

## A SURVEY ON THE INCIDENCE OF PSEUDO-THROMBOCYTOPENIA IN THE IN-PATIENTS

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**ABSTRACT:** Fever with thrombocytopenia is frequently encountered in the clinical settings. However some cases of thrombocytopenia are associated with clumping of platelets resulting in pseudothrombocytopenia. This results in disparity in the counts on subsequent manual examination of the peripheral smear. This apparent disparity in the counts witnessed, when performed with automated machines has been attributed to platelet clumping trait of commonly used anticoagulant EDTA. Currently there is paucity of reports documenting the incidence of pseudothrombocytopenia in patients with decreased platelet counts. We attempted to survey the incidence of such cases at our hospital particularly in those with febrile thrombocytopenia. Patients presenting with main complaint as fever or as one of the chief complaints were analyzed for the study. Our aim was to estimate the incidence of pseudothrombocytopenia in patients with thrombocytopenia & to prevent or reduce unnecessary platelet transfusion in patients with pseudothrombocytopenia. Of the 301 patients analyzed, 30% (no=90) were found to have thrombocytopenia; out of which 23% (no=21/90) had pseudothrombocytopenia. Platelet transfusion was required only in 30% (no=6/21). This documents the magnitude of the problem of pseudothrombocytopenia and its potential added burden on the laboratory costs and its propensity to dictate inappropriate treatment avenues based on inaccurate counts.

**KEYWORDS:** Pseudothrombocytopenia, EDTA, fever, platelet transfusion.

**INTRODUCTION:** Pseudothrombocytopenia occurs in both healthy subjects and in patients. It need not be associated with any particular disorder or medication.<sup>1</sup> False diagnosis of thrombocytopenia have led to serious problems like postponement of surgery, discontinuation of medications, unnecessary glucocorticoid therapy and splenectomy.<sup>2</sup> So initial observation of thrombocytopenia reported by an automated particle counter must be confirmed by microscopic examination of blood film.

Data from several surveys reported a consistent incidence of pseudothrombocytopenia of 0.09-0.21%.<sup>3-8</sup> Most common artifact causing pseudothrombocytopenia is invitro clumping of platelets in blood sample collected into EDTA anticoagulant tubes.<sup>9</sup> Alternatively instead of clumping one to another, platelets may attach to leucocytes (platelet leucocyte rosette, platelet satellitism or platelet leucocyte adherence phenomenon).<sup>10</sup>

Pseudothrombocytopenia i.e., spontaneous aggregation of platelets occurs due to antibodies directed against antigens related to glycoprotein IIb IIIa complex.<sup>11</sup> These crypt antigens are not exposed by conformational changes of platelet membrane structures occurring when calcium ions is removed by chelating agents.<sup>12</sup> Platelet clumping is detected by examination of blood film made from EDTA anticoagulant samples; demonstrating more platelets than

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expected from reported count with many in large clumps. Typically artefact is most prominent in the presence of EDTA, whether abnormality in platelet clumping or platelet satellitism.<sup>13, 14</sup>

Several remedies have been proposed, such as warming the sample to 37°C or using additives or specific formulations of anticoagulants including buffered sodium citrate, heparin, ammonium oxalate,  $\beta$ -hydroxyethyl theophylline, sodium fluoride, CPT (trisodium citrate, pyridoxal 5'-phosphate and Tris), antiplatelet agents, potassium azide, amikacin, kanamycin or other aminoglycosides, and calcium replacement with the simultaneous addition of calcium chloride/heparin. According to available evidences, the most suitable and practical approach so far for most clinical laboratories seems, however, the recollection of blood samples using sodium citrate, CPT or calcium chloride/heparin as additives, maintaining the specimen at 37°C until the platelet count has been completed.<sup>15</sup>

We attempted to find the incidence of pseudothrombocytopenia in 301 in-patient cases who presented with fever as chief complaint or one of the chief complaints.

**MATERIALS AND METHODS:** We documented details of 301 febrile in-patient admissions from March 2010 to March 2012. Patients with thrombocytopenia were further categorized into those exhibiting pseudothrombocytopenia (table 1). Very low platelet counts with platelet aggregation at those counts were subjected to a repeat pathological examination of blood smear & the corrected platelet counts were documented [table- 2]. Subsequent to the completion of the study, the percentage of patients with febrile thrombocytopenia exhibiting pseudothrombocytopenia was compared with that available in current literature.

CLINICAL CONDITIONS	NO. OF CASES	NO. OF THROMBOCYTOPENIA CASES	NO. OF PSEUDOTHROMBOCYTOPENIA CASES
Pneumonia	33	9	2
Dengue	31	25	7
Malaria fever	20	12	5
Viral fever	18	8	3
Leptospirosis	4	4	2
PUO	3	1	1
Bacterial meningitis	2	1	1
			21

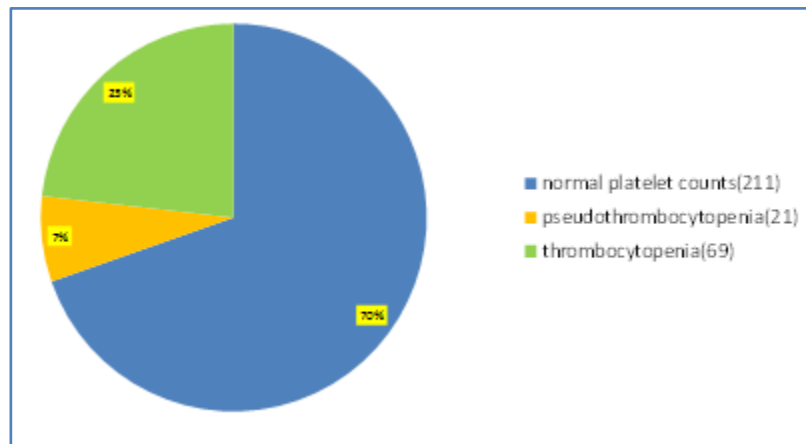
Table 1

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CLINICAL CONDITIONS	NO. OF CASES	INITIAL PLATELET COUNT	REVISED PLATELET COUNT
Pneumonia	2	50, 000	88, 000
		70, 000	90, 000
Dengue	7	44, 000	60, 000
		25, 000	40, 000
		63, 000	81, 000
		92, 000	1, 40, 000
		56, 000	82, 000
		23, 000	43, 000
Malaria	5	30, 000	56, 000
		27, 000	30, 000
		46, 000	52, 000
		22, 000	26, 000
		75, 000	90, 000
Viral fever	3	1, 00, 000	1, 30, 000
		90, 000	1, 25, 000
		60, 000	92, 000
Leptospirosis	2	25, 000	48, 000
		62, 000	86, 000
PUO	1	75, 000	1, 00, 000
Bacterial meningitis	1	60, 000	92, 000
	21		

Table 2

**RESULTS:** Sample size considered for the study was 301 patients. Blood count on the automated machine revealed thrombocytopenia in 30% (90 cases). Of these, pseudothrombocytopenia was diagnosed in 23% (n-21/90) cases (fig. 1). The range of platelet count in pseudothrombocytopenia cases varied from 22,000 to 1lakh. The revised platelet count in pseudothrombocytopenia cases was above 30,000. Platelet transfusion was required in 30% (n-6/21) of pseudothrombocytopenia cases.



**Figure 1**

(n=301)

**DISCUSSION:** Pseudothrombocytopenia cases were diagnosed based on the peripheral clumping of platelets, concurrent increase in leucocyte count, cross verification with manual checking of platelet counts and by the absence of bleeding. Cases with pseudothrombocytopenia included dengue fever, malaria, pneumonia, leptospirosis, PUO and bacterial meningitis. Platelet transfusion required in 30% (n-6/21) of pseudothrombocytopenia cases which included 2 patients of PUO and malarial fever associated with severe anemia respectively, 2 cases of serologically confirmed dengue fever and 2 cases of malarial fever with platelet count of 30, 000.

**CONCLUSION:** The study documents the magnitude of the problem of misleading false low platelet count (pseudothrombocytopenia) and physician's dilemma in deciding about the subsequent need for platelet transfusion. This also adds to the burden on the laboratory personnel and costs incurred both for patients and the laboratory in addition to the existing risk associated with platelet transfusion.

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