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Original Research Article

Hemostasis in Pregnancy Induced Hypertension (PIH)**P. Sathya**^{*1} and M. Praveen Kumar²¹Professor, Institute of Physiology & Experimental Medicine, Madras Medical College, Chennai, Tamilnadu, India²Director (Retired), Institute of Physiology & Experimental Medicine, Madras Medical College, Chennai, Tamilnadu, India

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Article History:*Received:** 02/06/2017**Revised:** 04/06/2017**Accepted:** 10/06/2017**DOI:** <https://doi.org/10.7439/ijbar.v8i6.4203>**Abstract**

Background: Pregnancy is a hypercoagulable state as the parturient is physiologically prepared against haemorrhage. Plasma fibrinogen level increases and platelet count decreases. Pregnancy induced Hypertension (PIH) is a syndrome complex of hypertension, oedema and proteinuria. In PIH, the physiological changes that occur in normal pregnancy are further aggravated and the woman is prone to develop Disseminated Intravascular Coagulation (DIC) which is a chief pathogenic factor in PIH.

Objective: 1.To estimate platelet count and serum fibrinogen in normal pregnant women and women with PIH.2.To do bleeding time and clotting time in normal pregnant women & women with PIH& compare both.

Material & methods: Two groups of pregnant women were involved. The first group (control) comprises normal pregnant women. The study group consists of pregnant women with PIH. Platelet count was done by direct method. Serum Fibrinogen was estimated by Rapid Turbidimetric method. Bleeding time was measured by Duke Method & Clotting time was measured by Wright's capillary tube method. Statistical analysis was done using appropriate student t test & SD.

Results: In PIH group, platelet count is moderately reduced (Mean 1.72, P=< 0.05) and bleeding time is prolonged (mean 117.45, P0.001), Serum fibrinogen level is reduced (mean 237.14, P 0.001) and clotting time is prolonged(mean 16.9,P 0.001).

Conclusion: Pregnant women with PIH are more prone to develop coagulation abnormalities which may result in bleeding tendency. Hence, serial estimations of platelet count & bleeding time can be used to assess primary hemostatic function. Plasma fibrinogen level & clotting time measurement may be used to assess secondary hemostatic function.

Keywords: PIH, Fibrinogen, Platelet count.

1. Introduction

In normal pregnancy, the components of coagulation are altered to facilitate hemostasis. Some factors are increased while others remain normal or decreased. Plasma fibrinogen (clotting factor I) in normal non-pregnant women averages about 300 mg/dl and ranges from 200 to 400 mg/dl. During normal pregnancy, plasma fibrinogen concentration increases about 50% above non-pregnant level with a range from 300 to 600 mg/dl[8]. The increase in the concentration of fibrinogen undoubtedly contributes

greatly to the striking increase in Erythrocyte Sedimentation Rate (ESR) in pregnancy. There is a moderate decrease in platelet concentration as pregnancy progresses which may be the consequence of increased platelet consumption throughout the pregnancy [16]. Bleeding time and clotting time are unchanged by normal pregnancy.

Pregnancy Induced Hypertension (PIH) is a syndrome characterized by hypertension, edema and proteinuria. In India, the incidence of PIH is about 7-10%.

According to a WHO report, the perinatal mortality in hypertensive disorders of pregnancy is about 20 percent or more in developing countries. During pregnancy, there are profound changes in hemostatic mechanism to protect the pregnant women from hemorrhage, particularly at delivery. These changes tilt the balance of hemostasis towards clotting. Such changes are further aggravated in PIH and the woman is more prone to develop DIC (Disseminated Intravascular Coagulation)[11]. One theory holds that in PIH, thromboplastin of placental origin invades maternal circulation to produce a slow DIC. This is manifested as intravascular disappearance of procoagulants especially fibrinogen [5] and platelets [6]. Severe neglected PIH may lead to a dreadful complication called HELLP syndrome (Hemolysis, Elevated Liver enzymes and Low platelet count)[18]. In normal pregnancy, there is a decreased pressor response to angiotensin II but in PIH, there is an abnormal increase in sensitivity to angiotensin II weeks before onset of clinical disorder due to defective trophoblast invasion of spiral arterioles. Generalized vasospasm with secondary interruption of blood flow and haemorrhage in the microcirculation has long been recognized as part of pathophysiology of PIH. These changes may lead to endothelial cell damage [17] and interendothelial cell leaks through which blood constituents, including platelets and fibrinogen are deposited subendothelially[19]. Thrombocytopenia in PIH is the result of endothelial damage [15] and is frequently associated with prolonged bleeding time [10].

Damaged endothelium also promotes excess intravascular thrombin formation. The action of thrombin on fibrinogen generates Fibrin Degradation Products (FDP) including D-dimer. Hence serum fibrinogen level decreases in women with PIH [14]. The decrease is directly proportional to the severity of PIH.

PIH is classified in to 3 types based on the severity:

Mild PIH

- BP 140/90 – 160/100mmHg
- urine- trace of protein

Moderate PIH

- SBP 160-180mmHg& DBP 100-110mmHg

Severe PIH

- BP>180/110mmHg
- oliguria, proteinuria
- Patient may complain of headache, epigastric pain & visual disturbances.

Eclampsia is a complication of uncontrolled PIH, characterized by tonic, clonic convulsions. The pathophysiology is due to cerebral vasospasm leading to ischemia and cerebral oedema.

The rationale behind the study is to do serial estimation of platelet count and bleeding time to assess the integrity of Primary hemostasis and plasma fibrinogen level and clotting time to assess the integrity of secondary hemostasis in women with PIH to prevent complications like HELLP syndrome.

2. Materials and methods

The study was done on patients attending the antenatal clinic in Kasturba Gandhi Government Hospital for Women and Children, Chennai(T.N) for the period from March 2001 to March 2002.

2.1 Inclusion criteria

- 1) 50 pregnant women with normal blood pressure with a gestational age of 20 weeks and above – Group 0
- 2) 100 pregnant women with PIH (mild, moderate, severe PIH and eclampsia).- Group 1.

2.2 Exclusion criteria

- 1) Pregnant women with <20 weeks of gestation
- 2) Pregnant women with any known hematological disorders
- 3) Pregnant women with any other medical illness.

After permission from institutional ethical committee, an informed written consent was obtained from the patients. They were subjected to general obstetric examination. BP was taken in supine position. A deep finger prick was made with a sterile lancet. Bleeding time was noted by Duke's method using filter paper. Another deep finger prick was made and clotting time was noted by Wright's capillary tube method.

About 5ml of venous blood was taken. Platelet count was done by Direct method using Reese-Ecker fluid and platelets were counted in a hemocytometer. About 2ml of same venous blood was taken in a test tube. From this sample, 0.2 ml of serum was used to estimate fibrinogen level by Rapid Turbidimetric method. The turbidity was read in a colorimeter at 490nm and the OD value was noted.

2.3 Data analysis

The results were tabulated and analysed. Descriptive statistics was used to determine mean and Standard Deviation (SD) of BT, CT, Platelet count and fibrinogen levels.

Student 't' test was used to compare between the two Groups. p value of <0.05 was considered statistically significant.

3. Results and observations

Bleeding time (sec) in PIH subject (117.45 ± 36.7) was observed to be significantly increased in comparison with control (79.4 ± 9.07). Clotting time (sec) in PIH subject (234.3 ± 16.09) was observed to be significantly increased in comparison with control (215.15 ± 59.68).

Fibrinogen level (mg/dl) in PIH subject (257.10 ± 56.77) was observed to be significantly decreased in comparison with control (417.04 ± 86.64). Platelet count (lakhs/ μ l) in PIH subject (1.99 ± 0.478) was observed to be significantly decreased in comparison with control (2.44 ± 0.462). (Tables 1-4, Figure 1, 2)

Table 1: Bleeding time in seconds

Group	n	Mean \pm SD	't' test value	P value	Significance
Control	50	79.40 \pm 9.07	7.25	0.001	Significant
PIH	100	117.45 \pm 36.47			

Table 2: Clotting time in seconds

Group	n	Mean \pm SD	't' test value	P value	Significance
Control	50	215.5 \pm 59.68	2.23	0.001	Significant
PIH	100	238.30 \pm 16.09			

Table 3: Fibrinogen level in mg/dl

Group	n	Mean \pm SD	't' test value	P value	Significance
Control	50	417.04 \pm 86.64	13.55	0.001	Significant
PIH	100	257.10 \pm 56.77			

Table 4: Platelet count in lakhs/ μ l

Group	n	Mean \pm SD	't' test value	P value	Significance
Control	50	2.44 \pm 0.462	5.51	0.001	Significant
PIH	100	1.99 \pm 0.478			

Tables 1, 2, 3, and 4 shows that bleeding time, clotting time, blood platelet count and serum fibrinogen levels are all reduced in PIH group compared to control group and it is statistically significant.

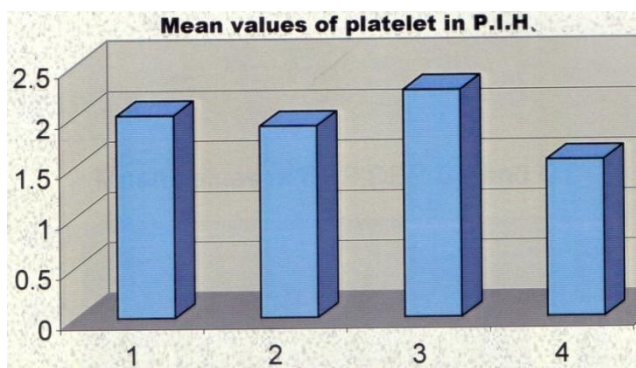


Figure 1: Shows that the platelet count is lowest in PIH group 4 i.e. eclampsia

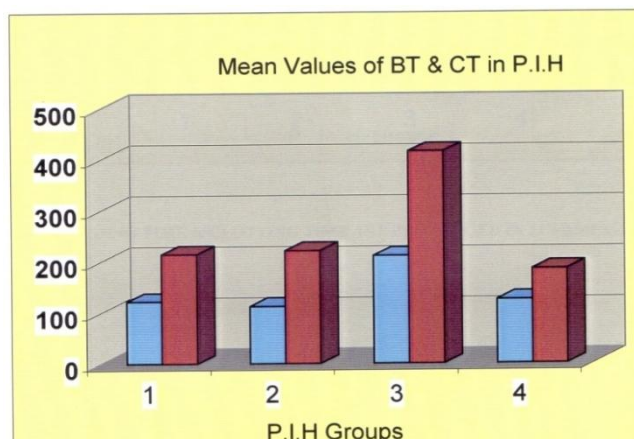


Figure 2: Shows that bleeding time and clotting time are prolonged in PIH group 3 i.e. severe PIH

Figures 1 and 2 shows that the hemostatic dysfunction in PIH becomes severe as the severity of PIH increases.

4. Discussion

In the present study, two parameters of primary hemostasis namely bleeding time and platelet count and two parameters of secondary hemostasis namely clotting time and plasma fibrinogen levels were estimated in pregnant women with PIH and without PIH. The findings reveal that the pregnant women with PIH are more prone to develop coagulation abnormalities which may result in bleeding tendency.[7].

Bleeding time (BT) is prolonged in the study group compared to the control group which is statistically highly significant. In mild PIH group, there is a positive correlation between BP and BT. In severe PIH group, a very high positive correlation is observed between diastolic BP and BT. The finding of prolonged BT in PIH mothers is in conformity with the observation of Burrows *et al*[12] and Kelton *et al* [10]. This may be due to increased platelet consumption in PIH which could be due to increased thrombin activity [8] or mediated by thrombin independent mechanism.

There is a statistically significant reduction in platelet count in study group compared to control group. This finding concurred with the results of Borok *et al*[3], Leduc *et al*[9] and Metz *et al*[13]. The damaged endothelial cells in PIH favour coagulation. Platelets may either be consumed in thrombus formation or may suffer membrane damage on contact with abnormal endothelial surface and be prematurely removed from circulation [7].

Clotting time (CT) is prolonged in study group compared to control group. In mild PIH, there is a positive correlation between systolic BP and CT, which may be due to hypofibrinogenemia.

It is observed in the present study that the fibrinogen levels are significantly lower in study group than that of the control group. This observation concurred with the results of Dube *et al*[12]. One theory in favour of this findings is that the thromboplastin of placental origin invades the maternal circulation to produce DIC. The activation of coagulation system is manifested as the intravascular disappearance of procoagulants, especially fibrinogen to a degree sufficient to produce spontaneous haemorrhage.

5. Conclusion

In the present study, 100 pregnant women with PIH and 50 healthy pregnant women with normal BP with more than 20 weeks of gestation were taken as the study group and control group respectively to assess hemostatic functions. Bleeding time, blood platelet count, clotting time and plasma fibrinogen levels were estimated in both groups as parameters for primary and secondary hemostasis respectively. The above said hemostatic parameters revealed a decreased efficiency of primary and secondary hemostatic functions in PIH [14].

Bleeding time and clotting time, which are simple, inexpensive and quick to perform tests, have proved to be reliable and easy bedside tests that should be recommended to be estimated in all PIH cases. If bleeding time is prolonged, platelet count should be done to assess primary hemostatic function. Serial estimations of platelet count can be used to monitor such patients so that when the count becomes less than $1\text{L}/\mu\text{l}$, the obstetrician may contemplate heroic intervention. If clotting time is prolonged, plasma fibrinogen level estimation may be useful to assess secondary hemostatic function.

It may be suggested that bleeding time and clotting time should be tested in all pregnant women with PIH at their first visit to the hospital and should be repeated in all subsequent visits to detect hemostatic abnormalities early so that maternal morbidity and mortality and in turn perinatal mortality may be reduced to a minimum.

6. Limitations of the study

- 1) More sophisticated methods may be used to assess bleeding time and clotting time.
- 2) Estimation of Fibrin Degradation Products (FDP) may be done to assess the severity of hemostatic alterations.
- 3) Serial Doppler and Ultrasonic methods of pregnant uterus may be done in women with PIH to identify the vascular changes reducing the blood flow to the foetus resulting in Intra Uterine Growth Retardation (IUGR).

Conflict of interest: None

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