Coagulation Abnormalities in Pre-Eclampsia-A Study of 40 Subjects.

M H MENGAL* M TAYYAB** Z HUSSAIN*** S ANJUM****
*Department of Pathology, Bolan Medical College Quetta
** Department of Pathology, Postgraduate Medical Institute, Lahore
*** Department of Pathology, King Edward Medical College, Lahore
**** Department of Pathology, Ayub Medical College, Abbottabad
Correspondence to Dr. Muhammad Hanif Mengal

A study of forty diagnosed cases of Pre-eclampsia (P.E) was carried out in Services hospital , Ganga Ram hospital and Lady Wellingdon hospitals of Lahore. Pre-eclampsia complicates about 10-12% of pregnancies .Some of these patients are at risk of developing coagulopathies such as DIC and HELLP syndrome . In the present study coagulation profile and liver function tests were performed in the pre-eclamptic cases to see whether some tests could be used to predict coagulopathy in such cases. The study showed that prothrombin time, activated partial thromboplastin time and liver function tests were normal in all the cases. The hemoglobin level and platelet count were low while ESR was high in pre-eclamptic cases when compared with comparable normal control pregnant women .The FDP's and D-dimers were raised in most of the cases of P.E especially those with severe pre-eclampsia .It was also concluded that D-dimer test is more sensitive as compared to FDP's.

Key words Coagulation, pre-eclampsia

Hypertensive disorders of pregnancy especially pre-eclampsia and eclampsia are important causes of both maternal and infant morbidity and mortality worldwide (Rana 1998). Young primigravida under 20 years and all patients over the age of 30 years have an increased incidence of pre-eclampsia with increased perinatal mortality (Davey 1995). Depending upon the severity of clinical and laboratory features P.E is classified as mild to moderate and severe P.E . The term severe P.E is applied when the blood pressure is more than 160/110 mmHg . Such patients have low (<100,000/μl) platelet counts. The HELLP syndrome is a form of severe P.E (Crombleholme1997) .The HELLP syndrome is seen in 2-12 ‰of P.E patients (Neiger et al 1995). It is characterized by hemolysis, elevated liver enzymes and low platelet count. HELLP syndrome is associated with a poor outcome for the mother and her infant (Geary 1997) . According to Lindheimer and Katz (1985) pre-eclampsia complicates 5-10% of all gestations .The incidence is slightly lower (6-7%) in USA while it complicates 10 – 12 % of pregnancies in our population (Parveen and Baig 2000).

Pre-eclampsia is a multi system disorder of pregnancy, with the clinical and diagnostic features of hypertension and proteinuria .Although the causes of this disorder are still unknown, current concepts of pre-eclampsia suggest that generalized dysfunction of the maternal vascular endothelium is a central pathogenic feature . Increased serum levels of factor VIII related antigen , factor VIII coagulation activity, increased serum levels of fibronectin , a disturbance of thromboxane A2/prostacyclin balance and disturbance of nitric oxide production , all support the hypothesis that endothelial cell damage is ultimately involved in the aetiology of pre-eclampsia (Olusi et al 2000). Studies have shown that coagulation abnormalities appear to be an important link in the pathogenesis of pre-eclampsia . It has been confirmed by the findings that the severity of coagulation abnormalities is closely correlated with the severity of the illness (Savelieva eral1995).Early detection of thrombotic changes associated with pre-eclampsia may lead to a better prognosis for the mother and the fetus (Hart et al 1994).The present study was aimed at early detection of thrombotic changes associated with pre-eclampsia . It was designed to see whether some tests could be reliably used to identify cases with increased chances of coagulation abnormalities since such an identification is important to save the mother and the fetus .

Materials and Methods:

A total of sixty subjects were included in the present study. The subjects were selected from Obstetrics and Gynae wards of services hospital, Lady Wellingdon hospital, Lady Aitchison hospital and Sir Ganga Ram hospital of Lahore . The subjects were divided into patient group and control group. The patient group included forty diagnosed patients of pre-eclampsia . The control group included healthy pregnant women . Blood and 24 hours urine samples were collected in both groups. Blood samples were divided into different aliquots containing EDTA, 3.8% trisodium citrate and one without any anticoagulant. On the EDTA sample blood complete examination including haemoglobin ,ESR,TLC,DLC and platelet counts were performed . On the other sample with trisodium citrate, PT, APTT, FDP's and D-dimer tests were performed. On the clotted sample serum bilirubin and SGPT enzyme levels were estimated . The urine sample was subjected to 24 hours urinary protein estimation ..

Results

Clinical features

In the patient group 15(37.5%) subjects were in the subgroup of mild to moderate pre-eclampsia i.e their blood pressure was less than 160/110 mmHg ,while 25 (62.5%)

patients had marked elevation of BP (i.e above 160/110mmHg) and they were labelled as having severe pre-eclampsia.

Pre-eclampsia was seen more in primigravida i.e., 26(65%) while only 14(35%) patients were multigravida .Pre-eclampsia was commonest in the 30-39 years age group i.e 30(75%) followed by 20-29 years age group i.e., 8(20%) patients. Minimum number of patients 2(5%) were seen in the 40 years or above age group.

Laboratory findings

Haemoglobin and platelet count was low while TLC, ESR 24 hour urinary protein, FDP's and D-dimer levels were high in the patient group, when compared to the normal control group. PT, APTT and liver functions tests were normal in both the patient and control groups.

	Mild to moderate P.E (mean±SD)	Severe P.E (mean±SD)	Control (Mean ± S.D)
Hb	9.4 ± 1.39	8.84 ± 1.5	11.42±0.27
TLC	6.08 ± 1.18	9.22 ± 1.95	6.0±0.93
ESR	23.4 ± 12.03	46.8 ± 25.41	9.75±3.37
Platelets	146.2 ± 66.99	129.44 ± 63.75	256.2±69.91
PT	14.86 ± 3.14	14.68 ± 3.57	12.85±1.46
APPT	38.37 ± 4.28	37.72 ± 5.88	34.0±2.88
S Bilirubin	0.67 ± 0.16	0.76 ± 0.38	0.58±.09
AST	25.93 ± 7.02	26.2 ± 4.39	22±5.03
Urinary Protein	2.1 ± 0.88	6.08 ± 0.79	0.11±0.05

FDP's

<10µg/ml	Mild to Mod P.E Cases	Severe P.E Cases	Control Cases
<10mg/ml	11(73.33%)	11(44.0%)	20(100%)
≥ 10<40	03(20%)	11(44.0%)	
≥40 mg	01(6.67%)	03(12.0%)	
Total	15	25	20

D-dimer test:

ng/ml	Mild to Moderate Cases	Severe Cases	Control Cases
<250	09(60%)	09(36%)	20(100%)
250-500	03(20%)	09(36%)	
500-1000	02(13.33%)	04(16%)	
1000-2000	01(6.67%)	04(16%)	
>2000	-	04(16%)	
Total	15	25	

Discussion

Though haemoglobin level was low in the control group but it was even lower in the patients of pre-eclampsia. These findings are consistent with those of Bain(1989) and Firkin(1989) . Total leucocyte count was within the normal range in both the patients & control groups. In the pre-eclamptic patients ESR was higher than the controls. In severe pre-eclamptic cases it was higher than that seen in the patients of mild to moderate pre-eclampsia. These findings are consistent with the findings of Rehmani et al (1997) who concluded that ESR increases with the severity of pre-eclampsia.

The platelet count is lower in the patient group and it closely correlates with the severity of pre-eclampsia. The same was reported by Pritchard et al (1954) Bonnar et al (1971) and Trofatter et al (1989) and according to them the fall in platelet count is due to their consumption during intravascular coagulation. The fall in platelet count seems to be an early detectable abnormality in pre-eclampsia and according to Redman et al (1978) the fall in platelet count is related to the severity of pre-eclampsia . The results of PT & APTT are not much different in the patient and control groups. The same was observed by Kelton et al (1985) and Trofatter et al (1989). The findings of Serum Bilirubin and AST enzyme level were within normal limits in both groups (i.e patient & control). Proteinuria was significantly higher in the patient group. Davey et al (1995) also found a close correlation in the severity of Pre-eclampsia and proteinuria.

FDP's

In the present study significantly higher levels of FDP's were detected in the patients with pre-eclampsia when compared with normal pregnant controls. These findings were consistent with the observations of Henderson et al (1970). Kobayashi and Terao (1987) in their extensive study observed the same and they considered pre-eclampsia as a transitory state between normal pregnancy and acute disseminated intravascular coagulation (DIC) and termed the condition as chronic DIC.

D-dimmer assay:

In the present study D-dimmer levels were significantly higher in patients of pre-eclampsia than normal pregnant controls. Trofatter et al (1989) also observed the same and concluded that D-dimmer is more sensitive than FDP assay. In the present study D-dimmer levels were higher in many subjects of pre-eclampsia in whom FDPs were negative. The same was concluded by Kobayashi and Terao (1987) and according to them the D-dimmer test was more sensitive. In the present study it is concluded that D-dimmer assay is a very sensitive, adequate and cost effective screening test as compared to other routine parameters for the detection of coagulation abnormalities accompanying pre-eclampsia . It is also concluded that in all cases of P.E blood complete examination including ESR and platelet count and D-dimmer tests should be performed at regular intervals in order to detect an impending coagulopathic crisis at an early stage.

References

1. Olusi S O, Diejomaoh M, Omu A, Abduaziz A, Prabha K. Interlenkins in pre-eclampsia . Ann Saudi Med 2000; 20(1): 4 - 7
2. Saveliera G M,EffimoveVS, Grislim V L, Sahalina R I, Kashezheva A Z. Blood coagulation changes in pregnant women at risk of developing pre-eclampsia . Int J Gynaecol Obstet 1995;48(1):3 – 8.
3. Hart R, Bate I, Dinh D, Elms M, Bundesen P, Hillyard C, Rylatt D B. The detection of D-dimmer in plasma by enzyme immunoassay: improved discrimination is obtained

with a more specific signal antibody. Blood coagulation 1994;.5: 27 – 32.
4. Bain BJ. In eds . Blood cells, practical guide . Philadelphia JB Leppincot co 1989; 144 – 64.
5. Firkin F, Chesterman C, Pennigton D, Rush B eds. De Gruchy s clinical heamatology in medical practice 5th Ed. Oxford : Blackwell scientific publications 1989; 37 – 61, 102 – 18, 216 – 35.
6. Rehmani MT. Antithrombin III levels in pre-eclampsia .Thesis, Lahore. University of the Punjab 1997.
7. Pritchard JA, Weisman R, Ratnoff OD, Vosburgh GT. Intravascular hemolysis, thrombocytopenia and other hematologic abnormalities associated with severe toxemia of pregnancy . N Eng J Med 1954; 250: 89 – 98.
8. Rana S . Hypertessive disorders in pregnancy. In Rana S eds. Obstetrics and perinatal care for developing countries. 1st ed. Islamabad S A F publications 1998;1176 – 99.
9. Davey DA . Hypertensive disorders of pregnancy In: Whitfield CR eds. Dewhurst's test of obstetries and Gynaecology for post Graduates.
10. 5th Ed. Philadelphia: Blackwell scientific publications 1995:175 – 215 .
11. Lindheimer MD, Katz AI. Pre-eclampsia : pathopliysiology, diagnosis and management. Ann Rev Med 1989; 40: 233 – 50.
12. Parveen K, Baig M. Influence of blood pressure changes with and without proteinuria upon outcome of pregnancy .The professional 2000; 7 (1) 62-65.
13. Cromble holme RD. Obstetrics current Medical Diagnosis and Treatment 35th Ed. Lange Medical Book 1997: 671 – 92.
14. Neiger R, Trofatter MO, Trofatter KF. D-dimer test for early detection of HELLP syndrome. South Med J 1995;88(4):416 – 19.
15. Geary M. The HELLP syndrome. Br J Obstet Gynaecol 1997;104:887-91.
16. Bonnar J, McNicol GP, Douglas AS . Coagulation and fibrinolytic system in pre-eclampsia . Br Med J 1971; 2 : 12 – 6.
17. Trofatter KFT, Howell ML, Greenberg CS, Hage ML. Use of the fibrin
18. D-dimer in sereening for coagulation abnormalities in pre-eclampsia . Obstet Gynaecol 1989; 73: 435.
19. Redman CWG, Bonnar J, Beilin L. Early platelet consumption in pre- eclampsia . Br Med J 1978;1:467.
20. Kelton JG, Hunter DIS, Neame PB. A platelet function defect in pre-eclampsia . Obstet Gynaecol 1985;65:107 – 109.
21. Handerson AH, Pugsley DJ, Thomas DP, Fiber degradation products in pre-eclamptic toxemia and eclampsia .Br Med J 1970; 3 : 545 – 7.
22. Kobayadshi T, Teroa T. pre-eclampsia as chronic disseminated intravascular coagulation. Study of two parameters.Thrombin Antithrombin III complex and D-damers.Gynecol obstet Invest 1987;24:170 – 8.
23. Terao T, Maki M, Ikenour T, Gotoh K, Murata M, Iwasaki H et al. The relationship between clinical signs and hypercoagulable state in toxemia of pregnancy .Gynaecol obstet Invest 1991; 31 : 74 – 85