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PT AND aPTT TRENDS IN DENGUE FEVER

General Medicine

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ABSTRACT

Dengue is the the most common mosquito borne arboviral disease in tropical regions of the world. Common hematological abnormalities seen with dengue fever are leukopenia followed by thrombocytopenia. Coagulopathy may also be seen in dengue fever. This study aims to observe the trends of PT and aPTT profile in dengue fever. **Materials and methods:** This was an observational study done at Narayana medical college and hospital, Nellore, from June 2021 to October 2022 on 180 dengue patients satisfying inclusion and exclusion criteria. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) values of all the study patients were noted. Laboratory control value for PT was 13.1sec, aPTT control value was 34sec. Values above these were considered abnormal. PT and aPTT values of all the 180 patients included in the study were noted at admission and median values were calculated. **Results:** Out of 180 dengue patients studied, 95.6% of the patients had normal PT and 78.8% of the patients had prolonged aPTT . Median value of PT observed in this study was 13.8 sec, median value of aPTT observed in this study was 48.9sec. **Conclusion:** Isolated aPTT prolongation with a normal PT is seen in dengue fever as commonly as thrombocytopenia. Moreover, in addition to thrombocytopenia, coagulopathy as represented by prolongation of aPTT is an important contributor of bleeding risk to be noted in patients with dengue fever.

KEYWORDS

Dengue, Prothrombin time , PT, activated partial thromboplastin time, aPTT, Coagulation profile

INTRODUCTION:

At present, the most common mosquito borne arboviral disease in tropical regions of the world is dengue[1]caused by dengue virus (DENV). WHO estimated that 50 million dengue infections per year occur across approximately 120 countries. Dengue virus belongs to family flavivirdae and has four distinct but closely related serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). 5th serotype has been discovered recently. The primary vector that transmits dengue virus is Aedes aegypti mosquito[2].

The first infection with any DENV serotype is usually mild and provides lifelong immunity against that serotype, due to production of neutralizing antibodies that circulate for a lifetime in the body. Subsequent infection with any other serotype results in antibody dependent enhancement of virus infection leading to severe dengue[3].
Dengue virus is a single stranded RNA virus made up of 3 structural proteins namely nucleocapsid protein (C), membrane associated protein (M), envelope protein (E), and 7 nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5). NS proteins are required for replication of virus[4].

Dengue manifestations may range from asymptomatic, mild symptoms to severe forms like dengue hemorrhagic fever or dengue shock syndrome or organ impairment[3]. Common hematological abnormalities seen with dengue fever are leukopenia followed by thrombocytopenia as a result of INF-α mediated transient bone marrow suppression and increased peripheral destruction of platelets[5]. Coagulopathy may also be seen in dengue fever. Recent studies highlighted the prolongation of aPTT in most of the dengue cases. This study is to reinforce the effect of dengue over (Prothrombin time) PT and (activated partial thromboplastin time) aPTT.

AIMS AND OBJECTIVES

To study the trends of PT and aPTT in Dengue fever.

MATERIAL AND METHODS

An observational study was done at Narayana medical college and hospital, Nellore, from June 2021 to October 2022 on 180 patients satisfying inclusion and exclusion criteria.

Inclusion criteria : All the patients presenting to emergency department or OPD, who were admitted and tested positive for Dengue NS1 antigen or dengue IgM serology or both were included in the study.

Exclusion criteria:

1. Patients with only dengue IgG positive on rapid card test were excluded from the study.
2. Patients with any other febrile illness like malaria, typhoid, leptospira, scrub typhus, Covid-19, or other microbial infections coexisting with dengue were excluded from the study.
3. Patients who were known cases of primary bleeding disorders were excluded from study.
4. Known cases of chronic liver disease were excluded from study.
5. Patients on anticoagulants were excluded from study.
4. Critically ill patients were excluded from the study.

History of presenting illness, clinical features of all the study patients were noted. Investigations done include complete hemogram, renal function tests, dengue serology (NS1Ag, IgM, IgG) by ELISA method, Malaria parasite smear, leptospira serology (IgM, IgG), scrub typhus serology (IgM, IgG), RTPCR-COVID 19, complete urine examination, coagulation profile (PT, INR, aPTT), liver function tests. Laboratory control value for PT was 13.1sec, aPTT control value was 34sec. Values above these were considered abnormal. PT and aPTT values of all the 180 patients included in the study were noted at admission and median values were calculated. Abnormal aPTT values were compared with platelets and bleeding manifestations.

RESULTS

180 patients were studied, of which 112 (62.2%) were males, 68 (37.8%) were females

Table 1: Age wise distribution of study patients

AGE IN YEARS	NUMBER OF PATIENTS	PERCENTAGE
18-30	72	40%
31-40	48	26.7%
41-50	25	13.9%
51-60	16	8.9%
>60	19	10.5%

Table 2: Distribution of serology for dengue fever

DENGUE SEROLOGY	NUMBERS OF PATIENTS	PERCENTAGE
NS1Ag positive	91	50.5%
IgM positive	21	11.7%

NS1Ag and IgM positive	50	27.8%
IgM, IgG positive	18	10%

Table 3: Distribution of clinical features among study participants

CLINICAL FEATURES	NUMBER OF PATIENTS	PERCENTAGE
Fever	138	76.7%
Headache	102	56.7%
Myalgia	63	35%
Vomitings	32	17.8%
Bleeding manifestations	87	48.4%

Table 4: Distribution of various bleeding manifestations among study participants

BLEEDING MANIFESTATION	NUMBER OF PATIENTS	PERCENTAGE
Bleeding gums	21	11.7%
Petechea	14	7.8%
Palatal haemorrhage	36	20%
Conjunctival haemorrhage	7	3.9%
Malena	9	5%

Table 5: Platelet counts among study individuals

PLATELET COUNT (cells/cu.mm)	NUMBER OF PATIENTS	PERCENTAGE
<20,000	94	52.2%
20,000-50,000	64	35.5%
50,000-1,00,000	18	10%
>1,00,000	4	2.3%

Table 6: PT levels among study participants

PT	NUMBER OF PATIENTS	PERCENTAGE
Normal	172	95.6%
Prolonged (>13.1 sec)	8	4.4%

Table 7: aPTT levels among study participants

aPTT	NUMBER OF PATIENTS	PERCENTAGE
Normal	38	21.2%
Prolonged (>34 sec)	142	78.8%

Table 8: Comparision of aPTT levels, thrombocytopenia and bleeding manifestations

	BLEEDING MANIFESTATIONS		TOTAL
	Yes	No	TOTAL
aPTT (>34 sec)	80 (56.3%)	62 (43.7%)	142
Platelets (<50,000cells/cu.mm)	76 (48.1%)	82 (51.9%)	158

No patients had bleeding manifestations with platelet count >50,000cells/cu.mm. None of the patients with prolonged PT had bleeding manifestations, unless if it was associated with prolonged aPTT as seen in 2 cases.

DISCUSSION

This study conducted in a tertiary care centre on 180 patients with dengue fever highlighted the common coagulation abnormality seen in patients with dengue fever.

In our study, out of 180 patients, 95.6% of the patients had normal PT and 78.8% of the patients had prolonged aPTT. Median value of PT observed in this study was 13.8 sec, median value of aPTT observed in this study was 48.9sec. Hence a conclusion of normal PT in most of the patients and prolonged aPTT in majority of the patients with dengue fever can be drawn. Huan-Yao Lei, et al7 also reported there is a significance raise of APTT in dengue fever. APTT elevation was reported and advocated as an associated factor for disease severity .Wei Liu et al8 observed prolongation of APTT in 97.5% cases of dengue hemorrhagic fever. These observations support the statement of isolated aPTT prolongation seen in dengue fever.

Recent studies have given decent explanations for the above observation. Tissue plasminogen activator and Interleukin-6 are produced from endothelial cells as induced by the dengue virus. IL-6 can down-regulate the production of coagulation factor XII, the initiator of intrinsic pathway of the coagulation cascade5. Also, NS1 binds to thrombin in vivo to form NS1-thrombin complexes and inhibits prothrombin activation and prolongs activated partial thromboplastin time (aPTT) in human platelet deficient plasma[6].

In our study, patients with platelet count <50,000 were 87.8%. Bleeding manifestations were seen in 48.4% patients. 56.3% of the patients with prolonged aPTT and 48.1% of the patients with platelets <50,000 cells/cu.mm showed bleeding manifestations. From these observations a conclusion of bleeding risk in dengue patients being high with prolonged aPTT and platelets <50,000cells/cu.mm can be obtained. HP Tee, et al9 reported low platelet level and prolonged APTT had significant association with bleeding tendencies.

CONCLUSION

Isolated aPTT prolongation with a normal PT is seen in dengue fever as commonly as thrombocytopenia. Moreover, in addition to thrombocytopenia, coagulopathy as represented by prolongation of aPTT is an important contributor of bleeding risk to be noted in patients with dengue fever. So, an early attention and search for the prolonged aPTT in dengue patients especially with very low platelet count can give us a brief prediction on bleeding risk in the patients and when managed accordingly could prevent further complications with bleeding.

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