Coagulation Profiles in PIH – a) To Determine Coagulation Index to Distinguish Severe Preeclampsia from Normal Pregnancy b) To Assess the Correlation of Coagulation Parameters in Normal Pregnancy & in Varying Grades of Preeclampsia

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Abstract: Background: PIH is the most common medical complication of pregnancy & it affects 2-10 % of all pregnancies. Thrombocytopenia is the most common finding which occurs in 11% to 29% of patients with PIH. It contributes significantly to maternal and perinatal morbidity and mortality. Methodology & Results: The coagulation index in severe pre-eclampsia = 2.62 ± 2.64. Higher the coagulation index severe is the pre-eclampsia. Thus the coagulation index of more than 1 can be safely taken as cut off value to distinguish between normal pregnancy & severe pre-eclampsia. In severe pre-eclampsia, the platelet count = (105 ±63.65)x 10^3/mm^3 , PT = (19.6 ± 5.7) sec , APTT =(78.7± 22.7) sec & D dimer(0.48 ± 0.07)was noted . Conclusion: The degree of thrombocytopenia increases with severity of disease (lower the platelet count, greater are maternal and fetal morbidity and mortality. The coagulation parameters, especially Platelet count, aPTT and D-dimer can be safely used as an early indicator for reassessment of severity of PIH cases and can be used to monitor the progression of gestational hypertension to preeclampsia. So, it is concluded from this study that total platelet count with aPTT & D dimer can be taken as an early and rapid procedure for screening preeclampsia cases at admission followed by serial platelet counts while monitoring coagulation indices.

Keywords: Pre-eclampsia, PIH, D-dimer, Platelet count, Multivariate, PT, APTT

1. Introduction

Pregnancy Induced Hypertension (PIH) is defined as hypertension that occurs in pregnancy for the first time after 20 weeks of gestation and disappears following delivery. PIH is classified into (i) Gestational hypertension/mild PIH (ii) Pre-eclampsia (iii) Eclampsia. It is one of the most common medical complications of pregnancy & it affects 2-10% of all pregnancies. PIH is associated with 16% of all maternal mortality and 20% of all perinatal mortality in India. Thrombocytopenia is the most common finding which occurs in 11% to 29% of patients with PIH.1

According to the criteria of the International Society of the Study of Hypertension in pregnancy, Pre-eclampsia is defined as the Blood pressure ≥ 140/90 mm Hg occurring after week 20 of gestation with proteinuria 300 ≥ mg / day or urinary protein/creatinine ratio =30 mg/mmol

Eclampsia is occurrence of convulsion or coma with signs and symptoms of pre-eclampsia.2

Based on the classification of American College of Obstetrician & Gynaecologist (ACOG), The pre-eclampsia can be categorized into Mild (140-159 /90-109 mm Hg) and severe (≥160 /110).2,3,4

The basic pathology of preeclampsia is endothelial dysfunction, poor placentation and vasospasm of vessels along with alteration of haematological profile of which thrombocytopenia is the most common.

It has been noted in other studies that the degree of thrombocytopenia increases with severity of disease (lower the platelet count, greater are maternal and fetal morbidity and mortality). The dreaded complications of PIH are DIC & HELLP syndrome.

HELLP syndrome is Hemolysis, Elevated liver enzyme, low platelet count. It occurs in 2–12% women with severe pre-eclampsia or eclampsia.5 Early assessment of severity of PIH is necessary to prevent complications like HELLP syndrome and DIC. This has prompted me to undertake the present study

The main objective of this study is to
a) To determine Coagulation index to distinguish severe preeclampsia from normal pregnancy
b) To assess the correlation of coagulation parameters of normal pregnancy with varying grades of preeclampsia.
c) To assess the relationship between total platelet count and severity of preeclampsia.

2. Methodology & Results

This study was undertaken in a tertiary maternity & children hospital. A total of 100 pregnant females with pre-eclampsia constituted cases.
Inclusion criteria
- 100 pregnant females with pre-eclampsia in 3rd trimester, were taken as cases
- 100 normal pregnant females in 3rd trimester without any disease were taken as controls
- Controls were Age & parity matched with cases (controls chosen were of similar age groups & parity as compared to cases with only minor differences)

The preeclamptic women were selected based on the following criteria:
Pregnant women with blood pressure over the baseline ≥ 140 /90 mm of Hg with Proteinuria ≥ 0.3 gm / l or >1 + measured by dipstick. Cases were categorized into Mild (140-159 /90-109 mm Hg) and severe ≥160 /110 based upon classification of American College of Obstetrician &Gynaecologist (ACOG).

Exclusion criteria
- History of hypertension, diabetes mellitus, recurrent miscarriages, hepatic or renal disease, ITP
- Cases with history of hypertension, diabetes mellitus, recurrent miscarriages, hepatic or renal disease, ITP
- HELLP syndrome & DIC
- Cases Indirect bilirubin, LDH, ALT, AST were done to rule out HELLP syndrome & DIC
- If any of the cases shows features of hemolysis on PBS (fragmented RBCs, increased retic count) then only in such cases Indirect bilirubin, LDH, ALT, AST were done to rule out HELLP syndrome & DIC

Exclusion criteria
Cases with history of hypertension, diabetes mellitus, history, recurrent miscarriages, hepatic or renal disease, ITP were excluded from the study

Statistical analysis of data
All data were expressed as Mean +/- SD. Statistical analysis was done using unpaired students t test. A level of p value <0.05 was used to indicate statistical significance in all analyses.

3. Results
Total no. of pre-eclampsia cases in 3rd trimester of pregnancy = 100
Mild pre-eclampsia= 65 cases
Severe pre-eclampsia= 35 cases (HELLP syndrome= 04 cases & DIC= 08 cases)
Age & parity matched controls = 100

Table 1: To determine Coagulation index

<table>
<thead>
<tr>
<th>Coagulation parameters</th>
<th>Normal pregnancy (100 cases)</th>
<th>Severe Preeclampsia (35 cases)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta PLT = (PLT count before delivery – PLT count in early gestation)</td>
<td>(4.8 ± 1.2) x 10⁹/microL</td>
<td>(15.9 ± 1.7) x 10⁹/microL</td>
<td>P = 0.03</td>
</tr>
<tr>
<td>Antithrombin (AT) level</td>
<td>(91.7 ± 18.8)%</td>
<td>(24.2 ± 17.8)%</td>
<td>P = 0.026</td>
</tr>
<tr>
<td>Thrombin-antithrombin (TAT) complex,</td>
<td>(11.8 ± 4.9) ng/ml</td>
<td>(19.7 ± 4.6) ng/ml</td>
<td>P = 0.06</td>
</tr>
<tr>
<td>D-dimer</td>
<td>(0.33± 0.08) microg/mL</td>
<td>(0.48± 0.07) microg/mL</td>
<td>P = 0.07</td>
</tr>
</tbody>
</table>

Coagulation index was calculated using multivariate logistic regression analysis =
Y = (-0.019 x AT activity) + (0.067 x TAT) + (0.067 x D-dimer) + (-0.064 x DeltaPlt) + 0.706.

The coagulation index in normal pregnant females= -0.59 ± 0.38
The coagulation index in severe pre-eclampsia = 2.62 ±2.64

Table 2: Comparative analysis of coagulation parameters in PIH

<table>
<thead>
<tr>
<th>Coagulation parameters</th>
<th>Normal pregnancy Control (100)</th>
<th>Mild pre-eclampsia (65 cases)</th>
<th>severe pre-eclampsia (35 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLT Count x 10⁹/mm</td>
<td>(192 ±41.9) x 10⁹/mm</td>
<td>(181 ±52) x 10⁹/mm</td>
<td>(105 ±63.65) x 10⁹/mm</td>
</tr>
<tr>
<td>PT (sec)</td>
<td>(10.9 ± 2.1) sec</td>
<td>(11.8 ± 3.2) sec</td>
<td>(19.6 ± 5.7) sec</td>
</tr>
<tr>
<td>PLT is low in DIC = 08 65% of severe D dimer++ preeclampsia cases HELLP synd.= 04 cases PBS = fragmented RBCs, Retic ++, Liver enzymes +++</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Platelet count was low in 25% of mild pre-eclampsia (78.7 ± 22.7) of severe pre-eclampsia cases

Table 3: Platelet count versus other coagulation parameters

<table>
<thead>
<tr>
<th>PLT COUNT</th>
<th>PT</th>
<th>APTT</th>
<th>D dimer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal preg &amp; mild pre-eclampsia</td>
<td>0.5-1x10^1/mm</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td>Severe preeclampsia &amp; eclampsia</td>
<td>1.5x10^1/mm</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td>Severe preeclampsia &amp; eclampsia</td>
<td>2.5x10^1/mm</td>
<td>0.06</td>
<td>0.06</td>
</tr>
</tbody>
</table>

There was a strong correlation between APTT and marked thrombocytopenia & also with D dimer APTT is prolonged in more than 50 % of total cases and platelet count were reduced in 38 % of total cases. The platelet count in mild preeclampsia was not significantly lower than that in controls. It was (181 ± 52)x 10^7/mm with P value > 0.05. It has been seen that the platelet count in severe preeclampsia and eclampsia was very significantly lower than that in normal healthy pregnant controls. The mean platelet count in severe preeclampsia(105 ± 63.65)x 10^7/mm.

Thrombocytopenia is relatively frequently reported in severe preeclampsia with the occurrence range of 30-50%. The incidence of thrombocytopenia in our study was 50%. This high incidence probably occurred because we included only the cases with severe preeclampsia or eclampsia, many of whom were admitted in the intensive care unit.

Table 4: Comparison of platelets in various studies

<table>
<thead>
<tr>
<th>Authors</th>
<th>Control (x10^11/mm)</th>
<th>Mild preeclampsia (x10^11/mm)</th>
<th>Severe Pre-eclampsia (x10^11/mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Srivastava et al. (1995)</td>
<td>1.94</td>
<td>1.79</td>
<td>1.64</td>
</tr>
<tr>
<td>Jambhulkar et al. (2001)</td>
<td>2.38</td>
<td>2.3</td>
<td>1.7</td>
</tr>
<tr>
<td>Joshi et al. (2004)</td>
<td>2.2</td>
<td>2</td>
<td>1.4</td>
</tr>
<tr>
<td>J. Davies et al. (2007)</td>
<td>2.57</td>
<td>2.3</td>
<td>1.77</td>
</tr>
<tr>
<td>Ellora Devi et al. (2012)</td>
<td>2.44</td>
<td>1.82</td>
<td>1.42</td>
</tr>
<tr>
<td>Present study</td>
<td>192 ±41.9</td>
<td>181 ±52</td>
<td>105 ±63.65</td>
</tr>
</tbody>
</table>

5. Conclusion

This present study along with few other studies showed that the degree of thrombocytopenia increases with severity of disease (lower the platelet count, greater are maternal and fetal morbidity and mortality. Early assessment of severity of PIH is necessary to prevent complications like HELLP syndrome and DIC.

The coagulation parameters, especially Platelet count, APTT and D-dimer can be safely used as an early indicator for the assessment of severity of PIH cases and can be used to monitor the progression of gestational hypertension to preeclampsia. Coagulation index can be used as an effective tool in assessment of severity of PIH. Higher the coagulation index severe is the pre-eclampsia. Coagulation index of more than 1 can be safely taken as to distinguish between normal pregnancy & severe pre-eclampsia. If the coagulation index is > 1.3, then the pregnancy should be terminated by cesarean section as there is increased risk of fetal & maternal mortality due to hypercoagulability.

So, it is concluded from the study that total platelet count with APTT & D dimer can be taken as an early and rapid procedure for screening preeclampsia cases at admission.
followed by serial platelet counts while monitoring coagulation indices.

References