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Original Research Article

Do the small blood cells have a big impact as prognosticators in dengue – A study

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ABSTRACT

Introduction: Dengue is an arboviral disease endemic in India. Severe dengue has a high morbidity. The progression to severe dengue may be diagnosed by clinical and lab parameters, are of the useful lab tests is platelet count, as thrombocytopenia is a consistent feature in dengue. There is confusion about the role thrombocytopenia in dengue. Our study aims to study the platelet count patterns and its relevance to severity of dengue.

Materials and Methods: We conducted a study on 132 dengue positive cases with relevant hematology data in November 2016.

Results: We had predominance of young people and males in the study group. Thrombocytopenia was uniform across the ages and sexes. Severe thrombocytopenia constituted 56%, had significant association with atypical lymphocytosis, rise in hematocrit and antibody patterns.

Conclusion: Platelet counts are marker of dengue, can serve as predicators of severity, platelet count monitoring helps guide transfusion therapy.

1. Introduction

Dengue caused by dengue virus (DENV), is endemic in India and a cause of public health concern due to high mortality of severe forms. It can manifest as asymptomatic, mild to severe dengue.[1,2] The milder forms presenting as flu like fever have overlap with other diseases like Influenza, Malaria etc and sometimes evolve rapidly to severe dengue with or without warning signs. Bleeding & shock are dreaded complications of severe dengue.[1–3] Dengue needs to be diagnosed early as there is no specific therapy.[3,4] Clinical features are of limited utility in diagnosing impending rapidly developing severe dengue and have to be supplemented by certain lab tests for accurate and early diagnosis of progression.[2–7] Severe dengue is characterized by thrombocytopenia (<1 lakh/cumm) preceding rise in hemocrit.[2,3,6,7] Thrombocytopenia is a consistent feature in dengue and a major reason for hospitalisation due to the risk of bleeding.[1,8] Complete blood counts including platelet counts are routinely performed simple, inexpensive tests available even in rural areas, where it may be checked by microscopy. There is confusion about the role of platelet counts in dengue, while it is confirmed as an initial dengue marker and are of the diagnostic criteria for dengue haemorrhagic fever(DHF),[8,9] correlation with severity of bleed and complications in dengue is debated in various studies.[10–16]

2. Aims a nd Objectives

To study patterns of platelet count, its association with other lab parameters in dengue.

3. Materials and Methods

This study was conducted in hematology section over one month in November 2016 on 132 serologically

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positive dengue cases. The data retrieved from hematology (complete blood counts tested by Sysmex 1800i) and microbiology records (dengue serology) was tabulated, along with visual check of platelets differential counts on leishman stained smears (as per hospital protocol) and analysed.

4. Inclusion criteria

All serologically positive dengue cases with thrombocytopenia and other relevant hematology data.

4.1. Exclusion criteria

Dengue cases with associated diseases, incomplete hematology data, high or normal platelet counts and pseudothrombocytopenia.

4.2. Ethical committee clearance

The study maintains anonymity of patient identity by recording only age & gender against the unique hospital identification number along with relevant data. The study was approved by ethical committee of hospital.

5. Results

Our study showed an age range of 5months to 65yrs with an average of 32yrs, with male predominance (male: female = 1.2:1)[Table 1].

Thrombocytopenia was graded as and showed

Grade	Count (cumm)	Cases(%)
Mild	$\geq$ 0.76- 1.5	31 (24%)
Moderate	$\geq$ 0.51- 0.75	27(20%)
Severe	$\geq$ 0.5	74(56%)

55% paediatric, 56% adults, 57% males and 55% females had severe thrombocytopenia.

The analysis of severe thrombocytopenia [Table 2] showed only one case <10,000/cumm (critical value)

The lowest platelet count noted in adult females was 8,000/ μl as against 11,000/ μl in adult males and in paediatric group. The maximum cut off in thrombocytopenia was 1.3lakhs/ μl with an average of 69,000/μl.

5.1. Total count patterns

Leucopenia was noted in 38% overall with 26/74 (35%) , 13/31 (42%) cases in severe and mild thrombocytopenia as against 8% and 13% respectively of leucocytosis[Table 3].

5.2. Differential count patterns

Lymphocytosis was noted in 82/132 (62%), 46/74 (62%) in severe and 20/31 (65%) in mild thrombocytopenias as against neutrophilia noted in 11% and zero respectively[Table 4].

Significant atypical lymphocytosis was noted in 42/74 (57%) and 12/31 (39%) of severe and mild thrombocytopenias respectively [Table 5].

5.3. Hematocrit pattern

66/132 (50%) showed an rise in hematocrit (according to age & sex of person) as against 6/132 (5%) with low hematocrit, 57% of severe as against 42% with mild thrombocytopenia showed rise in haematocrit [table6]. 8% showed hematocrit $\geq$20% above baseline hematocrit of which 80% had severe thrombocytopenia[table7]. A rise in hematocrit was noted maximally in severe thrombocytopenia across all ages and both sexes [table8].

5.4. Serology pattern

There were 38/132 cases with NS1 and 53/132 with antibody patterns. 16/74 (22%) of NS1 and 32/74 (53%) of antibody as against 10/31 (32%) of NS1 and 12/31 (38%) of antibody patterns had severe and mild thrombocytopenias respectively[table9].

6. Discussion

Thrombocytopenia is a prominent feature in dengue. It is a WHO criteria for DHF.[8,11,17]

Cause for thrombocytopenia includes

Platelet consumption, activation by surface band C3 + Ig G with complement moderated lysis, peripheral sequestration, destruction due to antibodies against viral antigens on platelets and direct damage to megakaryocyte precursors with decreased production[1,4,5,11,14,17].

Thrombocytopenia is usually mild, asymptomatic but may be associated with bleeding[18] along with vasculopathy, coagulopathy and platelet dysfunction.[5]

It may[13,17,19] or may not correlate with severity of bleeding[15,18] and complications.[10,15]

Platelet counts drop between 3^{rd}- 7^{th} days, normalise by 8th- 10^{th} days reach a nadir between 4-7^{th} day[5,8,11,14] coinciding with late febrile and early critical preshock period which precedes the rise in hematocrit[2,6,15]. It may drop to <4,000 cells/cumm.[15] Platelet counts are diagnostic, prognostic and recovery parameters in dengue[4,8,9,11].

Thrombocytopenia impacts management raising concerns about transfusions, their effects and hospitalisation[1,7,8,10,16]. Our study showed a predominance of dengue in young age and males in accordance with few studies[5,12,16].

Thrombocytopenia patterns showed predominance of severe cases in accordance with few[9,18,19] and discordance with other studies[17,20]. Severity being uniform between sexes and all ages.[15] 35% of thrombocytopenia were transfusion triggers according to few[8,14,16] differed in other

Table 1: Age & Sex Distribution

Gender	Paediatric ≤ 12yrs		Adult >12yrs		Total (n)	Percent (%)
	n	%	n	%		
Males	16	40	54	59	70	53
Females	24	60	38	41	62	47
Total	40	100	92	100	132	100

Table 2: Severe thrombocytopenia patterns (l/cumm)

<10,000		10,000 -25,000		26,000-50,000		Total	Percent (%)
n	%	n	%	n	%		
01	01	25	34	48	65	74	100

Table 3: Total white cell count & thrombocytopenia (l/cumm)

Total count(cells/cumm)	≤ 0.5		0.51 -0.75		0.76- 1.5		Total
	n	%	n	%	n	%	
Decreased (<4,000)	26	35	11	44	13	42	50
Normal	42	57	14	52	14	45	70
Increased (>11,000)	06	08	02	04	04	13	12
	74	100	27	100	31	100	132

Table 4: Differential cell count pattern & thrombocytopenia (1/cumm)

Differential cell count pattern	≤ 0.5		0.51 -0.75		0.76- 1.5		Total	Percent (%)
	n	%	n	%	n	%		
Lymphocytosis	46	62	16	59	20	65	82	62
Neutrophilia	8	11	04	15	00	0	12	9
Normal differential cell count (for age & sex)	20	27	07	26	11	35	38	29

Table 5: Atypical lymphocytosis & thrombocytopenia (1/cumm)

Atypical lymphocytes	≤ 0.5		0.51 -0.75		0.76- 1.5		Total	Percent (%)
	n	%	n	%	n	%		
<20	32	43	13	48	19	61	64	48
≥20 (significant)	42	57	14	52	12	39	68	52
Total	74	100	27	100	31	100	132	100

Table 6: Hematocrit (%) & Thrombocytopenia (1/cumm)

Hematocrit	≤ 0.5		0.51 -0.75		0.76- 1.5		Total	Percent (%)
	n	%	n	%	n	%		
Increased (as per age & sex)	42	57	11	41	13	42	66	50
Normal	27	36	15	55	18	58	60	45
Low	05	07	01	04	00	00	06	05
Total	74	100	27	100	31	100	132	100

Table 7: Range of hematocrit rise with thrombocytopenia

Hematocrit range (%)	≤ 0.5		0.51 -0.75		0.76- 1.5		Total	Percent (%)
	n	%	n	%	n	%		
≥ 20	08/74	11	02/27	08	00	00	10/132	8
>50	09/74	12	03/27	11	02/31	06	14/132	11
Total	74		27		31			

Table 8: Increased hematocrit & thrombocytopenia (1/cumm)

Platelet count range	Adults				Paediatric		Total	Percent (%)
	Males		Females					
	n	%	n	%	n	%		
≤ 0.5	16	38	10	24	16	38	42	100
0.51 – 0.75	04	29	04	29	06	42	14	100
0.76 – 1.5	03	30	02	20	05	50	10	100

Table 9: Serology with thrombocytopenia (1/cumm)

Pattern	≤ 0.5		0.51 -0.75		0.76- 1.5		Total	Percent (%)
	n	%	n	%	n	%		
NS1	16	22	12	44	10	32	38	29
Mixed	26	35	06	22	09	30	41	31
Antibody	32	43	09	34	12	38	53	40
Total	74	100	27	100	31	100	132	

studies.[21] We had one case of critical thrombocytopenia

in concordance with few[22], discordance with other studies.[15] The average platelet count was similar to few,[10,16] varied in others.[7,8]

Our study was in agreement with authors noting lower platelet counts, severity of dengue in females[13,22,23] than males and in adults than children[5,20], other varied.[8,24]

Leucopenia noted in 38% in accordance with few,[15] varied in other[16,18] being associated with mild than severe thrombocytopenia in support of few studies claming association with dengue fever than severe dengue.[23]

We had 62% cases of lymphocytosis with equal distribution in mild and severe thrombocytopenia in accordance with few studies, suggesting it was a consistent feature in the course of dengue,[4,12] other differed.[25] Significant atypical lymphocytosis, noted in 52%, had highest association with severe than mild thrombocytopenias and was in accordance with few studies indicating it to be a marker and severity prognosticator for dengue.[26,27]

Rise in hematocrit (above reference for age and sex) was noted in 66/132, 11% showed >50% (cut off severity-predicator,[28]) 8% showed ≥20% above baseline hematocrit in accordance with few[12] varied in other[4,29]. Rise in hematocrit is a severity predicator[30] and WHO criteria of severe dengue. 80% of severe thrombocytopenias had ≥20% above baseline hematocrit as against 20% with moderate and none with mild thrombocytopenias, suggesting that platelet counts could be severity predicators in accordance with few,[10,11,31] other disagree.[32]

The study showed that thrombocytopenia was consistent through the course of dengue. We had 29% NS1 and 40% antibody patterns. Severe thrombocytopenia was noted in 22% of NS1 as against 43% of antibody patterns, in concordance with studies claiming platelet counts drop from 3^{rd} day to 10^{th} day and reach a nadir between 4^{th}- 7^{th} day[5,8,11,14]. This is in agreement with studies indicating a rise in NS1 antigen from 1-5 days, IgM- 3^{rd}- 5^{th} day and IgG from 7^{th} day onwards.[2,33]

7. Conclusion

We conclude thrombocytopenia is a prominent feature and initial marker in dengue. Young children and females are at risk population. It could be a useful prognosticator of severe dengue, especially in association with other lab features. Platelet transfusions instituted due to concern about the platelet count drop and haemorrhagic tendencies, are guided by a study of platelet count patterns which helps to avoid harmful, wasteful transfusions.

8. Source of Funding

None.

9. Conflict of Interest

None.

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