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CORRELATION OF PLATELET COUNT WITH ULTRASONOGRAPHICALLY ASSESSED PERIRENAL FLUID IN SEROLOGICALLY POSITIVE PATIENTS OF DENGUE VIRAL FEVER

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ABSTRACT

*Introduction***:** Dengue fever constitutes one of the most common arthropod borne viral febrile illness, caused by a flavivirus. Ultrasonography is a safe, low cost imaging method, that helps in determining severity of the disease and knows the prognosis in patients.

*Aim***:** To correlate perirenal fluid collection with platelet count in serologically positive dengue cases.

*Materials and Methods***:** The study was conducted prospectively for a period of 6 months in a tertiary care hospital, Bengaluru in the year 2015 between July and December. Study was carried out on 252 serologically positive dengue cases. Ultrasound of abdomen, pelvis and thorax was performed and perirenal fluid collection was noted down and correlated with the platelet count to assess the severity of the disease. The data was analysed by using SPSS software. Chi-Square / Fisher exact test was employed to estimate the association between two variables.

P values ≤ 0.05 was considered to be statistically significant.

*Results***:** The study participants were in the age group of 4 to 87 yrs with mean age of 41.7 yrs. out of which 120 were males (47.6 %) and 132 were females (52.4 %). Maximum cases were in the middle age group of 21-60 yrs (67.9 %). Out of 252 dengue positive cases, 236 (93.7 %) had platelet count less than 1 lakh/microlitre of blood. All the study samples were positive for NS 1 antigen, 202 samples were positive for IgM antibodies and 232 samples for IgG antibodies.

Among 252 patients, fluid accumulation was seen in perirenal space in 41 patients. Right side fluid accumulation was seen in all 41 patients but left side fluid accumulation was noted down only in 15 patients who were severely ill. All the patients with right perirenal fluid collection had platelet count less than 60,000 platelets/microlitre of blood (44.1%) and patients with left perirenal fluid collection and bilateral fluid accumulation had platelet count less than 25,000 platelets/microlitre of blood (3.6%), thus left side fluid accumulation indicates that the disease is more severe. Thus decrease in platelet count correlated with the perirenal fluid accumulation and was statistically significant ($p\leq0.05$).

Conclusion: The degree of thrombocytopenia showed a significant statistical correlation with the perirenal fluid collection , indicating severity of the disease.

Keywords: Dengue, Thrombocytopenia, Serology, Ultrasonography, Platelet Count

INTRODUCTION

Dengue fever constitutes one of the most common arthropod borne viral febrile illness, caused by a flavivirus and endemic in tropical and subtropical countries with outbreaks occurring during monsoon (Ukey *et al.,* 2010). It is transmitted by the bite of infected *Aedes aegypti* mosquito and has 4 serotypes, namely DEN-1, DEN-2, DEN-3 and DEN-4 (Kulkarni *et al.,* 2011; Apurba *et al.,* 2016). It affects up to 100 million people annually, with 5,00,000 cases of dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS), and around 30,000 deaths, mostly among children .[3] Serious forms of dengue may be a hypersensitivity or enhancement response to sequential dengue virus infection in persons sensitized by prior exposure to other serotypes of the virus (Ananthnarayana and Paniker, 2017).

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Table 1: Correlation of Perirenal Collection with platelet count

Platelet Count	Right Perirenal Collection				Fisher Exact Test	p-value
	No	Less than 2cc	2cc - 5 cc	More than 5 cc		
5000 - 20000	0 (0.0)	0 (0.0)	0 (0.0)	9 (56.3)		
20000 - 40000	0 (0.0)	10 (66.7)	10 (100.0)	7 (43.8)		
40000 - 60000	70 (33.2)	5 (33.3)	0 (0.0)	0 (0.0)		
60000 - 80000	83 (39.3)	0 (0.0)	0 (0.0)	0 (0.0)		
80000 - 100000	42 (19.9)	0 (0.0)	0 (0.0)	0 (0.0)		
≥ 1 Lakh	16 (7.6)	0 (0.0)	0 (0.0)	0 (0.0)	185.914	< 0.05
Total	211 (100.0)	15 (100.0)	10 (100.0)	16 (100.0)		
	Left Perirenal Collection					
5000 – 20000	0 (0.0)	0 (0.0)	5 (100.0)	4 (100.0)		
20000 – 40000	21 (8.9)	6 (100.0)	0 (0.0)	0 (0.0)		
40000 – 60000	75 (31.6)	0 (0.0)	0 (0.0)	0 (0.0)		
60000 – 80000	83 (35.0)	0 (0.0)	0 (0.0)	0 (0.0)		
80000 - 100000	42 (17.7)	0 (0.0)	0 (0.0)	0 (0.0)		
≥ 1 Lakh	16 (6.8)	0 (0.0)	0 (0.0)	0 (0.0)	87.187	< 0.05
Total	237 (100.0)	6 (100.0)	5 (100.0)	4 (100.0)		
	Bilateral Perirenal Collection					
	No	Yes				
5000 – 20000	0 (0.0)	9 (60.0)				
20000 – 40000	21 (8.9)	6 (40.0)				
40000 – 60000	75 (31.6)	0 (0.0)				
60000 – 80000	83 (35.0)	0 (0.0)				
80000 - 100000	42 (17.7)	0 (0.0)				
≥ 1 Lakh	16 (6.8)	0 (0.0)			74.05	< 0.05
Total	237 (100.0)	15 (100.0)				

Increased capillary permeability is the main pathological process that leads to various clinical, hematological and ultrasonographic manifestations of dengue (Setiawan *et al.,* 1998).

Diagnosis of dengue can be done by various clinical and laboratory parameters. Thrombocytopenia serves as predictive marker for early diagnosis of dengue (Jyothi and Metri, 2015). Ultrasonography is a safe, low cost imaging method that helps in determining severity of the disease and know the prognosis in patients (Basawaraj *et al.,* 2015).

Objectives
1. To correlate the amount of accumulation of perirenal fluid by ultrasonography with the platelet count in the serologically positive dengue fever cases, thus assess the severity of the disease.
2. Correlation of various serological markers of dengue with the platelet count.
3. Correlation of above parameters in different age groups.

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MATERIALS AND METHODS

The present study was conducted prospectively for a period of 6 months during the recent outbreak of dengue fever in a tertiary care hospital, Bengaluru in the year 2015 between July and December. A written informed consent was obtained from all the patients who participated in the study after explaining the patient's diagnosis, the nature and purpose of the study. The study was approved by Institute Ethical Committee and procedures followed in this study are in accordance with the ethical standard laid down by ICMR's ethical guidelines for biomedical research on human subjects (2006).

Inclusion Criteria
Serologically positive dengue infections, which were sent for Ultrasonography were included.

Exclusion Criteria
1.   Patients with thrombocytopenia but serologically negative were not included.
2.   Patients with clinically suspected dengue but serologically negative were not included.

Methodology
*   A total of 252 serologically positive dengue cases of all age groups were included in the study.
*   Under proper aseptic precautions, blood samples were collected from patients
*   Samples were tested for dengue serology (NS1 Ag, IgM, IgG) and platelet count.
*   Serologically positive dengue cases were taken for ultrasonography of abdomen and pelvis.
*   Ultrasonography of abdomen and pelvis was done by experienced radiologist to assess the severity and prognosis of the disease.
*   Accumulation of perirenal fluid was noted down, whether it is unilateral or bilateral and also the amount of accumulation.

Statistical Analysis
Data was entered in the SPSS software. Chi-Square/Fisher exact test was employed to estimate the association between two variables. P values ≤ 0.05 was considered to be statistically significant.
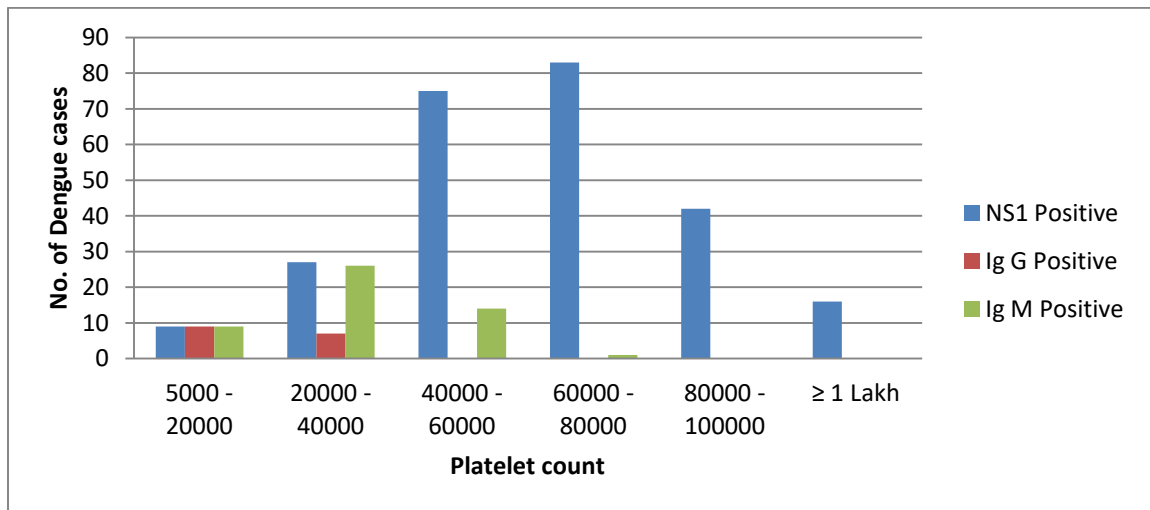
**Graph 1: Serological markers of dengue with the platelet count**

RESULTS

Total of 252 serologically positive dengue cases were included in the study. They were in the age group of 4 to 87 yrs with mean age of 41.7 yrs. out of which 120 were males (47.6 %) and 132 were females (52.4 %). Maximum cases were in the middle age group of 21-60 yrs (67.9 %). Out of 252 dengue positive cases, 236 (93.7 %) had platelet count less than 1 lakh/cu mm of blood. Out of 252 serologically positive cases, all were positive for NS1 Ag, 202 were positive for IgM and 232 for IgG antibodies.

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Table 2: Comparison of all the parameters with age group

	Age group							
	0-20	21-40	41-60	61-80	81-100	Total		
SEVERITY	**Right Perirenal Collection**							
No	16	83	63	41	8	211	chi-square	36.943
Less than 2cc	7	6	2	0	0	15	p value	< 0.05
2cc - 5 cc	3	5	1	1	0	10		
More than 5 cc	5	5	6	0	0	16		
	Left Perirenal Collection							
No	28	93	66	42	8	237		
Less than 2cc	0	4	2	0	0	6	Fisher exact	9.329
2cc - 5 cc	2	1	2	0	0	5	p value	< 0.05
More than 5 cc	1	1	2	0	0	4		
	Bilateral Perirenal Collection							
No	28	93	66	42	8	237	Fisher exact	4.591
Yes	3	6	6	0	0	15	p value	0.289
Serological markers	**NS 1 Positive**							
Yes	31	99	72	42	8	252		
	Ig G Positive							
No	26	94	66	42	8	236	Fisher exact	7.979
Yes	5	5	6	0	0	16	p value	0.063
	Ig M Positive							
No	16	76	62	40	8	202	Fisher exact	23.780
Yes	15	23	10	2	0	50	p value	< 0.05
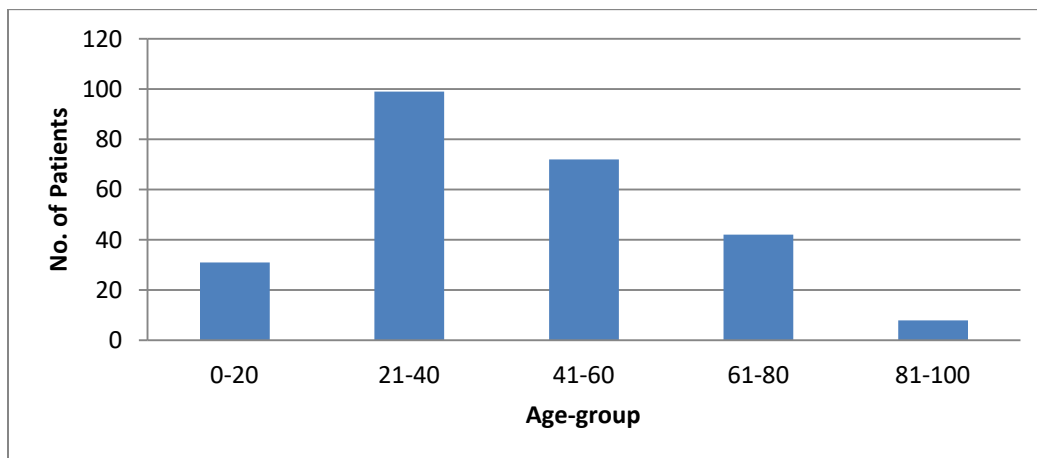
Graph 2: Age-Distribution of Patients

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Figure 1: Perirenal fluid collection

Ultrasonographic perirenal fluid collection was noted down. Among 252 total scanned patients, fluid accumulation was seen in perirenal space in 41 patients. Right side fluid accumulation is seen in all 41 patients but left side fluid accumulation was noted down only in 15 patients who were severely ill. Thus bilateral collection was noted down in 15 patients. All the patients with right perirenal fluid collection had platelet count less than 60,000 and patients with left and bilateral fluid accumulation had platelet count less than 25,000, thus left side fluid accumulation indicates that the disease is more severe.

DISCUSSION
Arboviruses are diverse group of RNA viruses transmitted by blood sucking arthropods and vary greatly in their geographical distribution. Dengue virus is the most common arbovirus in india transmitted by Aedes mosquito with 2.5 billion people at risk of infection, more than 100 million cases and 25,000 deaths reported annually (Apurba and Sandhya, 2016; Mustafa *et al.,* 2011). Clinically dengue manifests with sudden onset of high fever with chills, intense headache, muscle and joint pain, retro-orbital pain and severe backache. Hemorrhagic diathesis and thrombocytopenia with concurrent hemoconcentration are a constant finding (Government of India, 2006). NS1 is a glycoprotein that is common to all dengue serotypes and can be used to detect either primary or secondary infections in the earliest stages. Serology testing for dengue virus-specific antibodies, types IgG and IgM, can be useful in confirming primary or secondary diagnosis (Dussert *et al.,* 2006). USG is a relevant and important tool for the early diagnosis of plasma leakage signs and for prediction of the disease severity (Vedaraju *et al.,* 2016). Sonographic findings express the increase in capillary permeability (a sign of plasma leakage) and include cavitary effusion (ascites, pleural and pericardial effusion), and gallbladder wall thickening present in one third of patients affected by the mild presentation, and in 95% of cases with the severe presentation of DHF. Additionally, the presence of fluid in the perirenal space can be visualized (Oliveira *et al.,* 2010).
In our study maximum cases were in the age group of 21-60 yrs. Right Perirenal collection was noted when the platelet count was less than 60,000. Bilateral perirenal collection was noted when the platelet count was less than 40,000. That means perirenal collection is related to the severity of the disease. More than 5cc bilateral Perirenal collection is seen when the platelet count is less than 20,000. That means perirenal collection can also be taken as an indicator of severity of dengue fever along with the platelet count.
In a study conducted by Basawraj *et al.,* in 2015 also noted that bilateral renal collection was seen when platelet count was less than 40,000 (Basawaraj *et al.,* 2015). Study conducted by Nawali *et al.,* in 2016 also noted that perirenal oedema was seen only in severe cases of dengue.

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CONCLUSION
In our study the sonographic abnormality perirenal collection was noted mostly in the severe cases. Low platelet count was also noted in severe cases. Bilateral Perirenal collection was mostly seen when the platelet count was low. The degree of thrombocytopenia showed a significant statistical correlation with the perirenal collection , indicating severity of the disease. Thus platelet count and ultrasonography are a simple and valuable tools in diagnosing and predicting severity of dengue fever.

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