ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 1, January - 2023, Page No. : 465 - 475

Association of Thrombocytopenia with Microcytic and Macrocytic Anemia in Pregnant Women

[1]Dr.Kausar Jahan, Senior Resident, Lok Nayak Hospital, Governmet of NCT of Delhi, New Delhi, India.

[2]Dr.Tamkin Khan, Professor in Department of Obstetrics &Gynaecology, Jawaharlal Nehru Medical College and Hospital (JNMCH), AMU, Aligarh, Uttar Pradesh, India.

[3]Dr.Kafil Akhtar, Professor in Department of Pathology, Jawaharlal Nehru Medical College and Hospital (JNMCH), AMU, Aligarh, Uttar Pradesh, India.

Corresponding Author: Dr. Kausar Jahan, Senior Resident, Lok Nayak Hospital, Governmet of NCT of Delhi, New Delhi, India.

How to citation this article: Dr. Kausar Jahan, Dr. Tamkin Khan, Dr. Kafil Akhtar, "Association of Thrombocytopenia with Microcytic and Macrocytic Anemia in Pregnant Women", IJMACR- January - 2023, Volume – 6, Issue - 1, P. No. 465 – 475.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Objectives: To find out association of Thrombocytopenia with Microcytic and Macrocytic Anemia in pregnant women.

Background: Thrombocytopenia is defined as platelet count less than 150,000f/mm^3. It is a second common hematological disorder in pregnancy, anemia being the most common. The exact mechanism of Iron Deficiency Anemia (IDA) and Thrombocytopenia is not well understood. The present study was planned to evaluate the effect of anemia on platelet count and functions.

Methodology: This was a cross-sectional, observational study conducted from 2019-2021 in the Department of Obstetrics and Gynaecology, with the collaboration of Department of Pathology, JNMC, AMU, Aligarh (U.P) on 360 pregnant women at 26-32 weeks of gestation. Complete Blood Count (CBC) and Red cell indices were calculated by Automated Haemotology (H3D Premier Diagnova) Analyzer. Type of anemia was determined on the basis of General Blood Smear and on indices. All the qualitative variables were analyzed using Pearson's Chi-square test while all quantitative variables were analyzed using independent sample test and Kruskal-Wallis one-way ANOVA test.

Results: The prevalence of Thrombocytopenia in Iron Deficiency Anemia was 57.97%, in Megaloblastic Anemia it was only 18.92% and in Dimorphic it was 70.10%. The association was highest in the cases of Dimorphic Anemia and lowest in the cases of Megaloblastic Anemia while only 15% of control were having Thrombocytopenia in the present study. This

difference in prevalence among cases and control was statistically significant.

Conclusion: An association exists between haemoglobin and platelet count. Dimorphic Anemia is commonest form of anemia during pregnancy. Further studies need to be conducted for confirming the association of Anemia with Thrombocytopenia.

Keywords: Anemia, Microcytic, Macrocytic, Throm Bo cytopenia, Pregnant women.

Introduction

Platelets were discovered by an Italian Pathologist Giulio Bizz zero in the year 1882. Platelets are disc-shaped a nuclear cell fragment that are shed from megakaryocytes in the bone marrow into the blood stream. They play a critical role in haemostasis by forming the primary plug that initially seals vascular defects and by providing a surface that binds and concentrates activated coagulation factors [1]. Thrombocytopenia is defined as platelet count less than 150,000/mm^3 [2].

The association of anemia with Thrombocytosis has been known for over 70 years but its etiology has not been clearly understood [3]. However, reports of Thrombocytopenia associated with iron deficiency anaemia have served to confuse the issue [4, 5]. Normal platelet count has also been reported [5-8].

The following hypothesis has been suggested by Karp Atkin et al. for the maintenance of platelet count at steady-state levels and for the changes leading to reactive Thrombocytosis [9]. According to them, Iron either directly or indirectly inhibits the rise in platelet count above steady-state levels via some inhibitory mechanisms, possibly against Thrombopoietin, their hypothesis also considered that iron is required for the synthesis or production of an integral portion of the platelet [9].Iron deficiency anemia is commonly associated with ThromBo cytosis; however cases of Thrombocytopenia have been reported. The first case of iron deficiency associated trombocytopenia in literature was reported in 1964 by Gross et al. Moderate Erythropoietin stimulation, i.e. that produced by standard doses of Recombinant Human Erythropoietin short-term hypoxia or moderate iron deficiency causes a moderate elevation of platelet counts, whereas intense Erythropoietin stimulation, as produced by high doses of Recombinant Human Erythropoietin, prolonged hypoxia or severe iron deficiency, causes some degree of Thrombocytopenia [17].The exact mechanism of Iron Deficiency Anemia (IDA) and Thrombocytopenia is not well understood. Apar Kishor Ganti et al. suggested that it may be related to the alteration in the activity of iron-dependent enzymes in thrombo-and leucopoiesis [18].

A thorough literature search was conducted on med line with search parameters “anemia AND thrombocytopenia AND pregnancy” using the bole anword“AND”on15thJanuary2022.Itshowed1250results. There is scarcity of literature on association between Anemia and Thrombocytopenia. PubMed mostly revealed case reports and case series with only a few studies related to our topic. It is pertinent to mention here that most of the studies have been conducted on Paediatric age group. Literature search with the keyword’s anemia, Thrombocytopenia and pregnancy revealed study on prevalence of Thrombocytopenia in pregnancy, causes of thrombocytopenia in pregnancy and incidence of anemia in the cases of Thrombocytopenia. Therefore, the present study is planned to evaluate the effect of anemia on platelet count and functions.

Materials and Methods

The study was conducted after taking informed consent from the patients in the Department of Obstetrics and Gynaecology, with the collaboration of Department of Pathology, JNMC, AMU, Aligarh (U.P). It was a cross-sectional, observational study, conducted in 2019-2021. The details of the patients were noted in pre-designed Proforma.A total number of 360 pregnant women at 26-32 weeks of gestation were enrolled. Lost to follow up were 40 and remaining 320 were contributed by 20 control and 300 cases.

Inclusion Criteria

was Pregnant women at 26 to 32 weeks of gestation.

Exclusion Criteria

was Fever (>100 F), Known case of dengue, Any other viral infection like HCV, Pregnancy induced hypertension, Malaria, Idiopathic Throm bocytopenia of pregnancy, History of any drug intake which affects platelet counts (Aspirin, Warfarin).

Procedure methodology

Hb%, Platelet counts MCV, MCH, MCHC, TLC, DLC, GBP, BT CT, RFT, LFT, HBsAg, HCV, HIV, DENGUE(IgM), PTINR, MPQBC/MP smear was performed and divided the patients intofour groups:

Group-A: Microcytic Anemia with Thrombocytopenia, Group-B: Macrocytic Anaemia with Thrombocytopenia, Group-C: Dimorphic Anemia with Thrombocytopenia & Group-D: Control.

The above cited Groups were provided appropriate treatment depending on the type of anemia. Response of therapy seen after 4 to 6 weeks (by Hemogram & General Blood Picture).Hemogram and GBP were done at term or in labour. Hemogram and GBP were repeated after 48 hours of delivery. Statistical analysis was done using Pearson's Chi-square test while all quantitative variables were analyzed using independent sample test and Kruskal-Wallis one-way ANOVA test.

All the tests were performed using computer programme i.e., SPSS version 25.0.

Results

Table 1: Demographic characteristics

Groups	Age			Mean Gestational Age	Area of Residence		Literacy Status		Socio-Economic Status				
	20-25Year (%)	26-30Year (%)	31-35Year (%)	Gestational Age Mean ± SD	Urban (%)	Rural (%)	Literate	Illiterate	Upper	Upper-Middle	Lower-Middle	Upper-Lower	Lower
Group-A	20.29	72.46	7.25	29.04±3.05	91.30	8.70	81.16	18.84	1.45	30.97	56.52	28.99	4.35
Group-B	21.62	59.46	18.92	30.49±1.03	81.08	18.92	67.57	32.43	0.00	21.62	40.54	18.92	18.92
Group-C	9.79	87.63	2.58	29.02±3.61	96.39	3.61	75.77	24.23	2.06	1.03	77.32	18.04	1.55
Group-D	25.00	60.00	15.00	29.58±2.00	75.00	25.00	90.00	10.00	25.00	60.00	15.00	0.00	0.00

Both the Cases and Control were comparable for age, gestational age, literal cyst at us and area of residence as age of study group in our study was between 20-35year with majority of Cases and Controlbelongingto26-30-yearagegroup.

Mean gestational age was 29.04 ± 3.05, 30.49 ± 1.03, 29.02 ± 3.61in Group-A, Group-B and Group-C. There was no statistically significant difference in theme an gestational age in all groups i. e, comparable.

Maximum number of cases and controls were literate and belong to urban locality. However, there was difference in socio- economic status of the Cases and the Controls. Maximum number of cases was from lower middleclass while maximum Control was from upper middle class. The results were significant.

Table 2: Prevalence of Thrombocytopenia among four study groups.

S. N	Groups	Thrombocytopenia						Ch^2-Value	p-Value
		Yes		No		Total			
		No. of Cases	(%)	No. of Cases	(%)	No. of Cases	(%)		
1	Group A(n=69)	40	57.97	29	42.03	69	100		
2	Group B(n=37)	7	18.92	30	81.08	37	100		
3	Group C(n=194)	136	70.10	58	29.90	194	100		
4	Group D(n=20)	3	15.00	17	85.00	20	100	50.084	p<0.001

Thrombocytopenia was present in 70.1% cases in Group-C and 57.97% in Group-A. This difference of prevalence of thrombocytopenia among the study groups was statistically significant**.**

Table 3: Comparison of mean hemoglobin before and after therapy according to severity of anaemia in study population.

Groups	Severity	Before therapy	After therapy	t-Value	p- Value
Group A	Mild	10.90±3.48	10.88±3.44	-0.015	p >0.05
	Moderate	9.99 ±4.02	10.00±4.58	0.004	p >0.05
	Severe	7.01 ±4.52	7.00 ±3.58	-0.008	p >0.05
Group B	Mild	10.71±4.29	10.80±5.89	0.028	p >0.05
	Moderate	9.95 ±4.98	10.10±4.56	0.031	p >0.05
	Severe	6.99 ±3.25	7.01 ±3.59	0.006	p >0.05
Group C	Mild	10.71±4.92	10.72±5.58	0.008	p >0.05
	Moderate	9.92 ±5.02	9.81 ±4.23	-0.063	p >0.05
	Severe	7.10 ±4.34	7.00 ±4.85	-0.144	p >0.05

Mean rise in hemoglobin after appropriate therapy in Microcytic, Macrocytic, and Dimorphic groups is statistically non-significant.

Table 4: Comparison of mean platelet count and after therapy according to severity of anemia in study population.

Groups	Severity	Before therapy	After therapy	t-Value	p-Value
Group-A	Mild	1.50 ± 0.98	1.56 ± 0.56	0.192	p >0.05
	Moderate	1.01 ± 0.54	1.02 ± 0.39	0.04	p >0.05
	Severe	0.50 ± 0.21	0.51 ± 0.19	0.158	p >0.05
Group-B	Mild	1.51 ± 1.98	1.71 ± 1.89	0.163	p >0.05
	Moderate	0.98 ± 0.48	1.20 ± 0.99	0.283	p >0.05
	Severe	0.51 ± 0.35	0.56 ± 0.45	0.124	p >0.05

Group-C	Mild	1.52 ± 0.86	1.54 ± 0.92	0.093	p >0.05
	Moderate	0.99 ± 0.82	1.21 ± 0.99	0.64	p >0.05
	Severe	0.34 ± 0.08	0.51 ± 0.19	7.736	p <0.001

Mean rise in platelet count after therapy in Dimorphic anemia with thrombocytopenia in severe group is statistically significant (p<0.001).

Table 5: Mean hemoglobin and platelet counts at term or in labour.

Sn.	**Groups**	**Mean ± SD**				
		Hb	Platelet	MCV	MCH	MCHC
1	Group-A	9.84±0.65	2.09±0.41	87.24±10.19	30.19±1.49	32.23±1.87
2	Group-B	9.91±0.84	2.04±0.23	87.21±9.68	29.29±1.09	30.83±2.02
3	Group-C	10.19±5.16	2.52±6.47	87.11±10.85	30.86±2.44	32.21±2.00
4	Group-D	11.91±0.56	2.36±0.24	95.13±2.72	30.69±1.23	32.83±1.30
5	F-Value	1.149	0.099	3.703	2.3	1.867
6	p-Value	p>0.05	p>0.05	p<0.05	p>0.05	p>0.05

Mean hemoglobin at term or in labour was 9.84 ± 0.65 in Group A, 9.91±0.84 in Group B, 10.19±5.16 in Group C and 11.91±0.56 in Group D, this difference was statistically non-significant.

Table 6: Mean hemoglobin and platelet count after 48 hours of delivery.

Groups	**Mean ± SD**				
	Hb	Platelet	MCV	MCH	MCHC
Group-A	9.88±0.83	2.16±0.30	88.95±10.03	30.89±1.78	32.92±2.06
Group-B	10.06±0.76	2.04±0.26	89.66±8.14	30.70±2.00	32.34±1.58
Group-C	10.88±8.53	2.23±0.39	88.88±7.90	32.04±7.14	32.89±1.91
Group-D	11.82±0.47	2.27±0.20	93.86±3.09	30.23±1.34	32.09±1.40
F-Value	0.449	1.194	2.3	0.964	1.276
p-Value	p>0.05	p>0.05	p>0.05	p>0.05	p>0.05

Mean hemoglobin in Group A after 48 hours of delivery was 9.88 ±0.83, in Group-B it was10.06±0.76, in Group-C it was10.88±8.53 and in Group-D it was 11.82 ±0.47, this difference among the Cases and the Control after 48 hours of delivery in mean hemoglobin and mean platelet count was statistically non-significant**.**

Table 7: Mean VitaminB_{12} level in the cases.

Groups	**B12**	**F-Value**	**p-Value**
	Mean ± SD		
Group-A	812.12±216.25	126.158	p<0.001
Group-B	350.00±52.23		
Group-C	352.70±227.02		

Vitamin B_{12} level was found 812.12±216.25, 350.00±52.23and352.70±227.02 in Group A, Group B and Group C respectively, this difference was statistically significant**.**

Table 8: Mean Folic Acid level in the cases.

Groups	Folic Acid	F-Value	p-Value
	Mean ± SD		
Group-A	17.41±8.4	0.157	p>0.05
Group-B	20.60±0.00		
Group-C	16.00±10.15		

The mean folic acid level was 17.41±8.40, 20.60±0.00 and 16.00±10.15 in Group- A, Group-B and Group-C (respectively). This difference was statistically non-significant**.**

Discussion

Thrombocytopenia, defined as a platelet count less than 150,000/mm^3, is the second most common Haematological abnormality in pregnancy after anemia, occurring in up to 6-10% of pregnancies [20, 21, 22]. Platelet counts less than 100,000/mm3 are less common and are observed in less than1% of pregnancies [23]

Most cases of thrombocytopenia in pregnancy are mild and have no adverse outcome form other or fetus, moderate to severe thrombocytopenia may lead to bleeding during delivery and occasional cases may be related to a life-threatening systemic disorder such as thrombotic micro angiopathy [24]. The first case of iron deficiency-associated thrombocytopenia in the literature was reported in 1964 by Gross et al. [25]. We found limited studies similar to ours on association between Anemia and Thrombocytopenia in literature.

Age of study group in our study was between 20 & 35 year. Majority of Cases and Control belong to 26-30 year i.e., in both the Cases and the Control group age was comparable and the results were found to be statistically significant($p<0.001$). Our observations were different with the studies conducted on prevalence of thrombocytopenia among pregnant women by Sumaya Elgodwi et al. [26] (2021) as they concluded that maximum patients in their study were in the age group of 40-49 years old and also in that study they concluded that Thrombocytopenia increased with increasing age. Our study was also contradictory with Mbanaya et al. (2007), SHO reported that pregnant women with thrombocytopenia were aged from 15-40 years [27]. Al Kouatly et al. (2003) found that mean maternal age of Thrombocytopenic pregnant women was 34.3 ±5.4 years [28]. Also, Parrnas et al. (2006) reported that pregnant women with thrombocytopenia were significantly older compared with pregnant women without Thrombocytopenia [29].

In our study we found findings contradictory to the above studies. There was no correlation of Thrombocytopenia with increasing age. The finding may be because most of the pregnant women in our study were of a younger age group and had anemia which could be the confounding factor while other authors were studying only the prevalence of thrombocytopenia in pregnancy un related to anemia.

In present study mean gestational age was 29.04±3.05,30.49±1.03, 29.02±3.61 in Group-A, Group-B and Group-C (respectively). There was no statistically significant difference in the mean gestational age in all groups. It was comparable among all groups which were related to our inclusion criteria. Sumaya Elgodwi et al. (2021) found that the prevalence of moderate Thrombocytopenia increased with increasing gestational age [26]. Fikir, Bamlaku, Zegeye (2017) showed that there was no association between the trimester and thrombocytopenia [30].

In present study, maximum number of the Cases and Controls were from urban locality, the results were statistically significant ($p<0.001$). Fikir, Bamlaku, Zegeye (2017) concluded from their study on prevalence

of thrombocytopenia in pregnancy conducted in Ethiopia that thrombocytopenia was higher among pregnant women in patients from rural areas [30]. In an Indian study by Jeetendra et al. [31] (2017) on prevalence of anemia, the authors reported higher prevalence of anemia urban areas similar to our study but they also reported that severe anemia is more prevalent in rural areas in India but this was not so in our study. Urban population is expected to be more aware about antenatal checkups and easier access to a health care setting but it was not found to be so in our study. Only 20 patients out of 300 women in our study belonged to rural areas. The reason for this could be that it was conducted during the COVID period which affected the delivery of RMNCH services and frequent lockdowns prevented patients from peripheral areas from reaching health care facilities.

In present study maximum number of cases and control were literate, which were statistically non-significant ($p>0.05$). It was surprising to find the high prevalence of anemia in a literate population. Similar findings have been reported by other authors. Ali Eram et al. (2017) reported that in their study all women with anemia were literate [32].

Present study shows that the maximum number of the Cases having thrombocytopenia were from lower middle class according to modified Kuppuswamy scale while maximum Control were from upper middle class and the results were significant($p<0.001$). Both SumayaElgodwi et al. (2021) and Fikir, Bamlaku, Zegeye (2017) did not report on the socio-economic status of their study population [26, 30].

The socio-economic status correlates with nutritional status and access to antenatal care and this was the reason why most of our cases of anemia belonged to a lower middle-class stratum.

Only 4.35%, 18.92% and 1.55% cases in each group were fromlower class.This is surprising as our center caters to a wide area but the reason could be that our study was conducted during the COVID period when lockdowns and loss of work for daily wagers. Women from lower class were not seeking antenatal or emergency obstetric care during this period.

Prevalence of thrombocytopenia in Anemia: In the present study table-7 shows that the prevalence of thrombocytopenia in iron deficiency anemia was 57.97%, %,in Megaloblastic anemia it was only 18.92% and in Dimorphic anemia, it was 70.10%. The association was highest in cases of dimorphic anemia and lowest in cases of megaloblastic anemia. This was statistically significant.

In a study by Tabinda Ijaz et al. 2016 in Lahore, the prevalence of anemia and thrombocytopenia was reported as 70.5% & 16.5% (respectively). However, they did not attempt to co-relate the two conditions [33].

However, Fikir, Bamlaku, Zegeye (2017) found 8.8% prevalence of thrombocytopenia in pregnant women in North-West Ethiopia while Sumaya Elgodwi et al. (2021) found 18% prevalence of thrombocytopenia among pregnant women in Tripoli region [26, 30]. However, both the studies were different from the only studied the prevalence of thrombocytopenia. Sumaya et al. studied the various conditions associated in thrombocytopenia and found that anemia was present in 96 patients (31%) out of 312 thrombocytopenic pregnant patients [26].

We have studied the prevalence of thrombocytopenia in cases of anemia and found a prevalence of 60%. The results corroborate the finding of Mbanya et al. (2007) who reported that the major factor associated with

thrombocytopenia was anemia among pregnant women in Cameroon [27].

In present study after giving therapy according to type of anemia, we found statistically non-significant rise in haemoglobin and platelet counts among study groups. In Dimorphic group with severe anemia, correction of anemia resulted in significant rise in platelets($p<0.001$). Non-significant rise in mean platelet counts after iron therapy, may be due to the fact Erythropoietin shares same structural features with thrombopoietin. The levels of endogenous erythropoietin initially significantly decrease during the correction of iron deficiency. This reduction in endogenous erythropoietin might decrease the productivity of megakaryocytes and lead to transient thrombocytopenia which is known as iron therapy induced thrombocytopenia. Akan H, GüvenN, Aydogdu I, Arat M, Beksaç M, Dalva K (2000).[34]. Various case reports and case series have correlated iron deficiency anemia and thrombocytopenia. Van K. et al. (2010)reported a case series of four paediatric age group patients in all the four cases hemoglobin and platelet counts normalized within 1 to 3 weeks of iron supplementation[35]. Nataly, Calvo, Pak (2018) also reported a case of a 30 year non pregnant female whose low platelet count responded on iron therapy [15]. Ramy et al. (2012) also report a case of non-pregnant40-year female whose thrombocytopenia improved on treating severe anemia with blood and iron [36].

Mahmoud, Al-Tikrity, Babikikir, Yassin (2020) also report a case of severe anamia 32 year non pregnant female along with thrombocytopenia, her platelet count improved on injectable iron [37]. Tessa et al (2019) also conducted a study to correlate anemia with Throm bocytopenia but on non-pregnant patients [38]. Their study was a case control study, which showed an increase in mean platelet count on correcting severe iron deficiency. Vaibhav et al. (2015) analyzed the relationship between severe anemia and Throm bocytopenia, they also found that all thrombocytopenic patients respond rapidly on an anemia therapy [39]. Faisal, Shridhar, Samprathi and Vemgal (2021) also reported correlation of severe iron deficiency anemia with thrombocytopenia, but these case reports were also in paediatric age group [40]. All the above case report and case series were conducted either on paediatric age group or on non-pregnant population, so differ from our study.

Mean Hb and platelet count during labour and after 48 hours of delivery: The mean platelet count normalized as pregnancy reached term or in labour and 48hours, and mean platelet count was normal after 2 days of delivery. Red cell indices, however did not improve as they take 4to12 weeks to get normalized [41].

The mean vitaminB_{12} level was low in the three study groups (cases) including Iron Deficiency Anemia group but the deficiency was most marked in dimorphic and macrocytic group. In present study Megaloblastic anemia was associated with thrombocytopenia, this finding was comparable to study conducted by Raj Laxmi Birur Rajashekar et al (2017) but the study was conducted on non-pregnant patients which is different from our study population [14]. In contradictory to above studies Moghadam, Sand Ghor Bani, M.(2016) reported a case of a 33-year-old pregnant woman, who was having megaloblastic anemia and severe thrombocytopenia. After managing her megaloblastic anemia, her platelet count did not change [42].

The mean folic acid level was low in all three study groups, but was normal in megaloblastic anemia. Though both folic acid and B12 deficiency is implicated

in megaloblastic anemia but deficiency of Vitamin B_{12} was found to be more common than folic acid deficiency in our study. Wintrobes Clinical Hematology also mentions that B_{12} deficiency is more commonly associated with megaloblastic anemia [43].

Conclusions

It can be concluded that both anemia and Thrombocytopenia disorders in pregnancy are common even among literate younger pregnant women living in urban locality who come from lower-middle socio-economic strata. Dimorphic anemia is commonest form of anemia during pregnancy. It can also be concluded that there is an association that exists between haemoglobin and platelet count.

In order to reduce maternal and neonatal morbidities, careful surveillance is required of all pregnancies for early detection and treatment of anemia. Type of anemia should be investigated before therapy. Further studies to be conducted for confirming the association of anemia with thrombocytopenia.

References

1. Kumar V, Abbas AK, Aster JC. Robbins basic pathology e-book. Elsevier Health Sciences; 2017 Mar 8.

2. Sullivan CA, Martin Jr JN. Management of the obstetric patient with thrombocytopenia. Clinical obstetrics and gynecology. 1995 Sep 1;38(3):521-34.

3. Richardson FL. Effect of severe hemorrhage on the Number of Blood Plates in Blood from the Peripheral Circulation of Rabbits. The Journal of Medical Research. 1904 Dec;13(1):99.

4. Lopas H, Rabiner SF. Thrombocytopenia associated with iron deficiency anemia: A report offivecases. ClinicalPediatrics.1966Oct;5(10):609-16.

5. Dincol K, Aksoy M. On the platelet levels in chronic iron deficiency anemia. ActaHaematologica.1969; 41:135-43.

6. Gross S, Keefer V, Newman AJ. The platelets in iron-deficiency anemia. I. The response to oral and parenteral iron. Pediatrics. 1964 Sep;34(3):315-23.

7. Choi SI, Simone JV. Platelet production in experimental iron deficiency anemia. Blood.1973Aug;42(2):219-28.

8. Choi SI, Simone JV, Jackson CW. MegakaryoCyto poiesis in experimental iron deficiency anemia. Blood. 1974 Jan;43(1):111-20.

9. Karp Atkin S, Garg SK, Freedman ML. Role of iron as a regulator of thrombopoiesis. The American journal of medicine. 1974 Oct;57(4):521-5.

10. Xavier-Ferrucio J, Scanlon V, Li X,Zhang PX, Lozovatsky L, Ayala- Lopez N, Tebaldi T, Halene S, CaoC, Fleming MD, Finberg KE. Low iron promotes megakaryocytic commitment of megakaryocytic-erythroid progenitors in humans and mice. Blood. 2019Oct31;134(18):1547-57.

11. Nishikawa M.Thrombocytopenia due to deficient platelet production. Nihonrinsho.Japanese Journal of Clinical Medicine. 2003Apr1;61(4):575-80.

12. Borkataky S, Jain R, Gupta R, Singh S, Krishan G, Gupta K, Kudesia M. Role of platelet volume indices in the differential diagnosis of thrombocytopenia: a simple and inexpensive method. Hematology. 2009 Jun1;14(3):182-6.

13. Katti TV, Mhetre SC, Annigeri C. How far are the platelet indices mirror image of mechanism of Thrombocytopenia-mystery still remains.

14. Rajashekar RB, Mahadev Appa A, Patel S. Evaluation of thrombocytopenia in megaloblastic anemia by platelet indices and megakaryocytes-

comparison with hypoproduction and hyper destruction. National Journal of Laboratory Medicine. 2017.

15. Torrejon N, Calvo A, Pak S. Iron Deficiency Anaemia Leading to Thrombocytopenia: A Case Report. Int J Res Reports Hematol. 2018; 1:1-4.

16. Daza DO, Larhammar D. Evolution of the receptors for growth hormone, prolactin, erythropoietin and Thrombopoietin in relation to the vertebrate tetraploidizations. General and Comparative Endocrinology.2018Feb 1; 257:143-60.

17. BeguinY. Erythropoietin and platelet production. Haematological. 1999;84(6):541-7.

18. Ganti AK, Shonka NA, Haire WD. Pancytopenia due to iron deficiency worsened by iron infusion: a case report. Journal of Medical Case Reports.2007 Dec;1(1):1-3.

19. McDonald TP, Clift RE, Cottrell MB. Large, chronic doses of erythropoietin cause thrombocytopenia in mice [see comments].

20. Sullivan CA, Martin Jr JN. Management of the obstetric patient with thrombocytopenia. Clinical obstetrics and gynecology. 1995 Sep1;38(3):521-34.

21. Salnlo S, Kekomäki R, Rllkonen S, Teramo K. Maternal Thrombocytopenia at term: a population-basedstudy. Actaobstetriciaetgynecologic aScandinavica.2000Jan1;79(9):744-9.

22. McCrae KR. Thrombocytopenia in pregnancy. Hematology 2010, the American Society of Hematology Education Program Book. 2010 Dec 4;2010(1):397-402.

23. Rodeghiero F, Stasi R, Gernsheimer T, Michel M, ProvanD, Arnold DM, etal. Standardization of terminology, definitions and outcome criteria in immune Thrombocytopenic purpura of adults and children: report from an international working group. Blood [Internet].2009;113(11):2386–93.

24. Chaturvedi S, McCrae KR. Thrombocytopenia in pregnancy. In Platelets in Thrombotic and Non-Thrombotic Disorders 2017 (pp. 813-823). Springer, Cham.

25. Gross S, Keefer V, Newman AJ. The platelets in iron-deficiency anemia. I. The response to oral and parenteral iron. Pediatrics. 1964;34: 315-323.

26. Elgodwi S, LA war M, Saad Allah A. Prevalence of Thrombocytopenia Among Pregnant Women in Tripoli Region/Libya. International Journal of Biomedical Science and Engineering. 2021 Oct 29;9(4):83.

27. Mbanya D, TayouTagny C, Takoeta E, Mbu R, Kaptue L. Factors associated with thrombocytopenia among pregnant women in Cameroon. Sante [Internet]. 2007;17(4):213–7.

28. Al-Kouatly HB, Chasen ST, Kalish RB, Chervenak FA. Causes of thrombocytopenia in triplet gestations. American journal of obstetrics and gynecology. 2003 Jul 1;189(1):177- 80.

29. G,Yerushalmi R. Moderate to severe thrombocytopenia during pregnancy. European Journal of Obstetrics & Gynecology and reproductive biology. 2006Sep1;128(1-2):163-8.

30. Asrie F, Enawgaw B, Getaneh Z. Prevalence of thrombocytopenia among pregnant women attending antenatal care service at Gondar University Teaching Hospital in 2014, north-west Ethiopia. Journal of blood medicine.2017;8:61.

31. Yadav J, Yadav AK, Srinadh R. Rural-urban disparities in prevalence of anemia among adolescent girls in India. IntJ Community Med Public Health [Internet].2017;4(12):4661.

32. Eram A, Trivedi Shubha S, Manisha K, Naqvi Sayyed EH. A Cross Sectional Study of Prevalence of

'Anemia in Pregnancy' and Its Outcome in Urban Population of New Delhi.

33. Ijaz T, Atif MJ, Ullah M, Arshad S, Ashraf S, Munir S, et al. Prevalence of Anemia and Thrombocytopenia in Pregnant Females of Lahore Research; Life Sciences International Journal 2016 Jan.10(1):38-42;

34. Akan H, Güven N, Ayogdu İ, Arat M, Beksaç M, Dalva K. Thrombopoietic cytokines in patients with iron deficiency anemia with or without thrombocytosis. Actahaematologica. 2000;103(3):152-6.

35. Morris VK, Spraker HL, Howard SC, Ware RE, Reiss UM. Severe Thrombocytopenia with iron deficiency anemia. Pediatric hematology and oncology. 2010 Jul 30;27(5):413-9.

36. Ibrahim R, Khan A, Raza S, Kafeel M, Dabas R, Haynes E, Gandhi A, Majumder OL, Zaman M. Triad of Iron Deficiency Anemia, Severe Thrombocytopenia and Menorrhagia–A Case Report and Literature Review. Clinical Medicine Insights: Case Reports. 2012 Jan;5: CCRep-S9329.

37. Eisa MS, Al-Tikrity MA, Babikikir MM, Yassin MA. Thrombocytopenia secondary to iron deficiency anemia responding to iron therapy. Clinical Case Reports. 2021 Jul;9(7).

38. Huscenot T, Darnige L, Wagner-Ballon O, Ronchetti AM, Lousteau V, Limal N, Morbieu C, Gobert D, Rohmer J, Mathian A, Le Cann M. Iron deficiency, an unusual cause of Thrombocytopenia: results from a multicenter retrospective case-controlled study. Annals of Hematology. 2019 Oct;98(10):2299-302.

39. Verma V, Ayalew G, Sidhu G, Ramnaraign B, Cutler J, Khandekar S, Weedon J, Sharma G, Braverman AS. An analysis of the relationship between severe iron deficiency anemia and thrombocytopenia. Annals of hematology. 2015 Mar;94(3):535-7.

40. Mohammad F, Sridhar M, Samprathi M, Vemgal P. Thrombocytopenia in severe iron deficiency anemia: A report of two cases. Tropical Doctor. 2021 Jul;51(3):448-50.

41. Barbara J B, Imelda B, Michael A.L. Megaloblastic Anaemia and RBC indices. In Dacie and Lewis Practical Haematology, 12th Edition, Churchill Livingstone Publishers, New York, 2019; pp121-123.

42. Moghadam S, Ghorbani M. A Case of Megaloblastic Anemia with Thrombocytopenia. Open Journal of Obstetrics and Gynecology. 2016;6(09):534.

43. John PG, John F, George MR, Frixos P, Bertil G, Daniel AA et al. In Wintrobe's Clinical Hematology. Anaemia and Thrombocytopenia. Lippincott Williams & Wilkins, Fourteenth Edition, 2019; pp 217-221.