NEONATAL PROTEIN C IN TERM VERSUS PRETERM BABIES

THESIS

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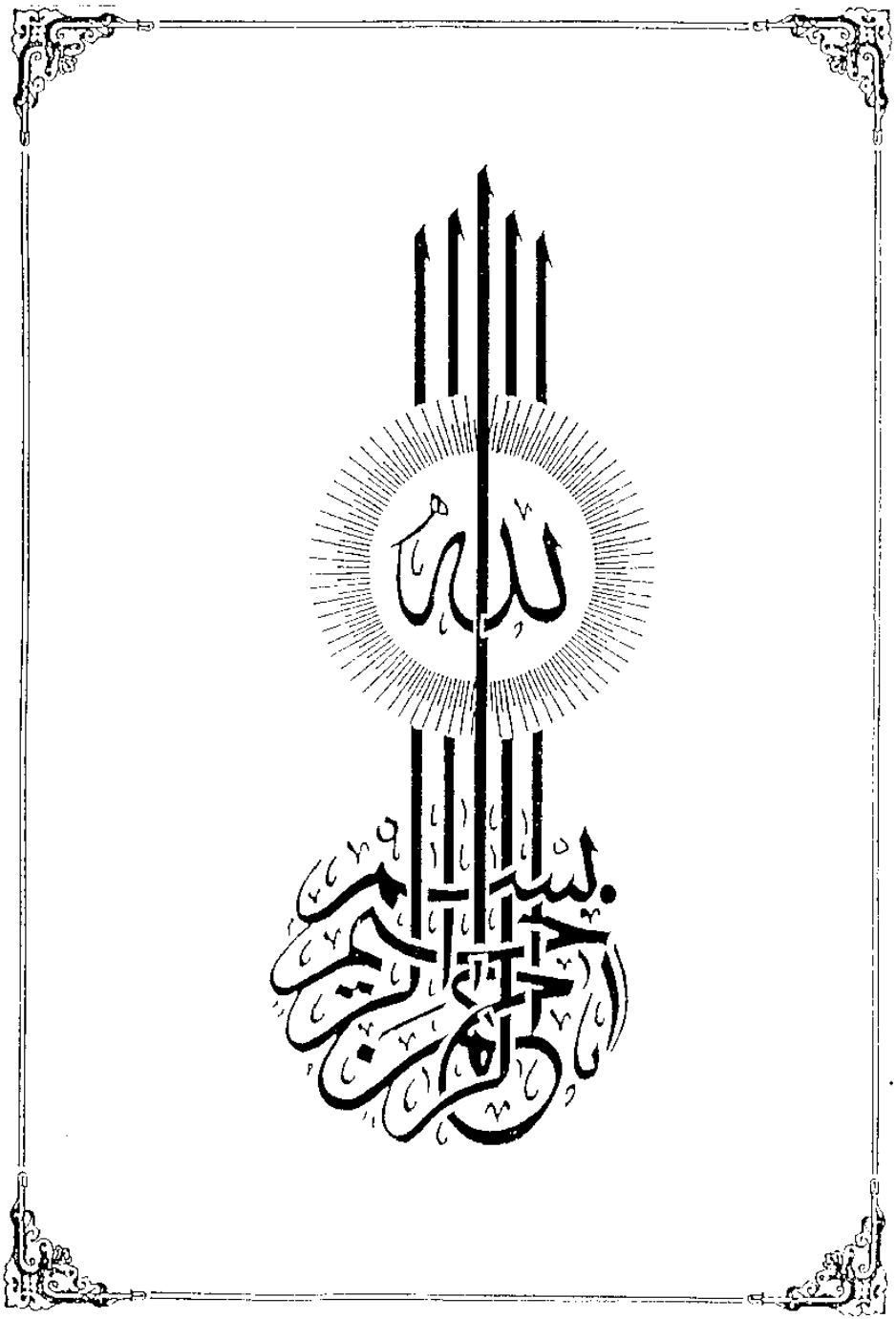

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Introduction

INTRODUCTION

Thromboembolic accidents are known to be dependent upon many haemostatic factors. The haemostatic dynamic equilibrium is mainly related to the delicate balance between the fibrinogenic and the fibrinolytic processes.

The neonatal period is probably the only period when a higher incidence of spontaneous thromboembolic complications may occur in the otherwise normal healthy individuals and this may be related to the activation of the coagulation system at the time of parturition (*Lao et al.*, 1990). Parturition leads to a degree of activation of the newborn coagulation system. As their anticoagulant and fibrinolytic activity levels are presumed to be lower and fibrinolytic inhibitory activity is higher, the newborns are thus predisposed to thrombosis even in the absence of complications such as sepsis (*Takamiya et al.*, 1989; *Lao et al.*, 1990).

A few years ago, previously known as autoprothrombin II-A, plasma protein was found to have a central regulatory action on the dynamic equilibrium of haemostasis. This protein was first described by *Stenflo* (1976) and named it as "protein C" because it was purified from a protein fraction (pool C) obtained after gradual elution of a prothrombin

complex concentrate on the third peak of DEAE-sephadex column chromatography.

Protein C is a vitamin K-dependent and coumarin-sensitive serine protease that circulates in plasma as zymogen (*Greffe et al.,* 1989).

Following activation by thrombin, protein C acquires a proteolytic activity and functions as a potent native inhibitor of the coagulation system and acts as an anticoagulant by proteolysing factors Va and activated factor VIII:C in the blood clotting cascade (*Kisiel et al.*, 1979; *Marlar et al.,* 1982; *Comp et al.,* 1984; *Greffe et al.,* 1989).

Protein C also enhances fibrinolysis promoting the blood clot lysis, at least in part, by increasing the levels of circulating plasminogen activator (*Karpatkin et al.*, 1985; *Greffe et al.,* 1989).

Many recent works are trying to correlate between protein C deficiency and conditions associated with hypercoagulable states.

AIM OF THE WORK

This work aims at comparing the protein C levels in healthy term and preterm newborns in order to detect its maturity levels and the effect of gestational age on its activity and also the incidence of occurrence of thrombosis and DIC in this vulnerable group.

Review of Literature

PHYSIOLOGY OF NORMAL HAEMOSTASIS

Definition: It is the interaction of a group of mechanisms by which animals with cardiovascular system are protected from blood loss from intact vessels and could arrest bleeding from injured ones (*Heimark et al.*, 1980).

These mechanisms include:

A. Active mechanism.

B. Passive mechanism.

(*Penner*, 1980).

The active one includes:

1. The role of the blood vessels and the blood platelets in the formation of a primary haemostatic plug.

2. The interaction between the soluble coagulation factors leading to the formation of a fibrin clot.

While the passive mechanism is the counter part of blood coagulation which controls the active mechanism, it includes:

1. The role of naturally occurring blood coagulation inhibitors in the maintenance of blood fluidity.

2. The role of the fibrinolytic system in the removal of fibrin deposits.

A. Active Mechanism

I. Role of Blood Vessel and Blood-Platelets in the Formation of Haemostatic Plug

a. The Blood Vessel Functions to Keep Normal Haemostasis via Many Mechanisms

1. It has a physiological function without trauma, in which the intact structure of the vessel wall acts to close the gaps in-between the endothelial cells of the blood vessel (*Jorgensen et al.*, 1972).

2. In case of trauma it acts to close the wound by vasoconstriction and retraction of the vessel wall (*Nalbandian and Henry*, 1979).

   The blood vessel also responds by VC to serotonin, thromboxane A_2 (Tx- A_2), adenosine diphosphate (ADP) and endothelin.

   Endothelin is a peptide which is synthesized and secreted by endothelial cells leading to long standing vasoconstriction. (*Yanagisawa et al.*, 1988).

3. Endothelial cells have also a powerful influence on haemostasis by the effect of 2 groups of factors they synthesize and release or bind onto their surfaces:

Group concerned with the control of haemostatic plug formation which includes:

- Von Willebrand factor that stimulates both platelet aggregation and adhesion (*Julie et al.*, 1987).

- Fibronectin that induces adhesion of both platelets and fibroblasts (*Cheresh*,1987).

- Thrombospondin that supports platelet aggregation (*Ketis et al.*, 1988).

- Prostaglandin I_2 (PGI_2) which is a good inhibitor of platelet aggregation and adhesion to prevent extension of platelet plug beyond the immediate vicinity of endothelial injury (*Kenneth et al.*, 1987).

- Ectoenzymes that antagonize ADP and 5-HT, both of which are powerful vasoconstrictors and induces platelet aggregation, so this reaction acts to localize the haemostatic plug (*Rao and Maria*, 1987).