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Analytical study of reactive thrombocytosis prevalence in microcytic hypochromic anemia

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ABSTRACT

Background : In routine hematology blood samples, every now and then when reporting peripheral smears, we come across cases of microcytic hypochromic anemia with increased platelet count more often in iron deficiency anemia. We have to differentiate is it the cases are just reactive thrombocytosis or else we are neglecting any platelet disorders. Iron deficiency is the commonest cause of secondary thrombocytosis.
Aims and Objectives: To know the prevalence of reactive thrombocytosis in microcytic hypochromic anemia cases. To analyze the range of hemoglobin levels and MCV values in which reactive thrombocytosis is more consistent.
Materials and Methods: The study includes 500 blood samples of patients of all the age groups and both the gender with microcytic hypochromic anemia. The samples were scrutinized for the corresponding thrombocytosis by using a hematology analyzer and confirmed by peripheral smear examination. Serum iron studies were done in confirmed samples of microcytic hypochromic anemia with valid thrombocytosis.
Results : Out of 500 cases of microcytic hypochromic anemia analysed 115 cases had associated thrombocytosis. out of which 17(14.78%) cases were males and 98 (85.22%) cases of females showed thrombocytosis. The majority of cases showed mild thrombocytosis which is frequently seen in cases with MCV 60-70 fl and moderate degree of anemia with hemoglobin level 7-9.9g/dl.
Conclusion : The utmost prevalent cause of reactive thrombocytosis in microcytic hypochromic anemia is iron deficiency. It is rational to distinguish between reactive and clonal thrombocytosis. However, the distinction cannot be always made with certainty, and the diagnosis often depends on watching the platelet count over a while. By identifying the etiology of increased platelet count and type of anemia treatment will be ease.

1. Introduction

The platelet count > 4,50,000/μl in the peripheral blood sample is referred to as thrombocytosis, by the rampant usage of electronic cell counters diagnosis of thrombocytosis is made easily and more often observed as an unexpected finding.[1,2]

In the peripheral blood, numerous disease conditions can lead to increased platelet count. The causes may be primary in elderly patients due to myeloproliferative disorders or secondary to infection or inflammation.[3]

Reactive thrombocytosis has to be differentiated from primary or clonal platelet disorders which are neglected many times which is of practical clinical importance and a diagnostic challenge. However, the distinction is not always made with certainty, and the diagnosis often depends on observing the platelet count over a period of time following the treatment.[4]

The commonest non- infectious cause of secondary thrombocytosis is iron deficiency anaemia. Thrombocytosis is either due to a reactive process (Secondary) or because of clonal disorders (primary thrombocytosis). It is critical

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concern to distinguish, because thrombo-haemorrhagic complications are frequent in clonal rather than reactive thrombocytosis.[5,6]

2. Aims and objectives of the study

1. It is a prospective study of 500 cases of microcytic hypochromic anemia.
2. How often microcytic hypochromic anemia cases present with thrombocytosis and in what range of hemoglobin level and MCV values it is affecting more consistently.
3. Which age group and sex are affected more commonly.

3. Methods

3.1. Selection of samples

All blood samples of patients of all the age groups were included in the study from January 2019 to December 2019 in a tertiary care center.

All EDTA blood samples were run in electronic cell counter for recording the Haemoglobin levels, MCV, and platelet counts along with platelet indices (PDW, Plateletcrit, and MPV) Patients who have low hemoglobin levels and MCV less than 80fl were screened for microcytic hypochromic anemia on peripheral smears stained by Leishman stain to confirm RBC morphology.

Random 500 blood samples with microcytic hypochromic anemia were selected and analyzed for the corresponding thrombocytosis. Platelet counts were confirmed by peripheral smear examination.

Confirmed cases of microcytic hypochromic anemia associated with thrombocytosis were sent for iron profile.

3.2. Inclusion criteria

Blood samples of all age groups received in the hematology laboratory who are diagnosed with microcytic hypochromic anemia were included in the study

3.3. Exclusion criteria

Blood samples of all age groups presenting with anemia and thrombocytosis for various reasons other than the microcytic hypochromic anemia were excluded.

In our study, the normal values of hemoglobin are considered according to the age and sex of the individual cases concerning WHO criteria for anemia.

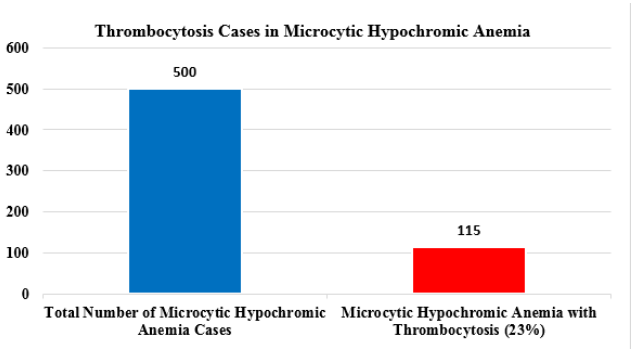
World Health Organization classification graded as hemoglobin level 11-12.9 g/dL as mild anemia in males and 11-11.9 g/dL in females.[7]

Hemoglobin level 8-10.9 g/dL as moderate anemia and <8 g/dL as Severe anemia both in males and females

Dame and Sutor[8]have categorized thrombocytosis into mild (5 to 7 lakhs/cumm) moderate (>7 to 9 lakhs/cumm) and severe (9lakhs/cumm) and extreme (> 10lakhs/cumm) and the same criteria is used in this study

4. Results

In the present study of 500 patients of Microcytic hypochromic anemia, 23% (n =115) of the total cases showed thrombocytosis (Graph 1)



Graph 1: Total number of Microcytic hypochromic anemia with thrombocytosis

Table 1 In the present study out of 500 cases of microcytic hypochromic anemia, 22.6 % (n = 113) were male patients and 77.4 % (n = 387) were female patients. In males microcytic hypochromic anemia is more prevalent in age group between 41 to 60 and then cases are more in the age group more than 70 years.

In females microcytic hypochromic anemia is more prevalent in the age group between 21 to 50 years, which is common in the reproductive age group.

Table 2 Out of 113 total male patients, 17 (15.04%) of them showed thrombocytosis associated with microcytic hypochromic anemia.

Out of 387 female patients, 98 (25.3%) of them showed thrombocytosis which is almost 10% more when compared to males (15.04%) with thrombocytosis associated with microcytic hypochromic anemia.

Table 3 In male patients microcytic hypochromic anemia with thrombocytosis is more common in the age group above 70 years (23.52%) and then in less than 10 years. (17.64%)

In female patients Microcytic hypochromic anemia with thrombocytosis is more frequent in the age group between 41 to 50 years (29.59%) and then in 31-40 years. (28.57%)

Table 4 In our study of male patients showed mild thrombocytosis (70.58%) in majority of the cases and commonly associated with moderate anemia (47.05 %) and only 5.88% showed severe thrombocytosis with one patient with platelet count more than 10 Lakhs/cumm.

In this study majority of the female patients showed mild thrombocytosis (86.74%) and commonly associated with moderate anemia (74.48%) and only (2.04%) showed severe

Table 1: Showing age wise distribution of male and female patients with microcytic hypochromic anaemia.

Age (in years)	1-10	11-20	21-30	31-40	41-50	51-60	61-70	> 70	Total
Number of cases	10	32	125	112	119	43	30	29	500(100%)
Total number of Males	08	07	13	11	23	18	11	22	113(22.6%)
Total number of Females	02	25	112	101	96	25	19	07	387(77.4%)

Table 2: Distribution of male and female patients with microcytic hypochromic anemia associated with thrombocytosis

Total number of male patients with microcytic hypochromic anemia	Total number of males with microcytic hypochromic anemia and thrombocytosis
113 (100 %)	17 (15.04 %)
Total number of females with microcytic hypochromic anemia	Total number of females with microcytic hypochromic anemia and thrombocytosis
387 (100 %)	98 (25.3 %)

Table 3: Showing age wise distribution of male and female patients with microcytic hypochromic anaemia associated with thrombocytosis.

Age (in years)	**1-10**	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**	**>70**	**Total**
Total number of patients presented with thrombocytosis	03	10	23	29	31	08	06	05	115 (100 %)
No of male patients presented with thrombocytosis	03	02	01	01	02	02	02	04	17 (14.78 %)
No of female patients presented with thrombocytosis	02	08	20	28	29	06	04	01	98 (85.22 %)

Table 4: Distribution of severity of thrombocytosis in males and females in relation to severity of anaemia.

Males			
Severity of anemia (gm/dl)	**No of male patients presented with mild thrombocytosis**	**No of male patients presented with moderate thrombocytosis**	**No of male patients presented with severe thrombocytosis**
Mild (Hb 11-12.9)	2	0	1
Moderate (Hb 8-10.9)	6	2	0
Severe (Hb < 8)	4	2	0
Total (n = 17)	12 (70.58 %)	4 (23.52 %)	1 (5.88 %)
Females			
Severity of anemia (gm/dl)	**No of Female patients presented with mild thrombocytosis**	**No of Female patients presented with moderate thrombocytosis**	**No of Female patients presented with severe thrombocytosis**
Mild (Hb 11-11.9)	7	1	0
Moderate (Hb 8-10.9)	64	**7**	2
Severe (Hb < 8)	14	3	0
Total (n = 98)	85 (86.7 %)	11 (11.22 %)	2 (2.04 %)

thrombocytosis with both the cases with platelet count more than 9 Lakhs/cumm

Table 5 In male patients most cases of microcytic hypochromic anemia with thrombocytosis presented within the range of 60.1 to 70fl MCV (52.94 %) and majority of the cases showed mild thrombocytosis (58.8%). In female patients most cases of microcytic hypochromic anemia with thrombocytosis presented within the range of 60.1 to 70fl MCV (68.36%) and majority of the cases showed mild thrombocytosis (84.69%).

Platelet indices analysed like MPV (Mean platelet volume), PDW (Platelet Distribution width), and PCT (Plateletcrit) were well within the normal range and no significant variations noted in all the cases of thrombocytosis associated with microcytic hypochromic anemias in the present study.

Most of the cases of microcytic hypochromic anemia with thrombocytosis (115) were sent for Iron studies and the majority of them were confirmed as iron deficiency anemia, which again proved that iron deficiency anemia is the most prevalent cause of reactive thrombocytosis

5. Discussion

There are various disease states that can bring about the elevated levels of platelets. The causes may be primary

Table 5: Showing severity of thrombocytosis in males and females in relation to MCV.

Male			
MCV (fl)	**No of male patients presented with mild thrombocytosis**	**No of male patients presented with moderate thrombocytosis**	**No of male patients presented with severe thrombocytosis**
70.1-79.9	2	1	1
60.1-70	6	2	1
<60	4	1	0
Total (n=17)	10 (58.8 %)	5 (29.41 %)	2 (11.76 %)
Female			
MCV (fl)	**No of Female patients presented with mild thrombocytosis**	**No of Female patients presented with moderate thrombocytosis**	**No of Female patients presented with severe thrombocytosis**
70.1-79.9	12	1	1
60.1-70	57	8	2
<60	14	2	1
Total (n = 98)	83 (84.69 %)	11 (11.22 %)	4 (4.08 %)

in elderly patients due to myeloproliferative disorders or secondary to infectious or inflammatory disorders.

Reactive thrombocytosis needs to be differentiated from primary or clonal platelet disorders, which are neglected many a times.[8]

It is extremely challenging to understand the reactive and clonal thrombocytosis process based upon clinical findings and laboratory test results even though there are underlying pathophysiological differences and clinical implications. The various physiological and pathological processes which contributes to the elevated platelet count has become clinically significant in routine practice. However, the distinction cannot be made with certainty, and the interpretation often depends on observing the platelet count variations periodically following the treatment.[9]

Iron deficiency anemia is the most common cause among the non-infectious causes of secondary thrombocytosis. This approach nevertheless is not without dangers, because thrombohemorrhagic complications are more common in clonal rather than reactive thrombocytosis.[10]

Study done by Ramu. R et al[11] about iron deficiency anemia with thrombocytosis and erythropoietin levels also showed that majority of the cases in their study had moderate degree of anemia and presented frequently with mild thrombocytosis which is similar to our study. They also depicted that novel data advocate the symbiotic effect of both erythropoietin and thrombopoietin on the bipotential progenitor cells of the erythroid/megakaryocyte precursors. Despite, this decline to clarify that not all the patients with elevated levels of erythropoietin, and iron-deficiency anemia cases present with thrombocytosis. Hence, there may be boundless added mechanisms that aid in the evolution of thrombocytosis in few cases of iron deficiency anemia.

Tania O et al[12] described that bone marrow examination cannot prove the causes of chronic myeloproliferative disorders, especially essential thrombocythemia. In iron deficiency anemia with associated thrombocytosis after an increase in hemoglobin level closer to normal values with packed red cell transfusion, platelet counts become normal with lowering erythropoietin levels. The probable mechanism in iron-deficiency anemia associated thrombocytosis is still a matter of deliberation of the concept of thrombopoietin and erythropoietin amino acid structural homology of might justify the cause of thrombocytosis in children associated with iron-deficiency anemia.

Mehri T et al[13] reported that in normal individuals, MPV is inversely related to Platelet count. The reference values of MPV may differ with the platelet count. In majority of the cases of myeloproliferative disorders, MPV is usually increased. Platelet counts are unusually increased in primary myeloproliferative disorders than secondary thrombocytosis cases. PDW in both primary and secondary thrombocytosis also varies accordingly. In our present study all the cases of thrombocytosis, the platelet indices were within normal limits.

Sandoval.C[14] and Nathiya S et al[15] defined that amidst of all the anemia types, anemia with iron deficiency most often presents with thrombocytosis and is more persistent in children below 2 years of age, because of the greater prevalence of iron deficiency in this age group. In this study more the severity of anemia was directly proportional to severity of thrombocytosis. The mean MPV and PDW were found to be higher in primary thrombocytosis when compared to secondary thrombocytosis. In the present study most cases were in the reproductive age group in females.

Jonathan S et al[16] and Akan et.al determined in his study that cytokines IL-6, IL-11, and TPO were not increased in patients associated with iron deficiency anemia associated with thrombocytosis, in correlation with iron deficiency anemia with normal platelet counts. This shows that the cytokine levels do not have any significant portrayal in iron deficiency associated thrombocytosis.[17]

Secondary thrombocytosis is usually favorable and platelet becomes normal with prompt treatment of the underlying cause without any thrombotic complications. [18]

6. Conclusions

In our routine reporting of peripheral smear examination, we come across many cases of increased platelet count in microcytic hypochromic anemia more often in iron deficiency anemia. It is of practical clinical importance to be readily able to distinguish between reactive and clonal thrombocytosis.

However, the distinction cannot be always made with certainty, and the diagnosis often depends on watching the platelet count over a while. By knowing the cause of increased platelet count and type of anemia treatment will be ease

To conclude, as there are only fewer articles published regarding the prevalence of thrombocytosis in microcytic hypochromic anemias involving all the age groups

This study was embarked upon, hemoglobin levels, MCV, and platelet count in all the age groups and both the genders. From the current study, we conclude that mild thrombocytosis is frequently seen in microcytic hypochromic anemia cases in females in the age group 21-50 years in which the majority of them proved to be iron deficiency anemia.

Ruling out the secondary causes of thrombocytosis should be the priority, then primary clonal disorders, whenever there is a suspicion. We have to differentiate that the cases are just reactive thrombocytosis or else we are neglecting any platelet disorders.

Among the non-infectious causes of secondary thrombocytosis, iron deficiency is a common one, since it is the single most common nutritional deficiency worldwide which can be treated efficiently next to Vitamin B12 and folic acid deficiency

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8. Conflict of Interest

The authors declare they have no conflict of interest.

References

1. Kumar CA. Incidence of thrombocytosis in iron deficiency anemia in pediatric age group in rural population. *Indian J Basic Appl Med Res*. 2013;3(1):45–9.
2. Kadikoylu G, Yavasoglu I, Bolaman Z, Senturk T. Platelet parameters in women with iron deficiency anemia. *J Natl Med Assoc*. 2006;98(3):398–402.
3. Fernández CM, J PMC, García GP, de Julián CE, Bieler BC, et al. Thrombocytosis in the oncology haematology clinic: description, aetiological diagnosis and progression thrombocytosis. An Pediatr. *An Pediatr*. 2008;69(1):104.
4. Mantadakis E, Tsalkidis A, Chatzimichael A. Thrombocytosis in childhood. *Indian Pediatr*. 2008;45:669–77.
5. Abha C. Iron deficiency anemia with thrombocytosis: a diagnostic challenge. *Int J Healthc Biomed Res*. 2014;03(1):43–6.
6. Buss DH, Cashell AW, O'Connor ML, Richards F, Case LD. Occurence, etiology, and clinical significance of extreme thrombocytosis: A study of 280 cases. *Am J Med*. 1994;96(3):247–53. doi:10.1016/0002-9343(94)90150-3.
7. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity in Vitamin and Mineral Nutrition Information System. Geneva, World Health Organization; 2011.
8. Hoffman R. Primary thrombocythemia. In: Hoffman R, J BE, SJ S, editors. Hematology: Basic Principles and Practice. vol. 129. Philadelphia, Pa: Churchill Livingstone; 2000. p. 165–77.
9. Waldhör T. Iron deficiency generates secondary thrombocytosis and platelet activation in IBD: the randomized, controlled thromboVIT trial. *Inflamm Bowel Dis*. 2013;19(8):1609–16.
10. Voigt W, Jordan K, Sippel C, Amoury M, Schmoll HJ, Wolf HH, et al. Severe thrombocytosis and anemia associated with celiac disease in a young female patient: a case report. *J Med Case Rep*. 2008;2(1):1752–947. doi:10.1186/1752-1947-2-96.
11. Ramu R, and NCM. Study of iron deficiency anemia with thrombocytosis in association with serum erythropoietin levels. *Trop J Path Micro*. 2017;3(1):71–6.
12. Tania O, Alka B. To Study Hematological Abnormalities of Platelet Count in Children with Iron Deficiency Anemia In India. *IntlJ Scientific Res*. 2016;5(4):90–5.
13. Mehri T, Mohammad RK, Rahim V. Etiology of Thrombocytosis and the Use of Platelet Parameters to Distinguish Between Clonal and Reactive Thrombocytosis. *Int J Hematol Oncol*. 2006;16:71–6.
14. Sandoval C. Thrombocytosis in Children With Iron Deficiency Anemia: Series of 42 Children. *J Pediatr Hematol/Oncol*. 2002;24(7):593. doi:10.1097/00043426-200210000-00025.
15. Subramaniam N, Mundkur S, Kini P, Bhaskaranand N, Aroor S. Clinicohematological Study of Thrombocytosis in Children. *ISRN Hematol*. 2014;2014:1–4. doi:10.1155/2014/389257.
16. H JSWJ. Thrombocytosis: Diagnostic Evaluation, Thrombotic Risk Stratification, and Risk-Based Management Strategies. *Thrombosis*. 2011;2011:1–16. doi:10.1155/2011/536062.
17. Akan H, Güven N, Ayogdu İ, Arat M, Beksaç M, Dalva K, et al. Thrombopoietic Cytokines in Patients with Iron Deficiency Anemia with or without Thrombocytosis. *Acta Haematol*. 2000;103(3):152–6. doi:10.1159/000041038.
18. Vora AJ, Lilleyman JS. Secondary thrombocytosis. *Arch Dis Child*. 1993;68:88–90. doi:10.1136/adc.68.1.88.

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