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BLEEDING TIME AND CLOTTING TIME: PROGNOSTIC ROLE IN PREGNANCY INDUCED HYPERTENSION.

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ABSTRACT Pregnancy is a physiological process but can cause hypertension in normotensive females. Pre - eclampsia is a multisystem disease which is seen only in humans. The dyed of hypertension and proteinuria, which manifests after 20 weeks of pregnancy, is referred to as pre-eclampsia. In normal pregnancy there are many changes in haemostatic mechanism which are associated with hypercoagulable state, in PIH there is derangement in the haemostatic mechanism. The degree of coagulation derangement increases with severity of the disease. Bleeding time and Clotting time are easy to perform, bedside inexpensive tests, so we have undertaken BT and CT as a means of assessing haemostatic status of PIH patient.

Aim and objectives: To study prognostic value of clotting time and bleeding time in pregnancy induced hypertension.

MATERIALS AND METHOD: The present study is a comparative prospective study. The study was started after taking the approval from the ethical committee of MGM's Medical College and Hospital. The study was carried out in 60 normal healthy pregnant females and 60 PIH patients of age group between 20 to 35 years.

RESULT: Our study revealed, statistical increase in the bleeding time and clotting time in the patients of pre-eclampsia and eclampsia, when compared to normotensive pregnant females and the increase is directly proportional to the severity of the disease .

CONCLUSION: There is unambiguous derangement of the haemostatic parameters in the patients of pre-eclampsia and eclampsia as compared to the normal pregnant females, patients showing a linear trend with disease, and as the disease progresses the haemostatic picture is deranged more.

KEYWORDS : Bleeding time, clotting time, pregnancy induced hypertension.

INTRODUCTION:

Pregnancy is a physiological process but can cause hypertension in normotensive females[1]. Pre - eclampsia is a multisystem disease which is seen only in humans and is characterized by hypertension with its effect on various systems of pregnant females[2,3]. The dyed of hypertension and proteinuria, which manifests after 20 weeks of pregnancy, is referred to as pre-eclampsia[4] Pre-eclampsia is a disorder of pregnancy which is stated to complicate at least 7-10% of all pregnancies world-wide [4]and it remains a nightmare to the obstetrician, every year nearly 1 lakh females die due to the eclampsia [5]. .It is studied that every 3minutes a woman dies due to the complications of PIH worldwide[5] In India, the incidence of PIH is reported to be around 8-10% of all pregnancies. It is the third leading cause of maternal mortality that is 17% of all maternal mortality.

Eclampsia is easily recognized entity and is studied back since 4200 year[6]. the most comprehensive epidemiologic work on PIH should still be credited to Chesley[7], whose classic masterpiece was published in 1978[8]. PIH is considered as "disease of theories" and has been a subject of large body of research [9,10].

According to NHBPEP (National High Blood Pressure Educational Programme) also known American college of obstetricians and Gynaecolists, PIH is defined as hypertension occurring in pregnant lady for the first time, is seen after 20 weeks of pregnancy , is accompanied by proteinuria and disappears following delivery [11]The classification system was based on the clinical symptoms such that it can guide the management of PIH.

Pre-eclampsia:

Systolic BP ≥140mm of Hg, diastolic BP ≥90mm of Hg.
Proteinuria ≥300mg/24 hrs or 1+dipstick value.

Eclampsia:

Pre-eclampsia associated with convulsions/coma is called as eclampsia [12,13]Historically the first case seen was of eclampsia, reported 2000 years back, where Celsus accounted a case of seizures in a pregnant female. Due to its rapid and unexpected occurrence, it was named as eclampsia which in Greek language means 'lightning'[14].

In normal pregnancy there are much changes in haemostatic mechanism which are associated with hypercoagulable state, having increased levels of coagulation factors [14,15]. This is believed to occur in the late third trimester and thus prevent major hemorrhage during parturition [16,17] There is distinct possibility of accentuation of these hypercoaggulative changes in PIH [18].

In few patients these complications may lead to further increase in DIC, intracranial hemorrhages, renal failure, HELLP syndrome, retinal detatchment, pulmonary edema, liver rupture, abruption placentae, more severity can lead to convulsions, cerebrovascular accidents and even may lead to morbidity or mortality. For fetus it is associated with growth retardation and even fetal demise [19]. Studies have shown that coagulation cascade occur early in the course of PIH often antedating clinically recognizable disease[6].

From above all studies we know that to prevent complications of PIH, we should do early intervention by anticipating coagulation disturbances. Clinical studies have demonstrated a good correlation between the haematological parameters and clinical severity of pregnancy induced hypertension[12]

BT and CT are easy to perform bedside, inexpensive tests, these tests can be performed in remote centers where more sophisticated tests are not available.

AIM: To study prognostic value of clotting time and bleeding time in pregnancy induced hypertension.

MERIALS AND METHODS:

The present study is a comparative prospective study; it was conducted in the Department of Physiology in collaboration with the Department of Obstetrics and Gynaecology. The study was conducted after taking the approval from the ethical committee of MGM's Medical College and Hospital and written and informed consent.

The study was carried out in 60 normal healthy pregnant females and 60 PIH patients of age group between 20 to 35 years.

Patients who satisfy our inclusion and exclusion criteria were divided into two groups;

1] Case group: patients with PIH,
2] Control group: normotensive pregnant females, by simple randomization technique.

The patients of pre-eclampsia (case group) were again categorized into two groups based upon the classification according to the scheme of the National High Blood Pressure Education Programme[1,20], third group was of patients who developed eclampsia

1) Mild PIH patients:
With SBP, 140-159mm of Hg and DBP 90-109mmof hg appearing for the first time after 20 wks of gestation.

2) Sever PIH patients:
With BP≥160/110 mm of hg.

3) Eclampsia patients:
Pre eclampsia associated with convulsions/coma before or during 24 hours of parturition Haematological parameters performed for the study were; bleeding time and clotting time.

1] Bleeding time [21]: Bleeding time was determined by using Duke's method. Normal BT is in the range of 2-5 minutes

2] Clotting time [21]: Clotting time is determined by Wrights capillary tube method.Normal CT is in the range of 3-7 minutes.

Statistical Analysis:
The data was compiled in master chart i.e. in MS-EXCEL Sheet and for analysis of this data; SPSS (Statistical package for social sciences) Version 24th was be used.

Analysis of variance (ANAOVA) was used to do the comparison between the subgroups.

Frequencies and percentages were calculated for qualitative data.
The significance level of this test was checked at $p < 0.05$.

RESULTS:
Table 1. – Comparison of Mean BT in mins of patients in Groups:

BT in mins.	Mean ± SD	Z-value	P-value
Case Group	5.31±1.29	9.46	P<0.0001
Control Group	2.87±0.54		S

The above table shows the comparison between the BT values in the cases and controls, when compared the result was found to be highly significant.

Table 2 –Comparison of mean BT in PIH Mild, PIH Severe and eclampsia

	Mean	SD	F-value	P-value
PIH Mild	4.79	1.59	3.85	P=0.027
PIH Severe	5.75	0.95		S
Eclampsia	5.49	0.64		

The above table shows the comparison of BT between the subgroups of PIH, the result was significant.

Table 3 – Comparison of Mean CT in mins of patients in Groups:

CT in mins.	Mean ± SD	Z-value	P-value
Case Group	6.01±1.23	8.48	P<0.0001
Control Group	4.38±0.82		S

The table shows comparison of CT between ,case group &control group which was found to be significant.

Table 4 –Comparison of mean CT in PIH Mild, PIH Severe and eclampsia

	Mean	SD	F-value	P-value
PIH Mild	5.44	1.39	14.7	P<0.0001
PIH Severe	6.84	0.58		S
Eclampsia	5.30	0.70		

The above table shows the comparison of CT between the subgroups of PIH, the result was significant.

DISCUSSION:
The study revealed increase in the BT in cases as compared to the control group, BT takes into account primary haemostasis i.e. defect in the platelet plug formation (platelet function) and/or vascular component defects. The rise in BT in PIH can be due to thrombocytopaenia which can be due to consumptive coagulopathy, the platelets adhere to the damaged endothelium resulting in destruction of platelets and also there are qualitative defects in the platelets showing less response to the aggregation stimulus[1]. BT is also prolonged due to generalized vasoconstriction which cannot cause further vasoconstriction for the platelet plug formation [18]

Our study result is in correlation with the study done by Girija P[22]. et al were the mean BT in case group was 5.03±1.52min and in control group was 3.65 ±0.9min, with $p<0.01$, the study by Vijaya Lakshmi et al[23] , were the mean BT in PIH patients was increased than the mean BT of normal control group with highly significant $p<0.0005$.

Our study result is in antagonism to the study done by Vennila et al [24], Chaware S. et al showing, that the bleeding time is not significantly prolonged in pre-eclamptic cases as compared with the control group of normal pregnant females.

Comparison of BT in subgroups of PIH cases:
In our study, BT in mild pre-eclampsia was less affected and it was much prolonged in severe pre-eclampsia group. This signifies that there is prolongation of bleeding time with the severity of the disease

Our study result is analogous to the study done by Upam Kumar Sharma[5], Priyanka Chauhan[25] Vijaya Lakshmi[23] also showing significant increase in BT values when the subgroups were compared among themselves $p<0.05$.

Our study results were in oppose to the results of S R Joshi[12], Suresh Arjunrao[18], Chaware S A [6], where the prolongation of BT among the sub-groups when compared among each other was not statistically significant. Study done by many authors Agrawal et al, Jambhulkar et al [26], Antony et al found that, there is no correlation of prolongation of BT with the severity of PIH.

CLOTTING TIME:
The study revealed increase in the CT in cases as compared to the control group. Clotting time done by capillary tube method utilizes both the intrinsic pathway and extrinsic pathway, so any defect in intrinsic or extrinsic pathway can lead to prolongation of clotting time. In PIH there can be prolongation of CT values, due to the coagulation failure which is the most dreaded complication of pre- eclampsia and eclampsia [27]

Our study is in correlation with the study done by Vennila et al[24] ,Girija Priyadarshini[22] et al Vijaya Lakshmi et al [23]where the increase in the clotting time in cases of PIH was found to be increased significantly as compared to controls with the $p<0.0005$.

Many studies have shown that there is no correlation between the cases and controls in the CT values; study done by Suresh et al[18] showed there is minimal increase in the CT values in PIH cases which is not statistically significant. Study done by Chaware S. A.[6] also shows no significance with $p>0.05$.

Comparison between CT values among the PIH subgroups:
In our study, CT in mild pre-eclampsia was less affected and it was much prolonged in severe pre-eclampsia group, this signifies that there is prolongation of clotting time with the severity of the disease. In severe cases there is increased consumption of platelets with decrease in the synthesis of platelets and clotting factors due to the involvement of liver, which can prolong the CT.

Our study is in correlation with the study done by vijaya Lakshmi[23] et al, where there is statistically significant prolongation of CT with increase in the severity of PIH. Upam Kumar [5], Shete Anjali and Bellar et al also showed a prolongation of CT with the increase in the severity of the disease, but it was not statistically significant.

Our result is in opposition to the study done by jambhulkar et al[26], Priyanka Chauhan [25]where when the subgroups were compared there was no significant change in values.

CONCLUSION
There is unambiguous derangement of the haemostatic parameters in the patients of pre-eclampsia and eclampsia as compared to the normal pregnant females.

- The change in the coagulation profile seen in the PIH patients shows a linear trend with the increase in the severity of the disease,

and as the disease progresses the haemostatic picture is deranged more.

- So bleeding time and clotting time, is a prognostic marker in the study of PIH, and its early detection can prevent lethal complications like DIC and HELLP syndrome.

Recommendations of the study are:

- Coagulation study is the simple, cost effective and easily available tool in many hospitals, so baseline complete blood count should be mandatory for all the pregnant females, as nadir platelet count can be detected early in the cases of PIH, should be under regular scanning by doing bedside BT and CT.
- We feel there is need for more sophisticated studies (platelet count), to know the pathophysiology of the disease, so it can be detected early in the course and can be managed more effectively.

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