EFFECT OF TOXAEMIAS OF PREGNANCY ON LEVELS OF FIBRINOGEN & FDP IN BLOOD

Thesis

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By

EMAD M. EZZAT

M.B., B.Ch.
Ain-Shams University

Under Supervision of

Prof.Dr. MOHAMED NAGY EL-MAKHZANGY
Prof.of Obstetrics & Gynaecology.
Ain-Shams University

Prof.Dr. SALAH EID
Prof. of Biochemistry
Ain-Shams University

Dr. ALAA EL-DIN EL-ETRIBY
Lecturer of Obstetrics & Gynaecology
Ain-Shams University

FACULTY OF MEDICINE

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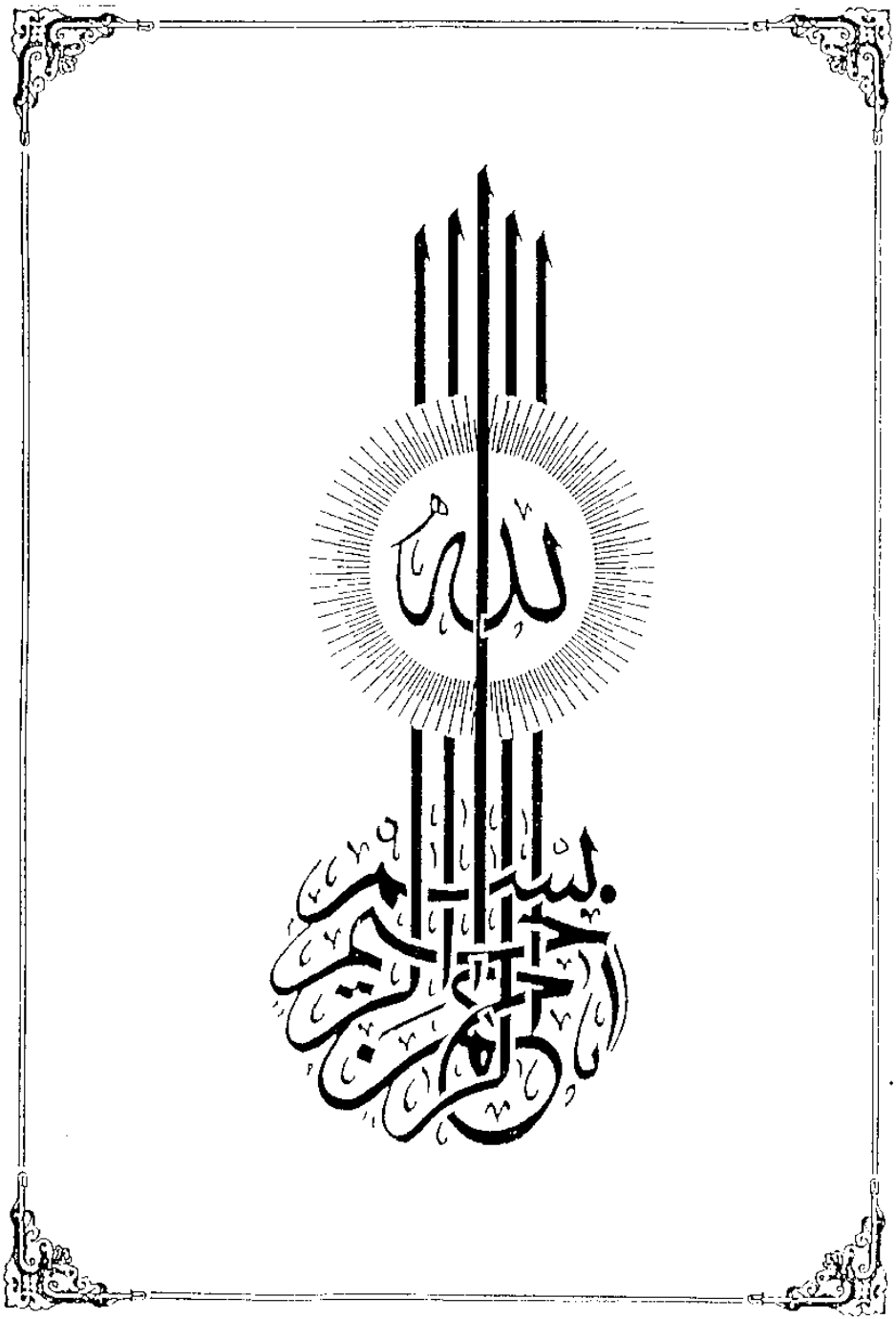
بسم اللـــه الرحمـن الرحيـم

"قالوا سبحانك لا علم لنا الا ما علمتنا
انك أنت العليم الحكيم"

صدق الله العظيم

"الآية ٣٢ من سورة البقرة"



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INTRODUCTION

Although the aetiology of preeclampsia/eclampsia is unclear, there is much evidence for intravascular coagulation in the disease. Widespread fibrin deposition has been a prominent histologic finding in fatal cases of eclampsia (Mc Kay et al., 1953).

Electron microscopy of renal biopsy material from patients with preeclampsia has shown fibrinoid material in the glomeruli, and this material stained with fluorescent-labeled antiserum to fibrinogen indicated intraglomerular deposition and endothelial cell phagocytosis of fibrinogen derivatives (Morris et al.,1964). Also, intervillous fibrin deposition and placental infarcts were accentuated in preeclampsia which resulted in placental insufficiency (Mc Kay, 1964).

Disseminated intravascular coagulation (DIC) has been suggested as a cause or an important secondary mechanism in toxaemia of pregnancy (Pritchard et al.,1954 and Kasper, 1956).

Pritchard et al.,(1976) reported that the coagulation changes in eclampsia may evolve primarily from platelet adherence at sites of vascular endothelial

damage as the consequence of segmental vasospasm and vasodilatation rather than be triggered by escape of thromboplastin from the placenta into the maternal circulation.

Regocczi and Hobbs,(1969) stated that in cases of pregnancy toxaemia, the fibrinogen levels may be even higher than in normal pregnancy where the turnover rate is increased. However Starkie et al.,(1971) stated that appoximately 50% of preeclamptic patients developed either thrombocytopenia, hypofibrinogenemia, hypoplasminogenemia, or combination of the three at some stage before delivery. Lang et al.,(1984) observed an increase in plasma fibrinogen level in cases with preeclampsia compared with control subjects matched for age and gestation, also they noticed an elevation of serum fibrinogen degradation products (FDP) levels in women complicated by preeclampsia.

Henderson et al.,(1970) stated that there is a significant rise in serum FDP in toxaemia, and strikingly increased in eclampsia and this increase is the most sensitive index of DIC. Also, this significant increase in serum FDP in preeclamptic women was reported by Howie et al.,(1971) and Bonnar et al.,(1971).

The measurement of serum FDP provides an accurate method for monitoring the extent of intravascular coagulation and lysis in preeclampsia as the precise determination of serum FDP levels is related to the severity of the disease (Gordon et al., 1976).

AIM OF THE WORK

The objective of this work is to measure the plasma fibrinogen and serum FDP levels in cases of pregnancy-induced hypertension (PIH) in comparison to normal pregnant control group, also to find out if these haematologic parameters have any correlation to the degree of hypertension or amount of proteinuria.

NORMAL PREGNANCY

COAGULATION FACTORS IN NORMAL PREGNANCY

Factor I "Fibrinogen":

Fibrinogen is a plasma glycoprotein synthesised in the liver, serum FDP may be the major regulator for its synthesis through a feed back mechanism (Biggs, 1972). The molecular weight of fibrinogen is approximately 344,000 and the molecule consists of three pairs of polypeptide chains linked by means of disulphide bonds. When fibrinogen is proteolysed by thrombin, two pairs of fibrinopeptides (A and B) are split off producing fibrin monomer (Hermans and McDonagh, 1982). Fibrin monomers polymerize together to form unstable fibrin clot which is stabilized by factor XIII.

Fibrinogen is the only coagulation factor present in sufficient quantity to allow its measurement in terms of milligrams of protein. Its level in plasma normally lies between 2.5 and 4.0 gm per litre, and the level needed for haemostasis is about 1 gm/litre (Letsky, 1985). The fibrinogen half life is about 3 - 6 days.

The plasma fibrinogen level shows a progressive rise starting from the third or fourth month of pregnancy reaching about 6.0 gm/L during late pregnancy and labour. If the increase of plasma volume is taken into consideration, the amount of circulating fibrinogen during late

pregnancy is at least double that of the nonpregnant state. This marked rise in fibrinogen results from increased synthesis (Bonnar, 1978).

This rise in plasma fibrinogen level explains the striking rise in erythrocyte sedimentation rate (ESR) during normal pregnancy (Wintrobe, 1974; Ozanne and co-workers, 1983).

About 5 - 10% of plasma fibrinogen is consumed in the fibrin mesh covering the placental bed after placental separation (Ludwig, 1971).

Factor II "Prothrombin" :

Naumann and Weinstein,(1985) stated that there was no change in the level of prothrombin during normal pregnancy.

Factors III, IV, VI :" in old terminology thromboplastin, calcium ion, and accelerin respectively": Their numbering has been discarded after Ingram et al.,(1982).

Factor V: "Proaccelerin, Labile Factor" :
Naumann and Weinstein,(1985) reported that there was no change in plasma level of factor V in normal pregnancy.

Factor VII: "Proconvertin, Stable Factor" :

Gjonnaesse,(1973) reported that there was an elevation in the level of factor VII during normal pregnancy reached as much as tenfold the non pregnant level.

Factor VIII: "Antihaemophylic factor A, Antihaemophylic globulin (AHG):

A considerable elevation in factor VIII level in late pregnancy including both factor VIII-coagulant activity (factor VIII - C) and factor VIII-related antigen (factor VIII-RA), (Whighan et al., 1979 and Fournie et al., 1981).

Bennett and Ratnoff,(1972) found a parallel increase in both factor VIII - coagulant activity and factor VIII-related antigen, while an increase in the ratio between the antigenic and coagulant activity of factor VIII was observed by Bouma et al.,(1973), and Van Royen & Tengate (1973).

Factor IX: "Christmas factor, Antihaemophylic factor B. Plasma thromboplastin component (PTC)" :

Bonnar,(1978) observed an elevation in factor IX level during normal pregnancy.

Factor X : "Stuart - Prower factor" :

There is higher levels of factor X during normal pregnancy compared with non pregnant controls (Naumann and Weinstein, 1985).

Factor XI : "Plasma thromboplastin antecedent (PTA)" :

Bonnar, (1978) reported that there was a decrease in the level of factor XI during normal pregnancy down to 60 - 70% of the non pregnant value.

Factor XII : "Hageman factor":

An increase in factor XII levels have been observed during normal pregnancy (Van Royen and Tengate, 1973; Biland and Duckert, 1973).

Factor XIII : "Fibrin stabilizing factor":

A gradual fall in factor XIII reaching at term to about 50% of the normal non pregnant value was observed by Coopland et al.,(1969); Kasper et al.,(1964); Talbert and Langdell, (1964).

Some of these altrations in coagulation factors during normal pregnancy may be equated with a continuous low grade process of intravascular coagulation (Fletcher and co-workers, 1979).