Original Research Article

Clinical profile of dengue fever and utility of WHO classification in the assessment of its severity

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Abstract

Background: Over the past few years, dengue has emerged as a serious public health concern especially in India. It is estimated that around 2.5 billion people, in urban areas of tropical countries, are at a risk of developing dengue infection. DF presents a broad clinical spectrum, ranging from a benign self-limiting infection (85–90% of cases) to the most severe forms (approximately 10–15% of cases) such as dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF). **Aims and objectives:** To study the clinical profile of Dengue Fever and utility of Who Classification in the assessment of its severity. **Materials and method**: The study included all diagnosed dengue on Dengue Card Test of 12 years or older admitted to medical wards from January 2017 to December 2018. Study was performed on 100 patients admitted in the study institute. A prestructured proforma was used to collect the information of patients. Detail history and clinical examination was done and the findings were recorded. Patients were classified as dengue fever, dengue hemorrhagic fever or dengue shock syndrome according to WHO guidelines and laboratory diagnosis of dengue is established by demonstration of specific NS1/IgM/IgG antibodies to dengue in serum (Dengue Card Test). **Results:** Majority of the patients belonged to the age group 20-29 years age group (38%) followed by 13-19 years (28%) and then 30-39 years age group (18%). Males were affected more (62%). Most common positive serology test which was NS1 in 61%, IgM was positive in 29% patients and 10% patients had mixed positivity (NS1/IgM ± IgG). Fever was the most common clinical feature (96%) followed by headache 82%, myalgia 78%, backache 52%, nausea and vomiting 36%, arthralgia 25%, abdominal pain 21%. Dehydration was the most common clinical sign (41%) followed by ascites 29%. **Conclusion:** Thus we conclude that Majority of the patients suffering from dengue were young male. Fever, headache, myalgia, backache, rash along with thrombocytopenia, leukopenia, elevated liver enzymes with signs of plasma cell leakage should prompt a clinician on the possibility of dengue fever. Statistically significant association was observed association was observed platelet count and HCT with sever type of dengue. Mortality of dengue was observed in Severe Dengue cases as compared to Dengue without Warning Signs and Dengue with Warning Signs. Thus WHO classification helps to predict the outcome of Dengue.

Key Word: Dengue Fever, clinical profile, Dengue with warning Signs.

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INTRODUCTION

Dengue fever is an ancient disease. The earliest record found to date is in a Chinese encyclopaedia of disease, symptoms and remedies, edited in 610 A.D and again in 992 A.D.[1] Globally some 2.5 billion people – two fifths of the world's population in tropical and subtropical countries – are at risk. Epidemics of dengue are increasing in frequency. During epidemics, infection rates among those who have not been previously exposed to the virus are often 40% to 50% but can also reach 80% to 90%.[2] The number of dengue cases reported annually to WHO has increased from 0.4 to 1.3 million in the decade

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1996–2005, reaching 2.2 million in 2010 and 3.2 million in 2015.[3] Over the past few years, dengue has emerged as a serious public health concern especially in India. It is estimated that around 2.5 billion people, in urban areas of tropical countries, are at a risk of developing dengue infection.[4] Most of the cases of Dengue Fever are being reported from Southeast Asian and the western Pacific regions.[5] The emergence of dengue in India has gone into epidemic proportions and dengue outbreaks are frequently engulfing different parts of the country in both urban and rural populations. Dengue infections may vary from flu-like self-limiting illness to life-threatening dengue hemorrhagic fever. In recent years some new presentations of dengue have been reported. Many atypical presentations have led to delayed suspicion and diagnosis of dengue. Some presentations have been completely different from any of the features of dengue described until now in literature.[6] DF presents a broad clinical spectrum, ranging from a benign self-limiting infection (85–90% of cases) to the most severe forms (approximately 10–15% of cases) such as dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF). Currently, the most severe cases do not always fit the four strict criteria (fever, hemorrhage, thrombocytopenia, and plasma leakage) of the 1997 WHO disease classification into DF or DHF/DSS. The WHO in 2009 improved the dengue case classification based on clinical severity, and this has been included in the WHO 2009 guidelines and therefore it would be better to use this as a reference. Although the 2009 WHO classification was designed primarily for use as a clinical tool, it also enables cases of SD to be differentiated into three specific subcategories; Severe vascular leakage, severe bleeding, and severe organ dysfunction, that could allow clinicians to evaluate the severe disease progression or pathogenesis in a more focused way, providing a new framework for scientific research. It is known that host and viral factors play a role in the development of more severe dengue cases.[7]

AMIS AND OBJECTIVES

To study the clinical profile of Dengue Fever and utility of Who Classification in the assessment of its severity.

MATERIALS AND METHOD

The present study was conducted in the department of Medicine of the tertiary care institute with the aim to study the clinical profile of Dengue Fever and also assess the utility of Who Classification in the assessment of its severity. The study included all diagnosed dengue on Dengue Card Test of 12 years or older admitted to medical wards from January 2017 to December 2018. Study was performed on 100 patients admitted in the study institute. The patients not willing to participate in study, with age less than 12 years and Fever diagnosed with other than dengue were excluded from the study. A prestructured proforma was used to collect the information of patients. Detail history and clinical examination was done and the findings were recorded. The investigations were done to diagnose and to know severity, etiology and complications of dengue fever in these patients. Hematological profiles, dengue card test, PSMP and biochemical investigations were done at the time of admission and were followed by daily (or bi-daily) investigations as required until discharge. Patients were classified as dengue fever, dengue hemorrhagic fever or dengue shock syndrome according to WHO guidelines[8] and laboratory diagnosis of dengue is established by demonstration of specific NS1/IgM/IgG antibodies to dengue in serum (Dengue Card Test).The collected information was entered in Microsoft excel. The statistical analyses performed using the Statistical Package for Social Science (SPSS) version 21 for Windows. The p-value of < 0.05 was considered statistically significant.

RESULTS

Table 1: Distribution according to type of serology among patients

Type Of Serology	Number Of Patients	Percentage
NS1	61	61%
IgM	29	29%
MIXED (NS1/IgM+IgG)	10	10%
TOTAL	100	100%

It was observed that that most common type of serology test which was positive was NS1 (61%), IgM was positive in 29% patients and 10% patients had mixed positivity (NS1/IgM ± IgG).

Table 2: Age and sex wise distribution of patients

Age (In Years)	Male	Female	Total	Percentage
13-19	18	10	28	28%
20-29	23	15	38	38%
30-39	12	6	18	18%

40-49	3	3	6	6%
50-60	4	3	7	7%
>60	2	1	3	3%
TOTAL	62	38	100	100%

In present study majority of the patients belonged to the age group 20-29 years of age (38%) followed by 13-19 years (28%) and then 30-39 years age group (18%). It was seen that males (62%) were more affected than females (38%).

Table 3: Distribution of the patient according to clinical symptoms and clinical signs

		Number of Patients	Percentage
Symptoms	Fever	96	96%
	Headache	82	82%
	Myalgia	78	78%
	Backache	52	52%
	Retro Orbital Pain	9	9%
	Arthralgia	25	25%
	Rash	16	16%
	Conjuctival Suffusion	5	5%
	Cough	9	9%
	Breathlessness	16	16%
	Hemorrhagic Manifestations	15	15%
	Nausea and Vomiting	36	36%
	Abdominal Pain	21	21%
	Increased Frequency of Stool	7	7%
	Altered Sensorium/ Neurological Manifestations	3	3%
	Siezures	4	4%
Signs	Dehydration	41	41%
	Pallor	10	10%
	Jaundice	7	7%
	Bradycardia	4	4%
	Hypotension	12	12%
	Hepatomegaly	9	9%
	Splenomegaly	14	14%
	Pleural Effusion	15	15%
	Ascites	29	29%
	Tourniquet Test Positive	20	20%
	Neck Rigidity And Altered Sensorium	3	3%

It was observed that dengue fever patients present with varying manifestations. Fever was the most common clinical feature with which patients present to the hospital. Fever is observed in 96% patients followed by headache 82%, myalgia 78%, backache 52%, nausea and vomiting 36%, arthralgia 25%, abdominal pain 21% rash 16%, breathlessness 16%, hemorrhagic manifestations 15%, retro- orbital pain 9%, cough 9%, increased frequency of stool 7%, conjunctival suffusion 5%, seizures 4% and altered sensorium in 3% of patients. In the present study dengue fever patients had varying signs. Dehydration was the most common clinical sign (41%) followed by ascites 29%, tourniquet test 20%, pleural effusion 15%, splenomegaly 14%, hypotension 12%, pallor 10%, hepatomegaly 9%, jaundice 7%, bradycardia 4%, neck rigidity and altered sensorium in 3% of patients.

TABLE 4: Distribution of patients according to site of bleeding and complication

		Number of Patients	Percentage
Site Of Bleeding	Petechiae/Purpura/Echymosis	3	3%
	Epistaxis	4	4%
	Gums	1	1%
	Melena	2	2%
	Hematuria	3	3%
	Menorrhagia	1	1%
	Hematemesis	1	1%
Complications	Hepatic Dysfunction	21	21%
	Renal Dysfunction	18	18%

	Multiorgan Failure	13	13%
	Myocarditis	4	4%
	Myositis	1	1%
	ARDS	4	4%
	Encephalopathy	3	3%
	Hypotension	12	12%

Hemorrhagic manifestations of varying degree and from different sites were observed in 13% of the patients. Epistaxis was the commonest bleeding manifestation in 4% of the patients, followed by hematuria 3%, skin 3%, melena 2%, gums 1%, menorrhagia 1%, hematemesis in 1% of patients. In present study, hepatic dysfunction was the most common complication in 21% of the patients followed by renal dysfunction 18%, multiorgan failure 13%, hypotension 12%, myocarditis 4%, ARDS 4%, encephalopathy 3%, myopathy in only 1% of the patient.

Table 5: distribution of dengue cases according to WHO case classification

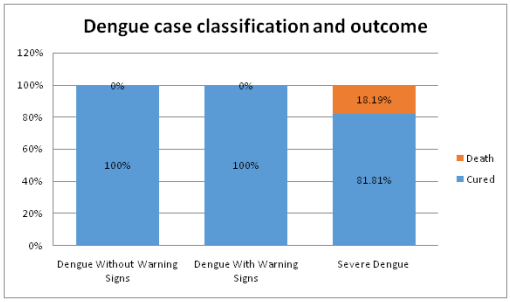
Count	Values	Number Of Patients	Dengue Without Warning Signs	Dengue With Warning Signs	Severe Dengue	P value
Platelet ×10⁹/L	<20	21	3	13	5	**p<0.001**
	20 - 50	28	4	21	3	
	51 - 100	38	27	8	3	
	>100	13	13	0	0	
WBC (X 109/L)	<4	44	16	21	7	**p>0.05**
	>4	56	31	21	4	
HCT (%)	<35	29	17	12	0	**p<0.001**
	35 – 45	40	25	13	2	
	>45	31	5	17	9	
Total		100	47	42	11	

In the present study, 47% patients were classified into dengue without warning signs, 42% patients were classified into dengue with warning signs and 11% were classified into severe dengue. It was observed that, 21% patients had platelets count less than 20000, out of which 3% patients were diagnosed with dengue without warning sign, 13% patients were diagnosed with dengue with warning signs and 5% patients were diagnosed with severe dengue. The difference observed was not statistically significant (Chi-square 47.17; df-6; $p<0.001$; highly significant). It was observed that 44% patients had WBC count less than 4000, out of which 16% patients were diagnosed with dengue without warning sign, 21% patients were diagnosed with dengue with warning signs and 7% patients were diagnosed with severe dengue. And the difference observed was not statistically significant (Chi-square 4.22; df-2; $p>0.05$; not significant) In the present study, 29% patients had HCT less than 35%, out of which 17% patients were diagnosed with dengue without warning sign, 12% patients were diagnosed with dengue with warning signs. 40% patients had HCT count in between 35% to 45%, out of which 25% patients were diagnosed with dengue without warning sign, 13% patients were diagnosed with dengue with warning signs and 2% patients were diagnosed with severe dengue. 31% patients had HCT count more than 45%, out of which 5% patients were diagnosed with dengue without warning sign, 17% patients were diagnosed with dengue with warning signs and 9% patients were diagnosed with severe dengue. And the difference observed was statistically significant (Chi-square 24.90; df-4; $p<0.001$; highly significant).

Table 6: Dengue case classification to assess its severity and outcome

Dengue Case Classification	Cured	Death	Total	Percentage Of Cured Patients
Dengue Without Warning Signs	47	0	47	100%
Dengue With Warning Signs	42	0	42	100%
Severe Dengue	9	2	11	81.81%

In the present study, 47 patients were classified into dengue without warning signs of which all cured. 42 patients were classified into dengue with warning signs of which all cured. 11 were classified into severe dengue of which 2 patients died and 9 patients cured. Thus 81.81% patients were cured in severe dengue group.



DISCUSSION

The emergence of dengue in India has gone into epidemic proportions and dengue outbreaks are frequently engulfing different parts of the country in both urban and rural populations. Dengue infections may vary from flu-like self-limiting illness to life-threatening dengue hemorrhagic fever. In recent years some new presentations of dengue have been reported. Many atypical presentations have led to delayed suspicion and diagnosis of dengue. Some presentations have been completely different from any of the features of dengue described until now in literature. The WHO in 2009 improved the dengue case classification based on clinical severity, and this has been included in the WHO 2009 guidelines and therefore it would be better to use this as a reference. We observed in present study that most common type of serology test which was positive was NS1 in 61% while IgM was positive in 29% patients and 10% patients had mixed positivity (NS1/IgM ± IgG). This was corresponding with other studies by Rabbani MU *et al*[9], Tejaswi CN *et al*[10], Chhotala YH *et al*[11]. In Krishnamurthy V *et al*[12] NS1 was positive in 39.7% followed by mixed infection (35.6%) which was higher than that reported in the present study and IgM (24.7%). In the present study, majority of the patients belonged to the age group of 20-29 years age group (38%) followed by 13-19 years (28%) and then 30-39 years age group (18%). This was corresponding with other studies by Sreenivasulu T *et al*[13], Shah V *et al*[14], Laul A *et al*[15], Chhotala YH *et al*[11]. In the present study males were more affected than females. Males were affected in 62% while females are affected in 38% with Male to female ratio was 1.6:1. This was corresponding to the other studies done by Rabbani MU *et al*[9], Deepa L *et al*[16], Sreenivasulu T *et al*[13], Morlawar R *et al*[17], Chhotala YH *et al*[11]. It was observed that Fever (96%) was the most common clinical symptom. In the study conducted by Tewari K *et al*[18], Tejaswi CN *et al*[10], Laul A *et al*[15], Deshwal R *et al*[19], Ali M *et al*[20], Lima FR *et al*[21] fever was most common symptom which was present in 99.8%, 90.3%, 100%, 100%, 100% and 98.3% respectively. In present study, headache (82%) was the second most clinical symptom, which was correlated with the study done by Tejaswi CN *et al*[10] (71.9%), Laul A *et al*[15] (87%), Deshwal R *et al*[19] (94.8%). It was observed that dehydration was the most common clinical sign with which patients presented to the hospital. Dehydration was observed in 41% patients followed by ascites 29%, tourniquet test 20%, pleural effusion 15%, splenomegaly 14%, hypotension 12%, pallor 10%, hepatomegaly 9%, jaundice 7%, bradycardia 4%, neck rigidity and altered sensorium in 3% of patients. In the study conducted by Chhotala YH *et al*[11] and Spoorti *et al* (2015)[22] also observed dehydration was the most common presenting sign in (61%) and (38%) respectively. In contrast to present study Sreenivasulu T *et al*[13] observed hepatomegaly (56%) was the most common presenting sign. Hemorrhagic manifestations of varying degree and from different sites were observed in 13% of the patients. Epistaxis was the commonest bleeding manifestation in 4% of the patients, followed by hematuria 3%, skin 3%, melena 2%, gums 1%, menorrhagia 1%, hematemesis in 1% of patients. In contrast with present study, petechiae, purpura and ecchymosis were the most common bleeding manifestation in studies conducted by Tewari *et al*[18] (4.5%), Jahnavi K *et al*[23] (31%), Sreenivasulu T *et al*[13] (66%), Lima FR *et al*[21] (51.61%). Gum bleeding (16%) was the most common bleeding observed in study conducted by Deepa L *et al*[16]. In the present study, hepatic dysfunction was the most common complication in 21% of the patients followed by renal dysfunction 18%, multiorgan failure 13%, hypotension 12%, myocarditis 4%, ARDS 4%, encephalopathy 3%, myopathy in only 1% of the patient. Similarly, hepatic dysfunction was found most common complication in many other studies conducted by Jahnavi K *et al*[23] (17%), Tejaswi CN *et al*[10] (4.3%), Mohan Kashinkunti *et al*[24] (34%). In the present study, 47% patients were classified into dengue without warning signs, 42% patients were classified into dengue with warning signs and 11% were classified into severe dengue. It was observed that 21% patients had platelets count less than 20000, out of which 16% patients were diagnosed with dengue with and without warning signs, 5% patients were diagnosed with severe dengue. 28% patients had platelets count in between 20000 and 50000, out of which (25%) patients were diagnosed with dengue with and without warning signs, and (3%) patients were diagnosed with severe

dengue. Thus maximum number of severe dengue cases were classified under platelets less than 20000. Similar findings were seen in studies done by Jayaratne SD *et al*[25] and Fernando S *et al*[26]. It was seen that 44% patients had WBC count less than 4000, out of which 37% patients were diagnosed with and without warning signs, and 7% patients were diagnosed with severe dengue. Maximum number of severe dengue cases were classified under WBC count less than 4000. Similar findings were seen in studies done by Jayaratne SD *et al*[25]. Studies by Shah V *et al*[14], Krishnamurthy *et al*[12], Deshwal R *et al*[19], Spoorti *et al*[22] showed leukopenia in 15.2%, 32,9%, 20.1%, and 34.1% respectively and this was in comparable with the present study. In the present study, 31% patients had >45% HCT and 69% patients had <45% HCT. Similar findings were seen in studies conducted by Shah V *et al*[14], Krishnamurthy V *et al*[12], Deshwal R*et al*[19], Spoorti *et al*[22]. In the present study, 47% patients were classified into dengue without warning signs of which all cured. 42% patients were classified into dengue with warning signs of which all cured. 11% were classified into severe dengue of which 2% patients died and 9% patients cured. 81.81% patients were cured in severe dengue group. In study done by Tewari K *et al*[18], 85.8% patients were classified into dengue without warning signs of which all cured. 11% patients were classified in to dengue with warning signs of which all cured. 3.2% patients were classified into severe dengue of which 1% patients died. In study done by Lima FR *et al*[21], 24.86% patients were classified into dengue without warning signs of which all cured. 59.11% patients were classified in to dengue with warning signs of which all cured. 16.02% patients were classified into severe dengue of which 1.1% patients died. In study done by Pozo Aguilar *et al*[27], 36.2% patients were classified into dengue without warning signs of which all cured. 43.6% patients were classified in to dengue with warning signs of which all cured. 20.2% patients were classified into severe dengue of which 1.8% patients died. Similar to our study, in studies done by Tewari K *et al*[18], Lima FR *et al* [21], Pozo Aguilar *et al*[27] all patients were cured in dengue with/without warning signs. All death occurred in severe dengue group. Similar to our study, maximum patients were classified under dengue without warning signs in the study done by Tewari K *et al*[18]. In contrast to our study, maximum patients were classified under dengue with warning signs in the studies done by Lima FR *et al*[21], Pozo Aguilar *et al*[27].

CONCLUSION

Thus we conclude that Majority of the patients suffering from dengue were young male. Fever, headache, myalgia, backache, rash along with thrombocytopenia, leukopenia, elevated liver enzymes with signs of plasma cell leakage should prompt a clinician on the possibility of dengue fever. Statistically significant association was observed association was observed platelet count and HCT with sever type of dengue. Mortality of dengue was observed in Severe Dengue cases as compared to Dengue without Warning Signs and Dengue with Warning Signs. Thus WHO classification helps to predict the outcome of Dengue.

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