

FREQUENCY OF THROMBOCYTOPENIA IN PREGNANCY RELATED HYPERTENSIVE DISORDERS IN PATIENTS PRESENTING AT TERTIARY CARE HOSPITALS OF PESHAWAR

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ABSTRACT

Objective: To find the frequency of thrombocytopenia in women with pregnancy related hypertensive disorders in patients presenting at tertiary care hospitals of Peshawar.

Methodology: This cross sectional study was conducted from January 2009 to January 2010 in the tertiary referral health care facilities of Peshawar. A total of 312 women of gestational age of >20 weeks with pregnancy related hypertensive disorders were investigated. They were subdivided into 102 women with gestational hypertension (Group A), 100 women with pre-eclampsia (Group B), and 110 women with eclampsia (Group C). Ninety healthy pregnant women (group D) were chosen as control. All the subjects were selected from the Gynecology and Obstetrics units of three tertiary health care facilities of Peshawar. Platelet count was measured by using Hematology Analyzer. The data was processed on SPSS version 10.

Results: The frequency of thrombocytopenia in all patient groups was 21.8% (n=68/312). Individual groups showed thrombocytopenia in 14.6% (Group A), 15% (group B), 34.6% (group C) and 4.5% in controls (group D). Out of 68 patients with thrombocytopenia, 38(55.9%) were eclamptic. Overall severe thrombocytopenia was recorded in 27(8.7%) patients, of whom 15(55.6%) were eclamptic. These patients were nine times more likely to have eclampsia as compared to those having platelet count > 150,000/ μ L (OR: 9.41; CI: 1.33-188.8; p= 0.008).

Conclusion: A high frequency of thrombocytopenia was recorded in the patients with pregnancy related hypertensive disorders in the tertiary care hospitals of Peshawar. The severity of thrombocytopenia is proportional to the severity of pregnancy related hypertensive disorders.

Key Words: Pregnancy Related Hypertensive Disorders; Platelet Count; Thrombocytopenia; Gestational Hypertension, Pre-Eclampsia.

This article may be cited as: 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):101-105.

INTRODUCTION

Thrombocytopenia is second only to anemia observed as the most common hematological abnormality during pregnancy. The overall prevalence of thrombocy-

topenia in pregnancy is 8%¹. Hypertensive disorders accounts for 21% of cases of thrombocytopenia in pregnancy². The causes of thrombocytopenia from pregnancy-induced hypertension and HELLP (Hemolysis, Elevated Liver enzymes, Low Platelet count) syndrome are unknown. One explanation is that it might be initiated by microvascular damage that results in platelet activation. Degranulation of the platelets is followed by vasospasm and further endothelial damage³. The only known therapy for this cycle is delivery of the fetus. Thrombocytopenia occurs more commonly in patients with eclampsia (30%) compared to patients with both mild and severe forms of pre-eclampsia (15%-18%).¹ Recent studies have documented that increased plasma levels of soluble vascular endothelial cell growth factor (VEGF) receptor type 1 (sFlt1)⁴, as well as endoglin, an endothelial cell-derived member of the tumor growth factor-2 (TGF- β) receptor family⁵, are present in patients intended to develop preeclampsia as early as the late first trimester. Increased levels of sFlt1 and endoglin mRNA are present in preeclamptic placentae, suggesting this is the source of these proteins^{4,6}. sFlt1 binds and neutralizes

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Date Submitted: May 11, 2012

Date Revised: September 26, 2012

Date Accepted: September 27, 2012

VEGF and placental growth factor (PLGF), another important VEGF family member whose levels normally increase during pregnancy, whereas endoglin blocks the binding of TGF- β^2 to endothelial cells⁷. These types of pregnancies are also associated with qualitative alterations suggesting increased platelet turnover. There is a shortened platelet life span, increased number of megakaryocytes in the bone marrow, accompanied with an increased number of immature platelets seen in the peripheral blood smear⁸. Many investigators believe that increased platelet consumption is due to disseminated intravascular coagulation while others suggest an immune mechanism⁸.

The degree of thrombocytopenia increases with the severity of disease and the prevalence of thrombocytopenia depend on the severity of the disease process⁹. Lower the platelet count, greater are maternal and fetal morbidity and mortality¹⁰. Overt thrombocytopenia (platelet count $< 100,000/\text{mm}^3$) indicates severity of the diseases process, where, in most cases delivery is indicated because platelet number continue to fall¹¹. HELLP Syndrome having platelet count $< 100,000/\text{mm}^3$ shows poor fetal outcome¹². It occurs in 2–12% women with severe pre-eclampsia or eclampsia⁹. Early assessment of severity of disease is necessary to prevent complications like HELLP syndrome and increased maternal and fetal morbidity and mortality risk. The platelet estimation method is reliable, rapid, cheaper, and simple; therefore prognosis of diseases could be monitored by measuring platelet count.

The frequency and intensity of maternal thrombocytopenia vary among studies. The purpose of this study was to find the frequency of thrombocytopenia in patients with pregnancy related hypertensive disorders in the major tertiary care hospitals of Peshawar, Khyber Pakhtunkhwa Province, Pakistan.

METHODOLOGY

This cross sectional study was conducted during the period of January 2009 to January 2010 in the tertiary referral health care facilities of Peshawar, viz. Khyber Teaching Hospital, Post Graduate Medical Institute (PGMI) Lady Reading Hospital and PGMI Hayatabad Medical Complex Peshawar, Khyber Pakhtunkhwa Province-Pakistan. Ethical approval for the study was obtained from the Institutional Ethical Research Board (IERB) at Post Graduate Medical Institute, Hayatabad Medical complex, Peshawar.

Women with pregnancy related hypertensive disorders and normotensive pregnant women at gestational age of > 20 weeks were registered in the study. The study subjects were divided into four groups, with three patient (A, B, C) and one control group (D). Group-A comprised of women with gestational hypertension (102), group-B with pre-eclampsia (100), group-C with eclampsia (110) and group-D of healthy women having normal uncomplicated pregnancy without hypertension (90). All

these cases were randomly selected through convenient sampling technique either from Gynecology and Obstetrics units or undergoing prenatal care at tertiary referral health care facilities. After explaining the objectives, informed consent was obtained from each subject for participation in this study.

History of patients was recorded on a properly designed questionnaire, which included maternal age, gestational age at screening and parity. Blood pressure, height and weight of all the participants were measured at the time of enrolment by using standard methods.

Venous blood samples were obtained in EDTA vacutainers and appropriately labeled. Platelet count was done using three dimensional, Hematology Auto Analyzer Humacount Plus in the research labs of Pakistan Medical Research Council, Khyber Medical College, Peshawar. Platelet Count > 150 thousand/ μL was considered as normal, 100-150,000/ μL as low (thrombocytopenia) and $< 100,000/\mu\text{L}$ as very low (severe thrombocytopenia). The data was processed on a computer software package SPSS version 10 and presented as mean + SEM (standard error of mean). Logistic regression procedures were used to calculate maximal likelihood estimates for the coefficients and their standard errors were used to calculate odd ratio (OR) and 95% CI. Groups A, B, and C ($n=312$) were combined as patients group to calculate OR & CI.

RESULTS

The demographic and reproductive characteristics of the patient and control groups are summarized in table-1. All the subjects were in the age range of 15 - 45 years. The age of patients in the eclampsia (group C) was significantly lower (25.24 ± 0.54 years) as compared to other groups. An increase in the mean systolic/diastolic blood pressure and decrease in the platelet count was observed in all the patient groups. Women in group 'A' were found to be more obese with Body Mass Index (BMI) of $30.96 \pm 1.08 \text{ kg/m}^2$ as compared to those in control group ($28.94 \pm 0.82 \text{ kg/m}^2$).

Table II compares various ranges of platelet count in four study groups as very low (< 100), low (100-150) and normal platelet count $> 150,000/\mu\text{L}$. Overall frequency of thrombocytopenia (platelet count $< 150,000/\mu\text{L}$) was 68(21.8%) in three patient groups and 38(55.9%) in the patients of eclampsia group, whereas severe thrombocytopenia was recorded in 27(8.7%) of three patient groups. It has been observed that very low count is more prevalent in the patients with eclampsia: 15(13.6%) versus 1.1% in the control women. Normal platelet count $> 150,000/\mu\text{L}$ was recorded in 86(95.5%) of control group against 72(65.4%) in the group of eclampsia patients.

When the value of platelet count was compared among control and patient groups of pregnancy related hypertensive disorders, a significant decrease in platelet count was observed (Table III). Overall prevalence of

COMPARISON OF DEMOGRAPHICS, VITAL SIGNS AND PLATELET COUNT (PATIENT SUB-GROUPS & CONTROL)

| Variables | Group-A (N=102) Mean \pm SEM | Group-B (N=100) Mean \pm SEM | Group-C (N=110) Mean \pm SEM | Group-D (N=90) Mean \pm SEM |
|-------------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|----------------------------------|
| Age (years) | 30.03 \pm 0.66 | 29.54 \pm 0.68 | 25.24 \pm 0.54 ^c | 30.04 \pm 0.66 |
| Gestation age (weeks) | 30.01 \pm 0.49 | 31.39 \pm 0.48 | 31.83 \pm 0.45 | 29.72 \pm 0.55 |
| Systolic BP (mmHg) | 146.49 \pm 1.25 ^c | 151 \pm 1.79 ^c | 155.58 \pm 1.97 ^c | 116 \pm 0.91 |
| Diastolic BP (mmHg) | 96.91 \pm 0.84 ^c | 99.45 \pm 1.34 ^c | 103.66 \pm 1.53 ^c | 75.28 \pm 0.91 |
| BMI (kg/m ²) | 30.96 \pm 1.08 | 29.41 \pm 1.04 | 29.27 \pm 1.12 | 28.94 \pm 0.82 |
| Platelets count (thousand/ μ L) | 223.24 \pm 7.64 ^c | 227.50 \pm 9.35 ^c | 198.60 \pm 9.28 ^c | 261.44 \pm 8.27 |

(Level of significance when compared with control)

a P < 0.05

b P < 0.01

c P < 0.001

Table I

PLATELET COUNT STATUS: PATIENT SUB-GROUPS Vs. CONTROL (GROUP D)

| Platelet count (thousand/ μ L) | Patient groups | | | | | | Control group | | | |
|---------------------------------------|----------------|------|---------|-----|---------|------|---------------|------|---------|------|
| | Group-A | | Group-B | | Group-C | | Overall | | Group-D | |
| | N | % | N | % | N | % | N | % | N | % |
| < 100 (very low) | 6 | 5.8 | 6 | 6 | 15 | 13.6 | 27 | 8.7 | 1 | 1.1 |
| 100-150 (low) | 9 | 8.8 | 9 | 9 | 23 | 21.0 | 41 | 13.1 | 3 | 3.4 |
| > 150 (Normal) | 87 | 85.4 | 85 | 85 | 72 | 65.4 | 244 | 78.2 | 86 | 95.5 |
| Total | 102 | 100 | 100 | 100 | 110 | 100 | 312 | 100 | 90 | 100 |

Table II

CALCULATED ODD RATIO WITH 95% CONFIDENCE INTERVAL & P VALUES

| Platelet count (thousand/ μ L) | Patients | | Control | | OR* | 95% CI** | P ^o | χ^2 |
|---------------------------------------|----------|------|---------|------|------|-------------|----------------|----------|
| | N | % | N | % | | | | |
| < 100 (very low) | 27 | 8.7 | 1 | 1.1 | 9.41 | 1.33-188.85 | 0.008 | 6.99 |
| 100-150 (low) | 41 | 13 | 3 | 3.4 | 4.76 | 1.37-19.80 | 0.005 | 7.79 |
| > 150 (Normal) | 244 | 78.3 | 86 | 95.5 | | Reference | | |

* Odd ratio

** Confidence interval

^o P value

Table III

thrombocytopenia was 68(21.8%) in three patient groups, while 27(8.7%) of pregnant women had severe thrombocytopenia compared to 1.1% in the control group. These

patients were nine times more likely to develop severe eclampsia as compared to those with platelet count > 150,000/ μ L (OR 9.41; CI- 1.33-188.8 and P 0.008).

DISCUSSION

Among the hematological changes that occur in pre-eclampsia and eclampsia, thrombocytopenia is the most common hematological abnormality found. Thrombocytopenia is reported¹³ relatively frequently in severe pre-eclampsia, with the occurrence range of 11-29%. In the present study, the overall prevalence of thrombocytopenia was 21.7% in women of pregnancy related hypertensive disorders, while 8.7% of them had severe thrombocytopenia. Our findings also indicate that the number of women with very low count is more in women with eclampsia (8.7%) versus 1.1% in the control women, resulting into wide confidence intervals. Severity of pregnancy related hypertensive disorders and thrombocytopenia observed are closely associated which indicates that thrombocytopenia is directly proportional to the severity of pregnancy related hypertensive disorders.

Thrombocytopenia, (platelet count < 100,000/mm³) was found in 11.6% of the patients with pregnancy related hypertensive disorders as reported by Romero et al¹⁴. This however is negating the results of another study from Pakistan which showed that platelet count was not significantly associated with the severity of hypertensive disorders during pregnancy.¹⁵ In the study logistic regression analysis was used to assess the relative contribution of thrombocytopenia, proteinuria, and the degree of hypertension to maternal and perinatal outcome. Thrombocytopenia was associated with a higher prevalence of preterm delivery and intrauterine growth retardation and was also found as an independent and important risk factor in the occurrence of maternal and perinatal complications in pregnancy related hypertensive disorders.

In a study reported by Leduce et al¹⁶, the prevalence of thrombocytopenia associated with preeclampsia was 50%. The reason given by the author for this high prevalence was that they included only women ill enough to be admitted in the intensive care unit. Burrows et al¹³ reported a prevalence of 35% in preterm proteinuria hypertensive patients.

A similar study from India reported platelet count in 30 normal pregnant women and 90 pregnant women with varying degree of pregnancy related hypertensive disorders¹⁷. Mean value of platelet count was 238,000/ μ L \pm 0.33 in control group, 223 \pm 0.19 (000/ μ L) in mild pre-eclampsia, 182 \pm 0.45 (000/ μ L) in pre-eclampsia and 121 \pm 0.49 (000/ μ L) in eclampsia patients.

In the present study a significant decrease in platelet number was observed in patients group. In comparison of women among various groups with normal, low and very low platelet number, it was found that the number of women with very low count was more in women with eclampsia, which shows that platelet count is inversely proportional to the severity of disease as reported by others¹⁸⁻¹⁹.

Limitations & recommendations

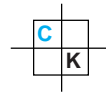
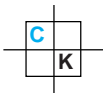
In our study sample size is small. The interpretation would be better if we take a large sample and follow the same pregnant women as its control. Platelet estimation method can be taken as a rapid procedure for assessing severity of pregnancy related hypertensive disorder, its management and prognosis.

CONCLUSION

A significantly high frequency of thrombocytopenia was recorded in the patients having pregnancy related hypertensive disorders. The severity of such disorders was increasing with the decrease in the number of platelets.

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- AUTHOR'S CONTRIBUTION**

Following authors have made substantial contributions to the manuscript as under

RN: Conception and design, Drafting the manuscript,

MAK: Analysis and interpretation of data,

TA: Critical revision, Final Approval of the manuscript

NSM, HA & JH: Acquisition of data
- CONFLICT OF INTEREST**

Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE

NONE DECLARED

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