PROTEIN-C IN DIABETIC PREGNANCY

THESIS

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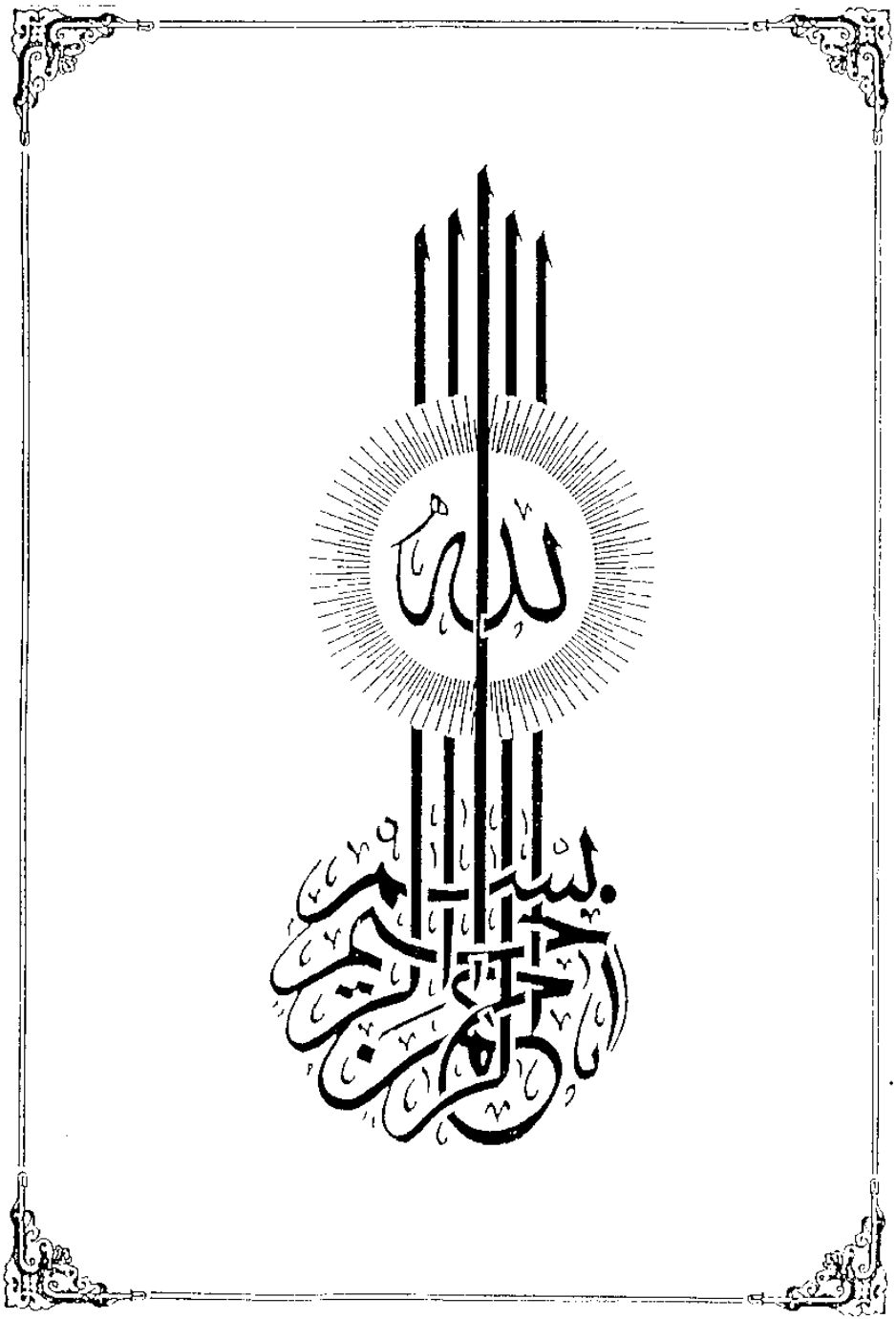

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TO MY FAMILY

INTRODUCTION

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Diabetes mellitus is a heterogeneous disorder of carbohydrate metabolism with multiple etiologic factors that generally involve absolute or relative insulin deficiency or insulin resistance or both (*Olefsky*, 1985).

The complications of diabetic pregnancy include an increased risk of maternal hypertension and sudden unexplained fetal death. Each of them may be associated with increased tendency for thrombosis (*Jones and Peterson*, 1981).

Intrauterine death may result from an episode of hyperglycemia in the presence of hypoxia, the combination of which leads to severe fetal acidosis (*Shelly et al.*, 1975).

More recently, fetal blood hyperviscosity has been suggested as a possible cause of sudden intrauterine death (*Foley et al.*, 1981).

During normal pregnancy, profound physiological changes occur in both the coagulation and fibrinolytic systems. Compared with non-pregnant state, there is general agreement that during pregnancy the

levels of several clotting factors rise to a peak during the third trimester (*Pechet and Alexander*, 1961; *Bonner and Douglas*, 1969).

In contrast to the increased potential of the coagulation system, the fibrinolytic activity is markedly depressed during normal pregnancy (*Bonner*, 1970), but rapidly returns to normal after delivery of the placenta (*Astedt*, 1972). The raised clotting factors and decreased fibrinolytic activity suggest that the intravascular fibrin formation is liable to occur during pregnancy.

Thromboembolism is the most common cause of fetal and maternal mortality associated with pregnancy (*Dewhurst*, 1981).

It is postulated that thrombosis only occurs if there is some added "risk" factor. Increasingly, it is becoming recognized that this added risk factor may be a hereditary or acquired disorder of hemostasis (*Morrison et al.*, 1988).

A variety of abnormalities of the hemostatic system have been reported in insulin-dependent diabetic patients. The interpretation of hemostatic abnormalities in diabetic patients with Microvascular disease is very difficult because the metabolic derangement as well as the

vascular disease influence the synthesis and catabolism of coagulation factors (*Bern et al.*, 1980).

However, since most of these abnormalities indicate a hypercoagulable state, they have been linked to the high risk of cardiovascular morbidity and mortality among diabetic patients (*Jones and Peterson*, 1981; *Garzia et al.*, 1987).

Strong evidence for such a link has been presented in a recent cross-sectional study that found significantly lower plasma levels of protein-C in type I diabetic patients than in age- and sex-matched control subjects (*Vukovich et al.*, 1986).

Protein-C is a vitamin K-dependent glycoprotein. It acts in its activated form as a natural anticoagulant by the inactivation of factor Va and factor VIIIa and by the promotion of fibrinolysis (*Messmore*, 1982).

The imbalance of hemostasis towards thrombophilicity in insulin-dependent diabetic patients, not completely correctable by glycemic control (*Schernthaner et al.*, 1989).

Unexplained or first trimester thromboembolism should therefore alert the physician to examine the levels of AT III, protein-C (the most

important anticoagulant) and protein S (protein-C cofactor) (*Brenner et al.*, 1987).

As the finding of hemostatic abnormality has serious implications, it is essential that women who develop thrombosis in pregnancy or in the purperium are fully investigated (*Morrison et al.*, 1988).

AIM OF THE WORK

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The aim of the study is to measure protein-C levels in diabetic pregnant patients compared to pregnant non-diabetic and non-pregnant non-diabetic healthy subjects.

REVIEW OF LITERATURE

Chapter I: Classification of Diabetes Mellitus