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Spot Urine Protein Creatinine Ration: A Valuable Tool for Assessing Severity of Dengue Infection

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Abstract
Dengue is a viral infection with different presentations, hence predicting the disease severity at admission is essential to triage patients requiring meticulous monitoring. In severe dengue, there is increase of urinary protein clearance due to the increase in systemic vascular permeability. Spot Urine Protein Creatinine Ratio (UPCR) as a tool in predicting the disease severity and adverse outcome in Dengue infection. A cross-sectional study conducted at Tertiary care center in 100 confirmed dengue patient with pre-defined inclusion criteria in South Gujarat. Daily morning first void clean catch mid-stream urine has been collected and sent for analysis. Daily morning complete blood counts are also collected. Statistically significant high UPCR level was found in patients with low platelet count, Dengue Hemorrhagic Fever (DHF), Dengue Shock Syndrome (DSS). spot urine protein creatinine ration (UPCR) analysis is valuable and handy tool to assess prognosis and complications of dengue fever.

INTRODUCTION

Dengue is an important arthropod-borne disease affecting millions of people in tropical and subtropical regions and is the most prevalent mosquito-borne viral disease in South East Asia with significant morbidity and mortality[1].

The global incidence of dengue fever has increased dramatically and about half of the world's population is now at risk. An estimated 100 million to 400 million infections occur each year, but more than 80% are generally mild and asymptomatic

Dengue fever is the fastest growing mosquito-borne viral disease. It is transmitted by the bite of infective, female, Aedes aegypti mosquito. Dengue virus is a part of Flaviviridae family and there are four different serotype that are closely related, [DEN1,DEN2,DEN3,DEN4][2]. Dengue has wide spectrum of clinical presentation ranging from non-severe and mild asymptomatic form or it can progress to more severe disease that is characterized by plasma leakage with or without hemorrhage.

WHO 2009 guideline[11] classify dengue into Dengue fever without warning sign, Dengue fever with warning sign and Severe Dengue

After being bitten by an infected mosquito, the dengue virus enters the host organism through the skin. Host humoral, cellular and innate immune responses are involved in disease progression, with rapid clearance of the virus from the host organism followed by more severe clinical manifestations. Hence, the most severe clinical presentation during the infection course does not correlate with a high viral load[3]. Changes in endothelial micro vascular permeability and thrombus regulatory mechanisms lead to increased protein and plasma loss. The proposed theory suggests that endothelial cell activation mediate by monocytes, T cells, the complement system and various inflammatory molecules mediate plasma extravasation. Thrombocytopenia may be associated with alterations in megakaryocytopoiesis manifested by infection of human hematopoietic cells and impaired proliferation of progenitor cells. This can lead to platelet malfunction, damage, or depletion, which can lead to significant bleeding. Studies shown that the onset and peak of proteinuria using the urine protein creatinine ratio (UPCR) was associated significantly with the development of Dengue Hemorrhagic Fever (DHF). The small hospitalized cohort comprised mostly DHF patients, as patients with DF are mostly treated in the community. The degree of proteinuria may indicate the severity of dengue infection. The significant peak proteinuria could be a manifestation of a pathogenic mechanism that the virus triggers on the lympho reticular system, resulting in glomerular leak age of protein associated with DHF. Proteinuria has been used as a method to assess the severity of dengue fever. Proteinuria is best measured by 24-hour urine protein, but it is a cumbersome method. Various texts show that urine spot PCR as fast, simple and alternative method of estimation of proteinuria. A Spot urine protein creatinine ratio of>20mg/mmol (0.2mg/mg) is the most commonly used cut off value for detecting proteinuria[4].

Aims and Objectives:

- To evaluate the spot urine Protein Creatinine Ratio (UPCR) as a tool of predicting severity of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) in dengue infection.
- To determine association between spot urine Protein Creatinine Ratio and severity of dengue hemorrhagic fever and dengue shock syndrome.

MATERIAL AND METHODS

Inclusion Criteria: IgM dengue ELISA positive, DengueNS1positive and Normal serum urea/creatinine at presentation.

Exclusion Criteria: Pre-existing Chronic Kidney Disease /nephrotic/ nephritic syndrome, Diabetes, Hypertensive, Urinary tract infections and Patients who refuse to give consent.

Sample Size: Study has included 100 confirmed cases of Dengue infection.

A cross-sectional study was conducted at a tertiary care hospital, Surat, South Gujarat.

Only patients with confirmed dengue by NS1 and IgM ELISA has been included. They were briefed on the purpose and procedure of the study, written informed consent in local language has been obtained. Daily morning first void clean catch mid-stream urine has been collected and sent for analysis. Daily morning complete blood counts are also collected.

RESULTS AND DISCUSSIONS

Present study found that highest number of participants (53%) were noted in 20-40 years age group and mean age was 38.5 years. The main clinical findings of present study were:

Incidence of DHF was observed in 19% and incidence of DSS was observed in 21% study participants. We have tried to correlate the level of spot urine protein creatinine ratio (UPCR) with other parameters in the following table.

Thus, high level of spot UPCR was clearly associated with DHF and DSS.

Present study found that all the participants who had spot UPCR value >1.5 and almost 86% of 1.0-1.5 spot PCR group had statistically significant very low platelets, whereas participants with low spot UPCR

Table 1: Analysis of Major Parameter[10]

Spot Urine Protein Creatinine ratio (UPCR) (mg/mg)	Number (n=100)
0.5	51
0.5-1.0	37
1.0-1.5	7
>1.5	5
Platelet Count (/µL of blood)	Number (n=100)
<50000	26
50000-1lakh	39
>1lakh	35
Bleeding Manifestations	Number (n=100)
Present	22
Absent	78

Table 2: Association between spot UPCR and dengue parameters

Parameter	Spot PCR Group (in mg/mg (%)				
	<0.5 (n=51)	0.5-1.0(n=37)	1.0-1.5(n=7)	>1.5(n=5)	p-value
PC					
<50000	7(13.7)	8(21.6)	6(85.7)	5(100)	
50000-1lakh	26(50.9)	12(32.4)	1(14.3)	0 (0)	0.001
>1lakh	18(35.4)	17(45.9)	0 (0)	0 (0)	
Bld. Meni.					
Yes	7(13.7)	7(18.9)	4(57.1)	4(80)	
No	44(86.3)	30(81.1)	3(42.9)	1 (20)	0.001
TSF					
Yes	10(19.6)	10(27)	5(71.4)	3(60)	
No	41(80.4)	27(73)	2(28.6)	2(40)	0.01
HV (%)					
<20	2(3.9)	5(13.5)	1(14.3)	1(20)	
20-30	2(3.9)	7(18.9)	3(14.3)	1 (20)	
30-40	44(86.3)	20(54.1)	2(28.6)	1(20)	0.003
>40	3(5.9)	5(13.5)	1(14.3)	2(40)	
DHF					
Yes	3(5.9)	6(16.2)	5(71.4)	5(100)	
No	48(94.1)	31(83.8)	2(28.6)	0 (0)	0.01
DSS					
Yes	6(11.7)	5(13.5)	5(71.4)	5(100)	
No	45(88.3)	32(86.5)	2(28.6)	0 (0)	0.001
Clinical out.					
Discharge	51(100.0)	37(100)	6(85.7)	2(40)	0.01
Death	0(0.0)	0 (0)	1(14.3)	3(60)	

value had higher platelets. These findings are correlated with the study done by Nimmannitya S. *et al*[9] and Vasanwala F F *et al*[5], Priyadarshi A *et al*[8], Venkataramanan R *et al*[7] and Joseph E *et al*[6].

The distribution of study participants according presence of bleeding manifestation and spot PCR level was statistically significant ($p<0.05$). Present study found that incidence of bleeding manifestation was observed in statistically significant number of participants who had spot UPCR value greater than 1.0 compared with participants with low spot UPCR. These findings are correlated with the study done by Nimmannitya S. *et al*[9] and Vasanwala FF *et al*[5], Priyadarshi A *et al*[8], Venkataramanan R *et al*[7], Joseph E *et al*[8]

Similarly, the incidence of third space fluid and high hematocrit value was observed in statistically significant number of participants who had spot UPCR value greater than 1.0 compared with participants with low spot PCR.

Present study found that all participants with low spot PCR group [0.5 and 0.5-1.0] were statistically significantly treated successfully. Almost 85.7% of 1.0-1.5 spot PCR group participants and 40.0% of >1.5 spot PCR group treated successfully. The overall mortality was 4% and all this observed in participants with higher spot PCR group (>1.0). Therefore, the present study noted that mortality was statistically significantly higher among who had higher spot UPCR value.

CONCLUSION

Spot urine protein creatinine ration (UPCR) analysis is valuable and handy tool for to assess prognosis and complications of dengue fever.

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