

# A study of clinical, radio-imaging and biochemical profile of Dengue patients in relation with outcome in central Indian hospital

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## Abstract

**Objective:** Dengue fever is most important arbo-viral disease in India and other tropical and subtropical countries with increasing prevalence in recent years with significant morbidity and mortality. This study was aimed to evaluate clinical & hematological features and outcome in central Indian adult population. **Methods:** A cross-sectional observational study undertaken among adult patients admitted in a teaching hospital. 105 patients were analyzed. All patients who were IgM-ELISA positive irrespective of their card test status were included in study. Clinical features and hematological, biochemical & radiological findings are noted. **Results:** Total 105 dengue patients were included 22 were of Dengue fever without warning signs (DFWOWS), 65 in Dengue fever with warning signs (DFWWS) and 18 were Severe Dengue (SD) group. Male: female ratio was 1.14:1. Most common age group affected was 21-30 Yrs. Most of cases reported in month of September and October. Clinical features noted most common was fever (96.2%); myalgia (57.1%), headache (40%), vomiting (24%), retro-orbital pain (26.6%), abdominal pain (26.6%), petechiae (34.2%), rash (41.9%), and positive tourniquet test (56.1%). Major bleeding (25.7%), among them most common was gut bleeding. Complications were noted in SD group. Blood transfusion required in 43.8% cases. Coagulopathy was noted in 72.2% cases of DSS. No mortality was noted in our study. **Conclusion:** Dengue is increased with increasing urbanization & poor sanitation. Dengue has wide spectrum of clinical and hematological presentation. Significant morbidity occurs in DHF and DSS. It is a low mortality illness if prompt diagnosis and proper fluid management instituted in DHF and DSS. Platelet transfusion has a little role in dengue management.

**Key words:** Dengue profile, IgM Elisa,

## Introduction

Dengue is the most rapidly spreading mosquito-borne viral disease in the world. Dengue is an acute viral infection with potential fatal complications. Dengue is the most common mosquito borne, endemo- epidemic arbo-viral infection in many tropical and sub-tropical regions of the world [1]. Dengue is one disease entity with different clinical presentations and often with unpredictable clinical evolution and outcome [2].

Dengue causes a wide spectrum of illness from mild asymptomatic illness to severe fatal dengue hemorrhagic fever and dengue shock syndrome [3]. According to National vector control program, total cases in India in 2013 were 75808 out of which 193 died, in 2014 it was 40571 and 137 died, in 2015 total

99913 cases reported and 220 deaths, July 2016 total 36110 total cases and 70 deaths reported. In Madhya Pradesh in year-2013, 1255 cases out of which 9 died, in year-2014, 2131 out of which 13 died, in year-2015 total 2108 cases out of which 8 died and till July-2016, 354 cases reported out of which 1 died [4].

In present study there is an attempt to collect data of adult population coming to a central Indian tertiary care hospital with dengue fever and compilation of various clinical manifestations and laboratory findings. Early prediction is very important to avoid unnecessary hospitalization to those with non severe dengue that are predicted to progress into severe dengue.

Awareness of clinical presentations and complication may be helpful in arriving early diagnosis and avoid morbidity and mortality.

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## Material and Methods

**Place and type of study:** This study was carried out in Department of Medicine, Gandhi Medical College and associated 1200 bedded Hamidia Hospital, Bhopal from March 2015 to July 2016. This study covered the population of Bhopal and its neighboring districts. This is a cross-sectional observational study and the informed consent was being taken from patients along with proper approval taken from ethical committee.

**Method and sample collection:** After detailed history and clinical examination, all the clinically suspected cases of dengue infection aged 12 years and above admitted in medicine wards and ICU were screened and IgMELISA positive confirmed cases (irrespective of antigen positivity) were included in this study. Patients with coexisting other febrile illness like malaria, leptospirosis, chikengunya, typhoid, pneumonia were excluded from study. Patients were categorized into classical dengue fever, dengue hemorrhagic fever and dengue shock syndrome according to WHO guidelines [4,5] was done for all the cases. Data collection of all study subjects was done in structured data collection forms.

**Laboratory measurements:** All the cases were subjected to Dengue IgM was done using the IgM capture ELISA kit, NS1 antigen (if available), CBC, Hb, TLC, DLC, platelet count, hematocrit by automated coulter counter method and peripheral smear for mp, Liver function test, ALT, AST by using Autozyme GPT and Autozyme GOT reagent respectively, Alkaline phosphatase by kinetic method.

Serum albumin by the BCG Dye binding method, total serum bilirubin by colorimetric method, Renal function test- urea, creatinine. PT and INR were done to assess the coagulation profile. Coagulopathy was defined as

INR > 1.5 or PT > 15 sec, widal test- by tube method, Chest X-ray was carried out to check for pleural effusion and features of ARDS and other lung pathology, Ultrasonography of abdomen was done to assess liver size and ascites, gall bladder wall thickness and splenomegaly.

Blood counts were monitored periodically during hospital stay other possible differential diagnoses were excluded using available appropriate laboratory tests and clinical findings. Ethical committee clearance was taken before commencement of study and informed consent was taken from each participants.

**Inclusion criteria:** Serologically confirmed (IGM positive alone or both IGM and IgG by ELISA) dengue fever patients admitted in Hamidia Hospital, Bhopal. All cases of the adult age group (>12 yrs) will be included irrespective of sex. Informed consent from all the patients will be taken before undergoing the study.

**Exclusion criteria** Dengue patients with other confirmed coexisting febrile illness (malaria, enteric fever, leptospirosis, RTI, UTI, CNS infections), Age less than 12 years. Patients with card test positive but not confirmed by IgM ELISA were excluded.

**Statistical analysis:** Continuous variables like age, laboratory parameters like serum bilirubin, ALT, AST, ALP, urea, creatinine were presented as mean  $\pm$  standard deviation. Categorical variables like sex, residence, symptoms, and Clinical signs were expressed in actual numbers and percentages. Categorical variables were compared across three groups by performing chi-square test. Pearson's chi-square test was used to compare outcomes with mortality. P value < 0.05 was considered as statistical significance.

## Results

**Table-1: Distribution of study population according to WHO classification [5,6].**

Who Classification	No. of cases	Percentage
Dengue fever without warning signs (DFWOWS)	22	20.95 %
Dengue fever with warning signs (DFWWS)	65	61.9 %
Severe dengue (SD)	18	17.14 %
Total	105	100%

Total 105 dengue patients were included, 22 were of DFWOWS, 65 in DFWWS and 18 were SD group. DFWOWS (dengue fever without warning signs). Most common age group affected was 21-30 Yrs in 42.8 % cases. 60.5% cases were from urban area. In our study population seasonal variability in the occurrence of cases were noted. 68.5% cases reported in month of September and October. Post monsoon season was with more cases.

**Table-2: Distribution of Clinical features in study population.**

Symptom/ SIGNS	DFWOWS N=22		DFWWS N=65		SD N=18		TOTAL N=105	
	Cases	%	Cases	%	Cases	%	Cases	%
Fever	22	100	62	95.3	17	94.4	101	96.2
Body ache	11	50	40	61.54	09	50	60	57.14
Major Bleeding	00	00	18	27.69	09	50	27	25.71
Petechie	00	00	33	50.77	07	38.89	36	34.28
Abdominal pain	03	13.63	10	15.38	15	83.33	28	26.66
Headache	05	22.72	21	32.31	16	88.89	42	40
Retro-orbital pain	04	18.18	11	16.92	13	72.22	28	26.66
Vomiting	02	9.09	09	13.84	13	72.22	24	22.85
Edema	00	00	16	24.61	09	50	25	23.81
Rash	00	00	37	56.92	07	38.89	44	41.90
Jaundice	00	00	03	4.61	06	33.33	09	8.57
Hepatic tenderness	06	27.27	18	27.69	08	44.44	32	30.47
Tourniquet test Positive	13	59.09	35	53.85	11	61.11	59	56.19
Ascites	01	4.54	02	3.07	05	27.78	07	6.66
Pleural effusion	01	4.54	06	9.23	08	44.44	15	14.28
Shock	00	00	00	00	17	94.44	17	16.19
Renal failure	00	00	03	4.61	17	94.44	20	19.04

Fever was most common symptom presented in 96.2% cases. Headache was more common in severe dengue group as compared to dengue fever with DFWOWS and DFWWS. Edema present in 40% cases out of which it was more common in dengue fever group. Vomiting 22.85% and abdominal pain 26.66% found in total cases, this was more prevalent in severe dengue group as compared to other groups. Rash was more common in subjects of DFWWS 56.92% cases followed by subjects of SD group. Patechie observed in 50.77% patients of DFWWS and 38.89% cases of severe dengue. Major Bleeding manifestations were more common in SD 50% as compared to DFWWS 18%. Ascites, renal failure, pleural effusion and shock were noted more commonly in severe dengue group. All complications ARDS, respiratory failure, encephalopathy, myocarditis were noted in severe dengue group. Out of total 105 cases 27 (25.71%) had major bleeding manifestations. Out of which Gut bleed 51.85% and gum bleeding 40.74% was the commonest types.

**Table-3: Distribution of patients according to dengue serology**

Dengue serology	DFWOWS N=22		DFWWS N= 65		SD N=18		Total N=105	
	Cases	%	Cases	%	Cases	%	Cases	%
IgM ELISA	22	100	65	100	18	100	105	100
NS1+	8	36.36	20	30.77	04	22.22	32	30.47
Both	8	36.36	20	30.77	04	22.22	32	30.47

All patients were IgM ELISA positive out of which 32(30.47%) cases had NS1 antigen positivity. NS1 antigen was not available in 37 patients. Only those who were having kit test considered here. NS1 Ag was negative in 34 cases who were IgM Elisa positive.

**Table-4: Mean hemoglobin, TLC, hematocrit & Platelet count**

Parameter	DFWOWS (Mean ± SD)	DFWWS (Mean ± SD)	SD (Mean ± SD)	TOTAL (Mean ± SD)
Hemoglobin (gm/dl)	11.70±2.20	11.71±1.73	11.42±1.84	11.61±1.84
Hematocrit (%)	40.81±3.86	39.86±5.56	41.5±4.44	40.72±5.06
Platelet count(/cumm)	72281±27633	49446±24012	35055±18235	51286±49930
TLC (/cumm)	5309±1927	7521±9872	6094±2289	6308±7903

Mean hemoglobin was 11.61 gm%. Mean hematocrit was 40.72%. Mean platelets count were 51286/cumm in total study population. Lowest mean platelets count 35055/cumm was noted in SD group compared to DFWOWS 72281/cumm and DFWWS 49446/cumm. Highest mean hematocrit was noted in severe dengue group.

**Table-5: Distribution of platelet count according to type of dengue.**

Platelet count (/cumm)	DFWOWS N=22		DFWWS n=65		SD n=18		TOTAL PATIENTS n=105	
	Cases	%	Cases	%	Cases	%	Cases	%
Less than 20000	03	13.63	09	13.84	05	27.78	17	16.19
20000-39999	03	13.63	11	16.92	05	27.78	19	18.09
40000-100000	15	68.18	44	67.69	08	44.44	67	63.81
More than 100000	02	9.09	02	3.07	00	00	04	3.80
<b>Total</b>	<b>22</b>	<b>100</b>	<b>65</b>	<b>100</b>	<b>18</b>	<b>100</b>	<b>105</b>	<b>100</b>

63.81% cases had platelet count between (40000-100000). 18.09% cases had platelet count between 20000-39999. platelet count <20000 were noted in 16.19% of total cases. 3.80% of total cases had normal platelet count more than 100000. Out of 105 cases 46 (43.81%) cases required transfusion of blood products. 94.44% SD cases required blood transfusion compared to DFWWS 41.54% and DFWOWS 9.09% .

**Table-6: Distribution according to mean urea and creatinine**

	DFWOWS (Mean ± SD)	DFWWS (Mean ± SD)	SD (Mean ± SD)	Total (Mean ± SD)
S. urea 9 (mg/dl)	33.5±6.06	39.07±13.26	65.33±12.34	42.46±16.06
s. creatinine (mg/dl)	0.95±0.21	1.09±0.46	1.68±0.30s	1.16±0.46

Mean serum urea & creatinine of study population was 42.46 mg/dl and 1.16mg/dl respectively. Higher mean serum urea & creatinine was noted in severe dengue groups compared to other groups of DFWWS and DFWOWS.

**Table-7: Distribution according to mean S.bilirubin, ALT, AST**

	DFWOWS (Mean ± SD)	DFWWS (Mean ± SD)	SD (Mean ± SD)	TOTAL (Mean ± SD)
ALTIU/dl	46.45±16.20	66.67±30.79	176.61±60.34	81.28±56.52
ASTIU/dl	49.72±16.23	55.50±19.70	69.94±19.96	53.83±19.91
Serum Bilirubin Mg/dl	1.18±0.29	1.21±1.03	1.65±0.85	1.27±0.90

Rise in serum transaminases noted in most of the study population. ALT > 45 IU/dl in 20/105, AST >45 in 20/105 Serum bilirubin >2 in 5 /105 cases. Mean ALT was 81.28 IU/dl of total study population, highest mean ALT was found in severe dengue group compared to other groups.

Mean AST was 53.83 IU/dl in total study population, highest mean AST was noted in severe dengue group. Mean serum bilirubin was 1.65 mg/dl in severe dengue group. Liver Functions was more deranged in severe dengue group.

Coagulopathy (INR>1.5 or PT prolongation >5 sec) was noted in 11.42% cases. Deranged INR was found in 72.22% cases of severe dengue followed by DFWWS 13.86%.

**Table-8: Distribution of USG - abdomen findings in dengue cases.**

USG FINDING	DFWOWS n=22		DFWW n=65		SD n=18		TOTAL n=105	
	cases	%	Cases	%	cases	%	cases	%
Hepatomegaly	07	31.82	22	33.84	16	88.89	45	42.86
Gall bladder wall thickening	04	18.18	25	38.46	16	88.89	43	40.95
Ascites	00	0	10	15.38	08	44.44	18	17.14

Hepatomegaly was noted in 42.86% cases. This was present in 88.89% of Severe Dengue cases while in DFWS 33.84% and DFOWS 31.82%. Gall bladder wall thickening was noted in 40.95% cases of which it was present in 88.89% severe dengue cases. Ascites was found in 17.14% cases of which it was in 44.44% severe dengue cases compared to DFWS 15.38% and DFOWS 0%.

Mean hospital stay was 7.43 day among dengue patients. Maximum patients had hospital stay of 7-14 day in 60.95% cases maximum in DFWS. <7 days stay was seen in 34.28% cases maximum in DFOWS. Co-morbidities present in 18.09% of total cases. In severe dengue group 50% patients had co-morbidities and DFOWS had in 27.27% cases while in DFWS it was in 6.15% cases. Major bleeding (25.7%), among them most common was gut bleeding. Coagulopathy was noted in 72.2% cases of DSS. Mean hospital stay was 7.43 days. No mortality was noted in our study.

## Discussion

Increase in the number in dengue cases over past few years has been noted which can be attributed to rapid unplanned urbanization and poor sanitation facilities contributing fertile breeding areas for mosquitoes. Total 105 cases of IgM-ELISA positive dengue fever admitted in Gandhi medical collage & Hamidia hospital during the study period included and epidemiological, clinical features, laboratory findings, complications& outcome of these patients has been described. In our study 20.95% classified as dengue fever without warning signs, 61.9% as dengue fever with warning signs and 17.14% as severe dengue. As only hospitalized patients were included in this study patients having dengue fever with warning signs were more than that without warning signs.

**Demography:** Male: female ratio was 1.14:1 in our study. Other authors have also found male preponderance in their study [7,8,9]. Male predominance may be due to greater vulnerability males for mosquito bite due to outdoor work. The commonest age group in our study was 21-30 years. Mohan et al [9] reported 15 – 40 yrs to affected more, Rachel Daniel et al [7] found nearly equal distribution among 12- 50 years, Rajesh Deshwal et al [8] reported maximum patients in 21- 40 yrs. At our hospital 60.95% patients came from urban areas.

Maximum cases were admitted in post monsoon season (68.57%) in September to October and (25.71%) in November to December. This highlights the relation

between post monsoon water stagnation and dengue infection. Preventive measures should focus on water stagnation in post monsoon season as concluded by Dr Mohan et al. Fever was most common presentation 96.2% in present study as stated by other authors [7-10]. Body ache / myalgia presented in 57.14% in present study, Dr Mohan et al [9] in 90% cases Rajesh Deshwal et al [8] reported in 90.8% cases.

Vomiting and abdominal pain in dengue can due to hepatitis, bowel wall ischemia or mesenteric lymphadenitis, in our study it was present in 22. 85% and 26.6% cases respectively. Rajesh Deshwal et al [8] reported in 5.4% and DrMohan et al [9] in 54% so presentation with vomiting is of variable phenomenon. Retro-orbital pain was in 26 .66% in our study. Rash was presented in 41.9% in our study, other authors reported same occurrence [8,10]. Positive tourniquet test was found in 56.19% of cases in present study, while Rachel Daniel et al [7] reported in 33.67% cases, Rajesh Deshwal et al [8]in 16% % cases. In our study Headache was seen in 40% cases, Rajesh Deshwalet al [8] reported in 94.8% cases Mohan et al [9]in 90% cases. Petechie was seen in 34.28% casesDr Mohan et al reported in 21% cases.Bleeding is common in dengue due to low platelet count and capillary leakage.

Major bleeding manifestations were noted in 25.71% cases includes gum bleeding, gut bleed, per vaginal bleed, hemoptysis, intracranial bleed, hematuria and nearly same frequency reported by other authors. [7-10]

In our study mean platelet count was 51286 /cumm. Platelet count, 40000-100000 noted in 63.81% cases, < 20000 in 16.19% cases and > 100000 /cumm platelets found in 3.80%. Rachel Daniel et al [7] found < 10000 /cumm in 8.6% cases, <50000/cumm in 47.4%. Rajesh Deshwal et al [8] noted platelets < 50000 /cumm in 59.51% cases. Sanjay Kumar Mandal et al [10] noted platelet count < 50000 in 37.84% and > 50000 in 62.16% cases.

Hematocrit >45% was noted in 14.8% cases present study. Rachel Daniel et al reported in 27.9% cases, Sanjay Kumar Mandal et al reported in 21.62% cases Rajesh Deshwal et al noted in 20.77%. Mean hemoglobin among study population was 11.61 gm% in our study population. 43.81% cases required blood products transfusion during their hospital course. Frequency of blood transfusion does not seem to be affected by low platelets count as bleeding manifested in subjects having count >50000 – 100000 also. Hepatic involvement was present in majority of cases in our study, we found serum ALT >45 in 22.85% cases and AST >45 seen in 19.04% cases. Deranged INR (>1.5) noted in 11.42% cases. Rise in serum transaminases and coagulopathy was more in group of severe dengue as compared to dengue fever with warning signs and dengue fever without warning signs. In a study done by Amrita et al [11] more than 10- fold increase in the levels of AST and ALT were observed mainly in dengue with warning signs (10.7%) and severe dengue (21.3%). There was 84.4% and 93.75% ALT and AST elevation respectively in dengue with warning signs and 94.5% and 95.9% ALT and AST elevation respectively in severe dengue and fulminant hepatic failure was observed in severe dengue.

In our study mean hospital stay was 7.4 days. 60.95% patients had stay 7-14 days. Stay was expectedly higher in severe dengue cases.

On USG-abdomen hepatomegaly was found in 42.86% cases, Rachel Daniel et al [7] reported in 17.6% cases. Gall bladder wall thickening found in nearly 40.95% cases in present study. In present study Ascites found in 17.14% cases, Rachel Daniel et al reported in 17.6%, Rajesh Deshwal et al [8] recorded in 16.31% cases.

No mortality was seen in our study. Rachel Daniel et al [7] reported 3.2% mortality Dr Mohan et al [9] reported 11% while; Rajesh Deshwal et al [8] reported 0.77% deaths. Mortality can be reduced by early and prompt diagnosis and active and timely interventions in suspected dengue cases. Presence of other co-

morbidities does not affect outcome in dengue cases in our study. Complications like ARDS, respiratory failure, encephalopathy, myocarditis, multi organ dysfunction observed in present study population was present in 9.52% cases which were seen in severe dengue cases. Dr. Mohan et al reported 52% cases to have complications.

Statistical analysis among demographic data, signs/symptoms and hematological parameters of dengue fever according to severity of dengue was done using appropriate tests p-value was found insignificant due to small sample size.

Limitations of present study was to have small sample size, interfering in making prompt and clear picture about clinical manifestations in dengue patients coming to our hospital. Another limitation is to leaving all outpatient department cases. Also entomological data was not collected. NS1 antigen was not taken as selection criteria instead of that only IgM ELISA positive included as NS1ag was not available at our hospital. Strategies to prevent dengue by government agencies should focus on awareness of signs and symptoms of dengue among general population. Further studies on broad scale needs to be done in future to understand dengue in more depth and to assess predictors of mortality and morbidity and residual effects on organs involved and to draw more specific management and prevention strategies.

## Conclusion

Dengue fever patients can have significant morbidity in the form of various symptoms and complications. Not so much difference found in distribution of symptoms and their relation with morbidity and outcome. Coagulopathy, liver dysfunction and prolonged hospital stay and various complications occurs more in severe dengue patients compared to other groups. Dengue infection is increasing with increased urbanization and poor sanitation measures. Dengue has a wide spectrum of clinical and hematological presentation. It presents with fever, headache, bleeding, retro-orbital pain, vomiting and abdominal pain and many other symptoms and signs. Significant morbidity occurs in dengue with warning signs and severe Dengue.

It is a low mortality illness if prompt diagnosis and treatment can be instituted on time. Proper fluid management is the most important in management of dengue hemorrhagic fever. Platelet transfusion has little role in management of dengue. Further large scale studies are required to understand more about dengue in terms of prediction of outcome on presentation.

## Original Research Article

**What this study adds:** In this study we found that dengue has wide spectrum of clinical and hematological presentation and they have not much difference in various WHO groups. Complications and mortality occurs in severe dengue group. With efficient in-hospital care and close hemato-radiological monitoring of clinical parameters with simple and quick tests both mortality and morbidity can be avoided to the significant extent.

**Contribution by authors:** Dr Gopal Krishna and Dr Anil have prepared the manuscript after doing various tests of admitted dengue patients. Dr Gopal Krishna was guided by Dr Deopujari in collecting and analyzing data during study period.

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