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Factor VIII Complex in Normal Pregnancy and Preeclampsia

TAYSSIR K. EYADA, M.D.; HODA A. SADEK, M.D.;
SHERIF M. KHATTAB, M.D. and TAREK, M. ELTERBY, M.D.
*The Departments of Clinical Pathology and Gynecology &
Obstetrics, Faculty of Medicine, Cairo University.*

Abstract

Factor VIII : C by immunodepleted plasma, von Willebrand factor by enzyme immunoassay and platelet count were determined in 30 adult pregnant females including 10 normal healthy pregnant females, 10 mild and 10 severe preeclamptic pregnant females. Factor VIII : C and von Willebrand factor were increased during normal pregnancy due to increase in synthesis, and markedly increased with the development of preeclampsia due to vascular injuries and uteroplacental lesions that occur with preeclampsia. Platelet count was nearly normal during normal pregnancy, but in mild preeclampsia, the platelet count was decreased and more significant decrease was found in severe preeclampsia. This decrease in the platelet count may be due to increased turnover of platelets and increased platelet consumption in the process of chronic disseminated intravascular coagulation present in preeclampsia. The measurement of factor VIII : C and von Willebrand factor and platelet count during pregnancy may be of help in the diagnosis and prognosis of preeclampsia.

Introduction

DURING pregnancy major changes occur in the components of the haemostatic system, these are detectable from as early as the first trimester and are presumably designed to prevent haemorrhage at delivery.

Fournie et al.[1] demonstrated that both factor VIII coagulant and the von Willebrand factor components of factor VIII complex increase progressively in nor-

mal pregnancy with the maximum values obtained at delivery. They also found that in pregnancies complicated by preeclampsia or intrauterine growth retardation, elevations of plasma von Willebrand factor levels were proportional to the severity of the disease. These findings were also reported by Thorp et al[2].

The aim of this work is to make a comparative study of factor VIII complex in normal pregnancy and pregnancy complicated by preeclampsia.

Material and Methods

Thirty pregnant females were included in this study. They were either attending the Outpatient Obstetrics and Gynecology Clinic or inpatients in the Obstetrics and Gynecology Department, Faculty of Medicine, Cairo University. They were categorized into three groups :

A) Normal pregnant females :

This group included 10 adult pregnant females. Their ages ranged between 20 and 37 years, with a mean of 28.20 ± 5.57 . They were all healthy with no clinical or laboratory evidence of preeclampsia, multiparae multigravidae, 35-38 weeks of gestation, with no fetal growth retardation and no fetal abnormalities. Also, they were not diabetic, with no rhesus disease, no twins, no placental abnormalities, so they all had completely normal, uncomplicated pregnancy.

B) Mild preeclamptic pregnant females :

This group included 10 adult pregnant females. Their ages ranged between 21 and 44 years, with a mean of 31.00 ± 6.67 . They were all hypertensive with a blood pressure of nearly 140/90 mmHg (30 mmHg rise in systolic pressure above the pregnant level and 15 mmHg rise in diastolic pressure, measured on at least two occasions, six or more hours apart). They were suffering from oedema of the lower limbs and proteinuria more than 3g/24 hours. All were multiparae multigravidae, 35-48 weeks of gestation, with no fetal growth retardation and no fetal abnormalities. Also, they were not diabetic, with no rhesus diseases, no twins; so all

had clinical and laboratory manifestations of mild preeclampsia.

C) Severe preeclamptic pregnant females :

This group included 10 adult pregnant females. Their ages ranged between 21 and 34 years, with a mean of 26.20 ± 6.76 . They were all hypertensive with a blood pressure of nearly 160/110 mmHg or higher on two occasions, six hours apart. They were suffering from oedema of the lower limbs and proteinuria of 5 or more/24 hours. All were multiparae multigravidae, 35-38 weeks of gestation, with no fetal growth retardation no fetal abnormalities. Also, they were not diabetic, with no rhesus diseases, no twins so they all had clinical and laboratory manifestations of severe preeclampsia.

All subjects were subjected to the following investigations :

A) Full clinical examination :

This included history taking, age, blood pressure recording, examination of oedema of the lower limbs, period of gestation and full obstetrical and gynecological examinations to assess the state of pregnancy whether normal or preeclamptic.

B) Full obstetrical and gynecological investigations :

To assess normal pregnancy and pregnancy induced hypertension.

C) Laboratory investigations :

I) General tests :

- a) Total proteins in urine.
- b) other tests to assess normal pregnancy and preeclampsia.

II) Specific tests :

1. Assay for factor VIII : C by immunodepleted plasma :

Principle :

It is one-stage assay which consists of the measurement of the clotting time in the presence of cephalin and activator, of a system in which all the factors are present, constant and in excess except factor VIII which is derived from the sample. Using log-log graph paper provided the percentage of factor VIII activity with its corresponding clotting time were plotted. Factor VIII : C level of the plasma to be tested was deduced from the calibration line.

2. Assay for von Willebrand factor by enzyme-linked immunosorbent assay (ELISA) :

Principle :

A plastic support coated with specific rabbit anti-human vWF antibodies captures the vWF to be measured. Next, rabbit anti-vWF antibody coupled with

peroxidase binds the remaining free antigenic determinants of vWF, forming the «sandwich». The bound enzyme peroxidase is then revealed by its activity in a predetermined time on the substrate orthophenylene-diamine, in the presence of hydrogen peroxide. After stopping the reaction with a strong acid, the intensity of the color produced bears a direct relationship with the vWF concentration initially present in the plasma sample.

3. Platelet count .

Results

Table (1) demonstrates statistical analysis of Factor VIII : C by immunodepleted plasma among normal pregnant and preeclamptic patients.

Table (2) demonstrates statistical analysis of vWF by ELISA among normal pregnant and preeclamptic patients.

Table (3) demonstrates statistical analysis of platelet count ($\times 10^3$) among normal pregnant and preeclamptic patients.

Table (1) : Factor VIII : C by Immunodepleted Plasma Among Normal Pregnant and Preeclamptic Patients.

Groups	Mean \pm S.D	Range	ANOVA Results*
Normal pregnancy	119.0 \pm 8.1	104 - 126	C
Mild Preeclampsia	135.2 \pm 4.1	130 - 140	B
Severe preeclampsia	153.8 \pm 10.9	140 - 170	A

P-value* < 0.001

Table (2) : vWF ELISA Among Normal Pregnant and Preeclamptic Patients.

Groups	Mean \pm S.D	Range	ANOVA Results*
Normal pregnancy	106.3 \pm 6.7	90 - 115	C
Mild Preeclampsia	125.3 \pm 3.7	120 - 130	B
Severe preeclampsia	145.0 \pm 9.1	135 - 160	A

P-value* < 0.001

Table (3) : Platelet Count ($\times 10^3$) Among Normal Pregnant and Preeclamptic Patients.

Groups	Mean \pm S.D	Range	ANOVA Results*
Normal pregnancy	286.0 \pm 111.9	150 - 430	A
Mild Preeclampsia	130.9 \pm 9.3	118 - 145	C
Severe preeclampsia	97.8 \pm 11.4	79 - 115	B

P-value* < 0.001

ANOVA results = Analysis of variance results, group means sharing same letter are not significantly different than each other.

P-value < 0.05 is considered significant.

Discussion

Factor VIII : C levels were 119.0 \pm 8.1 percent in normal pregnant females, 135.2 \pm 4.1 percent in mild preeclamptic group and 153.8 \pm 10.9 percent in severe preeclamptic group. The three groups were significantly different than each other. The highest level was found in the severe preeclamptic group, and the lowest level in the normal pregnant group.

During normal pregnancy the level of factor VIII complex increases, this phenomenon is possibly related to the develop-

ment of the uteroplacental vessels, a source of synthesis for factor VIII : The maximum value will be at delivery maybe due to the release of factor VIII from the uteroplacental vessels during stress and uterine contractions. This observation agreed with those reported by Bennet and Ratnoff[3]; Bonnar et al[4] and Fournie et al[1].

In preeclampsia, factor VIII : C level showed a progressive increase parallel to the severity of the disease. This was also noticed by, Robertson et al[5]; Boneu et al.[6] and Fournie et al[1].

Von Willebrand factor level were 106.3 ± 6.7 percent in normal pregnant female group, 125.3 ± 3.7 percent in mild preeclamptic group and 145.0 ± 9.1 percent in severe preeclamptic group and the three groups were significantly different than each other. The highest level was found in the severe preeclamptic group, and the lowest level in the normal group.

VWF is an acute phase adhesive protein, it increases in normal pregnancy due to increased synthesis in vascular endothelium. In preeclampsia vWF levels showed a progressive increase in accordance with the severity of the disease, so may provide a specific indicator of vascular injury and a guide to prognosis and treatment. This observation agreed with those reported by, Robertson et al[5]; Killam et al[7] and Fournie et al[1].

The ratio vWF/factor VIII : C was 0.89, 0.93, 0.95 for the three studied groups respectively. These values were nearly equal, and the three groups were not significantly different than each other. This finding agreed with that of Calvin et al[8] who found the ratios in patients and normal pregnancy were indistinguishable. Hellegren and Blomback[9], and Stiling et al.[10] reported that there was a steeper rise in this ratio in normal pregnancy and preeclampsia as the duration of gestation increased towards delivery.

There are many reports in the literature concerning factor VIII complex in normal and pathological pregnancies. All reported increase of factor VIII : C and vWF in normal pregnancies, and further

increase was observed in preeclampsia. The degree of increase was coinciding with the severity of the disease. Our results agreed with those reported by Bergmann et al.[11]; Lebarriere et al.[12]; Weiner[13] and Caron et al.[14].

Platelet counts were $(286.0 \pm 11.9) 10^3$, $(130.9 \pm 9.3) 10^3$ and $(97.8 \pm 11.4) 10^3$ for the three studied groups respectively. The highest count was found in the normal group, then the mild preeclamptic group and the lowest count in the severe preeclamptic group.

Regarding the normal pregnant group, our results agreed with other reported results[15,16].

As regards the mild and the severe preeclamptic groups, the platelet counts were significantly decreased as there is increased turnover of platelets in these women due to increased consumption in the process of chronic disseminated intravascular coagulation present with preeclampsia. These results agreed with other reported results [17,2,16,18,19].

In conclusion : the measurement of factor VIII : C and von Willebrand factor during pregnancy may help to predict vascular injuries and uteroplacental lesions that occur early in preeclampsia. Also they may be of help in the diagnosis and prognosis of preeclampsia.

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