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# Changes in Coagulation Profile in Dengue Patients with Hepatitis Attending to a Tertiary Care Hospital in Sri Lanka

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## Abstract

Dengue is a fast-growing global issue, which is endemic in Sri Lanka. Changes in coagulation is thought to contribute to complications of dengue but the evidence is lacking.

**Objective:** To assess the changes in coagulation profile in patients with dengue, with or without hepatitis in a tertiary care hospital, in Sri Lanka.

**Method:** A cross sectional survey was carried out in patients with dengue (n=139) in Sri Jayewardenepura General Hospital with confirmed dengue, in 2013.

**Results:** There was no statistically significant difference when either the APTT or PT result, compared with more than two-fold rise in aspartate aminotransferase level during the course of illness ( $p>0.05$ ).

**Conclusion:** Presence of hepatitis was not predictive of abnormal APTT/PT values. Further larger scaled studies are recommended in achieving conclusions.

**Keywords:** Dengue; Hepatitis; Coagulation profile; APTT; PT/INR

*albopictus*) [1]. Several genotypes have been identified within each serotype and "Asian" genotypes of DEN-2 and DEN-3 serotypes are frequently associated with severe disease [1].

While vast majority of infections are asymptomatic, some present with fever and thrombocytopenia, fluid leakage, shock, hepatitis, haemorrhage and myocarditis [2,3]. Rarely encephalitis and other neurological manifestations like cerebellitis and cranial nerve palsies were described. Natural history of dengue is considered in three phases; febrile phase, critical phase and recovery phase [4]. Severe dengue (previously known as dengue haemorrhagic fever (DHF)) is a leading cause of hospital mortality and morbidity in endemic areas [1]. Hepatitis in dengue is quite frequent and rarely may progress to liver failure. Coagulopathy sometimes contributing to hemorrhagic complications can occur in some patients, especially with severe hepatitis and disseminated intravascular coagulation (DIC), but also without any of these [5]. Transient elevation of APTT and decrease in fibrinogen level are also seen frequently even in the absence of hepatitis, the magnitude of the change thought to correlate with the severity of leakage [2]. There is a lack in data on coagulopathy associated with dengue and its relationship to hepatitis. This study designed to assess the coagulopathy in patients with dengue, especially those with hepatitis.

## Objectives

To assess the changes in coagulation profile in patients with dengue, with or without hepatitis in a tertiary care hospital, in Sri Lanka.

## Methodology

**Study design:** Cross sectional survey.

## Background

Dengue is a fast-growing global health issue with endemic areas (over 100 endemic countries), mainly distributed in Asia, Africa and Latin America, and is potentially a pandemic soon [1]. Dengue is an important infectious disease with significant health and economical impacts in Sri Lanka. Dengue is caused by four serotypes (DEN-1, DEN-2, DEN-3 and DEN-4) of viruses (belong to the genus *Flavivirus*, family *Flaviviridae*) transmitted by mosquitoes (*Aedes aegypti*, the primary vector and also *A.*

## Study population and sampling procedures

**Study population:** The study population includes the patients managed as dengue in ward 06 of Sri Jayawardenepura General Hospital, during the period of July 2013 to December 2013. Dengue was confirmed by detecting IgM antibodies to dengue virus.

**Sample:** All consenting, dengue patients who agree to participate, are included in to the study. Those who showed positive IgM antibodies during ward stay or after discharge were recruited for data collection. This survey will be carried out from July 2013-December 2013 at, Sri Jayawardenepura General Hospital, Sri Lanka.

**Data collection tools:** Data collected to data sheets.

**Variables:** The dependent variables are APTT, PT, Hepatitis and Platelet count and the independent variables are Age, Sex etc.

## Data Collection

After obtaining verbal consent, data was collected by the principal investigator using the data collection sheets and entered to SPSS analytic software. Data from 139 patients who were treated as dengue was collected and used for analysis, of whom the dengue IgM antibodies were found positive. Blood sampling for coagulation studies were done on 5<sup>th</sup> to 7<sup>th</sup> day of illness. Highest recorded APTT and PT value were taken as the value for analysis.

## Data Analysis

Analysis was done with SPSS statistical analysis software. Findings relevant to descriptive statistics will be summarized into proportions and averages (means/SD or percentiles) based on the scales of measurements. Comparisons will be evaluated using T-tests (continuous variables) or Chi square tests (discrete variables) based on retrospective groupings, variable distributional patterns and scales of measurements.

## Ethical Considerations

Ethical clearance for the study was obtained from the ethics review committee of the University of Sri Jayawardenepura.

## Results

Data from 139 patients were collected. Two of them were excluded due to inadequate information recorded, leaving 137 for analysis. They were of ages ranging from 12 to 82 years with a mean age of 33+/-15 SD, years. Seventy-one of them were males and 66 were females (M: F=1.167). Alanine Transferase level ranged from 11 to 753 with a mean of 181.3+/-162.3 SD. Hepatitis was defined as more than two times ULN of AST value, thus AST>80 was taken as having hepatitis, in this study. Thus 99/137 (about 72%) of patients had hepatitis.

There was no statistically significant difference when either the APTT or PT result, compared with more than two-fold rise in aspartate aminotransferase level during the course of illness ( $p>0.05$ ). Hence an abnormal APTT/PT result was not predictive by the presence of two-fold rise of AST levels from the upper normal margin.

## Discussion

Dengue virus (DENV) infection leading to DHF and complications are not fully understood. The blood level of dengue NS1 (Nonstructural protein) antigen has a correlation to development of DHF. Some studies suggested a possibility of NS1 binding to prothrombin and inhibition of its activation, thus leading to prolonged APTT [6]. Recent study published in August 2017 suggested PT (INR) as the most important predictor of severe bleeding, where they found both hepatic transaminases having high correlation with international normalized ration (INR) [7]. Similarly, APTT and PT levels have been suggested as predictors in bleeding in DHF [8].

Our study aimed at looking in to the connection between hepatitis and prolonged APTT/PT in patients with dengue. However, there were limiting factors like small number of patients, affordability for series of investigations to do, specially coagulation studies. Thus, in this small study we did not find a significant association of presence of hepatitis leading to deranged coagulation. Further studies with larger number of patients will be helpful in finding pathophysiological mechanism leading to deranged coagulation in dengue.

## Conclusion

Presence of hepatitis was not predictive of abnormal APTT/PT values. Further larger scaled studies are recommended in achieving conclusions.

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