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RESEARCH ARTICLE

EFFECT OF ASSOCIATION OF THROMBOCYTOPENIA WITH ANEMIA ON FETO-MATERNAL OUTCOME

Dr. Kausar Jahan[1], Dr. Tamkin Khan[2] and Dr. Kafil Akhtar[3]

1. Senior Resident, Lok Nayak Hospital, Government of NCT of Delhi, New Delhi, India.
2. Professor in Department of Obstetrics &Gynaecology, Jawaharlal Nehru Medical College and Hospital (JNMCH), AMU, Aligarh, Uttar Pradesh, India.
3. Professor in Department of Pathology, Jawaharlal Nehru Medical College and Hospital (JNMCH), AMU, Aligarh, Uttar Pradesh, India.

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Abstract

Objectives: To find out effect of association of thrombocytopenia with anemia on feto-maternal outcome.

Background: Thrombocytopenia is defined as platelet count less than 150,000/mm^3. It is a second common hematological disorder in pregnancy, anemia being the most common. The exact mechanism of Anemia and Thrombocytopenia is not well understood. 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. Therefore, the present study is planned to evaluate the effect of association of thrombocytopenia with anemia on feto-maternal outcome.

Methodology : 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 and Department of Pediatrics, JNMCH, 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. Appropriate therapy was given and response seen after 4 to 6 weeks. During labour and after delivery, feto-maternal outcome was evaluated. All the qualitative variables were analyzed using Pearson Chi square test while all quantitative variables were analyzed using independent sample test and Kruskal-Wallis one-way ANOVA test.

Results: The association of thrombocytopenia with anemia was highest in cases of dimorphic anemia and lowest in cases of megaloblastic anemia while only 15% of control were having thrombocytopenia in the present study. The maternal outcome in terms of preterm labor, PPH, duration of hospital stay after delivery, maternal sepsis, DIC, bleeding from any other site between cases and controls was not significant. Fetal outcome between cases and controls in terms prematurity, birthweight, neonatal infections, NICU admissions, intracranial hemorrhage, still

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

births was not statistically significant. Only the mean 1 minute Apgar score was lower in cases as compared to controls and this was statistically significant.

Conclusion : It can be concluded that there is an association that exists between hemoglobin and platelet count. Appropriate therapy corrects anemia and improves platelet count. Timely detection and correction of anemia with thrombocytopenia reduces intrapartum and postpartum complications. In order to reduce maternal and neonatal morbidities, careful surveillance is required of all pregnancies for early detection and treatment of anemia.

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Introduction:-

Thrombocytopenia is defined as platelet count less than 150,000/mm^3 [1] .It is a second common hematological disorder in pregnancy, anemia being the most common [1]. 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. The first case of iron deficiency-associated thrombocytopenia (IDA) in the literature were reported in 1964 by Gross et al. The cause of IDA-associated thrombocytopenia is unclear. There is an inverse linear relationship between platelet count and iron saturation, platelets tend to increase as iron saturation decreases and it has been hypothesized that iron may have an inhibitor effect on megakaryopoiesis [2]. Similarly, few studies have been conducted on association with macrocytic anemia. Therefore, the present study is planned to evaluate anemia with thrombocytopenia in pregnancy or on feto maternal outcome.

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 and paediatrics, 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 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 thrombocytopenia 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 into four groups: Group A- Microcytic Anemia with Thrombocytopenia, Group B- Macrocytic Anemia 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. During labour and after delievery, feto maternal outcome was evaluated. Statistical analysis was done using Pearson 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 3.1:- Demographic characteristics.

Groups	**Age**			**Mean Gestational Age**	**Area of Residence**		**Literacy Status**		**Socio-Economic Status**				
	20-	26-	31-	Gestation	Urb	Rur	Litera	Illitera	Upp	Uppe	Lowe	Uppe	Low

	25Year	30Year	35Year	al Age	an (%)	al (%)	te	te	er	r-Middle	r-Middle	r-Lower	er
	(%)	(%)	(%)	Mean±SD									
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, literacy status and area of residence as age of study group in our study was between 20-35 year with majority of cases and control belonging to 26 -30 year age group.

Mean gestational age was 2 9.04 ± 3.05, 30.49 ± 1.03, 29.02 ± 3.61 in Group A , Group B and Group C. There was no statistically significant difference in the mean gestational age in all groups i.e. comparable.

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

Table 3.2:- 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	50.084	p<0.001
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		

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 3.3:- Maternal outcome.

S.N.	Group	Pretermlabour	PPH	Duration of Hospital stay	MaternalInfection	Bleeding from a Other site	DIC
				(Mean±SD)			
1	Group A	0 (0.00%)	2 (2.90%)	4.53 ±1.34	9(13.04%)	0 (0.00%)	0 (0.00%)
2	Group B	0 (0.00%)	0 (0.00%)	4.57 ±0.53	2 (5.41%)	0 (0.00%)	0 (0.00%)
3	Group C	1(0.52%)	10(5.15%)	4.79 ±1.97	10(5.15%)	0 (0.00%)	0 (0.00%)

4	Group D	0 (0.00%)	0 (0.00%)	4.70 ±0.47	0 (0.00%)	0 (0.00%)	0 (0.00 %)
5	Total	1 (0.31%)	12(3.75 %)		21(3.56%)	0 (0.00%)	0 (0.00 %)
6	p-value	p>0.05	p>0.05	p>0.05	p>0.05	p>0.05	p>0.05

Maternal outcome in terms of preterm labor, PPH, duration of hospital stay after delivery, maternal sepsis, DIC, bleeding from any other site between cases and controls was not significant.

Table 3.4:- Fetal outcome.

Group	**Preterm**	**Birthweight**		**APGAR 1**	**APGAR2**	**Neonatal Infection**	**NICU Admission**	**Still Birth**	**ICH**
	n(%)	≤2.5kg	>2.5kg	**(Mean± SD)**	**(Mean ± SD)**	n(%)	n(%)	n(%)	n(%)
GroupA	1(1.45 %)	2(2.9 %)	67(97.10 %)	6.06±0.49	7.69±0.51	8(11.59 %)	2(2.90%)	0(0.00 %)	0(0.00 %)
GroupB	0(0.00 %)	0(0.00 %)	37(100%)	6.29±0.49	7.86±0.38	0(0.00%)	0(0.00%)	0(0.00 %)	0(0.00 %)
GroupC	9(4.64 %)	7(3.6 %)	187(96.39 %)	5.87±0.54	7.49±0.72	18(9.28 %)	15(7.73 %)	0(0.00 %)	0(0.00 %)
GroupD	0(0.00 %)	0(0.00 %)	20(100%)	5.92±0.52	7.60±0.60	0(0.00%)	0(0.00%)	0(0.00 %)	0(0.00 %)
Total	10(3.13 %)	9(2.8 %)	311(97.19 %)			26(87.13 %)	17(5.31 %)	0(0.00 %)	0(0.00 %)
p-value	p>0.05	p>0.05	p>0.05	P<0.05	p>0.05	p>0.05	p>0.05	p>0.05	p>0.05

Fetal outcome between cases and controls in terms prematurity, birthweight, neonatal infections, NICU admissions, intracranial hemorrhage, still births was not statistically significant. Only the mean 1 minute Apgar score was lower in cases as compared to controls and this was statistically 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 [1, 3, 4]

Most cases of thrombocytopenia in pregnancy are mild and have no adverse outcome for mother 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 microangiopathy [5]. The first case of iron deficiency –associated thrombocytopenia in the literature were reported in 1964 by Gross et al. [6].

We found limited studies similar to ours on association between Anemia and Thrombocytopenia in literature.

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.

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 cases and 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. [7] (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),who reported that pregnant women with thrombocytopenia were aged from 15-40 years [8] . Al Kouatly et al (2003) found that mean maternal age of thrombocytopenic pregnant women was 34.3±5.4years [9] . Also, Parrnas et al. (2006) reported that pregnant women with thrombocytopenia were significantly older compared with pregnant women without thrombocytopenia [10] .

In our study we found findings contradictory to the above studies there was no coorelation 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 unrelated to anemia.

In present study mean gestational age was 29.04±3.05, 30.49±1.03, 29.02±3.61 in GroupA, GroupB and GroupC. There was no statistically significant difference in the mean gestational age in all groups. It was comparable among all groups which was related to our inclusion criteria. Sumaya Elgodwi et al. (2021) found that the prevalence of moderate thrombocytopenia increased with increasing gestational age [7] . Fikir, Bamlaku, Zegeye (2017) showed that there was no association between the trimester and thrombocytopenia [11] .

In present study, study shows that maximum number of 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 [11] . In an Indian study by Jeetendra et al.[12] (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 healthcare 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 the study was conducted during the COVID period which affected the delivery of RMNCH services and frequent lockdowns prevented patients from peripheral areas from reaching healthcare facilities.

In present study, maximum number of cases and control were literate, the results was 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 [13]. In the present study, study shows that the maximum number of cases having thrombocytopenia were from lower middle class according to modified Kuppuswamy scale while maximum control were from upper middle class, the results were significant ($p<0.001$). Both Sumaya Elgodwi et al. (2021) and Fikir , Bamlaku, Zegeye (2017) did not report on the socio economic status of their study population [7, 11].

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 strata. Only 4.35%, 18.92% and 1.55% cases in each group were from lower 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.

In the present study 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 cases of dimorphic anemia and lowest in cases of megaloblastic anemia. This was statistically significant.

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 [14].

However, Fikir, Bamlaku , Zegeye (2017) found of 8.8% prevalence of thrombocytopenia in pregnant women in northwest Ethiopia while Sumaya Elgodwi et al. (2021) found 18% prevalence of thrombocytopenia among pregnant women in Tripoli region [7, 11]. However both the studies were different from they only studied the prevalence of thrombocytopenia. Sumaya et al studied the various conditions associated associated in thrombocytopenia and found that anemia was present in 96 patients (31%) out of 312 thrombocytopenic pregnant patients [7].

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 [8].

In Feto-maternal outcome we found that preterm labour was found only in Dimorphic group, the results were non significant ($p > 0.05$) . Katke RD et al (2014) showed that preterm labour was associated with thrombocytopenia in 10.9% cases [15]. Similarly anemia is also associated with preterm labour [16]. However in our study timely detection was done and therapy was given so the incidence was low.

In present study PPH was found in both Microcytic and Dimorphic group, the results were non significant ($p > 0.05$) The incidence in Dimorphic group was 5.15% that was comparable to Dwivedi et al (2012), (4.2%) [17].However, Gaba N. et al (2020) found 15.8% of women had primary PPH in thrombocytopenia during pregnancy [18]. As we had corrected the thrombocytopenia incidence was low in our study.

Maternal infection in the form of unhealthy stitch line, fever, UTI, respiratory infection, unhealthy lochia was found in cases but no single control was having the same. This difference was statistically not significant.

No cases complained of bleeding from any other site in our study, Gaba N.et al. (2020) found 3.2% of women having bleeding manifestation in their study in pregnancy with thrombocytopenia [18]. In the present study both the cases and control had comparable birth weight, the results were statistically non significant ($p>0.05$).

Studies have correlated small birth weight with maternal anemia but the difference was not found to be significant. However maternal anemia in the first trimester of pregnancy can be considered as a risk factor for negative pregnancy outcomes(SGA) [19].

In our study the anemia was detected and corrected early so no adverse effect on fetal weight was see. This emphasizes the importance of regular antenatal checkup, screening for anemia at least once a month and proper therapy to improve feto-maternal outcome.

In the present study Apgar1 was better in Group B. It was found to be statistically significant ($p<0.05$), though the mean hemoglobin and platelet count was maximum in GroupC at term. This could be because the Apgar score depends on a number of antenatal co-morbidities and intrapartum factors.

Neonatal infection was found in both the Microcytic and Dimorphic anemia group, the results were not statistically not significant ($p > 0.05$). Gaba N. et al (2020) found 1.6 %were having early onset sepsis [18].

NICU admissions were found in Microcytic and Dimorphic group, the results were not statistically significant ($p>0.05$).

Though Gaba N , et al. (2020) found 16.7 % were still born Katke RDet al. (2014) found 14.1% stillbirth while Parnas et al. (2006) found 6.5% cases had still birth .We did not have a single stillbirth in our study [10, 15,18].

This is because these authors were studying the prevalence of thrombocytopenia in pregnancy due to various causes and included other causes of fetal mortality like pregnancy induced hypertension. In this study, there were no cases of ICH while Gaba N, et al(2020) found that 1 neonate developed ICH but the mother was having HELLP syndrome. As we had excluded other causes of thrombocytopenia and corrected the anemia related thrombocytopenia this complication was not observed[18].

The maximum mean of duration of hospital stay was in Dimorphic Group, none of the cases went into DIC. Gaba N. et al. (2020) found DIC incidence was 4.2% in their study in pregnancy with thrombocytopenia [18].

In the present study both the cases and control had comparable birth weight, the results were statistically non-significant (p>0.05). Studies have correlated small birth weight with maternal anemia but the difference was not found to be significant. However maternal anemia in the first trimester of pregnancy can be considered as a risk factor for negative pregnancy outcomes (SGA) [19].

Conclusion:-

It can be concluded that there is an association that exists between haemoglobin and platelet count. Appropriate therapy corrects anemia and improves platelet count. Timely detection and correction of anemia with thrombocytopenia reduces intrapartum and postpartum complications.

In order to reduce maternal and neonatal morbidities, careful surveillances required of all pregnancies for early detection and treatment of anemia. Further studies to be conducted for confirming the association of anemia with thrombocytopenia.

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