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Lowered Platelet Count a Prognostic Index in Pregnancy Induced Hypertension

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Abstract

Introduction: Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection that contribute greatly to maternal morbidity and mortality.

Aim: To know the variation in platelet count between normal pregnancy and pregnancy induced hypertension (PIH) and correlate – fetomaternal outcome.

Materials and Methods: It is prospective study done in 100 pregnant women attending the gyneacology ward. Among these 50 were normal pregnant women, 15 were eclampsia, 20 were preeclampsia (sever PIH) 15 were mild pregnancy induced hypertension from the antenatal clinic and inpatient ward.

Results: More number of cases in eclampsia group came from rural area, from lower socio economic group and were unbooked for antenatal care. Both diastolic and systolic pressures are significantly correlating platelet count. Platelet count is significantly lower in cases of pre-eclampsia and eclampsia when compared to normal. Mean gestational period delivery was shorter in pre-eclampsia and eclampsia when compared to normal. Mean birth weight was reduced as the severity of the disease increased.

Conclusions: Thrombocytopenia is directly proportional to the severity of the pre-eclampsia. Reduction of platelet count below 1 lac per ml. increases the risk of developing DIC and HELLp syndrome significantly, thus an early prediction suggesting prompt management.

Keywords: Platelet Count; Prognostic Index; Pregnancy Induced Hypertension; Maternal morbidit

Introduction

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad along with hemorrhage and infections that result in much of the maternal morbidity and mortality related to pregnancy. There are multiple possible causes of elevated blood pressure during pregnancy but the overwhelming majority of cases can be included into 5 well defined groups: chronic hypertension, gestational hypertension, Preeclampsia, Eclampsia, Hellp syndrome. Hematological abnormalities develop as a complication of preeclampsia. Out of all hematological changes that occur in preeclampsia and eclampsia, thrombocytopenia is most common hematological abnormality found in pregnancy. Thrombocytopenia is defined as platelet count less than 1.5 Lac Though in normal pregnancy there is no effect on platelet count, studies show that platelet counts might fall to some extent but not

lesser than the normal range. This usually occurs during the third trimester and reverts back to normal immediately following delivery. Changes in platelet count is well established in preeclampsia and studies show, with evolution of severe preeclampsia there was a fall in circulating platelet count much earlier than expected [1].

Thrombocytopenia is attributed to two main causes. Failure of platelet production and early excessive platelet consumption, where the second cause is observed in eclampsia and pre eclampsia. Accelerated platelet activation and consumption is seen in normal pregnancy which explains the mild thrombocytopenia seen in normal patients and is termed as pregnancy associated thrombocytopenia or incidental thrombocytopenia. The incidence is 0.4 to 8.3%. In these cases the fetus is not at risk as perinatal outcome is quite satisfactory. HELLP syndrome is a severe form of preeclampsia and involves hemolytic anemia, elevated liver function tests and low platelet counts. The pathophysiology remains unclear. The findings of this multi system disease are attributed to abnormal vascular tone, vasospasm and coagulation defects. No precipitating factor has been found till date. This syndrome occurs as final manifestation of a series of endothelial damage and intravascular platelet activation. With platelet activation thromboxane A and serotonin are released, causing vasospasm, platelet agglutination and aggregation, and further endothelial damage. This begins a cascade that is only terminated after delivery [2,3].

The aim of the study is to know the variation in platelet count between normal pregnancy and pregnancy induced hypertension (PIH) and correlate – fetomaternal outcome.

Materials and Methods

It is prospective study done in 100 pregnant women attending the Gandhi medical college, secunderabad formed the basis of the study. Among these 50 were normal pregnant women, 15 were eclampsia, 20 were preeclampsia (sever PIH) 15 were mild pregnancy induced hypertension, according to ACOG classification, from the antenatal clinic and inpatient ward.

Besides complete obstetric examination, detailed history was takes with special attention to hemorrhagic disorders thromboembolic episode, epilepsy, hepatic or renal disorder and drug intake, which can alter platelet count four weeks, 24 hours after delivery and 7 days after delivery, for estimating HB%, total and differential white cell counts, blood sugar, blood urea, serum uric acid and total platelet count. Platelet count was done manually.

Classification of hypertensive disorders complicating pregnancy by the working group of the NHBPEP (national high blood pressure education program-2000). There are five types of hypertensive disease.

1. Gestational hypertension (formerly pregnancy induced hypertension that included transient hypertension.
2. Pre-eclampsia
3. Eclampsia
4. Preeclampsia superimposed on chronic hypertension
5. Chronic hypertension.

Both the study and test groups of patients belonged to the pregnancy induced hypertension of this classification. The demographic sheet included information about the name, age, parity of patient, duration of amoenorrea, last menstrual period, expected date of delivery, obstetric formula, compliant of the patient if any, blood pressure, systemic examination, abdominal examination, per speculum and per vaginal examination, mode of delivery, complications if any, baby details, investigations mainly platelet count done at interval along with other PIH investigations and USG.

After completing the demographic sheet, all the patients taken up for study were subjected to laboratory investigations. 5 ml of venous blood sample were aspirated from the participants ante cubital vein and mixed with EDTA (Ethylene diamine triacetic acid). The blood is mixed well and placed on a rack in an analyzer. The instrument has flow cells, photometers and apertures that analyses different elements in the blood. The cell counting components counts the number and types of different cells in the blood. The results are printed.

Blood counting machine aspirates a very small amount of the sample through narrow tube followed by an aperture and a laser flow cell. flow cytometry count the number of the cells passing through the aperture. The instruments identify the type of blood cell by analyzing data about the size and aspects of light as they pass through the cells (called front and side scatter). The counts are reported.

In patients with very low platelet count, the counts are rechecked using manual method. In manual method, whole blood is diluted with 1% ammonium oxalate solution. The isotonic balance of the diluents is such that all the erythrocytes are

destroyed while platelets and leucocytes remain intact. The standard dilution for platelet is 1:100. The dilution id prepared using leucocyte/platelet unopette system. The dilution is mixed well and incubated to permit the lysis of the erythrocytes following incubation period. The dilution is mounted on a hemocytometer chamber under the microscope. The cells are allowed to settle and then are counted in a specific area of hemocytometer under the microscope. The number of platelet is calculated per micro liter.

Platelet values. Normal Thrombocytopenia Critical count

1.5 to 4 Lakhs /mm^3 <1.5 lakhs/mm^3. <50,000/ mm^3.

The data thus collected were analyzed using appropriate statistical methods. The mean and standard deviations were completed. The statistical test used for analysis was.

Results

The study group of 100 women with PIH was distributed into mild and severe preeclampsia and eclampsia. In general, it was the middle and the lower income group of individuals that availed the government hospital, antenatal checkup facilities.

The socioeconomic status determined according to register - general's occupational classification as follows.

a. Low socioeconomic group: - laborers and people working ion daily wages unskilled occupation.
b. Middle income group: - non-manual skilled occupation and manual skilled occupation.
c. Higher income group: - professionals and managers.

The simple population of individuals in different groups of disease severity were classified into different social economic groups. The no of cases reporting to the hospital with mild and sever preeclampsia were in the lower and middle-income groups. It is significant that cases reporting with eclampsia were the highest in the lowered income groups (80%).

In the higher income group there no cases of eclampsia. Mild (15%) and severe preeclampsia (10%) also were less. Complications of PIH were more in low socioeconomic group. The normal cases lowest in the lower income group (20%) and higher income group (30%) the occurrence of mild PIH was more or less similar magnitude across the three socio economic groups. Severe preeclampsia was if similar magnitude in lower and middle-income groups (45%). But lower in higher income groups (10%) THE present number ofcases with eclampsia are the highest in lower income group (80%). And more at all the higher income group. (Table 1)

The number of cases reported to the hospital were more from the urban background rather than rural background. From the urban background, more or less equal number of cases were in the normal mild (16.4%), severe preeclampsia (21.6%) group and least in the eclampsia group (2.6%) where as it was the other way for the rural group with majority (86.7%) falling in the eclampsia group. The number of normal cases were the high (70%) among the women booked for antenatal care and low among the unbooked cases (30%). On the other hand, eclampsia was high in unbooked cases (93%) and low in the booked cases (6.6%) Percent distribution of cases according to urban and rural background

Table 1: Distribution of cases according to socio-economic class

Group of individuals	Total no of cases studied	Lower income	Middle income	Higher income
Normal	50	20% (10)	50% (25)	30% (15)
Mild PIH	15	40% (6)	45% (7)	15% (2)
Severe preeclampsia	20	45% (9)	45% (9)	10% (2)
Eclampsia	15	80% (12)	20% (3)	---
	100	37	44	19

Table 2: Occurrence of disease in urban and rural back ground, booked and unbooked population.

Group of Individuals	Number of Cases	Urban	Rural	Booked	Un-Booked
Normal	50	94% (47)	6%	70% (35)	30% (15)
Mild PIH	15	86.6% (13)	13.3 (2)	53.3% (7)	46.3% (7)
Sever preeclampsia	20	85% (17)	15% (3)	65% (13)	35% (7)
Eclampsia	15	13.3% (2)	86.6% (13)	6.6% (1)	93.3% (14)
Total	100	79	21	57	43

and cases booked and unbooked for antenatal care on each group of individuals in a disease (Table 2).

The lowest mean age was seen among the mild preeclampsia group (21) followed by the eclampsia group (20). Eclampsia was seen at the extremes of age (19-35 y). Though there are no large differences in the mean age in the four groups (Table 3) the mean age tended to be lower in the mild preeclampsia and normal group. The range in age was wider in severe preeclampsia and eclampsia group (Table 3).

Both the diastolic and systolic components of the blood pressure, as expected and on which the division into different groups was partly based, increase with increasing severity of the disease. Being the highest in eclampsia group the range in systolic blood pressure was the widest in the eclampsia group. The order in which the range varied were eclampsia > normal> severe preeclampsia > mild PIH.

< 50 > 40 > 20 >10 (Table 4).

The study group of 100 women with PIH was distributed into mild and severe preeclampsia and eclampsia. Platelet count was done by manual method. In control group and mild PIH. cases. Platelet count was done after 28 weeks of gestation and repeated after every 4 weeks till delivery. Platelet count repeated 24 hours after and 7 days after delivery the platelet count increased progressively to reach a normal level with in 3–5 days in all cases (Table 5).

For comparing the platelet count and to determine its increasing or decreasing trend, the mean value for each group was determined. There was a significant difference b/w platelet counts of severe PIH (p=0.001) eclampsia (p=0.001) and mild PIH (p=0.044) when compared to control group. To specify the relationship a comparison was made b/w no of cases in control and study with normal low and very low counts. minimum counts are seen in patients with severe PIH and eclampsia. In the present study in cases observed that 20% severe eclampsia 40%. The difference in the platelet count in normal and mild preeclampsia cases was not significant but the difference b/w the normal and severe preeclampsia cases was large and significant. The heterogeneity or variation from patients to patients which is indicated by variance was the largest for the platelet count. This heterogeneity was larger in normal group of individuals and those having mild PIH. It is reduced in severe preeclampsia and eclampsia group of patients. The minimum value recorded was the highest in normal group of individuals. Of the study five patients died,

Table 3: Age and occurrence of disease

Group of individuals	Mean	SD	Range
Normal	22.2	2.4	20-26
Mild PIH	21	2.2	18-25
Severe preeclampsia	25	2.8	19-30
Eclampsia	20	4.3	19-35

Table 4: Blood pressure and the disease

Character	Group of individuals	Mean	SD	Range
Diastolic blood pressure	Normal	73.5	8.75	60-80
	Mild PIH	97.3	5.49	90-100
	Severe preeclampsia	113.7	7.41	100-110
	Eclampsia	119.3	12.23	110-130
Systolic blood pressure	Normal	108	14.6	80-120
	Mild PIH	132	9.2	130-140
	Severe preeclampsia	147	11.7	140-160
	Eclampsia	173.2	23.2	160-210

Table 5: Mean platelet count in all groups

Group	No of patients	Mean platelet count	p value compares with
Mild PIH	15	2	0.044
Severe preeclampsia	20	1.4	0.001
Eclampsia	15	1.3	0.001
Control group	50	2.2	--

Table 6: Comparison of the platelet count between the control and study group

Platelet count lacs/cc	Control (n=50)	Mild PIH (N=15)	Severe PIH	Eclampsia (n=15)
Normal (>1.5)	38(76%)	11(73.3%)	9(45%)	2(16.6%)
Low (1-1.5)	12(24%)	3(20%)	7(35%)	7(46.6%)
Very low (<1)	--	1(6.6%)	4(20%)	6(40%)

Table 7: Distribution of gestation age in the four groups of individuals

Character	Group of individuals	Mean	S. D	Range
Gestation period in weeks	Normal	38.5	1.79	36-40
	Mild PIH	37.6	1.56	34-40
	Severe preeclampsia	34.2	2.37	32-40
	Eclampsia	33.1	1.6	30-37
Birth weight	Normal	2.72	0.3	2.0-32
	Mild PIH	2.42	0.33	1.8-3.0
	Severe preeclampsia	1.97	0.54	1.0-2.9
	Eclampsia	2.07	0.61	1.2-2.5

three of eclampsia and two of severe preeclampsia. of the eclampsia patients two died with DIC and HELLP syndrome, one of acute renal failure. While of severe preeclampsia both died of DIC. All these are unbooked cases having very low platelet count (<1 lac/c.c) (Table 6).

The mean gestational age at the time of delivery was equal in severe preeclampsia and eclampsia and much shorter when compared to normal and mild PIH. The mean birth weight was reduced as the severity of the disease increased. However, there was no difference in the severe preeclampsia and eclampsia group of individuals for this character (Table 7).

Discussion

Reduced platelet counts in patients with mild and severe PIH and very low counts in eclampsia in the present study were comparable to those reported by other authors (Table 9) all these studies confirm a marked thrombocytopenia in patients with severe PIH, which indicates severity of the disease.

In the present study, itwas observed that 20% of severe pre-eclampsia and 40% eclampsia patients had a platelet count, below one lakh per c.c. which is comparable to the study of sibai etal and of Pritchard who have reported platelet count less than one lakh per c.c. in 30% patients of eclampsia. however, redman noticed that if patients are followed serially with each woman acting as her own control a relative reduction in the clinical disease, suggesting platelet consumption occurring in the early part of the disorder.

Table 9: Comparison of mean plated count in Lacs/ml different series.

Group	Percent series	Kulkarni and sutaria [4]	Agarwal and buradkar [5]	Giles and inglis [6]
Normal	2.2	2.5	2.4	2.8
Mild PIH	2	1.84	2.1	2.4
Severe PIH	1.4	1.19.	2.1	2.1
Eclampsia	1.3	1.18	1.6	1.5

Thrombocypenia is directly proportional to the severity of PIH. Counts below one lac per ml. increased risk for DIC and HELLP syndrome. disseminated intravascular coagulation has been implicated in thepathogenesis of pre-eclampsia and eclampsia since a long time. Equally long standing is the reported incidence of thrombocytopenia in these cases.

Page et al. sought to demonstrate direct ties between placental hypoxia and the signs of PE. Using pregnant dogs as the model, they showed that constricting the abdominal aorta between the origins of the renal and uterine arteries increased blood pressure. There is a reduction in uteroplacental blood flow due to enhanced vascular reactivity and liable to hypertension as a consequence of which there is a placental damage and thromboplastin release [7,8].

A slow disseminated intravascular coagulation then occurs which occasionally fulminates. The most important aspect of the model is the suggested inter-relationship of placental blood flow, placental

pathology and disseminated intravascular coagulation. J.A. Pritchard [9] postulated the totally different theory that the coagulation changes when present in eclampsia in eclampsia are effects rather than a cause and that the changes may evolve primarily from platelet adherence at sites of vascular endothelial, as the consequence of segmental vasospasm and vasodilatation, rather than be triggered by the escape of thromboplastin from the placenta into the maternal circulation.It has also been assumed that the lowered platelet count is due to sequestration of platelets in the microcirculation of organs such as the placenta, kidney and liverthe exact extent to which platelets themselves contribute to the pathogenesis of preeclampsia is however not known.

Thrombocytopenia in pregnancy has been thought to be due to heamodilution by some and due to a compensated thrombocytolytic state by some. Immunological cause has also been implicated. Many theories have been put forward but none been accepted universally.Modern management of pre-eclampsia aims at controlling the disease in the mother for as long possible so that the fetus can mature. In doing so, we are confronted with a condition where the internal environment of the fetus is not only detrimental for its existence but is gradually deteriorating with time. In our anxiety if we deliver the fetus too early it may be so ill developed that it might not survive, on the other hand a long delay will cause intrauterine death. The ideal time of delivery on which the management [9].

Depends should be found out. Apart from the fetus, the mother herself is exposed to the risk of impending eclampsia. It has been seen that sometimesa woman with a very high blood pressure dose not throw a fit but the one with the moderately elevated blood pressure develops eclampsia.With the help of laboratory investigations, it is important to identify the critical time, over which the slow intravascular coagulation of pre-eclampsia fulminates into wide spread disseminated intravascular coagulation.Such an information will sever as a break-through and will be of tremendous help in the proper and efficient management of the disease. Pregnancy can then be terminated at the right time effectively minimizing / preventing the possibility of development of eclampsia in the better interests of both mother and child. In the development countries, a number of highly sophisticated laboratory investigations are being used to monitor changes in the coagulation system during the course of pre-eclampsia e.g. the study of platelet life span and adhesiveness, estimation of serum and urinary fibrin degradation products, estimation of ratio between factor 8 related antigen and factor 8 coagulated activity, cryfibrinogen and plasminogen estimations and platelet factor 8 availability.

In our country, such investigations are available at selected centers in big cities only. The highest incidence of eclampsia causing very maternal and perinatal morbidity and mortality in people belonging to rural areas is very clear in our studies and less been reposted by others has been reported by others as well. The reason appears to be.

1. The early age of marriage among our rural poor.
2. Lack of proper antenatal care and the reluctance to use it wherever available due to ignorance and illiteracy.

The other equally important cause is Poverty (Table 1). Providing proper antenatal care to this particular group of high risk patients is absolutely essential and demands immediate attention on high priority. The increasing severity of the disease is clearly related to the decreasing, fewer are the platelets in the blood (Table 5). These findings show that as pre-eclampsia progresses the platelet count decreases. The diastolic and systolic blood pressure both within and across the different disease severity groups are groups are highly negatively correlated with the platelet count. It indicates that higher the B.P. lower will be the platelet number. Whether it means that simple measurement of blood pressure can be used as a quick indirect measure of platelet number in the blood stream and therefore, the disease severity is worth further investigations and confirmation. However, platelet count would be a must in cases of pre-eclampsia and eclampsia. The negative relationship between the diastolic and systolic blood pressure with the gestation period and fetal weight is well known. The relationship was negative i.e., the high systolic and diastolic pressures were associated with decreased fetal weight in severe pre-eclampsia and eclampsia groups. The relationship b/w blood pressure and fetal weight appears to be curvilinear when cases arose severity is associated with lower platelet count and shorter gestation period and lesser mean birth weight. It is observed that the mean duration of pregnancy was significantly higher in control group, which means most of them were full term deliveries, whereas the duration of pregnancy was reduced in test group in patients with thrombocytopenia. Thereby suggesting early delivery as prompt treatment of the disease and preventing complications. A fact recorded

earlier by JK Vrunda et al. [10] The occurrence of coagulopathy associated with thrombocytopenia was significantly higher in test group. A fact recorded by other authors (MP Fitzgerald) [11]. There was a higher incidence of still born infants in women with thrombocytopenia in the test group suggesting a poor neonatal outcome in cases with maternal thrombocytopenia. A fact recorded by other authors (Carl H Backers et al.) [12].

Conclusion

The objective investigation clearly brings out the fact that disease severity indicated by increasing blood stream, higher the blood pressure lower is the platelet count. This opens out the possibility whether measurement of blood pressure can be taken as a simple, quick and good index of platelet no in order to screen out normal population and carryout extensive platelet counts in mild PIH and severe PIH group of patients. Sophisticated expensive laboratory techniques are available for a proper understanding of prevailing high-risk conditions as pre-eclampsia and low birth weight in the developed countries which are known to be helpful in early recognition and proper management of the maternal condition and hold a better prospect for the fetus.The extent to which pre-eclampsia cause maternal and perinatalmorbidity and pregnancy wastage in the rural and poor socioeconomic groups brings in focus the fact. To what extent the antenatal care is inadequate. Inspire of the massive effort both by the state and national agencies to provide maternal and child care services, this vulnerable group of women is not being benefitted. Does it mean that the programmed are not effective or too small to cater for such a widespread preventable disease is a debatebles question and needs to be investigated.

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