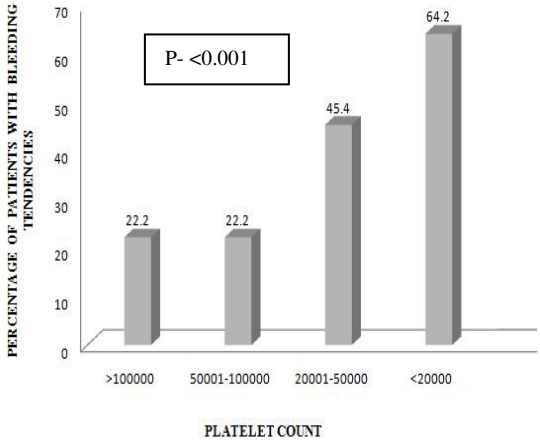

Figure-2: Bar diagram showing the percentage of bleeding tendencies in different ranges of platelet counts

Patients were categorized into different grades of dengue fever according to WHO classification. Majority of patients fell in to the classical dengue fever and grade 1 DHF, 9 patients with grade2 DHF, 6 patients with DSS and 2 patients among the DSS died.

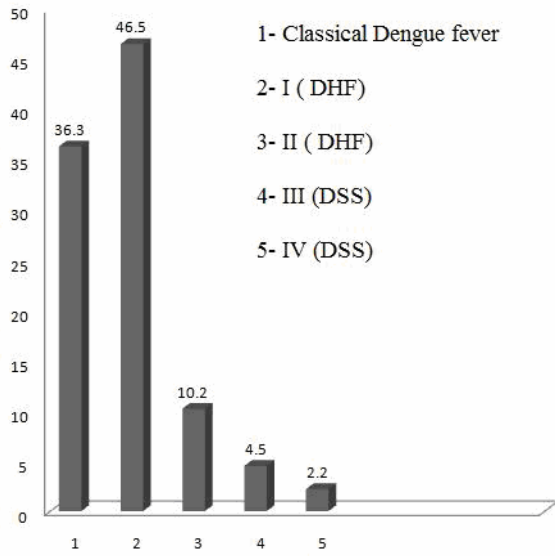

Figure-3: Bar diagram showing the percentage of patients in different WHO grades of dengue

In our study, as a marker of plasma leakage rise in haematocrit was seen in 10 patients (17.8%), evidence of pleural effusion in chest X ray in 15 patients (26.7%), ascites in 32 patients (65%) and hypoproteinemia in 9 patients (15%). Thrombocytopenia was found in 6 out of 32(3.1%) patients with classical dengue fever, 45 out of 56 (80.3%) patients

with DHF and all 6 patients with DSS. Plasma leakage markers were found in 2 patients with classical dengue fever, 48 patients with DHF and all 6 patients with DSS. We found that 41% patients with grade 1 DHF, 78% Patients with grade 2 DHF, all 6 patients in DSS required intensive care, fluid resuscitation and blood product transfusions

Table-2: Showing the management of patients in different WHO grades

	Observation	Icucare, Fluid Resuscitation, Blood Transfusion	Death
Dengue Fever	30(93%)	2(7%)	0
Grade 1 DHF	24(59%)	17(41%)	0
Grade 2 DHF	2(22.2%)	7(78%)	0
Grade 3 DSS	0	4(100%)	0
Grade 4 DSS	0	0	2(100%)

Mean hospital duration stay was found to be high in grade 2 DHF, DSS (mean -20 days) when compared to grade 1 DHF and classical dengue fever (mean – 6.8 days)

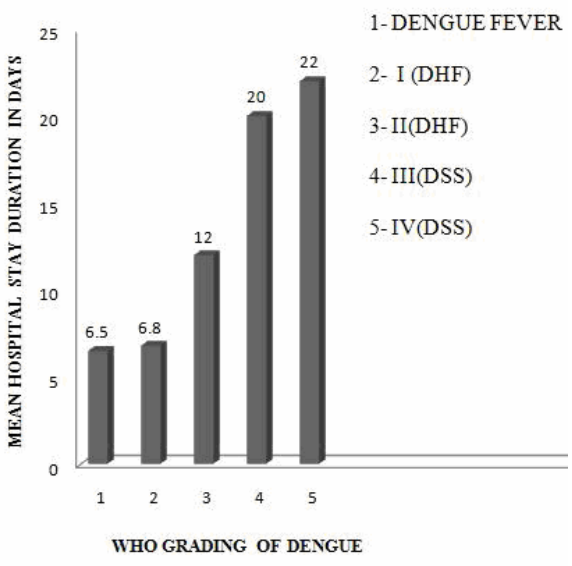

Figure-4: Bar Diagram Showing Mean Duration of Hospital Stay In Different WHO Grades of Dengue

Discussion

Epidemics of dengue have reported in India and many authors have applied WHO classification retrospectively to classify dengue cases [7]. In this study we have assessed the WHO criteria by applying them prospectively in adult patients diagnosed as dengue in a tertiary hospital. In our study, we assessed the WHO grading system for classification of dengue severity in adults. We classified the patients to their respective grades at the time of presentation, those patients who fell in to grades of DHF and DSS were admitted to ICU for intensive care and observation. Out of 88 patients who were Dengue positive, 32 were diagnosed to have Dengue fever (classical), 50 had DHF, and 6 had DSS. Majority of patients in DHF grades had thrombocytopenia and bleeding manifestations. In our study we were able to identify all patients according to the WHO grading. Many studies have shown that bleeding and thrombocytopenia are reliable indicators and prerequisites for subsequent development of shock syndrome [4,8]. We observed that thrombocytopenia was an important factor to differentiate dengue fever from DHF. The degree of thrombocytopenia was significantly more in grade 2 DHF followed by grade 1 DHF. Tourniquet test is an important diagnostic parameter as it is the only hemorrhagic manifestation in grade 1 DHF. Positive tourniquet test did not differ significantly between DF and DHF. It was not an effective variable to differentiate between the two entities. This finding is in conformity with observations of other workers [9-10].

As markers of plasma leakage, we assessed rise in haematocrit, hypoalbuminemia, pleural effusion and ascites individually. Clinical detection of pleural effusion and ascites is not reliable unless the volume of fluid is large [11]. Compared to chest radiograph, chest sonography has been proven to be highly efficient methods to detect small amounts of pleural fluid. Ascites which cannot be detected clinically can be easily diagnosed by ultrasonography [12-13]. In our study we have found ascites to be a significant marker for plasma leakage followed by pleural effusion when compared to other studies in which pleural effusion was significant [4].

Markers of plasma leakage had a significant difference between DF and DHF. Thrombocytopenia and increased vascular permeability i.e markers of plasma leakage are very useful in assessing and differentiating DF from DHF. Patients with these markers should be segregated and kept under close observation. WHO classification excludes severe dengue cases associated with unusual manifestations such as encephalopathy, encephalitis, hepatic failure, cardiomyopathy, acute respiratory distress syndrome. It is possible that these manifestations are complications from shock and might be prevented by early treatment [10, 14].

Out of the dengue confirmed cases, 17% of grade 1 DHF, 41% of grade 2 DHF, all patients with DSS needed intervention. Thus DHF as defined by the WHO criteria correlated strongly with the need for intervention [4]. Mean duration of hospital stay was more in grade 2 DHF and DSS [15]. Many studies have failed to show the importance of WHO grading system in estimating the severity of dengue [16-19]. Possible explanation for this would be lack of data on serial platelet counts and hematocrit values. Estimation of markers of plasma leakage by using the radiological techniques would not have been done in all patients [20]. In our study we diagnosed dengue disease by determining the serological evidence of dengue antibodies due to unavailability of nucleic acid probes. Due to small sample size we could not effectively study DSS patients. In a tertiary care centre where repeat platelet count and hematocrit values can be performed along with assessing plasma leakage by radiography and ultrasound, WHO grading system has been found to be very useful in estimating severity of dengue fever.

Conclusion

WHO criteria for grading of dengue can identify patients who need aggressive management and observation. Thrombocytopenia and markers of plasma leakage are key determinants in differentiating DHF from DF. Though Dengue cases are on the rise; proper diagnosis, statergical approach in segregating patients according to WHO classification and aggressive treatment can decrease the progression of the disease, hospital stay and mortality rates.

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References

1. Halstead SB. Dengue. *Lancet* 2007; 370: 1644-1652.
2. World Health Organization, Geneva. Dengue hemorrhagic fever: Diagnosis, treatment, prevention and control. 2nd edition 1997.
3. Rocha J, Idiaquez W, Alonso RE, Delgado MA, Campo LA, Acevedo F, Gonzalez A, Amador JJ, Balmaseda A: Clinical, Epidemiologic, And Virologic Features Of Dengue In The 1998 Epidemic In Nicaragua. *Am J Trop Med Hyg* 2000; 63:5-11.
4. Anon Srikiatkhachorn, Robert V. Gibbons, Sharone Green, Daniel H. Libraty**.** Dengue Hemorrhagic Fever: The Sensitivity and Specificity of the World Health Organization Definition for Identification of Severe Cases of Dengue in Thailand, 1994–2005. *Clinical Infectious Diseases.* 2010; 50:1135–1143.
5. Kalayanarooj S, Vaughn DW, Nimmannitya S, Green S, Suntayakorn S, Kunentrasai N, Viramitrachai W, Ratanachu-Eke S, Kiatpolpoj S, Innis BL, Rothman AL, Nisalak A, Ennis FA: Early Clinical And Laboratory Indicators Of Acute Dengue Illness. *J Infect Dis* 1997; 176: 313-321.
6. Murgue B, Deparis X, Chungue E, Cassar O, Roche C: Dengue: An Evaluation Of Dengue Severity In French Polynesia Based On An Analysis Of 403 Laboratory Confirmed Cases. *Trop Med Int Health* 1999; 4:765-773.
7. Kabra SK, Jain Y, Pandey RM, Madhulika, Singhal T, Tripathi P, Broor S, Seth P, Seth V. Dengue haemorrhagic fever in children in the 1996 Delhi epidemic. *Trans R Soc Trop Med Hyg* 1999; 93: 294-298.
8. Libraty DH, Endy TP, Houng HS, Et Al. Differing Influences Of Virus Burden And Immune Activation On Disease Severity In Secondary Dengue- 3 Virus Infections. *J Infect Dis* 2002; 185(9):1213–1221.
9. Phuong CX, Nhan NT, Wills B, Et Al. Evaluation of The World Health Organization Standard Tourniquet Test In The Diagnosis Of Dengue Infection In Vietnam. *Trop Med Int Health* 2002; 7:125-132.
10. Bandyopadhyay S, Lum LCS, Kroeger A: Classifying dengue: a review of the difficulties in using the WHO case classification of dengue hemorrhagic fever. *Trop Med International Health.* 2006;11:1238-1255.
11. Balasubramanian S, Janakiraman L, Kumar SS, Muralinath S, Shivbalan S. A Reappraisal of the Criteria to Diagnose Plasma Leakage in Dengue

Hemorrhagic Fever. *Indian Pediatr* 2006; 43: 334-339.
12. Srikiatkhachorn A, Krautrachue A, Ratanaprakarn W, Et Al. Natural History Of Plasma Leakage In Dengue Hemorrhagic Fever: A Serial Ultrasonographic Study. *Pediatr Infect Dis J* 2007; 26(4):283-290.
13. Venkata Sai PM, Dev B, Krishnan R: Role of Ultrasound in Dengue Fever. *Br J Radiol* 2005; 78:416-418.
14. Deen JL, Harris E, Wills B, Balmaseda A, Hammond S N, Rocha C, Dung NM, Hung NT, Hien TT, Farrar JJ. The WHO Dengue Classification and Case Definitions: Time for a Reassessment. *Lancet* 2006; 368: 170-173.
15. Nasim A. Khan, Esam I. Azhar, Suzan El-Fiky, Hosam H. Madani. Clinical Profile and Outcome of Hospitalized Patients during First Outbreak of Dengue in Makkah, Saudi Arabia. *Acta Tropica* 2008;105: 39-44.
16. Gupta P, Khare V, Tripathi S, Nag VL. Assessment of World Health Organization definition of dengue hemorrhagic fever in North India. *J Infect Dev Ctries.* 2010; 4(3):150-155.
17. Cao Xuan Thanh Phuong, Ngo Thi Nhan, Rachel Kneen, Pham Thi Thu Thuy. Clinical Diagnosis and Assessment of Severity of Confirmed Dengue Infections in Vietnamese Children: Is The world health organization classification system helpful?. *Am J Trop Med Hyg*. 2004; 70(2):172-179.
18. Tatty E Setiati, Albert TA Mairuhu, Penelopie Koraka, Dengue Disease Severity in Indonesian Children. An Evaluation of the world health organization classification system. *BMC Infectious Diseases.* 2007;7: 22.
19. Angel Balmaseda, Samantha Nadia Hammond, Maria Angeles Pérez, Ricardo Cuadra. Assessment of the World Health Organization Scheme for Classification of Dengue Severity in Nicaragua. *Am J Trop Med Hyg.* 2005; 73(6):1059-1062.
20. Rigau-Perez JG, Bonilla GL. An evaluation of modified case definitions for the detection of dengue hemorrhagic fever. Puerto Rico Association of Epidemiologists. *P R Health Sci J.* 1994; 18: 347-352.

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