COAGULATION ACTIVITY IN CORD BLOOD IN SEVERE PRE-ECLAMPSIA

THESIS

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By

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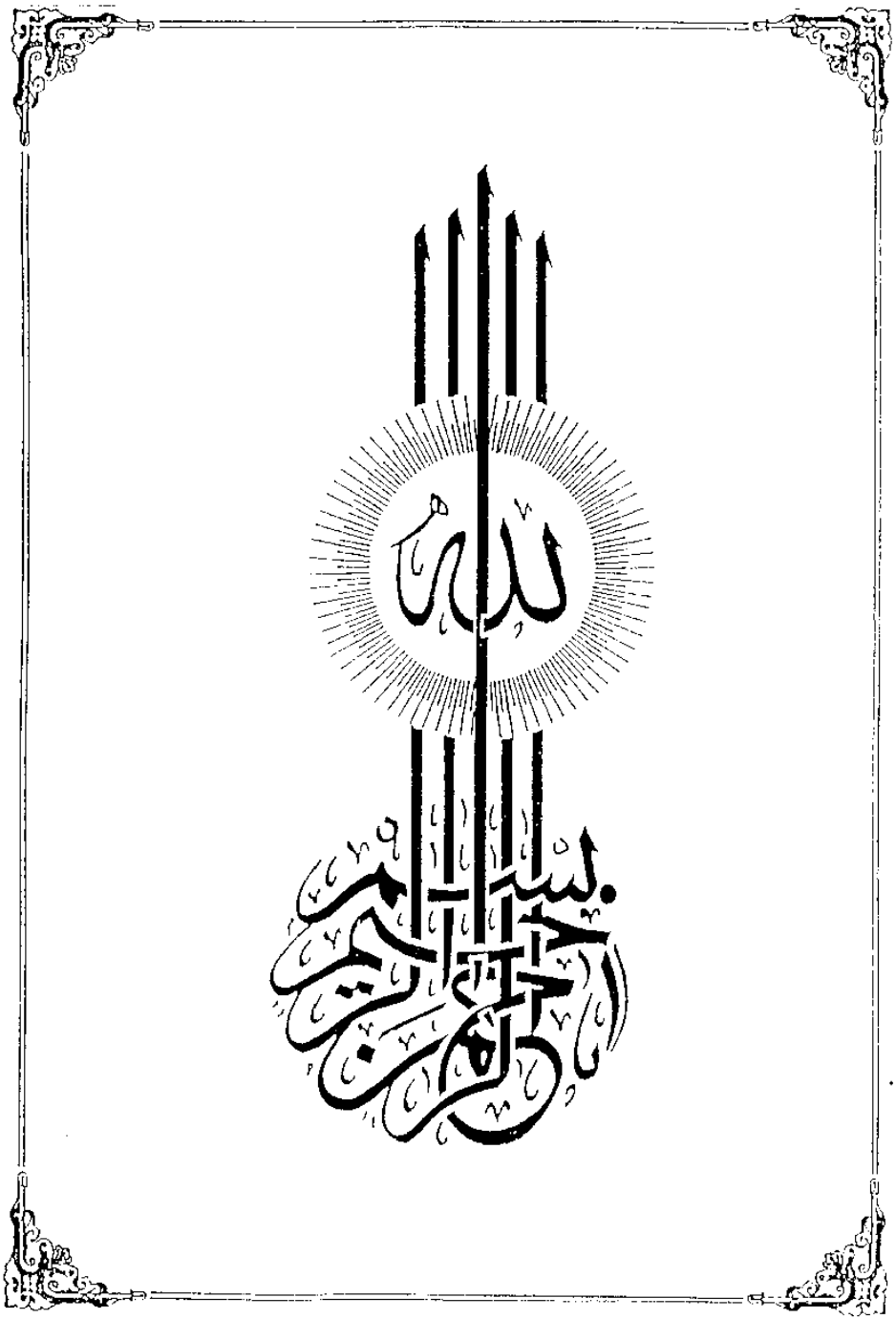

LIST OF ABBREVIATIONS

A.D.P.	=	Adenosine Diphosphate
A.P.T.T.	=	Activated Partial Thromboplastin time.
A.T.P.	=	Adenosine Triphosphate.
Ca^{++}	=	Calcium ions
D.I.C.	=	Disseminated intravascular coagulation
F.D.Ps.	=	Fibrinogen/fibrin degradation products
Fg.	=	Fragment.
5-HT	=	5-Hydroxy tryptamine
Ig	=	Immunoglobulin
n	=	Number
P	=	Level of significance
P.T.	=	Prothrombin time.
P.T.T.	=	Partial thromboplastin time
r	=	correlation coefficient.
RDS	=	Respiratory distress syndrome
S.D.	=	Standard deviation.
t	=	Student test.

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INTRODUCTION AND AIM OF WORK

Introduction

The pregnant human female is unique among all other species in the fact that she is liable to develop a pregnancy disease state characterized by hypertension, oedema and proteinuria. [Sandberg 1978].

The term pre-eclampsia is the state of hypertension, oedema and proteinuria which precede the occurence of convulsions (Percival 1969). The term "eclampsia" was introduced to describe the convulsive attacks that may accompany pre-eclampsia. Pritchard and Mac Donald in 1980 classified pre-eclampsia as "Severe" if any of the following abnormalities develop:-

1- Blood pressure of 160 mm/Hg or more systolic or 110 mm/Hg or more diastolic that does not decrease when the woman is hospitalized and at bed rest. 2- Proteinuria of 5 g. or more in 24 hours (3 or 4 plus on qualitative examination). 3- Oliguria (500 ml or less in 24 hours) and a rising plasma creatinine level. 4- Persisting cerebral or visual disturbances. 5- Epigastric or right upper quadrant pain. 6- Pulmonary oedema or cyanosis. 7- Severe thrombocytopenia or overt intra-vascular haemolysis. 8- Hepatocellular damage and lastly foetal growth retardation.

Howie 1977 suggested that DIC plays a part in the pathogenesis of pre-eclampsia but the stimulus which initiates

the haemostatic changes is still unknown. Page 1972 suggested that the trophoblastic fragments from the damaged placenta enter the circulation in pre-eclampsia and act as a stimulus to intravascular coagulation. Stander et al., 1971 found that intra-amniotic saline infusion can induce haemostatic changes suggestive of DIC, they suggested that the well known sodium retention in pre-eclampsia may act as a factor in stimulating DIC changes similar to what happened in intra-amniotic infusion. In pre-eclampsia there is greater inhibition of systemic fibrinolytic activity as compared with that in normal pregnancy (Bonnar et al., 1971). In a recent study carried by Goubran and Elyan 1985, it was reported that the marked rise in serum α_2-macro-globulin is responsible for supression of plasmin activity in pre-eclampsia. Sheppard and Bonnar 1976 found extensive fibrin deposition in utero-placental arteries in pre-eclamptic patients. Howie et al., 1971 and Dube et al., 1975 found raised levels of serum FDPs in Pre-eclampsia as compared with normal pregnancy. Some authers tried to correlate the haemostatic changes with the severity of pre-eclampsia. Thornton and Bonnar 1977 found that in patients with severe pre-eclampsia, the increase in the ratio of factor VIII related antigen and factor VIII clotting activity correlate with the severity of pre-eclampsia. Moreover Howie et al., 1975 found that a coagulation index,

based on changes in platelet count, plasma factor VIII activity and serum fibrin degradation products (FDPs) correlated with clinical index in reflecting the spectrum of disease in pre-eclampsia. They suggested that the index may be of value in monitoring the progress of the disease. The severity of the feto - placental damage could be related to the degree of abnormal coagulation activation changes (Mc Killop et al., 1976). Trading 1976 found that in pre-eclampsia, reduced maternal levels of circulating platelets were correlated with intrauterine growth retardation.

Aim of Work

The aim of this work is:

1- To ascertain if changes in maternal clotting activity during pre-eclampsia would be reflected on fetal clotting activity.

2- To correlate the changes in clotting activity with the growth retardation in utero which is a complication of pre-eclampsia.

REVIEW OF LITERATURE

Haemostasis

Haemostasis can be defined as the spontaneous arrest of bleeding from the injuried blood vessel. Since the vessels convey blood under pressure, the physical principles involved in haemostasis are basically simple. The blood will continue to flow from the vessel so long as the vessel remains patent and fluid pressure inside the vessel exceeds that outside it. When a blood vessel is injuried, a variety of chemical and physiological reactions are immediately set in motion to prevent loss of blood from the intravascular compartment. these reactions are generally subdivided into three lines of defense (Biggs 1976).

(1) Vascular component (contraction of the injuried blood vessel to seal the injuried site).

(2) Platelet reaction.

(3) Blood coagulation.

Vascular and platelet reactions combine together to form a temporarily plug to the vascular defect with a platelet aggregate. Clotting factors transform the plug into definitive seal. (Senyi et al., 1975).

Mechanisms Of The Platelets In The Formation Of A Haemostatic Plug:-

The formation of a haemostatic plug involves first adhesion of platelets to other tissues, followed by the aggregation of platelets to each other. Initially, the platelets adhere loosely to each other so that the plasma and cells continue to pass out of the vessel. Within few minutes the platelets become packed more closely so that the plug becomes more effective in its haemostatic function (Born and Hardisly, 1976).

Hellem and Stromorker (1969) described the formation of the haemostatic plug in four main steps:-

1. Platelet adhesion.
2. Local release reaction.
3. Platelets aggregation forming platelet plug.
4. Reinforcement of the platelet plug by plasma fibrin.

1. Platelet Adhesion

Platelets do not adhere to normal endothelial cells but adhere to subendothelial structures as collagen fibres,

basement membrane, and microfibrils in the gap between endothelial cells within 1 to 2 seconds after injury (Baumgartner et al., 1976). The adhesivness of platelets is markedly increased by ADP, the catecholamines and a potent agent, thrombin (Hardisty, 1976).

2. Release Reaction

Many important constituents necessary for platelet aggregation, blood coagulation and maintenance of haemostasis are liberated from the adherent platelets viz ADP, hydroxy tryptamin (5-HT), amino acids and small amounts of protein.

3. Platelet Aggregation:-

Platelets aggregate on top of the adhering layer by ADP, adrenalin, 5-hydroxy tryptamin, thrombin, collagen and certain fatty acids. This stage of aggregation is completely reversible.

The second or the irreversible phase is associated with the release of ADP from the platelets, and also other substances including adenosine triphosphate (ATP), 5-hydroxy tryptamin as well as platelet factor 3 which

accelerate coagulation of plasma (Hardisty and Hutton, 1966). This stage leads to the formation of an impermeable haemostatic plug.

4.Reinforcement of the Platelet Plug:-

This stage depends on the formation of fibrin by the plasma coagulation.

Finally, clot retraction in a wounded vessel would promote haemostasis if the walls of the vessel were pulled together to narrow the lumen. Early retraction of a coagulation thrombus could prevent the complete occlusion of a vessel and promotes its reopening to the flow of blood.

COAGULATION MECHANISM

Historical

The classical theory of blood coagulation derived from the work of Schmidt (1872), Hammeristein (1899), and Morawitz (1909), which remained unchanged for 50 years.

The above theory postulated the existence of 4 factors, thrombokinase (or thromboplastin) derived from damaged

tissue or blood cells, prothrombin and fibrinogen which are present in normal blood plasma, and ionized calcium.

Blood in the normal circulation, remains fluid because prothrombin and fibrinogen are inherently stable. Following tissue damage, thromboplastin enters the blood and reacts with prothrombin in the presence of calcium to form thrombin, which in turn reacts with fibrinogen to form the insoluble threads of fibrin (Fig. 1).

Many important discoveries and new blood coagulation factors were introduced. (The coagulation factors had been listed P. 9).

In (1964), Macfarlane, Davis and Ratnoff separately described two similar theories which were the Cascade and Water fall theories of blood cogulation.

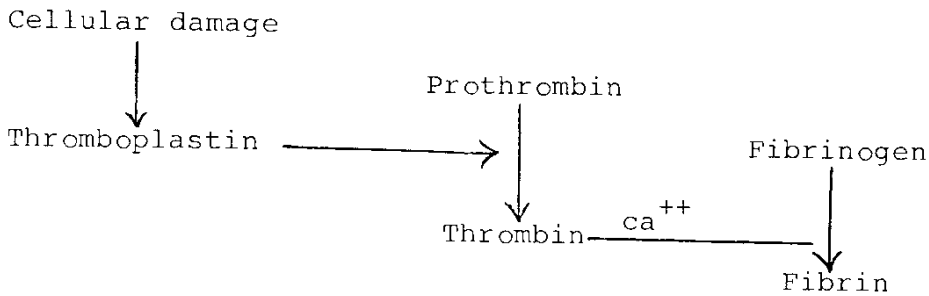

Fig. (1)
The mechanism of blood coagulation
(after Marcus, 1969)