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Age – Can it be a Navigational Factor in Dengue: A Study

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Abstract

Background: Dengue infections can occur as epidemics in India causing high morbidity and mortality. The awareness of risk factors can help in early recognising and treatment of severe forms and reduction in mortality. Age is one such intrinsic risk factor which can affect the outcome to a significant extent. *Objective*: To analyse the haematological variables affected by different age groups and its impact by comparison with other similar or clinical studies on complications of dengue. *Materials and Methods*: A total of 132 serologically proven Dengue positive cases were analysed along with relevant haematology data after tabulation against patients unique hospital identification number, age and sex. The data was collected over a one month period in November 2016 in Haematology Department of KIMS Hospital and Research Centre, Bengaluru. *Results*: Our study showed an age range between 5 months to 65 years with most patients in the 12-25 years group and an average of 32 years. We had 30% paediatric cases (≤12 years) and 70% non-paediatric cases (>12 years). The male to female ratio was 1.2:1 with a slight male predominance. The analysis of haematocrit patterns in association with age showed 70% paediatric cases with rise in haematocrit above reference range in comparison to 43% in adults. The highest haematocrit was 59.6 in adults as against to 47% in paediatric cases. Total white cell count patterns were uniform in both groups. The lowest count was noted in adults (1100 cells/cumm) as against paediatric (1900 cells/cumm) cases. The differential count showed marginal increase in lymphocytosis in non-paediatric (70%) as against paediatric (63%) cases, whereas neutrophilia (23% vs 50%) in paediatric and non- paediatric cases was more significant. Neutropenia was seen in a higher proportion of non- paediatric (38%) vs paediatric cases (18%). Platelet counts less than 1.0 lakhs/cumm was noted in 98% in non-paediatric as against 90% of paediatric cases. There was a significantly higher proportion of NS1 Antigen positivity noted in non-paediatric (34%) as against paediatric (15%). Paediatric cases had a higher association (85%) with antibody pattern as against non-paediatric (65%) cases. *Conclusion*: Age has a significant impact as a prognosticator in dengue and can play an important and decisive role in early diagnosis and management of severe cases.

Keywords: Dengue fever; Prognosticators; Age; Paediatric; Blood counts; Serology.

Introduction

Dengue, an arboviral infection presents as undifferentiated fever, dengue fever, dengue haemorrhagic fever and dengue shock syndrome [1]. It has been classified as non severe dengue without and with warning signs and severe dengue [2]. Most cases are self limited but complicated cases have a high morbidity and mortality [3].

Certain risk factors impact progression to severe dengue includes age, gender, race, nutritional status and blood group. These aid in early management and a reduction in morbidity and mortality [4,5].

Several studies have analysed the effect of age on dengue and claimed increased risk of severe dengue in children [6,7,8,9]. This is due to increased base line vascular permeability in children with increased plasma leakage leading to shock [9,10,11]. Some of these studies claim children < 5 years have a higher risk and evolve faster into severe dengue [11,12].

Other studies have suggested that adult have a higher risk for severity especially for internal haemorrhage [10,11] possibly due to increased risk of severe thrombocytopenia [13]. A few studies show elderly tend to have severe dengue (due to comorbidities and weaning immunity) [10].

Our study explores the haematological impact of age and its utility in predicting severity in dengue.

Aims and Obectives

The aim of the this study is to analyse the variations in haematological parameter seen in paediatric and non-paediatric group and to compare with similar clinical studies, to assess the risk group in dengue.

Materials and Methods

This is a prospective study conducted on 132 patients with dengue positive serology in KIMS Hospital, Bengaluru over a one month period in November 2016.

All patients with dengue positive serology (NS1, IgM, IgG or all) by rapid card method (standard diagnostic-Bioline alera) with results of relevant haematology tests – haematocrit, blood counts (obtained by automated haematology analyser – Syemex 1800e) with differentiated counts obtained from leishman stained peripheral smear (done as per hospital protocol to verify platelet counts) with age and sex details were included in the study.

The result of these tests were tabulated and analysed.

Patients with concomitant infection like Malaria, Typhoid along with dengue, those with normal, high platelet count and those without age details were excluded from the study.

Ethical Committee Clearance

This study consists of analysing data against the patients unique hospital identification number with age and sex details only. The anonymity of patients was maintained. The study was approved by Ethical committee of the hospital.

Results

Our study showed patients aged between 5 months to 65 years, most were in the 12-25 years age group and the average age was 32 years (Table 1).

There was a slight male predominance (M:F-1.2:1)

Non-pediactric group includes adolecents and adults and for simplicity sake will be categorised as adults in the study. The haematological parameters analysed included haematocrit and blood counts

Haematocrit: There was an increased proportion of paediatric cases showing a rise in haematocrit above reference range for age and sex, however rise in haematocrit over 20% for age and sex was seen more in adults (12%) than paediatric group (8%). The highest haematocrit in adult was 59.6% vs 47%

Table 1: Age and sex distribution of patients

Age Group	Number	Percent	Gender	Nember	Percent
Pediactric	40	30	Male	73	55
Non Pediatric	92	70	Female	59	45
Total	132	100		132	100

Table 2: Comparison of haematocrit (rise above reference range for ages)

Age Group	Normal		Rise in Haematocrit		Total (n)
	Number	Percent	Number	Percent	
≤12 years Pediactric	12	30	28	28	40
≥12 years Non Pediactric	52	57	40	40	92
Total	64	100	68	100	132

in children (Table 2).

Total WBC counts: There was no significant variation in the impact on WBC counts in the different age groups. Leucocytosis was marginally higher in non-paediatric group. The highest total count in paediatric group was 11350 cells/cumm, the lowest was 1000 cells/cumm whereas in non-paediactric it was 33410 cells/cumm and 1100 cells/cumm respectively (Table 3).

In both categories the percent of leucopenia was significant (40%)

Differential counts

There was a significant variation in the proportion of neutrophilia with 23% noted in paediatric group as against 5% in non-paediatric.

Differential counts cut off values were the standard reference ranges for particular age groups (Polymorphs-adults: 40-75%, children ≤ 12 yrs: 20-40%; Lymphocytes-adults: 20-45%, children: 40-60%) (Table 4).

Lymphocyte count: The highest lymphocyte count in non-paediatric group was 90% as against 80% in paediatric group lymphocytosis was marginally higher in adults

The number of significant atypical lymphocytosis (≥20%) was seen in a higher portion of paediatric cases as against to non-paediatric (57% vs 50%) significant variation was noted in the proportion of neutropenia cases which was higher in non-paediatric cases, 38% as against 8% in paediatric cases. The lowest neutrophil count in adults was 10%, in paediatric age 12% (Table 5).

Platelet Counts: An analysis of platelet counts showed lowest platelet count in paediatric group, was 15000 cells/cumm as against 8000 cells/cumm in non-paediatric group (Table 6).

There was a higher proportion of adults with

Table 3: Comparison of total WBC counts

Age Group	≤4000 cells/cumm		4000-11000 cells/cumm		≥11000 cells/cumm	
	Number	Percent	Number	Percent	Number	Percent
≤12 years Pediactric n=40	16	40	22	55	02	05
≥12 years Non Pediactric n=92	36	39	47	51	09	10
Total	52		69		11	

Table 4: Comparison of differential counts.

Age Group	Lymphocytosis		Neutrophilia		Normal pattern	
	Number	Percent	Number	Percent	Number	Percent
≤12 years Pediactric n=40	25	63	09	23	06	14
≥12 years Non Pediactric n=92	64	70	05	05	23	25
Total	89		14		29	

Table 5: Comparison of atypical lymphocyte counts

Age Group	<20%		≥20%	
	Number	Percent	Number	Percent
≤12 years Pediactric n=40	17	43	23	57
≥12 years Non Pediactric n=92	46	50	46	50
Total	63		69	

Table 6: Comparison of platelet counts.

Age Group	≤0.5 Lakhs/cumm		≤1.0 Lakhs/cumm		<1.5 Lakhs/cumm	
	Number	Percent	Number	Percent	Number	Percent
≤12 years Pediactric n=40	22	55	14	35	04	10
≥12 years Non Pediactric n=92	53	58	38	41	01	01
Total	75		14		05	

Table 7: Comparison of serology patterns

Age Group	NS1 Antigen pattern		NS1 +Ab pattern		Ab pattern	
	Number	Percent	Number	Percent	Number	Percent
≤12 years Pediactric n=40	06	15	18	35	16	40
≥12 years Non Pediactric n=92	31	34	26	41	35	38
Total	37		44		51	

thrombocytopenia 99% (≤1.0 lakh) as against to 90% in paediatric group.

Serology pattern: The serology pattern showed a higher proportion of non-paediatric cases in association with NS1 antigen (34%) and a higher proportion of paediatric cases in association with Ab pattern (85%) as against 65% in non-paediatric cases (Table 7).

Discussion

Our study showed most cases in in 12-25 years group, range 5 months -85 years (average age 32 years) in accordane with few studies [13] with slight male predominance.

There was higher proportion of cases with rise in haemocrit in paediatric group [14] where as 20% rise and highest haemocrit was more in non-paediatric cases. Few studies claim higher risk of Dengue shock syndrome in children [10,11] and others showed increased risk was more in adults [15].

The total WBC count showed no significant variations in our study in contrast to few studies which showed higher proportion of leukopenia in paediatric group [14,16].

Lymphocytosis was noted in a higher proportion of cases in paediatric category [16,17] but these included those ≤ 15 years unlike our study which included those ≤ 12 years.

There was significant atypical lymphocytosis in a higher proportion in children than adults, one study didn't find any difference between the two [15] in another it was more in non-paediatric group [14].

Neutropenia was noted in a higher proportion of cases in adults than children in accordance with few studies [14].

Few studies noted that leucopenia and lymphocytosis were prominent in adults (non paediatric) than paediatric group [13,16]. Our study noted that lowest total count and highest lymphocyte count were noted in non-paediatric group.

Platelet count showed that ≤ 1.0 lakhs/ cummwas seen in a higher proportion of non-paediatric as against paediatric group (99% vs 90%) in accordance with few studies [13,15,16]. But others claim higher proportion in paediatric group [11,17,18]. Our study showed higher proportion of severe thrombocytopenia ≤0.5 Lakhs/cumm in non-paediatric group [13]. The severity of thrombocytopenia was noted in non-paediatric group as the lowest platelet count was observed in this category [13]. Few studies noted that haemorrhagic tendencies were more in non-paediatric group [10,11,13].

The increased haemocrit was due to haemo concentration secondary to plasma leakage. An increase in plasma leakage is noted in children due to increased microvascular permeability [9,10,14].

Leucopenia is attributed to bone marrow suppression with lymphocytosis in acute phase [19]. Atypical (plasmacytoid) lymphocytes represent an augmented immune response to control the spread of the virus and neutropenia is due to marked degeneration of mature neutrophils with shift to left during febrile phase [20]. Thrombocytopenia is due to direct bone marrow suppression by virus and antibody mediated platelet destruction etc [21].

Leucopenia is an early severity predictor in dengue [4]. Atypical lymphocytosis was associated with thrombocytopenia and could be a marker of disease severity. Haemocrit and thrombocytopenia are criteria for diagnosis of Dengue haemorrhagic fever and thus prognosticators [4].

The serology pattern showed significant association of non-pediatric group with NS1 antigen (34%) as against the paediatric group (15%) whereas the Ab pattern (isolated and in combination with NS1 antigen) showed significant association (85%) with pediatric group than non-paediatric group (65%). NS1 antigen positivity correlates with increased viremia and is found in severe cases. Ab to NS1 antigen are cross reactive with platelets and endothelial cells and may cause haemorrhagic manifestations [18].

The take home points of the study could be

summarised as the risk of dengue shock syndrome is more in children than in adults, however in adults it could be more severe. This is in support of few studies claiming higher mortality in adults with dengue shock syndrome than children [15].

Neutropenia and thrombocytopenia were seen more in non-paediatric group suggestive of higher incidence of bone marrow suppression, contributing to severe disease with increased haemorrhagic manifestation in non-paediatric group, in accordance with few studies [10,11,13,15].

Limitation of study included small sample size, limited data to confirm findings and lack of clinical correlation.

Conclusion

Dengue can occur in epidemics in India. Early management is essential to limit the mortality rate. Age is an important factor which can influence the outcome in dengue infections as certain complications have an affinity to selective age groups. Awareness of this can go a long way in reducing morbidity and mortality in dengue.

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