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STUDY OF CLINICAL OUTCOME IN ADULT PATIENTS WITH SEROLOGICALLY PROVEN DENGUE SYNDROME AT A TERTIARY HOSPITAL

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Abstract

Background: Dengue fever is an acute febrile illness (AFI) caused by one or more dengue viruses belonging to genus Flavivirus and transmitted by Aedes aegypti mosquito. The exact clinical and laboratory profile is crucial for early diagnosis and management of patients. Present study was aimed to study clinical outcome in adult patients with serologically proven dengue syndrome at a tertiary hospital.
Material and Methods: Present study was hospital based, observational study, conducted in patients of age > 18 years, of either gender, with acute febrile illness, with serologically proven dengue syndrome admitted in wards & ICUs.
Results: We studied 210 serologically proven dengue patients in present study. Majority of patients were from 31-40 years age group (29.05%), were male (60.48%), NS 1 Positive (81.90%). In present study, non-severe dengue (83.81%) cases were more as compared to severe Dengue fever(DHF) (16.19%). Laboratory findings such as hematocrit < 36%, leukopenia, thrombocytopenia, reactive lymphocytes, prolonged PT, prolonged APPT, SGOT>40 IU/L & SGPT >40 IU/L were common in severe dengue group as compared to non-severe dengue group & difference was statistically significant ($p<0.05$). Ultrasound abdomen findings (thickened gall bladder, hepatomegaly & ascites) & chest X-ray findings of pleural effusion common in severe dengue group as compared to non-severe dengue. Pleural effusion, Renal failure, Hepatic failure, Shock, ARDS, Encephalopathy & Sepsis were common in severe dengue group as compared to non-severe dengue group & difference was statistically significant ($p<0.05$). Mortality was more common in severe dengue group as compared to non-severe dengue group (23.53%vs 1.7%).
Conclusion: Laboratory findings such as hematocrit < 36%, leukopenia, thrombocytopenia, reactive lymphocytes, prolonged PT, prolonged APPT, ultrasound abdomen findings (thickened gall bladder, hepatomegaly & ascites) & chest X-ray findings of pleural effusion common in severe dengue.

Keywords: Severe dengue, leukopenia, thrombocytopenia, hepatomegaly

Introduction

Dengue fever is an acute febrile illness (AFI) caused by one or more dengue viruses belonging to genus Flavivirus and transmitted by Aedes aegypti mosquito. Dengue infection is increasing substantially with un-planned rapid urbanization, high population density and poor waste management[1].

Clinically, the manifestations of DENV infection can range from mild-acute undifferentiated febrile illness to classical dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). DF is an acute febrile illness that presents symptoms such as bone or joint and muscular pains, headaches, leukopenia and rash. DHF has four major clinical manifestations: severe fever, hemorrhage, often with hepatomegaly and, in severe cases, circulatory failure[2].

The exact clinical and laboratory profile is crucial for early diagnosis and management of patients. Approximately 0.3-14.9% develop severe manifestations that result in ICU admission, and 1-5% die without early recognition and proper treatment[3].Timely access to proper treatment for dengue patients by primary healthcare professionals not only reduces the number of unnecessary hospital admissions but also lowers fatality rates below 1% [5].Present study was aimed to study clinical outcome in adult patients with serologically proven dengue syndrome at a tertiary hospital.

Material and Methods

Present study was hospital based, observational study, conducted in wards & ICUs under Department of General Medicine, Kamineni Institute of Medical Sciences, Narkatpally,, India. Study duration was of 3 years (January 2019 to December 2021). Study approved by institutional ethical committee.

Patients of age > 18 years, of either gender, with acute febrile illness, with serologically proven dengue syndrome (dengue NS1 antigen using Microwell ELISA test and dengue IgM antibody using Microwell Capture ELISA test), admitted in wards & ICUs were considered for present study.Patients with other co infections like malaria, typhoid, etc. or with any critical co-morbid diseases were not considered for study.

A detailed history was taken and a careful clinical examination was performed. All baseline investigations like complete blood count (Hb, TLC, DLC, haematocrit), coagulation profile, liver function test, kidney function test, X-ray chest & ultrasound abdomen were done at admission. Other relevant investigations were performed according to the clinical conditions of the patients.

The outcome of the study was in the form of an analysis of the varied clinical profile of dengue fever and the end result of treatment resulting in either discharge on recovery, discharge on request and discharge against medical advice or death of the patient.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Statistical analysis was done using descriptive statistics. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

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Results

We studied 210 serologically proven dengue patients in present study. Majority of patients were from 31-40 years age group (29.05%) & from 41-50 years age group (22.86%), were male (60.48%), had Hypertension (19.52%), Diabetes (10.48%). Majority of patients were NS 1 POSITIVE (81.90%) as compared to NS1 POSITIVE + ANTIBODY (IgM, IgG) (22.86%). In present study, non-severe dengue (83.81%) cases were more as compared to severe Dengue fever(DHF) (16.19%).

Table 1: General characteristics

Characteristics	No. of cases (n=210)	Percentage
Age distribution (in years)		
19-30	29	13.81%
31-40	61	29.05%
41-50	48	22.86%
51-60	41	19.52%
>60	31	14.76%
Gender		
Male	127	60.48%
Female	83	39.52%
Comorbidities		
Hypertension	41	19.52%
Diabetes	22	10.48%
Pregnancy	4	1.90%
Others (COPD/TB)	17	8.10%
Laboratory diagnosis		
NS 1 Positive	172	81.90%
NS1 Positive + Antibody (IgM, IgG)	48	22.86%
Classification		
Non-severe dengue	176	83.81%
Severe Dengue fever(DHF)	34	16.19%

In present study, common symptoms noted were fever (100.00%), headache (69.05%), nausea/vomiting (62.86%), myalgia (48.57%), gastrointestinal (43.33%), abdominal pain ((21.43%), diarrhea (10.95%), bleeding (8.10%), retro orbital-pain (7.14%) &rash (5.24%).

Table 2: Presenting symptoms

Symptoms	No. of cases (n=210)	Percentage
Fever	210	100.00%
Headache	145	69.05%
Nausea/vomiting	132	62.86%
Myalgia	102	48.57%
Gastrointestinal	91	43.33%
Abdominal pain	45	21.43%
Diarrhea	23	10.95%
Bleeding	17	8.10%
Retro orbital-pain	15	7.14%
Rash	11	5.24%

Laboratory findings such as hematocrit < 36%, leukopenia, thrombocytopenia, reactive lymphocytes, prolonged PT, prolonged APPT, SGOT>40 IU/L & SGPT >40 IU/L were common in severe dengue group as compared to non-severe dengue group & difference was statistically significant ($p<0.05$). Ultrasound abdomen findings (thickened gall bladder, hepatomegaly & ascites) & chest X-ray findings of pleural effusion common in severe dengue group as compared to non-severe dengue group & difference was statistically significant ($p<0.05$).

Table 3: Laboratory & radiological profile of cases

Laboratory profile	Non-severe dengue (n=176)	Severe dengue (n=34)	P value
Hematocrit < 36%	32 (18.18%)	21 (61.76%)	< 0.05
Total Leukocyte count (Leukopenia < $4x10^3$/all)	13 (7.39%)	19 (55.88%)	< 0.05
Platelet count < 150 $x10^3$/µl	11 (6.25%)	34 (100%)	< 0.05
Peripheral smear (Reactive lymphocytes present)	11 (6.25%)	30 (88.24%)	< 0.05
Prolonged PT	12 (6.82%)	21 (61.76%)	< 0.05
Prolonged APPT	4 (2.27%)	11 (32.35%)	< 0.05
SGOT >40 IU/L	20 (11.36%)	32 (94.12%)	< 0.05
SGPT >40 IU/L	24 (13.64%)	26 (76.47%)	< 0.05
Ultrasound abdomen			< 0.05
Thickened gall bladder	21 (11.93%)	29 (85.29%)	< 0.05
Hepatomegaly	13 (7.39%)	25 (73.53%)	< 0.05
Ascites	11 (6.25%)	10 (29.41%)	< 0.05
Pleural effusion	44 (25%)	18 (52.94%)	< 0.05

Pleural effusion, Renal failure, Hepatic failure, Shock, ARDS, Encephalopathy & Sepsis were common in severe dengue group as compared to non-severe dengue group & difference was statistically significant ($p<0.05$).

Table 4: Complications in Dengue

Laboratory profile	Non-severe dengue (n=176)	Severe dengue (n=34)	P value
Pleural effusion	5 (2.84%)	13 (38.24%)	< 0.05
Renal failure	4 (2.27%)	11 (32.35%)	< 0.05
Hepatic failure	11 (6.25%)	7 (20.59%)	< 0.05
Shock	1 (0.57%)	5 (14.71%)	< 0.05
ARDS	2 (1.14%)	3 (8.82%)	< 0.05
Encephalopathy	0	2 (5.88%)	< 0.05
Sepsis	0	1 (2.94%)	< 0.05

In present study, 197 cases (93.81%) were discharged, 2 cases were(5.24%) Discharged against medical advice & 5.24% mortality noted. Mortality was more common in severe dengue group as compared to non-severe dengue group (23.53% vs. 1.7%).

Table 5: Outcome

Outcome	Non-severe dengue (n=78)	Severe dengue (n=22)	Total (n=130)
Discharged	171 (97.16%)	26 (76.47%)	197 (93.81%)
Discharged against medical advice	2 (1.14%)	0	2 (0.95%)
Death	3 (1.7%)	8 (23.53%)	11 (5.24%)

Discussion

The pathogenesis of dengue fever has still not been elucidated completely. Host response is considered to be a significant contributor in the pathogenesis and pathology of dengue[5].The most common causes of mortality in dengue are prolonged shock, massive hemorrhage and fluid overload. The main problem leading to poor prognosis or death is not being diagnosed when presenting in critical conditions at the hospitals[6].

Early in the acute febrile period of disease, dengue fever presents with the same clinical symptoms as primary dengue. Later, during defervescence, patients can rapidly deteriorate, progressing to hemorrhage with or without vascular leak. During this period, patients can experience bleeding, thrombocytopenia with <100 000 platelets/μL, ascites, pleural effusion, increased hematocrit concentrations, severe abdominal pain, restlessness, vomiting and sudden reduction in temperature with profuse perspiration and adynamia[7].

Differential diagnosis of Dengue fever based on clinical criteria alone is not possible because of overlapping clinical presentations with other tropical fevers and the correct diagnosis is only possible by using pathogen specific diagnostic tests such as NS1 antigen, IgM detection.Studies have shown that NS1 protein is present early in dengue virus infection and offers a new technique to diagnose a dengue virus infection based on NS1 antigen capture ELISA. Rapid immunochromatographic tests to detect dengue IgM and IgG have demonstrated high sensitivity and specificity[8].Management in dengue is predominantly supportive and includes judicious fluid therapy in order to prevent or treat shock while at the same time preventing fluid overload due to capillary leak. Crystalloids were preferred over colloids for initial resuscitation[9].

In study by Nair KR *et al*.[10], out of 236, 183(77.5%) were diagnosed as primary dengue and 53 (22.5%) as secondary dengue infection. Common clinical symptoms were fever (100%), generalized body ache (53%), headache (42%), vomiting (22%), and abdominal pain (10%). Thrombocytopenia, leucopoenia and elevated liver enzymes were observed. All patients improved clinically and showed an improvement in their biochemical and hematological parameters.

Shastri PS *et al*.,[11] studied 137 cases,median age of study population was 36.0 (26.0-52.0) years. Liver (65.7%) was the main organ involved followed by acute kidney Injury (AKI) (18.6%). Dengue Shock Syndrome (DSS) was found in 18.6% of cases. 52 patients died and the crude mortality was 38.0%. On multivariate analysis APACHE Score >10, thrombocytopenia, hepatic dysfunction, AKI and dengue shock syndrome (DSS) were associated with the risk of mortality.

Of the 53 patients studied, by Abdul B A *et al*.,[12] majority were male. Fever (100%) was the major symptom followed by headache/retro-orbital pain (71.69%), myalgia (64.15%), arthralgia (52.83%), rash (26.21%), skin hemorrhage (26.21%), abdominal pain (22.6%), vomiting (18.86%), itching (18.86%), loose motion (16.98%), gum bleed (16.98%), epistaxis (15.09%), hepatomegaly (15.09%), pleural effusion (5.66%) and ascites (7.55%). Thrombocytopenia, leucopenia and deranged liver transaminases were significant laboratory abnormalities.

Tiwari M, *et al*.,[13] studied 75 cases, gender was not significantly associated with the outcomes. The duration of fever was significantly higher among those with ICU use, ventilator use and blood transfusion. Dengue patients with co-morbidities (diabetes, hypertension or chronic obstructive pulmonary disease) or co-infection had a significantly higher odds of the outcomes. The platelet level was significantly lower while liver enzymes were significantly higher among those with the outcomes. The clinical features, comorbidities and laboratory profile can help in identifying critical patients for ICU admission and timely intervention to improve outcome.

Tauqeer H M *et al*.,[14] studied 667 dengue patients (30.69 ± 16.13 years; Male: 56.7%) were reviewed. Typical manifestations of dengue like fever, myalgia, arthralgia, headache, vomiting, abdominal pain and skin rash were observed in more than 40% patients. DHF was observed in 79 (11.8%) cases. Skin rash, dehydration, shortness of breath, pleural effusion and thick gall bladder were more significantly ($P < 0.05$) associated with DHF than DF. Older age, secondary infection, diabetes mellitus, lethargy, thick gallbladder and delayed hospitalization significantly predict DHF. Prior knowledge of expected clinical profile and predictors of DHF/DSS development would provide information to identify individuals at higher risk and on the other hand, give sufficient time to clinicians for reducing dengue related morbidity and mortality.

Supportive treatment was the mainstay mode of management. Raised hematocrit, thrombocytopenia, leucopenia and atypical lymphocytes in the peripheral smear will aid in early diagnosis of Dengue infection[15].Where some known features are still manifesting, few atypical features are noted from several parts of the world. So a continuous sero-epidemiological surveillance and timely interventions are needed to identify the cases, so that its complications, outbreak and mortality can be minimized.

Bleeding, shock and raised SGOT and SGPT levels were identified as predictors of adverse outcomes and mortality in dengue fever. Knowledge of factors that predict worse prognosis can help the health workers in primary care centers to identify the patients requiring intensive medical management. Such patients need to be admitted to intensive care units in tertiary care centers so that mortality due to dengue can be controlled[16].

Conclusion

Mortality & complications were more in severe dengue group. Laboratory findings such as hematocrit < 36%, leukopenia, thrombocytopenia, reactive lymphocytes, prolonged PT, prolonged APPT, SGOT>40 IU/L & SGPT >40 IU/L, ultrasound abdomen findings (thickened gall bladder, hepatomegaly & ascites) & chest X-ray findings of pleural effusion common in severe dengue group as compared to non-severe dengue group. Early identification of these risk factors and active management is important to reduce dengue-related mortality.

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