Original Research Article

TO DETERMINE THE FREQUENCY OF THROMBOCYTOPENIA IN PRE ECLAMPTIC WOMEN PRESENTED AT ISRA UNIVERSITY HOSPITAL

ABSTRACT

OBJECTIVE: To determine the frequency of thrombocytopenia in pre-eclamptic women presented at Isra University Hospital Hyderabad.

PATIENTS AND METHODS: This cross sectional descriptive study of six months study was conducted at Isra university hospital from April 2019 to September 2019. All the patients between ≥18 - 45 years of age diagnosed as preeclampsia were admitted and evaluated for thrombocytopenia.

RESULTS: During six month study period, total 177 patients with preeclampsia were evaluated for thrombocytopenia. Majority of patients were from urban areas 125/177 (70.6%). The mean ±SD for maternal and gestational age of the preeclamptic patient was 32.75±8.85 and 28.75±7.63 whereas the mean platelet count was 93200±10.74 respectively. Majority of the patients were 21-30 years of age (54.8%) and the finding was statistically significant in relation to gestational age [p=0.002]. The thrombocytopenia was observed in 99/177 (55.9%) and is statistically significant in relation to maternal age, gestational age and parity while in context to gravida and duration of disease it is non significant.

CONCLUSION: A significantly high frequency of thrombocytopenia (55.9%) was recorded in the patients with preeclampsia and is statistically significant in relation to maternal and gestational age and parity.

KEY WORDS: Pre-eclampsia, Platelet, Thrombocytopenia

INTRODUCTION:

Pre-eclampsia is a common pregnancy complication that can cause high morbidity and mortality for both the mother and the fetus.[1] Its condition accounts for 4-8% of all pregnancies worldwide, and is characterized by high blood pressure, proteinuria, and edema[2]. It progresses to eclampsia if it is not treated correctly characterized by malignant hypertension and convulsions requiring emergency caesarean section. One study conducted by Rathore et al and reported prevalence of pre-eclampsia in Pakistan is around 19%[3]. In a study examining emergency obstetric care (EOC) in Bangladesh, 5% of patients in medical facilities were pre-eclampsia. However, the precise etiology of preeclampsia is unknown[4]. The outcomes from medical research showed the relationship between the aggravation of the hypertensive complication and the change in concentration of various chemistries in mother's serum[5-6].

Pregnancy is related to the physiological and pathological changes of platelet count and function, which may be a clinical concern because of the risk of bleeding from the fetus and mother. Thrombocytopia during pregnancy is commonly encountered in obstetrics and gynecological practice[7]. It affects 10 % of all pregnant women[8]. It can be considered, when platelet count below 150 $x10^9/L^9$.Normal range of platelet varies between 150 x109/L to 400 x109/L in pregnant women.11it can be classified as mild, moderate and severe thrombocytopenia as count between from 100-150 x109/L,50-100 x109/L and less than 50 x109/L respectively[10,11]. The reported prevalence for thrombocytopenia in preclampsia is 21%[12].

MATERIAL AND METHODS:

This was a cross sectional descriptive study of the 177 preeclamptic ladies at the department of Obstetrics and gynecological department of Isra University Hospital from April 2019 to September 2019. The study was conducted after taking permission from the ethical committee of Isra university Hospital.

All pregnant ladies aged between 18 - 45 years diagnosed as preeclampsia and cooperative patients who gave the written consent to participate in the study were included in

this study. Exclusion criteria were known case of idiopathic thrombocytopenic purpura (as platelets are lyzed in this disease), known case of aplastic anemia, myelodysplastic syndrome, osteopetrosis (in which platelet production is impaired), already on drug therapy (fansidar, septran, thiazides and chemotherapeutic agents that can lead to thrombocytopenia), had history of repeated blood / platelet transfusion, non cooperative patients who refused to give written consent for participation in the study. The data was collected by filling specified proforma by patient admitted in labour room after taking informed and written consent. All the pregnant preeclamptic ladies were admitted in ward and were further evaluate for thrombocytopenia for which 3cc venous blood sample was collected in disposable syringe, transferred to CP bottle and sent to laboratory for analysis.

RESULTS

During six month study period, total 177 patients with preeclampsia were evaluated for thrombocytopenia. Majority of patients were from urban areas 125/177 (70.6%). The mean±SD for maternal and gestational age of the preeclamptic patient was 32.75±8.85 and 28.75±7.63 whereas the mean platelet count was 93200±10.74 respectively. The distribution of maternal age in relation to gestational age, parity, gravida, duration of disease and thrombocytopenia. The distribution of gestational age in relation to parity, gravida, duration of disease and thrombocytopenia is shown in Table 1. The parity in relation to gravida, duration of disease and thrombocytopenia is shown in Table 13-15. The gravida in context to duration of disease and thrombocytopenia is shown in Table 2 whereas the thrombocytopenia in relation duration of disease is mentioned in 2.

TABLE No.1
AGE DISTRIBUTION IN RELATION TO DIFFERENT VARIABLE (n=177)

Variable	AGE DISTRIBUTION (Years)				
	18-20 years	21-30 years	31-40 years	41-45 years	P value
PARITY					
• **0**	3	8	9	1	0.01
• **1-2**	10	32	21	7	
• **3-5**	10	27	2	3	
• **>5**	6	30	7	1	
GRVIDA					
• **1-2**	7	16	7	0	0.63
• **3-5**	14	52	20	9	
• **>5**	8	29	12	3	
DURATION OF THE DISEASE (Weeks)					
• **21-25**	3	19	7	4	0.02
• **26-30**	24	53	17	5	
• **31-36**	2	25	15	3	
RELATION TO THROMBOCYTOPENIA					
• **Yes**	15	63	20	1	0.002
• **No**	14	34	19	11	

TABLE No.2
GESTATIONAL AGE IN RELATION TO DIFFERENT VARIABLE (n=177)

Variable	GESTATIONAL AGE (Weeks)			
	21-25 weeks	26-30 weeks	31-36 weeks	P value
PARITY				
• **0**	18	3	00	<0.01
• **1-2**	45	23	2	
• **3-5**	8	33	1	
• **>5**	00	65	38	
GRVIDA				
• **1-2**	17	9	4	0.27
• **3-5**	34	35	26	
• **>5**	20	21	11	
DURATION OF THE DISEASE (Weeks)				
• **21-25**	12	16	5	0.02
• **26-30**	47	33	19	
• **31-36**	12	16	17	
RELATION TO THROMBOCYTOPENIA				
• **Yes**	25	41	33	<0.01
• **No**	46	24	8	

DISCUSSION:

Thrombocytopenia is 2nd only to anemia, found as the most frequent hematological abnormality at some stage in pregnancy. Hypertensive problems represents 21% cases of thrombocytopenia in pregnancy[13,14].

The reasons of thrombocytopenia from being pregnant- triggered hypertension and HELLP (hemolysis, increased liver enzymes, low platelet count number) syndrome are unknown. One clarification is that it is probably initiated by means of microvascular damage that consequences in platelet activation. Degranulation of the platelets is observed through vasospasm and similarly endothelial damage [13]. The most effective acknowledged remedy for this cycle is delivery of the fetus. Thrombocytopenia occurs more commonly associated with mild and severe forms of pre-eclampsia (15%-18%)[15,16], whereas the present study observed 55.9% prevalence of thrombocytopenia in preeclamptic ladies. In current study the mean ± SD for maternal and gestational age observed was 32.75±8.85 and 28.75±7.63 and it is consistent with the study by Nazli R, et al.[17] Recent studies have recorded that increased plasma levels of soluble vascular endothelial cell growth factor (VEGF), receptor type 1 (sFlt1)[15], endoglin, an endothelial cell-derived member of the tumor growth factor-² (TGF-²) receptor family[18], are present in patients intended to develop preeclampsia as early as the late first trimester. The placentae of preeclamptic patients contain a significant level of sFlt1 and endoglin mRNA, these neutralizes VEGF and placental growth factor (PLGF). Another important member of the VEGF family, its level increases significantly during pregnancy, and endoglin inhibits TGF-² binding to endothelial cells[19].

Thrombocytopenia is said noticeably often in severe pre-eclampsia, with the prevalence range of 11-29%[20]. The seriousness of pregnancy related hypertensive issues and thrombocytopenia noticed are firmly related, which shows that thrombocytopenia is straightforwardly corresponding to the seriousness of pregnancy related hypertensive problems. An international study of Bockenstedt PL was reported 11.6% cases pregnancy related

hypertensive disorders associated with thrombocytopenia[21]. One more review from Pakistan, which showed that the platelet count was not essentially associated with the seriousness of hypertensive issues during pregnancy[22].

Study of Line et al reported that prevalence of thrombocytopenia associated with preeclampsia was 50%. The motive given by using the writer for this high incidence became that they included women unwell enough to be admitted inside the intensive care unit. Stavrou E, et al reported a prevalence of 35% in preterm proteinuria hypertensive patients. Thrombocytopenia is generally moderate and platelet remember not often decreases to less than 20,000/μl and constantly correlates with the severity of the sickness, reported by Perepu U, et al.[23,24].

In particular, it is not clear whether these peripheral changes are a cause or a consequence of the occlusive vascular lesions in the uteroplacental arteries associated with fetal growth retardation. Because of the variation in counts between patients no diagnostic importance can be attached to a single low reading; thus platelet counts would not be a good screening test for pre-eclampsia. They are simpler to obtain than other measurements of disturbed coagulation, however, and repeated readings in the same patient can be useful in showing a consistent trend towards lower counts, which may herald the onset of preeclampsia. Thus the platelet count can be helpful in monitoring high-risk pregnancies[25,26].

The haemostatic work starts when the platelets come into contact with damaged endothelial wall or with circulatory coagulation factors, particularly thrombin, bringing about platelet activation, aggregation and clot formation. Thus, the endothelial dysfunction and the increase in vascular reactivity are proven to be involved in preeclampsia pathogenesis: the generalized endothelial alteration from preeclampsia causes vasoconstriction and promotes the adhesion and aggregation of the platelets, as well as the activation of the coagulation factors, inducing supplementary hypoxic injury of the endothelium[27].

The etiopathogenic factors of preeclampsia are very complex: the endothelium is the key in comprehension a multi-step process in which the platelet likewise has a significant impact. It is necessary to recognize the molecular and cellular alterations, due to the fact those precede with quite a few months the clinical features, subsequently presenting a massive advantage and the possibility of prevention.

CONCLUSION:

A significantly high frequency of thrombocytopenia i.e. 99 patients (55.9%) was recorded in the patients had preeclampsia. It is important to remember that most patients have a benign condition but a few seriously ill patients are at risk of developing serious morbidity and mortality. These patients have good results as well and can be safely treated by family doctors of appropriate consultation with obstetricians and hematologists.

REFERENCES:

1. Story L, Chappell LC. Preterm pre-eclampsia: what every neonatologist should know. Early human development. 2017 Nov 1;114:26-30.
2. Punthumapol C, Kittichotpanich B. Comparative study of serum lipid concentrations in preeclampsia and normal pregnancy. J Med Assoc Thai. 2008;91(7):957-61.
3. Rathore R, Butt NF, Iqbal A. Khan MZU. Complications and outcome of patients of pre-eclampsia & eclampsia presenting to medical wards of Mayo Hospital Lahore. Ann King Edward Med Coll. 2010;16(1):17-9.
4. Apicella C, Ruano CS, Méhats C, Miralles F, Vaiman D. The role of epigenetics in placental development and the etiology of preeclampsia. International journal of molecular sciences. 2019 Jan;20(11):2837-45.
5. Dhungana A, Bharati A, Manandhar R, Karki C. A comparative study of serum uric acid, glucose, calcium and magnesium in pre-eclampsia and normal pregnancy. Journal of Pathology of Nepal. 2017 Sep 1;7(2):1155-61.
6. Dymara-Konopka W, Laskowska M, Oleszczuk J. Preeclampsia-current management and future approach. Current pharmaceutical biotechnology. 2018 Sep 1;19(10):786-96.
7. Kadir RA, McLintock C.Thrombocytopenia and disorder of platelet function in pregnancy.Semin Thromb Hemost.2011;37(6):640-52.
8. Khellaf M, Loustau V, Bierling P, Michel M, Godeau B, Thrombocytopenia and pregnancy. Rev Med Interne.2012;33(8);446-52.

9. Sadulla SM, Mahmood AY, Shamdeen MY. Gestational thrombocytopenia: maternal and fetal outcomes in Duhok. Duhok Med J. 2020;14(2):86-9.
10. Chitra TV, Panicker S. Maternal fetal outcome of dengue fever in pregnancy J Vector Borne Dis.2011;48(4):210-3.
11. Altarescu G, Geva TE, Grisaru-Granovsky S, Bonstein L, Miskin H, Varshver I, et al. Preimplantation Genetic Diagnosis for fetal neonatal alloimmune Thrombocytopenia due to Antihuman Platelet Antigen Maternal Antibodies. Obstet Gynecol.2012;119:338-43.
12. Kalagiri RR, Choudhury S, Carder T, Govande V, Beeram MR, Uddin MN. Neonatal thrombocytopenia as a consequence of maternal preeclampsia. American Journal of Perinatology Reports. 2016 Mar;6(01):e42-7.
13. Cines DB, Levine LD. Thrombocytopenia in pregnancy. Hematology 2014, the American Society of Hematology Education Program Book. 2017 Dec 8;2017(1):144-51.
14. Shehata N, Burrows R, Kelton JG. Gestational thrombocytopenia. Clin Obstet Gynecol.1999;42:327-34.
15. Maynard SE, Venkatesha S, Thadhani R, Karumanchi SA. Soluble Fms-like tyrosine kinase 1 and endothelial dysfunction in the pathogenesis of preeclampsia. Pediatr Res.2005;57:1-7.
16. Wenger NK, Arnold A, Bairey Merz CN, Cooper-DeHoff RM, Ferdinand KC, Fleg JL, et al. Hypertension across a woman's life cycle. J Am Coll Cardiol. 2018 Apr 24;71(16):1797-813.
17. Nazli R, Khan MA, Akhtar T, Mohammad NS, Aslam H, Haider J. Frequency of thrombocytopenia in pregnancy related hypertensive disorders in patients presenting at tertiary care hospitals of Peshawar. Khyber Med Univ J.2012;4(3):101-5.
18. Venkatesha S, Toporsian M, Lam C, Hanai J, Mammoto T, Kim YM, et al. Soluble endoglin contributes to the pathogenesis of preeclampsia. Nat Med.2006;12:642-9.
19. Young BC, Levine RJ, Karumanchi SA. Pathogenesis of preeclampsia. Annu Rev Pathol.2010;5:173-92.
20. Kadir RA, McLintock C. Thrombocytopenia and disorders of platelet function in pregnancy. Semin Thromb Hemost.2011;37(6):640-52.
21. Bockenstedt PL. Thrombocytopenia in pregnancy. Hematol Oncol Clin North Am.2011;25(2):293-310.

22. Hossain N, Shah N, Khan N, Lata S, Khan NH. Maternal and perinatal outcome of hypertensive disorders of pregnancy at a tertiary care hospital. J Dow Univ Health Sci.2011;5(1):12-6.
23. Stavrou E, McCrae KR. Immune thrombocytopenia in pregnancy. Hematol Oncol Clin North Am.2009;23(6):1299-1316.
24. Perepu U, Rosenstein L. Maternal thrombocytopenia in pregnancy. Proceedings in Obstetrics and Gynecology.2013;3(1):1-15.
25. Ciantar E, Walker JJ. Pre-eclampsia, severe pre-eclampsia and hemolysis, elevated liver enzymes and low platelets syndrome: what is new?. Womens Health (Lond Engl).2011;7(5):555-69.
26. Akcan AB, Oygucu SE, Ozel D, Oygur N. Mean platelet volumes in babies of preeclamptic mothers. Blood Coagul Fibrinolysis.2011;22(4):285-7.
27. Mussbacher M, Kral-Pointner JB, Salzmann M, Schrottmaier WC, Assinger A. Mechanisms of Hemostasis: Contributions of Platelets, Coagulation Factors, and the Vessel Wall. In Fundamentals of Vascular Biology 2019:145-169.
28. McElwain CJ, Tuboly E, McCarthy FP, McCarthy CM. Mechanisms of endothelial dysfunction in pre-eclampsia and gestational diabetes mellitus: windows into future cardiometabolic health?. Frontiers in Endocrinology. 2020 Sep 11;11:655.