Original Research Article

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

Anagha A Joshi1, Divyashree B N2,*, Rukmini Tanjore3, Gayathri B R1

1 Dept. of Pathology, Kempegowda Institute of Medical sciences and Hospital, Bengaluru, Karnataka, India
2 Dept. of Pathology, Pes Medical college and Research Hospital, Kuppam, Andhra Pradesh, India
3 Prathima Institute of Medical Sciences, Nagunoor, Telangana, India

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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.

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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 hematocrit.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 and 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
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   | ≥ 0.76- 1.5  | 31 (24%) |
| Moderate | ≥ 0.51- 0.75 | 27(20%)  |
| Severe | ≥ 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 1.3 lakhs/ 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 ≥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 bleeding18 along with vasculopathy, coagulopathy and platelet dysfunction.5

It may 13,17,19 or may not correlate with severity of bleeding15,18 and complications.10,15

Platelet counts drop between 3rd to 7th days, normalise by 8th- 10th days reach a nadir between 4-7th day5,8,11,14 coinciding with late febrile and early critical preshock period which precedes the rise in hematocrit2,6,15. It may drop to <4,000 cells/cumm.15 Platelet counts are diagnostic, prognostic and recovery parameters in dengue4,8,9,13.

Thrombocytopenia impacts management raising concerns about transfusions, their effects and hospitalisation1,7,8,10,16. Our study showed a predominance of dengue in young age and males in accordance with few studies5,12,16.

Thrombocytopenia patterns showed predominance of severe cases in accordance with few9,18,19 and discordance with other studies17,20. Severity being uniform between sexes and all ages.15 35% of thrombocytopenia were transfusion triggers according to few8,14,16 differed in other
### Table 1: Age & Sex Distribution

| Gender | Paediatric ≤ 12yrs | Adult >12yrs | Total (n) | Percent (%) |
|--------|--------------------|--------------|-----------|-------------|
|        | n  | %  | n  | %  | 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  | %  | 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 | Percent (%) |
|-------------------------|-------|------------|-----------|-------|-------------|
| 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 |
| Total                   | 74    | 100| 27 | 100| 31 | 100| 132|

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

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

### Table 5: Atypical lymphocytosis & thrombocytopenia (l/cumm)

| Atypical lymphocytes | ≤ 0.5 | 0.51 -0.75 | 0.76- 1.5 | Total | Percent (%) |
|---------------------|-------|------------|-----------|-------|-------------|
| <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 (l/cumm)

| Hematocrit | ≤ 0.5 | 0.51 -0.75 | 0.76- 1.5 | Total | Percent (%) |
|------------|-------|------------|-----------|-------|-------------|
| 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 (%) |
|----------------------|-------|------------|-----------|-------|-------------|
| ≥ 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 |     |     |     |     |     |
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 accordance with studies claiming platelet counts drop from 3rd day to 10th day and reach a nadir between 4th–7th day. This is in agreement with studies indicating a rise in NS1 antigen from 1-5 days, IgM- 3rd–5th day and IgG from 7th day onwards.

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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**Author biography**

**Anagha A Joshi** Tutor

**Divyashree B N** Assistant professor

**Rukmini Tanjore** Final Year MBBS

**Gayathri B R** Tutor

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