CIRCULATING PLATELET AGGREGATION IN PREGNANCY INDUCED HYPERTENSION

THESIS

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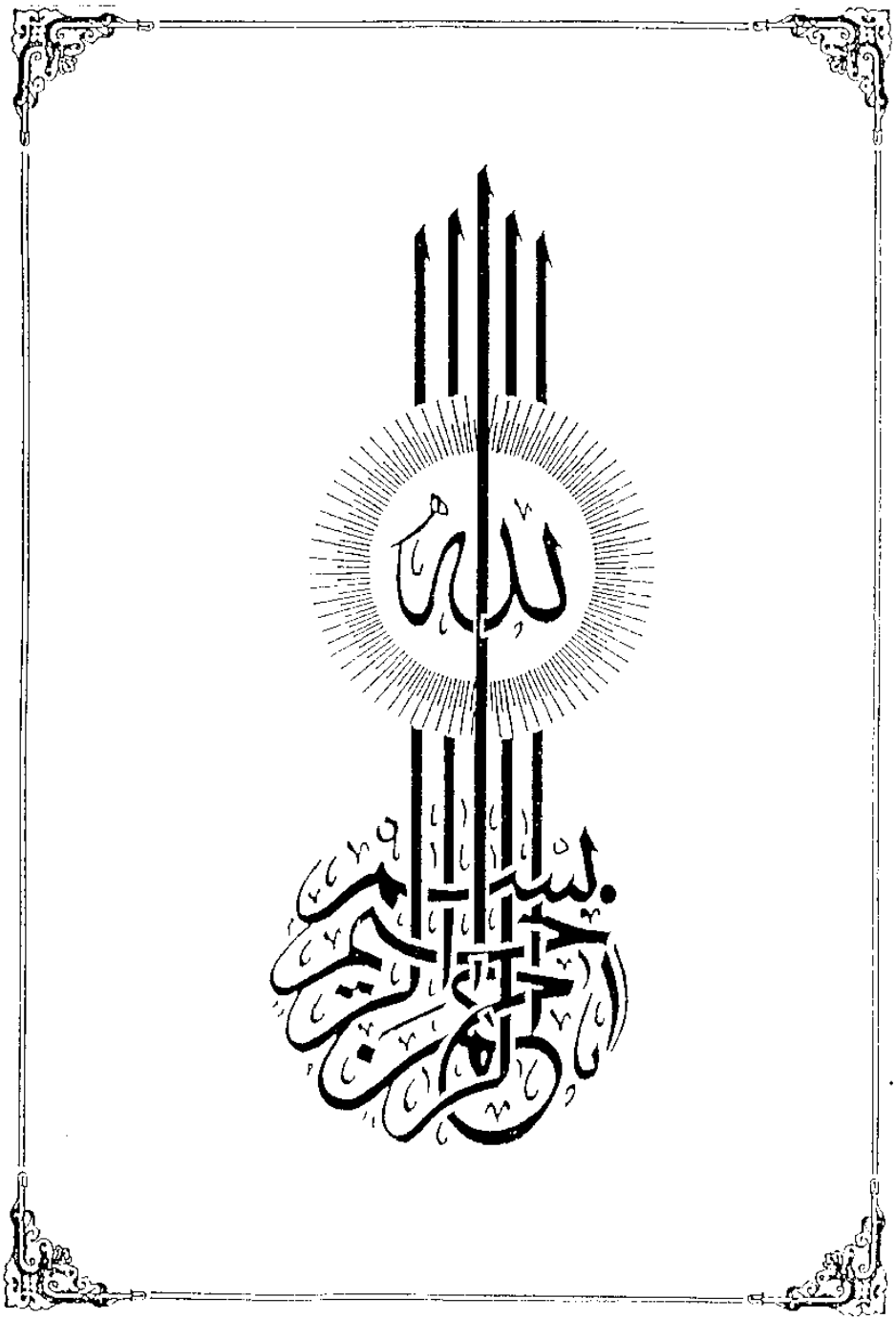

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INTRODUCTION

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Pregnancy induced hypertension is a hypertensive disorder unique to pregnancy occurring primarily in primiparae. Its complications are well understood, but the pathogenesis remains obscure (Gibson, et al, 1982)

Pregnancy induced hypertension involves mild or severe pre-eclampsia (Symonds, 1979). Platelet consumption is an early feature of the disease (Redman, Bonnar and Beillin, 1978).

In 1922, Stahnke stated that thrombocytopenia was present in severe cases of toxaemia of pregnancy associated with increased intravascular coagulation and haemolysis.

It was realized that platelets are not merely trapped passively in pregnancy induced hypertension but their aggregation and the release of their constituents may contribute to the pathogenesis and deterioration of the disease (Wigham, et al, 1978).

Aggregation of platelets in pregnancy induced hypertension may be the result of intra-vascular coagulation (Schneider, 1947) or interaction between platelets and endothelium (Pritchard, Cunningham, & Mason, 1976) or auto immune reaction (Bern, Driscoland Locavitit, 1981).

AIM OF THE WORK

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To study the circulating platelet aggregation (C.P.A.) in pregnancy induced hypertension, which may explain some aspects of pathogenesis of pregnancy induced hypertension.

Few reports have been published about C.P.A. in pre-eclampsia. Most of the reports study the platelet function abnormalities in pre-eclampsia by in vitro platelet aggregation test technique. But who knows that this highly artificial technique reflects the situation in vivo. so, we perform the present work to study the in vivo platelet behaviour in preeclampsia by the in vivo platelet aggregation test of Wu and Hoak (1974) which may directly reflects the behaviour of platelet activity in circulation.

REVIEW OF LITERATURE

I- Hypercoagulability in Normal Pregnancy.

II- The Hemostatic Mechanisms in Pre-Eclampsia.

III- Blood Platelets.

IV- Blood Platelets in Normal Pregnancy.

V- Platelets Changes in Pregnancy Induced Hypertension.

VI- Platelet Aggregation.

VII- Tests for Measurement of Platelet Aggregation.

CHAPTER (I)

HAEMOSTATIC MECHANISM IN NORMAL PREGNANCY

1. **Coagulation factors:**

The over-all effects of pregnancy is to increase the activity of coagulation factors, with the exception of factors XI and XII, and to lower slightly the coagulation innibitors antithrombin III and anti-factor Xa. Detectable changes in the circulating blood are present from the 2nd month of pregnancy.

The plasma level of fibrinogen gradually increases from the 2nd month to reach levels in the range 4.0-6.5 gm/L in late pregnancy and labour. Immediately follwoing delivery a further slight increase in fibrinogen concentration occurs followed by a decline from around day five of the Puerperium to normal values by the fourth week following puerperium (Bonnar; Nichol; Douglas, 1969, & Fletcher et al,1970).

Allowing for the increase of plasma volume, the amount of fibrinogen in the circulating blood near the end of pregnancy approaches double that of the non pregnant state. Fletcher and Colleagues (1970) found that the concentration of high molecular weight fibrin complexes correlate with plasma fibrinogen levels from the 2nd month of pregnancy onward,

reflecting an increase in fibrin formation around three folds over the physiological non-pregnant state at two months gestation and increasing to approximately five fold, or greater in late pregnancy and the early puerperium.

Factor XIII concentration falls steadily during pregnancy, reaching approximately 50 percent of control values at term (Coopland, Alkjaersig & Fletcher, 1969).

Prothrombin or factor II increases to about 117% of the normal level during pregnancy. Pechet and Alexender (1961), reported that only few out of 90 pregnant women showed a significantly elevated values and that the increase Was only to the upper limit of normal which was 120%.

Van Royen 1974 found moderate increase of factor V. Both factor VII and factor X undergo a marked elevation in pregnancy (Kenan & Bell 1957, & Fresh et al. 1956).

Factor VIII activity is markedly elevated in pregnancy, (Kasper,et al 1964), reported an increase in the level of factor VIII during pregnancy that reached 192% of the normal non pregnant value in the last trimester of pregnancy.

Most studies of factor IX during pregnancy have reported either no change or a slight elevation (Nilson and Kullander, 1967).

Factor XII is also increased in late pregnancy (Bonnar, 1978).

In contrast to the general increase of coagulation factors, factor XI is reported to decrease during pregnancy with average levels between 60-70% (Bonnar, 1978).

2. Coagulation inhibitors:

A slight lowering of the level of antithrombin III and antifactor Xa is also found in late pregnancy (Bonnar 1976).

3. **fibrinolytic enzyme system in pregnancy:**

Fibrinolytic activity in plasma decreases markedly during pregnancy, remains depressed during labour and delivery, and rapidly returns to normal within 30-60 minutes of delivery (Bonnar et al. 1970). Fibrinolytic capacity is also decreased, as shown by progressive diminution in the response to venous occlusion as pregnancy advances (Astedt et al. 1970).

The placenta has been shown to contain inhibitors which block urokinase induce fibrinolysis (Bonnar, 1978). This strongly suggested that the inhibition of fibrinolysis is in some way mediated through the placenta.

There is no doubt that fibrinolytic activity is substantially reduced during pregnancy (Biezenski, and Moore 1958), Brackman, 1966 and Shaper et al., 1968). In spite of much research, the mechanism by which this reduction in activity is still obscure. Some authors attributed it to an increaed content of inhibitors in the blood (Biezenski and Moore,

1958; Guest, 1954; Lauritsen, 1969), while others ascribe the condition to decreaed production or release of plasminogen activators (Brackman, 1966; Nilson and Kullander, 1967, Bonnar et al., 1969).

Bonnar, (1969) found high levels of fibrinogen and plasminogen, but in spite of that he found a Steep increase of euglobulin lysis time, which indicated a decrease in plasminogen activators. So, he beleived that decreased fibrinolytic activity during pregnancy is mainly due to decrease in plasminogen activators. During normal pregnancy, it seems that serum fibrin/fibrinogen degradation products increase which suggests a continuous, low grade process of intravascular coagulation (Bonnar, 1978; Woodfield, 1968). The increase was more marked in the third trimester (Woodfield, 1968). However other investigators found no significant increase in fibrin/fibrinogen degradation products until the onset of labour (Bonnar et al., 1970; Von Royen, 1974).

Bonnar (1969), found a sharp increase in serum fibrin/fibrinogen degradation products during