# MODIFICATIONS OF THE COAGULATION FACTORS DURING NORMAL AND PATHOLOGICAL PREGNANCIES

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## SUMMARY

Levels of fibrinogen and fibrin/fibrinogen degradation products (F.D.P.) have been misurated respectivelly by thrombin time and by staphylococcus clumping test in 33 pregnant patients, recovered in the Obstetric and Gynaecological Clinic - University of Padua, during the ninth month of pregnancy.

A control group of 16 normal pregnancies, a second group of 12 hypertensive patients, and a third group of 15 pregnancies who had given birth to rather small babies for date, were considered.

A significative increase (p<0,001) of the F. D. P. values was found both in the pregnant women with hypertension and in those with foetal insufficiency respect to the control group.

The fibrinogen levels did not vary in any of the three groups. During pregnancy, factors promoting and factors obstructing the coagulation are in a different equilibrium.

Among the first, the increase of fibrinogen (6, 15, 20) and of the factors VII, VIII and X (2, 16, 18, 23) is accepted. The increase of the factors II, IX and XII is less significant and not shared by all (4, 18, 19).

Concerning the fibrinolysis, besides the modest increase of plasminogen, there is a heavy fall of its circulating activator (5, 19, 25).

The rise in the concentration of some coagulation factors and, on the other hand, a decrease in the fibrinolysis, leads to a state of hypercoagulation with an increased tendency toward fibrin formation and thrombosis, and to a decreased tendency to thrombi lysis.

The fibrinolitic system acts upon the fibrinogen and fibrin molecules, reducing the primitive molecule into a series of fragments X, Y, D, E with different molecular weight and biological characteristics, but with a prevalently anticoagulant activity of direct antithrombinic type (table 1).

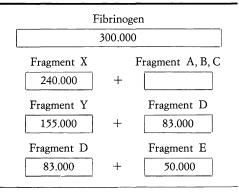
Various Authors have demonstrated an increase in Fibrin Degradation Products (F.D.P.) during the third trimester of pregnancy.

The latter could derive from the lysis of the fibrin deposits at placental level, very frequent during the last trimester of pregnancy.

According to an other hypothesis, the increase in F.D.P. is due to the liberation of activators by the myometrial plasminogen during contractions (23).

The disseminated intravascular coagulation (DIC) is a rare, but very severe complication of pregnancy. It could be due to the presence of circulating thromboplastinic factors, which lead to the conversion of prothrombin into thrombin and therefore to the formation of intravascular thrombi, particularly in the small peripheral vessels.

Tab. 1. — Scheme of the F.D.P. formation.



During pregnancy, the DIC can be associated to a premature separation of the placenta (1), to embolism of amniotic fluid, to prolonged retention of stillbirth (7), to eclampsia (3, 12, 22) and to septicemia.

These pathologic conditions are characterized by an abnormal consumption of fibrinogen, and by a local increase of fibrinolysin at peripheral microcirculating level, and they are associated to an increased concentration of circulating F.D.P.

The acute defibrination is characterized by a sudden clinical symptomatology, which requires a timely diagnosis and treatment.

Nevertheless, more often the modifications of the coagulation are not associated to evident clinical symptoms, since they have a subacute evolution which can only be demonstrated by laboratory examinations.

During pregnancy this occurs in some cases of preeclampsia, essential hyperten-

sion, chronic renal diseases, placental insufficiency.

This research aims to verify if the F.D. P. and fibrinogen serial plasmatic determination is a valid test for a precocious diagnosis of the latent process of intravascular coagulation, before the formation of fibrin's deposits or at least before the onset of irreversible lesions due to these deposits.

## MATERIAL AND METHODS

We have examined 33 pregnant women during the third trimester of pregnancy, classified as follows:

1° control group, including 16 cases of normal pregnancies, in which the outcome was evaluated on the basis of the foetal weight ranging between the 10th and the 90th centile, of the Apgar score higher than 7 and of the normality of the physical examination.

2° group including 12 women affected by hypertension with values of the arterial pressure higher than 100 for the diastolic pressure and 150 for the sistolic one.

3° group including 15 pregnant women who have delivered « small for date » infants.

The fibrinogen was evaluated by the thrombin time (normal values between 150 and 450 mg/ 100 ml).

The F.D.P. were dosed by the agglutination test of the staphylococci. This test is considered pathologic when the F.D.P. concentration is higher than 8 ng/ml.

### **RESULTS**

Table 2 reports the arithmetical mean  $(\bar{x})$  and standard deviation  $(\sigma)$  of the fibrinogen's values in the three groups examined (pregnancies with normal evolution, with hypertension and with chronic placental insufficiency).

Tab. 2. — Fibrinogen mg/100 ml.

Clinic report	N.	Χ	σ	N	CU%
Normal	16	455,25	119,36	29,84	26,22
Hypertension	12	454,58	101,41	29,27	22,31
Insufficient foetal development .	18	411,61	109,53	25,82	26,61

Tab. 3. — F.D.P. ng/ml.

Clinic report	N.	Χ	σ	N	CU%
Normal	16	8,79	12,26	3,07	139,54
Hypertension	12	21,67	21,33	6,16	98,47
Insufficient foetal development .	15	9,87	8,43	2,18	85,47

The fibrinogen levels do not undergo significative modifications in none of the three groups, passing from 455.25 mg/ml in the control group, to 454.58 mg/ml in the hypertension and to 411.61 mg/ml in the placental insufficiency.

The statistical analysis has not shown significant differences (p>0.7 and p<0.8) between the control group and the placental insufficiencies (p between 0.5 and 0.4) between the group of normal pregnant women and those affected by hypertension.

Table 3 shows the mean values and the standard deviation of the FDP in the three groups.

A highly significative difference was found (p<0.001) between the control group and that complicated by hypertension, and also between the control group and the cases of placental insufficiency (p < 0.001).

### DISCUSSION

The evidence of significative plasma levels of FDP shows the formation of fibrin deposits and of microthrombi, probably at hepatic, renal and placental microcirculation.

In the preeclampsia, the placental hystopathology shows a thickening of both the trophoblastic and vasal basal membrane of the villus, a coagulation in the intervillous spaces with formation of platelets and fibrin thrombi, and with a marked alteration of the vessel's endothelium.

The fibrin deposits in the utero-placental circulation, reduces the blood flow, and may be a cause of poor intrauterine foetal growth.

The FDP dosage, on the basis of our results, seems to represent a reliable test for the evaluation of the placental lesions due to alterated coagulation. In particular, this test could show an exagerated lysis of the fibrin deposits in the intervillous spaces, caused by the liberation of trophoblastic material, and by a proteolitic activity.

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