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Original Research Paper

General Medicine

A STUDY OF COAGULATION PROFILE IN DENGUE FEVER IN TERTIARY CARE HOSPITAL

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ABSTRACT

Background: In Dengue fever deaths are due to hemorrhagic complications. Hemorrhage in DF is due to thrombocytopenia or clotting factors abnormalities.There is limited literature on coagulation abnormalities, fibrin degradation products and D-dimer.thus it makes very important

Methods: The study was done in Yenepoya medical college hospital -A tertiary care hospital. Total of 60 patients were taken out of which 30 were cases and 30 were healthy controls. Detailed history, general, physical and systemic examination was done. Laboratory parameters for tests Dengue NS1, IgM and IgG, CBC, PT/INR, APTT, FDP, D-dimer, were done.

Results: The results of our study show that coagulation profile is impaired in Dengue Fever cases with FDP and D-dimer being positive and APTT being higher than that of controls. However impairment of APTT was clinically not significant. Also cases with DHF – were significantly associated with elevated D-dimer and FDP when compared with Dengue Fever cases.

Conclusion: In conclusion, coagulopathy in Dengue Fever with Thrombocytopenia may indicate secondary Dengue infection and may predict Dengue hemorrhagic fever and its complications. FDP or D-dimer could be a useful tool to predict which patient needs monitoring for bleeding. Since D-dimer is expensive, and not all set ups will have facilities to estimate the same, we strongly recommend that FDP can be a part of Dengue hemorrhagic fever work up.

KEYWORDS : FDP- Fibrin degradation products, D-DIMER-D-D-dimer ,APTT- Activated partial thromboplastin time, PT- Prothrombin time , INR- International normalized ratio.

INTRODUCTION

Dengue is one of the most common mosquito borne viral disease in the world. The incidence has been increased to 30 fold in the last five decades with increase in geographic distribution to new countries in the present decade from urban to rural settings1.According to WHO 50 billion people dengue infections occur annually and 2.5 billion people live in endemic areas.Dengue has been identified as a one of the 17 tropical diseases according to WHO[1]. Although the full burden of the disease in the globe is still uncertain the patterns are alarming to human as well as economy. Some 1.8 billion (more than 70%) of the population at risk for Dengue worldwide live in member states of the WHO South-East Asia Region and Western Pacific Region, which bear nearly 75% of the current global disease burden due to Dengue. The countries have been divided in to four distinct regions.Epidemic Dengue is a major public health problem in Indonesia, Myanmar, Sri Lanka,Thailand and Timor-Leste which are in the tropical monsoon and equatorial zone where Aedes aegypti is widespread in both urban and rural areas, where multiple virus serotypes are circulating, and where Dengue is a leading cause of hospitalization and death in children. In India Dengue virus was first isolated in India in 1945. The first evidence of Dengue was evidenced in the Vellore district of Tamil Nadu in 1956. First DHF outbreak was occurred in Calcutta in 1963. Aedes mosquito breeding is common in urban areas, the disease was observed is more prevalent in urban areas. The trend is changing now, due to socioeconomic and man made ecological changes this has led significantly increased even in rural areas.Recurrent out breaks has been reported in Andhra Pradesh, Chandigarh, Delhi, Goa, Haryana, Gujarat, Karnataka, Maharashtra, Rajasthan, Puducherry, Uttar Pradesh, Tamil Nadu and West Bengal.

According to National Vector Borne disease Control programme (NVBDCP) in India there is a persistent increase of Dengue Fever(DF) from 2010 (28292- cases) to 2017 (153635-cases)[2].In Karnataka total number of Dengue cases in 2017 according to NVBDCP are 165522 .In Dengue fever deaths are due to hemorrhagic complications. Hemorrhage in DF is due to thrombocytopenia or clotting factors abnormalities which can be due to auto antibodies or disseminated intravascular coagulation. There is limited literature on coagulation abnormalities, fibrin degradation products and D-dimer. Hence this study was planned to see coagulation abnormalities in Dengue fever and Dengue haemorrhagic fever.

AIMS OF STUDY:

To compare the coagulation profile in Dengue fever/Dengue hemorrhagic fever and controls.

MATERIALS AND METHODS:

The study had 60 participants including both Cases and controls. Cases included both dengue fever and dengue hemorrhagic fever. Each group had 30 participants. Healthy age and sex matched healthy individuals were matched and included in control group.Cases were taken from dengue fever patients meeting the inclusion and exclusion criteria. Assuming 50% DHF cases will have coagulation abnormalities and 1% DF cases will have coagulation abnormalities a sample size of 13 of was calculated using the unmatched case control formula of Open epi version 3.01 with confidence interval level of 95% and power of 80% and odd ratio of cases and controls as 1, hence sample size of 13 DHF cases and 17 DF were taken with a total sample size of 30. For convenience sake sample of 30 in each group was taken at a confidence level of 95% and power of 80%.Laboratory parameters for tests Dengue NS1, IgM and IgG, CBC, PT/INR, APTT, FDP, D-dimer, were done.

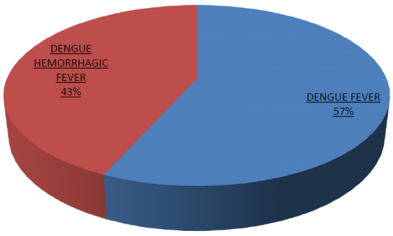
RESULTS:

In our study age and sex were nearly matched, which is given in the below table;

TABLE 1: GENDER DISTRIBUTION IN CASES AND CONTROLS

CASE	MALE	FEMALE	TOTAL
	18	12	30
	60.0%	40.0%	100.0%
CONTROL	23	7	30
	76.7%	23.3%	100%

GRAPH 1:SEVERITY OF DENGUE FEVER AMONG CASES:



Total 30 cases were taken, the above table shows percentage of severity of dengue fever.17 cases (56.7%) were dengue fever and 13 cases (43.3%) were DHF. Patients were classified based on WHO criteria2.

TABLE 2:COAGULATION COMPARISION BETWEEN CASES AND CONTOLS:

TESTS	GROUP	N	MEAN	S.D	T-test	P-value
APTT	CASES	30	41.8583	9.02999	4.012	<0.001
	CONTROLS	30	35.2133	0.86293		
PT TEST	CASES	30	16.113	2.1779	1.617	0.111
	CONTROLS	30	15.467	0.2324		
INR	CASES	30	1.0293	0.18873	0.851	0.398
PLATELET	CONTROLS	30	1.0000	0.00		
	CASES	30	62066.67	55603.63	-6.810	<0.001
	CONTROLS	30	193117.43	89535.418		

Above table shows the coagulation parameters between cases and controls. The following parameters were taken APTT, PT and INR.Mean of APTT test between cases and controls are 41.8 for cases and 35.2 for controls and p- value is less than 0.001. It is statistically significant between cases and controls. Mean of PT test for cases and controls are 16.1 and for controls are 15.4 with a p-value 0.111. PT test is not statistically significant between cases and controls. Mean of INR between cases and controls are 1.02 and 1.0 respectively. P- value is 0.3. INR is also not significant between cases and controls.Mean of platelets for cases and controls are 62066 and for controls it is 193117. The p- value is less than 0.001 which is statistically significant.

TABLE 3:COMPARISION OF FDP IN CASES AND CONROLS:

GROUP	FDP		
	NEGATIVE	POSITIVE	TOTAL
CASES	16	14	30
	53.3%	46.7%	100%
CONTROLS	30	0	30
	100%	0.0%	
CHI-SQUARE TEST $X_{2\ (1)}$	18.261		
P-VALUE	<0.001		

The above table shows association of FDP with severity of dengue fever. Out of 30 cases 17 were DF and 13 were DHF. In DF FDP is positive in only 1(5.9%).In DHF out of 13 all were positive for FDP. It is 100% associated with DHF. And p-value is less than 0.001 which is significantly associated statistically.

TABLE 5:COMPARISION OF D-DIMER IN DENGUE FEVER AND DENGUE HEMORRHAGIC FEVER:

SEVERITY	D-DIMER		TOTAL
	NEGATIVE	POSITIVE	
DENGUE FEVER	16	1	17
	94.1%	5.9%	100%
DENGUE HEMORRHAGIC FEVER	4	9	13
	30.8%	69.2%	100%
Chi-square test $x_{2(1)}$	13.30		
P-VALUE	<0.001		

The above table shows severity of D-dimer between DF and DHF. Chi-square test is used for comparison. Out of 30 cases 10 were positive for D-dimer. In DF out of 17 only 1(5.9%) is positive for D-dimer. In DHF out of 13, 9(69.2%) were positive and 4(30.8%) were negative. The p- value is less than 0.001. It is statistically significant.

DISCUSSION:

The results of our study show that coagulation profile is impaired in Dengue Fever cases with FDP and D-dimer being positive and APTT being higher than that of controls. However impairment of APTT was clinically not significant. Also cases with DHF – were significantly associated with elevated D-dimer and FDP when compared with Dengue Fever cases[3]. No statistical difference was found in mean platelet count, PT, APTT and INR between Dengue fever and Dengue hemorrhagic fever. Hence we can safely conclude that FDP and D-dimer are probably better markers of Dengue hemorrhagic fever indicating secondary infection as compared to platelet count, APTT, PT/INR .This may also indicate severity of illness and guide the clinician in anticipating clinical haemorrhage and also being vigilant and equipped to treat haemorrhage. Previous studies have found similar results. In a previous study done in 2004 Abhilash kannan et al[4]authors reported coagulopathy in 22.3% of the study population They had estimated D-dimer, APTT and PT/INR in the study subjects with thrombocytopenia. They reported increase in bleeding manifestations with increasing APTT and also concluded that platelet count falls with rise in APTT[5].

It was hypothesized that there APTT prolongation is due to abnormality in intrinsic pathway and not due to extrinsic pathway of coagulation. There are also some studies showing the role of activation of fibrinolytic system responsible for bleeding manifestation in Dengue fever patient's addition to thrombocytopenia and APTT prolongation[6]. In their study along with the prolongation of APTT there was also rise in D-dimer[7].

In a recent study by Muhammad et al[8] to find predictors of hospital stay and mortality in dengue virus infection reported that nearly 72.6% stayed less than 3 days and 27.4% people stayed more than 3 days due to AKI, prolongation PT and APTT. In their study they concluded that with increasing age and coagulopathy and length of hospital stay increased.

Thus it makes FDP and D-dimer test vital in dengue fever for prediction of coagulopathy complications in early phases of fever.

CONCLUSIONS:

In conclusion, Coagulopathy in Dengue Fever with Thrombocytopenia may indicate secondary Dengue infection and may predict Dengue Hemorrhagic fever and its complications[9] FDP or D-dimer could be a useful tool to predict which patient needs monitoring for bleeding[10] .Since D-dimer is expensive, and not all set ups will have facilities to estimate the same, we strongly recommend that FDP can be a part of Dengue hemorrhagic fever work up.

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