Journal of Clinical and Biomedical Sciences

Journal homepage: www.jcbsonline.ac.in

Brief Communication

Evaluation of plasma fibrinogen and plasma fibrin degradation product (FDP) in Preeclampsia.

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Received: 05th October –2013 Accepted : 25th November - 2013 Published: 30th December - 2013

Abstract

Background: Preeclampsia is one of the commonest complications of pregnancy. It is associated with a state of hypercoagulability. The present study aimed to estimate the plasma fibrinogen and plasma FDP levels in preeclampsia compared to normal pregnancies. ***Materials and Methods:*** This is a case-control hospital based study carried in the Department of Biochemistry M.G.M. Medical College and associated M.Y. Hospital, Indore (M.P., India). Normal pregnant women (n=36) and women with preeclampsia (n=64) in their third trimester were included in the study. Preeclamptic group was classified in to mild (n=42) and severe (n=22) preeclampsia. Plasma fibrinogen and FDP levels were analysed, and compared between the groups. ***Results:*** Preeclampsia and normal pregnancy groups were comparable for age and body mass index but preeclampsia group had higher blood pressures and less period of gestation ($p<0.0001$). The levels of plasma fibrinogen (654.5±131.74 vs. 491.52±81.7 mg/dL) and plasma FDP (10.96±2.32 vs. 5.54±0.8 µg/L) were higher in the preeclampsia group as compared to normal pregnancy ($p<0.0001$). Elevations in fibrinogen and FDP levels were more marked for severe preeclampsia group than mild preeclampsia group. ***Conclusion:*** Preeclampsia is associated with high fibrinogen and FDP levels as compared to normal pregnancies. Severe preeclampsia patients have greater elevations as compared to mild preeclampsia patients.

Key words: Fibrin degradation products, Fibrinogen, pre-eclampsia.

Introduction

Preeclampsia is a systemic disease characterised by hypertension, oedema and proteinuria. Haematological, genetic and immunological factors play role in preeclampsia aetiopathogenesis. Fibrin deposit in vascular and endothelial area of many organs and placenta is the well-known feature of this disease [1]. Preeclampsia is a major cause of maternal morbidity and mortality in the world. It develops in 5-8% of human pregnancies [2].

Normal pregnancy is associated with impressive changes in the haemostatic mechanism and is a hypercoagulable state associated with increase in many coagulation factors. Coagulation and fibrinolytic systems undergo major alteration associated with reduced fibrinolytic activity and increased levels of fibrinogen and FDP in normal pregnancy which has been reported in many studies[3,4]. It has been hypothesised that preeclampsia is a generalised intravascular inflammatory response, which occurs in normal pregnancy too, but is more exaggerated in preeclampsia [5]. Endothelial cell dysfunction and inflammation are considered to have a role in the pathophysiology of preeclampsia [6]. Mediators of an inflammatory response like plasma fibrinogen are altered in preeclamptic women. A systemic inflammatory response involves both the immune system and clotting and fibrinolytic system [7] . An excess of FDP with diminished or normal systemic fibrinolytic activity suggests that local intravascular fibrin deposition and fibrinolysis occur in preeclampsia. The high level of FDP is associated with the pathogenesis of the defective haemostasis in preeclampsia [8]. Increased fibrinolytic activity in preeclampsia patients has been reported earlier, resulting in increased levels of FDP [9,10] . So this study intended to estimate the plasma fibrinogen and plasma fibrin degradation product (FDP) levels in preeclamptic pregnant women and compare them with normal pregnant women

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Quick access Code

in their third trimester.

Materials and Methods

This case control study was conducted in the Department of Biochemistry M.G.M. Medical College and associated M.Y. Hospital, Indore, Madhya Pradesh, India. The subjects were pregnant women clinically diagnosed as preeclampsia during third trimester (28-40 weeks) with the age 18-35 years visiting obstetrics OPD and wards of MY Hospital, Indore. Sixty-four consecutive preeclampsia patients were included in the study. Preeclampsia patients were classified in to mild preeclampsia (n=42) and severe preeclampsia (n=22) women. As a control group 36 pregnant women without evidence of any illness were taken. The normal pregnant women were also in the third trimester (28-40 weeks) of their pregnancy with the age 18-35 years. Inclusion criteria for women included in the study were: should not be using any kind of oral contraceptives, anticoagulant drugs, should be non-smokers and non-alcoholics. Exclusion criteria were: past history of diabetes, systemic or endocrine disorder, chronic infection, chronic renal disease, previous history of hypertension, women in active labour, were excluded from the study.

Preeclampsia was diagnosed according to American College of Obstetrics and Gynecology (ACOG) criteria: a blood pressure higher than 140/90 mm Hg and proteinuria more than 300 mg/24hour were observed on at least two occasions more than 6 hours apart after the 20th week of pregnancy. Preeclamspia was classified as severe if diastolic blood pressure increased to at least 110 mmHg, proteinuria >5000 mg per day and the presence of headache, visual disturbances, epigastric pain, oliguria, elevated liver function tests, elevated renal function tests, thrombocytopenia.

Blood samples for plasma fibrinogen and FDP was collected into test tubes containing 1 ml of 3.8% sodium-citrate. Centrifugation of these specimens was done for ten minutes at room temperature and at 2500xg. Plasma fibrinogen was estimated by Clauss method using Start analyser -a compact 4-channel coagulation instrument. The levels of FDP were investigated using latex immunoturbidimetric method based on the principle of ELISA. The results were expressed as mean ± SD and groups were compared using ANOVA. Statistical analysis was carried out by using SPSS software, version 20. The level of significance was set at < 0.05.

Results

Maternal age and body mass index (BMI) were comparable in the preeclampsia and normal pregnancy groups (Table 1). Gestational age was lower while systolic and diastolic blood pressures were significantly ($p<0.0001$) higher in preeclamptic patients as compared to normal pregnant women (Table 1). Average values of fibrinogen and FDP were higher for the preeclamptic pregnant patients as compared to normal pregnancy group ($p<0.0001$), although the normal pregnant group also showed elevated levels of fibrinogen than the normal range (200-400 mg/dL). Fibrinogen (727.95 vs 616.02 mg/dL, $p<0.05$) and FDP levels were significantly higher in severe preeclampsia group than in the mild preeclampsia group (12.28 vs. 10.27 µg/L, $p<0.001$).

Parameters	Normal pregnant women (n=36)	Preeclamptic pregnant women (n=64)	Mild preeclamptic pregnant women (n=42)	Severe preeclamptic pregnant women (n=22)
Age (years)	23±2.62	23.14±2.97	22.90±2.96	23.59±2.98
BMI (kg/m^2)	24.17±1.91	24.66±1.84	24.87±1.76	24.26±2.07
Gestational age (weeks)	39.13±2.82	36.68±1.78	37.19±1.65	35.72±1.54
Systolic blood pressure (mm of Hg)	114.72±6.96	148.10±15.78	139.52±5.38	164.5±16.17
Diastolic blood pressure (mm of Hg)	74.44±5.03	100.15±12.11	94.04±7.26	111.81±10.97
Plasma fibrinogen (mg/dL)	491.52±81.7	654.5±131.74	616.02±124.65	727.95±118.91
Plasma FDP (µg/L)	5.54±0.8	10.96±2.32	10.27±2.39	12.28±1.57#

Table:1- Clinico-biochemical features in the normal and preeclampsia groups

Discussion

In the present study, the plasma fibrinogen and FDP levels were significantly higher in preeclampsia, more so in the severe preeclampsia women as compared to mild preeclampsia. Enhanced coagulation-fibrinolysis and coagulopathy are well known features of preeclampsia [11]. Fibrinogens are the major coagulation heterogeneous protein and it is symmetrical glycoprotein of 340 KD molecular weight. The results of our study showed that in preeclampsia the level of plasma fibrinogen was higher as compared to normal pregnancy and reconfirms the results from earlier studies[12,13].The increase of fibrinogen in preeclampsia results from the exaggerated inflammatory response and subsequent endothelial dysfunction and activation which are currently believed to be the key pathophysiological mechanism in preeclampsia [12]. The increase in fibrinogen in normal pregnancy is also due to the inflammatory responses which explain that fibrinogen

is the acute phase reactant-marker of inflammation, in both normal pregnancy and preeclamptic pregnancy. The increase of fibrinogen in normal pregnancy may also be due to utilisation in uteroplacental circulation, enhanced synthesis and also due to hormonal changes like oestrogen synthesis [14].

Fibrin degradation products (FDP) are components of the blood produced by clot degeneration. These are the substances left behind when clots dissolve in the blood. These are produced by the action of plasmin (proteolytic enzymes) on deposited fibrin. Excess FDP can cause severe haemostatic defects [15]. High plasma FDP levels in our preeclamptic patients are in agreement with the finding of others [16,17]. In this study, raised plasma FDP levels indicate increase in fibrinolytic activity and concurs with the previous finding which showed an intravascular coagulation disturbance observed in patients with preeclampsia [17,18]. However, more research in this field is warranted.

Our study concluded that increase in plasma fibrinogen explains it to be an acute phase reactant indicating the exaggerated inflammatory responses in preeclampsia and the endothelial activation which are believe to be the pathophysiological mechanism in preeclampsia. Also the elevated FDP indicates the increased intravascular coagulation in preeclampsia and increased in fibrinolytic activity. Both are thus the complementary predictors explaining the severity of the disease.

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