

Correlation of dipstick proteinuria with thrombocytopenia and leucopenia and its efficacy predicting the severity of kidney injury in dengue fever

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Abstract

Introduction: Dengue fever is one of the global viral epidemics with more than 50 million cases reported per year with more than 20 thousand deaths every year. Dengue virus infection is transmitted by the bite of *Aedes aegypti* and *Aedes albopictus* mosquitoes. Dengue fever manifests as undifferentiated fever, dengue fever (DF), and dengue hemorrhagic fever (DHF). **Objective:** This study was done in a tertiary care hospital in coastal region of Karnataka, India to correlate dipstick proteinuria with thrombocytopenia and leucopenia and its efficacy in predicting the severity of kidney injury in dengue fever. **Methods:** The data has been obtained from the patient records of laboratory and medical records section of the hospital. Laboratory testing of patients admitted in the hospital with fever was done. Dengue fever was detected by the positivity to NS1 antigen, IgM and IgG. Patients coming with fever in the out-patient departments were excluded from the study. The hematological parameters and proteinuria were analysed. The Wilcoxon method (nonparametric) and the Student t-test (parametric) were used for statistical analysis. Descriptive statistics were compared using the chi-square test for the variables of gender, age and the clinical forms of dengue. Hospital ethics committee clearance was obtained before starting the study. **Results:** Proteinuria is seen to significantly correlate with thrombocytopenia and leucopenia in our study. However there was no significant correlation with leucopenia and thrombocytopenia in our study. **Conclusion:** Hence injury to the kidney is more likely if there is presence of thrombocytopenia and leucopenia in patients with dengue fever. Thus severity of renal impairment in dengue fever can be predicted by presence of decreased total WBC count and decreased platelet count.

Key words: Dengue, Haematological profile, Leucopenia, Proteinuria, Thrombocytopenia.

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Introduction

Dengue fever is caused by single stranded RNA virus of flaviviridae family. The World Health Organization estimates that 50 to 100 million cases of dengue infection occur each year [1-3]. More than three lakh cases of dengue hemorrhagic fever are diagnosed each year. Dengue causes a fatality of 24,000 deaths per year. Dengue virus infection is transmitted by the bite of *Aedes aegypti* and *Aedes albopictus* mosquitoes. Kidney is affected in dengue fever in many cases as marked by proteinuria [4,5]. Few studies are available

regarding the utility of dipstick method of analysis of proteinuria in dengue fever. Our study aims to determine as to whether any laboratory parameter can predict the occurrence and severity of kidney injury in patients of dengue fever admitted in the hospital because early detection and timely intervention can decrease mortality associated with dengue fever.

Hence we studied cases of suspected dengue in patients admitted for fever in our hospital to correlate hematological profile with proteinuria using dipstick method.

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Materials and Methods

Study design: The study is a prospective cum retrospective study carried out in patients of a tertiary care hospital in coastal region of Karnataka admitted for fever from October 2012 to September 2013.

Setting: The data has been obtained from the patient records of laboratory and medical records section of the hospital.

Laboratory testing of patients admitted in the hospital with fever was done. Dengue fever was detected by the positivity to NS1 antigen, IgM and IgG.

The kit used was Dengue day 1 test kit (NS1 Ag, IgG and IgMAB) by J. Mitra and Co. Hematological tests and urine tests were done in confirmed cases of dengue. Hospital ethics committee clearance was obtained before starting the study.

Inclusion criteria: In-patients complaining of fever were included from the study.

Exclusion criteria: Patients in the out-patient department coming with fever were excluded from the study. Fevers proven due to reasons other than dengue were excluded from the study.

Results

A total of 433 cases of suspected dengue fever admitted in the hospital were tested within one year for dengue, out of which 146 cases (33.7%) were positive for dengue. Coexistent malaria with dengue was seen in 11 (7.5%) cases. 90.4% of dengue positive cases were males and 9.6% of dengue positive cases were females. Males were more commonly affected than women (9:1). Mean age is 30.38 years.

The oldest patient was 75 years and the youngest patient was 4 years. Maximum number of cases was in April month (summer climate) and least number of cases in february and march (spring climate).

74.65% of cases were positive for dengue NS1 Ag. 6.16% of cases were positive for both dengue NS1 Ag and IgM. 2.05% of cases were positive for dengue NS1 Ag and IgG.

48.63% of dengue positive cases had leucopenia. None of the dengue positive cases had leucocytosis. 47.26% of dengue positive cases had lymphopenia. 4.10% of the dengue positive cases had lymphocytosis. 48.63% of the dengue positive cases had normal lymphocyte count.

There was no proteinuria seen in category A. Total 22 (15%) cases belonged to category B, out of which 17 cases showed no proteinuria, 3 cases with 1+ proteinuria, 2 cases with 2+proteinuria. Total 52 (35.6%) cases were seen in category C with 41 cases showing no proteinuria, 9 cases showing 1+ proteinuria, 1 case showing 2+proteinuria, 1 case showing 3+ proteinuria. Total 42 (28.7%) cases were seen in category D with 35 cases showing no proteinuria, 6 cases showing 1+ proteinuria, 1 case showing 2+ proteinuria. Total 25 (17.12%) cases belonged to category E with 19 cases showing no proteinuria, 6 cases showing 1+ proteinuria (Table 1). Four dengue positive cases had no platelet and urine record. Significant association between platelet count and proteinuria was seen in our study (p value 0.001).

Study size: A total of 433 cases of suspected dengue fever admitted in the hospital were tested within one year for dengue, out of which 146 cases (33.7%) were positive for dengue.

Variables: All the participants were analysed for confirmation of dengue fever. Data regarding complete blood count and urine analysis were analysed. The hematological parameters was analysed by the Lablife H3D premier cell counter. The proteinuria was analysed by using DIRUI dipstick. The dengue positive cases based on platelet count was divided into A, B, C, D, E categories with category A having platelet count less than 20000/cumm, category B having platelet count 20000/cumm to 50000/cumm, category C having platelet count 50000/cumm to 100000/cumm, category D having platelet count 100000/cumm to 150000/cumm, category E having platelet count more than 150000/cu mm [1]. The proteinuria was classified as 1+, 2+, 3+ or nil using dipstick method.

Statistical methods: The Wilcoxon method (nonparametric) and the Student t-test (parametric) were used for statistical analysis. Descriptive statistics were compared using the chi-square test for the variables of gender, age and the clinical forms of dengue.

Table-1: Correlation between platelet count and proteinuria.

Platelet count/ Category	Nil proteinuria	1+ proteinuria	2+ proteinuria	3+ proteinuria	Total cases
< 20000/cumm (category A)	1	0	0	0	1 (0.68%)
20000-50000/cumm(category B)	17	3	2	0	22 (15%)
50000-100000/cumm (category C)	41	9	1	1	52 (35.6%)
100000-150000/cumm(category D)	35	6	1	0	42 (28.7%)
>150000/cumm(category E)	19	6	0	0	25 (17.12%)

64 out of 146 dengue positive cases had normal total WBC count, among these 56 cases had nil proteinuria, 6 cases had 1 +proteinuria and 2 cases had 2 + proteinuria. 71 out of 146 dengue positive cases had leucopenia. Out of these 71 cases with leucopenia, 52 cases had no proteinuria, 16 cases had 1 + proteinuria and 1 case had 2 + proteinuria, 2 cases had 3+ proteinuria (table 2). 11 dengue positive cases had no relevant records. Leucopenia was significantly associated with proteinuria in our study (p value 0.0004)

Table-2: Correlation of WBC count with proteinuria.

Total WBC count	Nil proteinuria	1+ proteinuria	2+ proteinuria	3+ proteinuria	Total cases
Normal	56	6	2	0	64
Leucopenia	52	16	1	2	71

One case in category A had leucopenia. 10 out of 20 cases in category B had leucopenia. Category C had maximum dengue positive cases (56 cases), out of which 14 cases has normal total WBC count (TC) and 38 cases had leucopenia. Category D had total 42 cases, out of which 24 cases had normal TC and 17 cases had leucopenia. Category E had total 24 cases, out of which 16 cases had normal TC and 7 cases had leucopenia (table 3). Total 9 dengue positive cases had no relevant records. There was no significant association between WBC count and platelet count in our study (p value 0.32).

Table-3: Correlation of WBC count with platelet count.

Total WBC count(TC)	A	B	C	D	E	Total cases
Normal	-	10	14	24	16	64
Leucopenia	1	10	38	17	7	73
Total	1	20	52	41	23	137

Discussion

Dengue fever is frequently associated with thrombocytopenia, leucopenia, deranged liver function tests, increased AST to ALT ratio [6]. The severity of dengue increases with decreasing platelet count in many studies [6,7]. Fever is the most common presenting complaint in dengue fever [6,7].

Hence all patients admitted in our hospital with fever and suspected to have dengue were analysed in our study. Kidney is affected in 76% of cases of dengue fever. In our study an attempt is made to correlate thrombocytopenia, leucopenia with proteinuria detected by urine dipstick method and efficacy of dipstick proteinuria to predict the severity of dengue fever as marked by kidney injury and thrombocytopenia.

Dengue causes thrombocytopenia due to bone marrow suppression and binding of dengue antigens to platelets and antibody mediated immunological destruction of platelets [7]. The changes in WBC count is useful in differentiating dengue infections from other febrile illnesses [8]. Thrombocytopenia is seen in 59% of cases in our study. Thrombocytopenia was seen significantly associated with dengue in most of the studies [6,9-11]. There is significant thrombocytopenia seen associated with dengue fever in our study, similar to many studies [12-14].

44% of cases had leucopenia in the present study. There is significant leucopenia seen associated with dengue fever in our study similar to many studies [6, 10, 11,

15]. However, a study observed only 4% cases of dengue fever had leucopenia and was statistically not significant [7]. 22% of cases had proteinuria in the present study. A significant association is found between thrombocytopenia and proteinuria. Association between leucopenia and proteinuria was also significant in our study. However no significant association between leucopenia and thrombocytopenia was seen in our study.

The World Health Organization (WHO) estimated that 40% of the world's population (approximately 2.5 billion) living in tropical and subtropical areas are at risk of getting infected by dengue virus. The global prevalence of dengue infection has increased dramatically in the recent decades, particularly in the Americas, Western Pacific and South-East Asian regions. DF has estimated 50 to 100 million infections and 200,000–500,000 cases of dengue hemorrhagic fever (DHF) per year. On an average, 20000 deaths occur every year due to dengue [1]. Case fatality rate is around 5%. Early diagnosis and aggressive fluid replacement therapy with good nursing care can reduce the fatality rates to 1% or less [1, 16]. In 2005, the world health assembly, through WHA resolution 58.3, in a review of the international health regulation (IHR), included dengue fever as an emergent public health disease, with implications for health safety due to spread of the epidemic beyond national boundaries[1].

The epidemic trend of dengue, in India, is on the rise in recent years with 28,292 cases in 2010 and increasing mortality. All four serotypes of dengue have been isolated in India. Dengue fever has been reported from India over a long time but DHF was first reported in 1963 from Calcutta. Dengue shows a cyclical trend with a peak in September-October every year. It is spread by female aedes mosquito which breeds exclusively in domestic man made water receptacles. Dengue outbreaks are common in rural areas of Haryana, Maharashtra, Andhra Pradesh and Karnataka. Coastal Karnataka has a tropical climate Favourable for breeding *Aedes aegypti* mosquitoes. Poor vector control, unplanned construction activities, poor sanitation contribute to increasing incidence of dengue fever [16]. Dengue has a huge economic impact and is largely preventable [7].

Dengue fever is one of the most common arboviral infections in humans caused by a single-stranded RNA virus of Flaviviridae family with four serotypes DEN-1,

DEN-2, DEN-3, and DEN-4 and is transmitted by the bite of *Aedes aegypti* and *Aedes albopictus* mosquitoes [1].

Dengue is a self-limiting infection which causes a spectrum of illness ranging from no symptoms to life threatening DHF/dengue shock syndrome. It shares some symptoms with other infectious diseases, most of which go undiagnosed and under reported.

Clinical manifestations result from uncomplicated dengue fever to dengue hemorrhagic fever (DHF) with/without shock. Most of the patients presented with classical features such as fever myalgia, arthralgia, pain abdomen, vomiting, headache, rash, and bleeding manifestations.

Hypotension, hemorrhagic spots, jaundice, pedal edema, ascites, pleural effusion, shock, hepatitis, and polyserositis may occur. The group progressing from no severe to severe disease is difficult to define, but this is an important concern since appropriate treatment may prevent these patients from developing more severe clinical conditions [1].

Serological testing is currently the standard diagnostic practice for confirmation of dengue infection. There is no specific antiviral treatment for dengue. Management includes supportive therapy, hydration and close monitoring for signs and symptoms suggestive of dengue shock syndrome [16].

Conclusion

Our study is one of the few studies that have found significant association of proteinuria with thrombocytopenia and leucopenia. However there was no significant correlation with leucopenia and thrombocytopenia in our study. Hence injury to the kidney is more likely if there is presence of thrombocytopenia and leucopenia in patients with dengue fever. Thus severity of renal impairment in dengue fever can be predicted by presence of decreased total WBC count and decreased platelet count.

Urine analysis for proteinuria along with complete blood count helps in early detection of kidney impairment in dengue fever and timely intervention in these patients decreases mortality in dengue fever.

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