Blood Investigations as Predictive Tool for Predicting Bleeding Manifestations and Death with Dengue like Illnesses

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Abstract

Background: Dengue has a broad range spectrum of clinical presentations and many times unpredictable clinical evolution and outcome. Though the disease is complex in its manifestations, management is relatively simple hence it is very important to be able to predict which patients are more likely to land up in complications like bleeding manifestation and death. There is a paucity of literature on this.

Objective: To study blood investigation parameters as predictive tool for predicting bleeding manifestations and death in children with dengue like illnesses.

Methods: We enrolled all the consecutive admissions to pediatric ward of a tertiary care teaching hospital satisfying the inclusion criteria from February 2014 to May 2015. Blood investigations were sent and patients were assessed for appearance of bleeding manifestations and death.

Results: 200 children were enrolled of age group 3 month to 12 years. Investigation parameters are predictors of outcome of bleeding in mortality group Vs survivals (TLC - 4.81±2.69 Vs 5.97±4.84; p=0.031, Platelet-65.50±32.89 Vs 79.66±39.46; p=0.010, Highest haematocrit-40.67±3.89 Vs 38.77±4.45; p=0.003). Patients having bleeding have more dengue positivity (p=0.0001) with maximum positivity for NS1 69%. Hb% on admission and lowest Hb% were significantly lower in mortality group than in survival group.

Conclusion: 3 patients died and bleeding manifestations were present in 74 patients out of 200 patients. Investigation parameters are predictors of outcome of bleeding in mortality group Vs survivals. Dengue positivity was not a significant factor for prediction of death.

Key words: Clinical Presentations; Dengue; Investigations; Predictors.

Introduction

Dengue is the one of the most important arthropod-borne viral infection of humans. Dengue has been an urban disease for many years but now has spread to rural areas of India as well.[1] Co-circulation of all four serotypes and hyperendemicity of dengue in India has been increased in last few years.[2,3] In addition, many other viral hemorrhagic fevers caused by various arboviruses other than dengue lead to similar manifestations but without laboratory confirmation of dengue infection are clubbed together under the popular umbrella diagnosis of "Dengue like illnesses".

Dengue has a more broad range spectrum of clinical presentations and known to have unpredictable clinical evolution and outcome.[4,5] The key to a good clinical outcome is understanding clinical problems that arise during the different phases of the disease, leading to appropriate approach in case management.[6,7]

The case fatality rate can be as high 15% but can be decreased to 1% by early diagnosis and prompt treatment.[8-10] Hence it is very important to be able to predict which patients are more likely to land up in complications.[11,12] Predictors will also help in monitoring the therapy and the course of illness in a dengue like illnesses.[13-15] Since there is a paucity of literature on this, and there exist many gaps in the current understanding of blood investigations as predictive factors.

Objectives

To study blood investigation parameters as predictive tool for predicting bleeding manifestations and death in children with dengue like illnesses.

Method

This cross sectional study was conducted in the Department of Pediatrics of Mahatma Gandhi Institute of Medical Sciences, Sewagram from February 2014 to May 2015 after obtaining clearance from the Institutional Ethics Committee. To detect a 25% difference in the prevalence of the predictive factors, the sample size was calculated for a one sided alpha error of 5%. Hence, we decided on a sample size of 200 expecting approximately 25% will turn out to be ineligible either because of refusal to give consent or failure to fit in inclusion criteria. We enrolled all the consecutive admissions to pediatric ward satisfying the inclusion criteria which were age 3 months to 12 years with history of fever as given by the patient or parents or a documented fever and thrombocytopenia of <1,00,000/cu mm that were ready to give written informed consent. Patients with proven bacterial infection as the cause for thrombocytopenia and fever were excluded. This assessment of predictive factors was done

in a standard case record form. For the reliability evaluation of physical examination, the assessment was done by two independent pediatric residents blinded to each other within one hour of each other. Bleeding manifestations assessed were patechiae/purpura/ecchymosis/bleeding spots, melena/bleeding PR, hematemesis/blood in RT/nasal bleeding, bleeding gums, haematuria, vaginal bleeding.

In blood investigations following parameters were studied as predictors HB%, Lowest Hb%, TLC, Lowest TLC, Platelet, Lowest Platelet, Haematocrit, Lowest Haematocrit, SGOT, SGPT, Rapid test for Dengue, Sr. Albumin.

Statistical Analysis

Calculations were done with standard methods using software version Epi info 7.5 versions, SPSS 21.0, graph Pad prism 6.0. A P-value less than 0.05 considered significant.
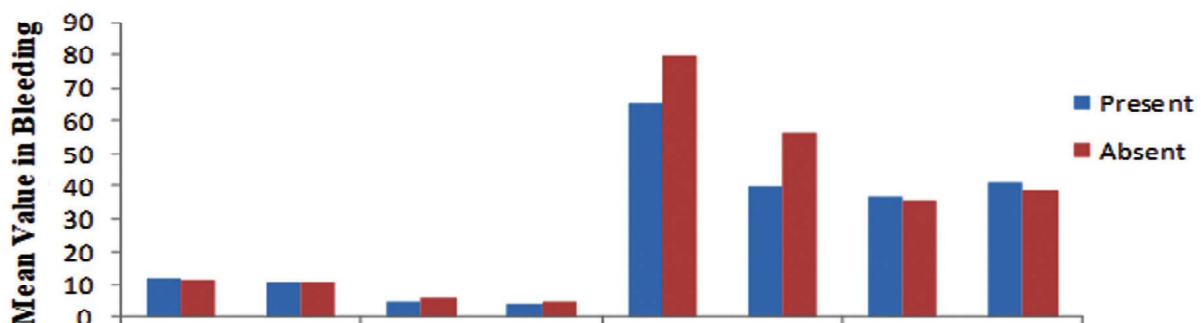
Results

All the patients which were enrolled in the study were investigated for rapid diagnostic test for dengue. Out of 200, 93 were negative and 107 tested positive. (Table 1).

Table 1: Dengue positivity in study sample.

Dengue	Yes	
	n	%
Negative	93	46.5
NS1	52	26
IGG	22	11
IGM	10	5
Other	23	11.5

Comparison of blood investigation parameters in

	Hb%	Lowest Hb%	TLC	Lowest TLC	Platelet	Lowest Platelet	Haematocrit	Highest Haemotocrit
Present	11.95	10.37	4.81	3.94	65.5	39.47	36.82	40.67
Absent	11.44	10.38	5.97	4.87	79.66	56.26	35.54	38.77

Fig. 1: Comparison of CBC in Patients With and Without Bleeding.

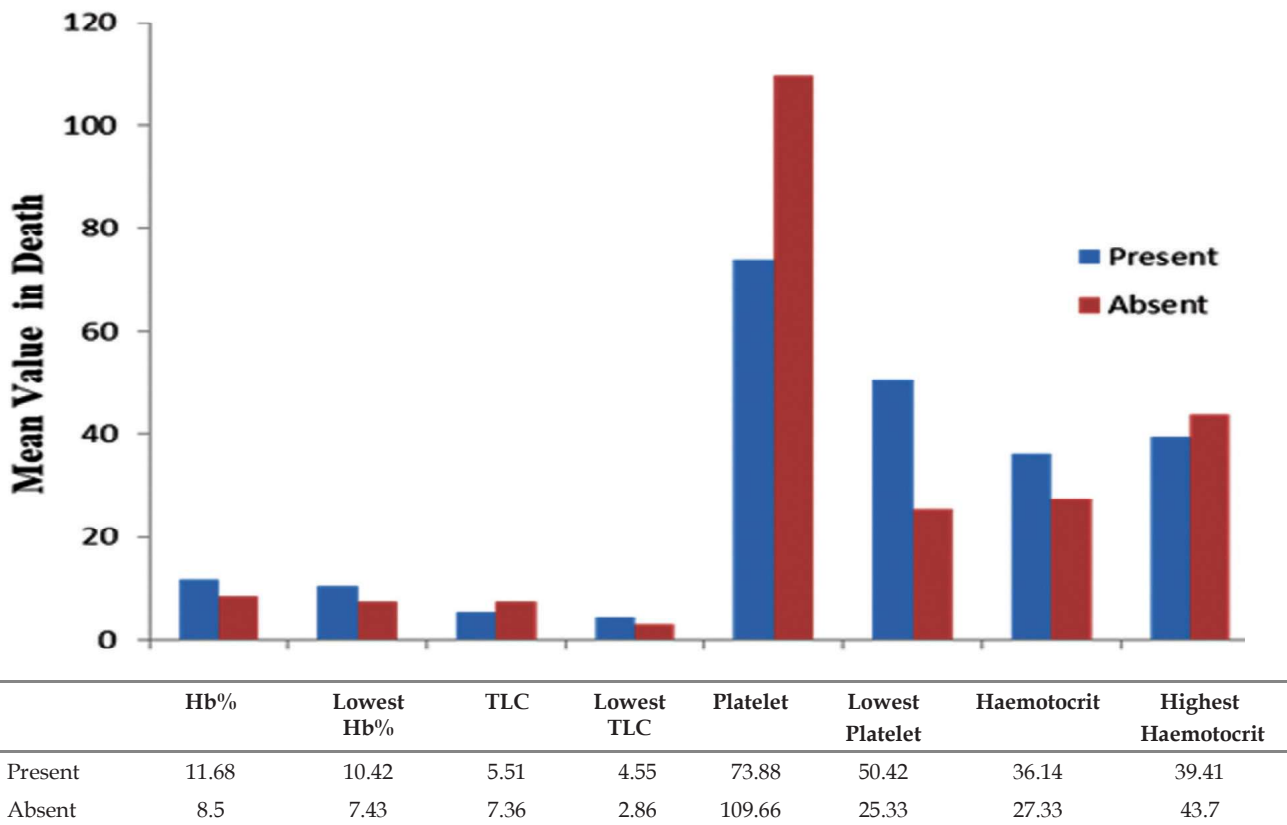|	Hb%	Lowest Hb%	TLC	Lowest TLC	Platelet	Lowest Platelet	Haemotocrit	Highest Haemotocrit
Present	11.68	10.42	5.51	4.55	73.88	50.42	36.14	39.41
Absent	8.5	7.43	7.36	2.86	109.66	25.33	27.33	43.7

Fig. 2 Comparison of CBC in Patients Died and Survived.

patients with and without bleeding manifestations -Bleeding manifestations were present in 74 patients out of 200 patients. Hb% on admission and lowest Hb% had no significant association with bleeding.

All other investigation parameters were common in patients with bleeding than in patients without bleeding manifestations (TLC - 4.81±2.69 Vs 5.97±4.84, p=0.031; Lowest TLC-3.94 ±1.71 Vs 4.87±3.07, p=0.018; Platelet-65.50±32.89 Vs 79.66±39.46, p=0.010; Lowest platelet- 39.47±21.26 Vs 56.26±21.88, p=0.0001; Highest haematocrit 40.67±3.89 Vs 38.77±4.45, p=0.003) (Figure 1)

SGOT level was significant higher in patients with bleeding than in patients without bleeding manifestations (p=0.03) while SGPT and serum albumin level was not significantly different in two groups.

Patients having bleeding had more dengue positivity than those in which bleeding was absent (p=0.0001) (Table 2)

Table 2: Dengue Positivity in Patients With and Without Bleeding.

Dengue	Bleeding		Total	χ2-value
	Present	Absent		
Negative	19	74	93	
NS1	36	16	52	
IGG	6	16	22	37.41
IGM	2	8	10	
OTHER	11	12	23	
Total	74	126	200	p=0.0001, S

2) Comparison of blood investigation parameters in patients died and survived- Out of enrolled 200 patients, 3 died (1.5%). Hb% on admission in mortality group was significantly lower than survival group (8.50±2.57 Vs 11.68±2.27; p=0.017). Lowest Hb% was also significantly lower in mortality group than in survival group (7.43±3.46 Vs 10.42±1.48 respectively; p=0.001). Haematocrit percentage on admission was significantly lower in mortality group than in survival group (27.36±6.624 Vs 36.14±5.33; p=0.005) (Figure 2)

SGOT, SGPT and serum albumin were done in only one patient out of total 3 patients who died which

were not significantly associated with death. Out of 3 deaths, 2 were positive for rapid diagnostic test of dengue (NS1 antigen) which was not statistically significant. (Table 3)

Table 3: Dengue Positivity in Patients Died and Survived.

Dengue	Outcome		Total	2-value
	Survive	Death		
Negative	92	1	93	
NS1	50	2	52	
IGG	22	0	22	2.88
IGM	10	0	10	
Other	23	0	23	
Total	197	3	200	p=0.57,NS

Discussion:

Our study included 200 pediatric in-patients aged 3 months to 12 years with fever and thrombocytopenia. We studied blood investigation parameters as predictors which will help the pediatricians in future to predict patients that are more likely to land up with complications like bleeding manifestations and death. 2009 classification, classifies dengue into severity levels which is considered to be more sensitive in capturing severe disease than the 1997 classification.

Out of total 200 patients, bleeding was manifested in 74 patients. We found that, TLC, lowest TLC, platelet and lowest platelet were significantly lower in patients with bleeding (p=0.031, 0,018, 0.010, 0.0001. Study by Narayanan et al had mean haematocrit and platelet count similar to our study which is significant predictor of bleeding (p=0.0002, 0.008).[16] Contrary to this, a study by Joshi et al found no correlation between platelet counts and bleeding manifestations which was attributed to multifactorial causes of bleeding in dengue.[17]

Another study by Kulkarni et al found that frequency of bleeding increased with decreasing platelet counts but 16.4% of cases with normal platelet count also had bleeding which again emphasizes nonthrombocytopenic causes of bleeding in dengue.[18] SGOT level was significantly higher in patients with bleeding which was similar to finding of other studies such as Narayanan et al, Kulkarni et al, Surangrat et al, Joshi et al.[16-19] No statistical significance was found for SGPT in our study which found in other studies.

There were 3 deaths out of total 200 patients included in our study population. Study by Joshi et al found that out of 2 deaths in total study population of 57 patients, bleeding and shock was manifested in both patients. Very low platelet count (<20,000/cu mm) was documented in both these patients.[17] But this study also found that there was no correlation between platelet counts and bleeding manifestations. Another study by Kulkarni et al. found that among 1.1% mortality in their study subjects and shock was present in 9 patients out of total 10 deaths.[18] Siddhart Bhave et al. has reported thrombocytopenia in 96% of dengue cases.[20] Bandyopadhyay D et al. observed that platelet count was low (64.4%) in dengue fever.[21]

Conclusion

Some basic investigations which we do as standard of care in patients presenting with fever and thrombocytopenia are cost effective and help in not only in diagnosing dengue but also for prediction of complications such as bleeding manifestations and death.

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