

## To Evaluate the Various Bone Marrow Changes in Thrombocytopenic Patients: An Institutional Based Study

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### ABSTRACT

**Background:** The present concept of thrombocytopenic purpura as a definite syndrome has gradually been evolved and separated from the maze of hemorrhagic diseases. Recent years have witnessed an upsurge in patients with thrombocytopenia resulting from a number of varying etiologies. Therefore, this work is undertaken to study the clinical profile of various symptomatic thrombocytopenic patients in our clinical setting and to evaluate the etiological factors responsible for thrombocytopenia.

**Materials & Methods:** The observational study done on 50 patients admitted with complaint of bleeding with documented thrombocytopenia in department of paediatrics, Pacific Institute of Medical sciences, Udaipur, Rajasthan. Each patient where systemic hemostatic disturbance is suspected after excluding the local causes were assessed by a battery of preliminary hematological tests viz. B.T., C.T., Platelet count, P.T., P.T.T. supplemented by bone marrow examination and other specific tests.

**Results:** Our study showed that maximum (30%) cases of thrombocytopenia were in age group 0-3 years and male to female ratio was 1.77 : 1. In idiopathic thrombocytopenic

purpura the bone marrow finding was normal marrow cellularity in 13 cases & increased cellularity in 4 cases. Mortality rate of children was 8% in our study due to septicemia & ITP with ICH.

**Conclusion:** We concluded that every case with bleeding and thrombocytopenia should be worked out in detail to rule out secondary causes which if missed may lead to high mortality.

**Key Words:** Idiopathic Thrombocytopenia, Bone Marrow Examination, Megakaryocyte, Cellularity.

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### INTRODUCTION

Bleeding disorder is labeled when a person bleeds from single or multiple sites on single or several occasions and does not respond to conventional local measures. Such disorder is a common problem in infancy and childhood.<sup>1</sup>

The functions of the normal haemostatic process are to prevent blood loss from intact vessels and to arrest bleeding from injured vessels. In general three organs or tissues are primarily involved in normal haemostatic mechanism. They are bone marrow: megakaryocytes, which produce the blood platelets and in turn furnish the thromboplastin; the liver; which supplies prothrombin, fibrinogen and other clotting factors; and blood vessels, with their endothelial function and capillary reactions.<sup>1</sup>

The spleen is a disturbing factor in some thrombocytopenic states and the gastrointestinal tract participates in the mechanism of Vitamin K formation and absorption. In our study we will include bleeding due to thrombocytopenia. (Quantitative changes of platelets only). The normal platelet count is 150 to 450x 10<sup>9</sup>/L. Thrombocytopenia refers to reduction in platelet count below

150x10<sup>9</sup>/L. Purpura is characterized by spontaneous bleeding into the skin or mucosa, manifesting as petechiae (small pin point hemorrhage) or ecchymosis (large superficial hemorrhage).<sup>2</sup>

The present concept of thrombocytopenic purpura as a definite syndrome has gradually been evolved and separated from the maze of hemorrhagic diseases. In the earliest fragmentary descriptions of purpura, it was noted in association with the pestilential fevers, later it was found apart from these, and still more recently, was separated as a distinct entity. A proper understanding of these conditions however awaited the discovery of blood platelets by Donne and Arnold<sup>3</sup> and the observation by Denys and Hayem.<sup>4</sup>

Recent years have witnessed an upsurge in patients with thrombocytopenia resulting from a number of varying etiologies. Therefore, this work is undertaken to study the clinical profile of various symptomatic thrombocytopenic patients in our clinical setting and to evaluate the etiological factors responsible for thrombocytopenia.

**MATERIALS & METHODS**

The observational study done on 50 patients admitted with complaint of bleeding with documented thrombocytopenia in department of paediatrics, Pacific Institute of Medical sciences, Udaipur, Rajasthan. Each patient where systemic hemostatic disturbance is suspected after excluding the local causes were assessed by a battery of preliminary hematological tests viz. B.T., C.T., Platelet count, P.T., P.T.T. supplemented by bone marrow examination and other specific tests.

**Inclusion Criteria**

- (1) Patients should have documented thrombocytopenia
- (2) Patients should have been evaluated for causes of thrombocytopenia.

**Bone Marrow Aspiration**

It is most important single differential diagnostic procedure. Bone marrow aspiration was done by Jamshidi aspiration needle. Upto 2 years of age tibia and after 2 years iliac crest was chosen for bone marrow aspiration. 0.2 ml bone marrow is aspirated and smear are prepared immediately. Before staining smears are fixed with acetone free methyl alcohol for 30 sec. - 1 min. in order to

prevent haemolysis. Staining of smear are done by Leishman stain. About 8 drops of stain in poured on slide. Wait for 2 minute and add 16 drops of buffered water. Wait for 7-10 minutes. The stain is flooded off with distill water and this should be completed in 2-3 seconds now the smear is seen under 10x, 40x and oil immersion lenses. Secondary thrombocytopenic purpura as in cases of leukemia, aplastic anemia is readily diagnosed and immediately separated from idiopathic thrombocytopenic purpura (Lucia S.P. 1942).<sup>5</sup>

In acute thrombocytopenic purpura a bone marrow reveals a uniform stimulation of megakaryocytes.<sup>6</sup> In chronic thrombocytopenic purpura diminution in number of megakaryocytes occur.

The characters of megakaryocytes are also variable. In acute phase of disease many megakaryocytes are of young form. In chronic phase most of the megakaryocytes are mature with an abundance of azurophilic granules in the cytoplasm. Some of megakaryocytes reveal morphologic changes such as a hyaline cytoplasm and absence of azurophilic granules.

**Table 1: Showing distribution of thrombocytopenic cases according to age**

Age in years	No. of cases	Percentage
0-3	15	30%
3-6	14	28%
6-9	11	22%
9- 12	6	12%
12- 14	4	8%

**Table 2: Bone marrow findings**

	n	C			E			M			G			Morphology of megakaryocyte						
		N		↑	↓	N		↑	↓	N		↑	↓	Normal		Budding/hyper-segmentation		Granularity		
		N	↑			N	↑			N	↑			N	↑	N	↓	N	↓	
<b>Idiopathic thrombocytopenia</b>	17	13	4	-	14	3	-	7	7	3	17	-	-	8	2	4	3	2	5	2
<b>Leukemia</b>	9	-	9	-	-	-	9	-	-	9	-	-	9	9	-	-	-	-	-	-
<b>Septicemia</b>	9	3	6	-	4	5	-	5	4	-	2	7	-	9	-	-	-	-	-	
<b>Dengue</b>	6	6	-	-	6	-	-	6	-	-	6	-	-	6	-	-	-	-	-	
<b>Aplastic anemia</b>	5	-	-	5	-	-	5	-	-	5	-	-	5	5	-	-	-	-	-	
<b>Hemolytic Uremic syndrome</b>	1	-	1	-	-	1	-	-	1	-	1	-	-	1	-	-	-	-	-	
<b>Thrombocytopenia associated with HIV infection</b>	1	1	-	-	1	-	-	1	-	-	1	-	-	1	-	-	-	-	-	
<b>Drug induced</b>	1	1	-	-	1	-	-	-	1	-	1	-	-	1	-	-	-	-	-	
<b>Malaria</b>	1	1	-	-	-	1	-	1	-	-	1	-	-	1	-	-	-	-	-	

C=Cellularity; E=Erythropoiesis; M=Megakaryopoiesis; G=Granulopoiesis

Table 3: Outcome of patients

Outcome	No. of Patients	Percentage
Improved & discharged	46	92%
Died	4	8%
Total	50	100%

## RESULTS

Our study showed that maximum (30%) cases of thrombocytopenia were in age group 0 - 3 years (table 1) and male to female ratio was 1.77: 1.

In idiopathic thrombocytopenic purpura the bone marrow finding was normal marrow cellularity in 13 cases & increased cellularity in 4 cases. Erythropoiesis was normal in 14 cases and increased in 3 cases. Megakaryocyte number was increased in 7, decrease in 3 & normal in 7 cases. The morphology was normal in 8 cases, while in remaining 9 cases hyper segmentation was present in 4 cases but decreased segmentation present in 3 cases & Granularity of cytoplasm was increased in 5 cases & decreased in 2 cases (table 2). Mortality rate of children was 8% in our study due to septicemia & ITP with ICH (table 3).

## DISCUSSION

Out of the total 50 cases taken into consideration, idiopathic thrombocytopenic purpura constituted 34% of the total cases and was the commonest cause of thrombocytopenia. Charles A. Doan (1960)<sup>7</sup> also reported a high incidence of idiopathic thrombocytopenia purpura as a cause of thrombocytopenia in his study.

Fowler W.M. (1936)<sup>8</sup> found 10.6% incidence of ITP in US children. This may be attributed to difference in geographical area.

Out of total 50 cases in study, in 66% cases secondary etiological factors were detected and this group was labeled as secondary thrombocytopenia. Out of these cases leukemia and septicemia with DIC were the leading causes, both constituting nearly 18% patients in each group.

These findings were in concordance with the finding of Fowler W.M.<sup>8</sup> of 24% and Charles A. Doan<sup>7</sup> reported a low incidence of leukemia (1.7%) in his study.

In our maximum incidence of idiopathic thrombocytopenic patients were found in age group 3-6 years constituting 47%. In age group 0-3 years it was 17.6% and in 7-9 years it was 23%. Similar high incidence in age group 3-6 years were reported by Lammi et al (1973)<sup>6</sup> - 33%, Simpons SS et al (1975).<sup>9</sup>

In patients of idiopathic thrombocytopenic purpura 76% patients were male and 24% patients were female. Doan et al (1960)<sup>7</sup> reported a high incidence of female (68%) in his study. Simpons et al (1975)<sup>9</sup> found an equal sex incidence in his study. Lammi et al (1973)<sup>6</sup> also found an equal sex incidence in their study. The negligence of the society to provide female children with competent medical aid might be the reason for this high female ratio in the discussed cases.

In idiopathic thrombocytopenic purpura marrow cellularity was normal in 76% and increased in 24%. Erythropoiesis was increased in 18%, normal in 82% and granulopoiesis was normal in all cases. Megakaryopoiesis was normal in 47% cases. Increased number of megakaryocytes was found in 41% cases and megakaryopoiesis was reduced in 18%.

Regarding morphology of megakaryocytes, cytoplasmic granulation was increased in 30% and decreased in 12%. In rest of the cases this was normal. Hyper-segmentation of megakaryocytes was found in 25% and decreased segmentation was found in 18% cases. Similar findings were reported by Fowler W.M. (1944)<sup>8</sup>, David Y Graham (1974)<sup>10</sup> and Calpin (1998).<sup>11</sup> McClare PD (1974) and Macmillan (1981) reported increased number of megakaryocyte with poor budding and granulation in their study while rest of marrow cells were reported normal.

In aplastic anemia, all cell lines were decreased and bone marrow was replaced by fatty cells. This finding was also reported by Fowler W.M.<sup>8</sup> And Calpin et al 1998.<sup>11</sup>

In leukemia, marrow cellularity was increased in all cases and in each case myeloblast and lymphoblast were present with decreased production of thrombocytes and erythrocytes.

Morphology of megakaryocyte was normal in all cases. Similar findings were reported by Fowler W.M. (1944)<sup>8</sup> and Calpin et al 1998.<sup>11</sup> In septicemia and disseminated intravascular coagulation, cellularity was normal in 33% cases and increased in 66%. Erythropoiesis was raised in 55% cases and was normal in 45%. Granulopoiesis was increased in 77% cases. Similar findings were reported by J.F. Ackroyd et al (1953).<sup>12</sup>

In dengue fever, marrow findings were normal in all subjects. In drug induced thrombocytopenia there was increase in cellularity as well as megakaryocyte number but the morphology of megakaryocyte remained normal. Similar finding were reported by Fowler W. M.<sup>8</sup>, J.F. Ackroyd<sup>12</sup> and M.A. Blajchtman et al.<sup>13</sup>

Out of 50 patients taken into study, 46 patients (92%) improved and 4 (8%) patients expired. Out of these 4 cases, one had intracranial haemorrhage due to idiopathic thrombocytopenic purpura and the other 3 expired due to septicemia with disseminated intravascular coagulation.

The presence of intracranial haemorrhage in idiopathic thrombocytopenic purpura is 5% in our study. Simpons et al (1975)<sup>9</sup> reported intracranial haemorrhage in 1.2% of idiopathic thrombocytopenic purpura.

## CONCLUSION

We concluded that every case with bleeding and thrombocytopenia should be worked out in detail to rule out secondary causes which if missed may lead to high mortality.

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