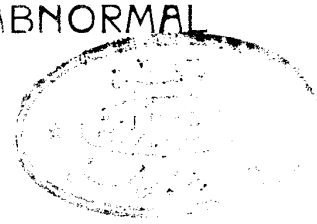
BIOCHEMICAL STUDIES ON CERTAIN ENZYMES AND AMINO ACID CONTENTS OF THE BLOOD AND PLACENTA IN NORMAL AND ABNORMAL PREGNANCY



A THESIS

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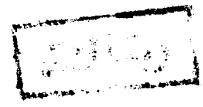

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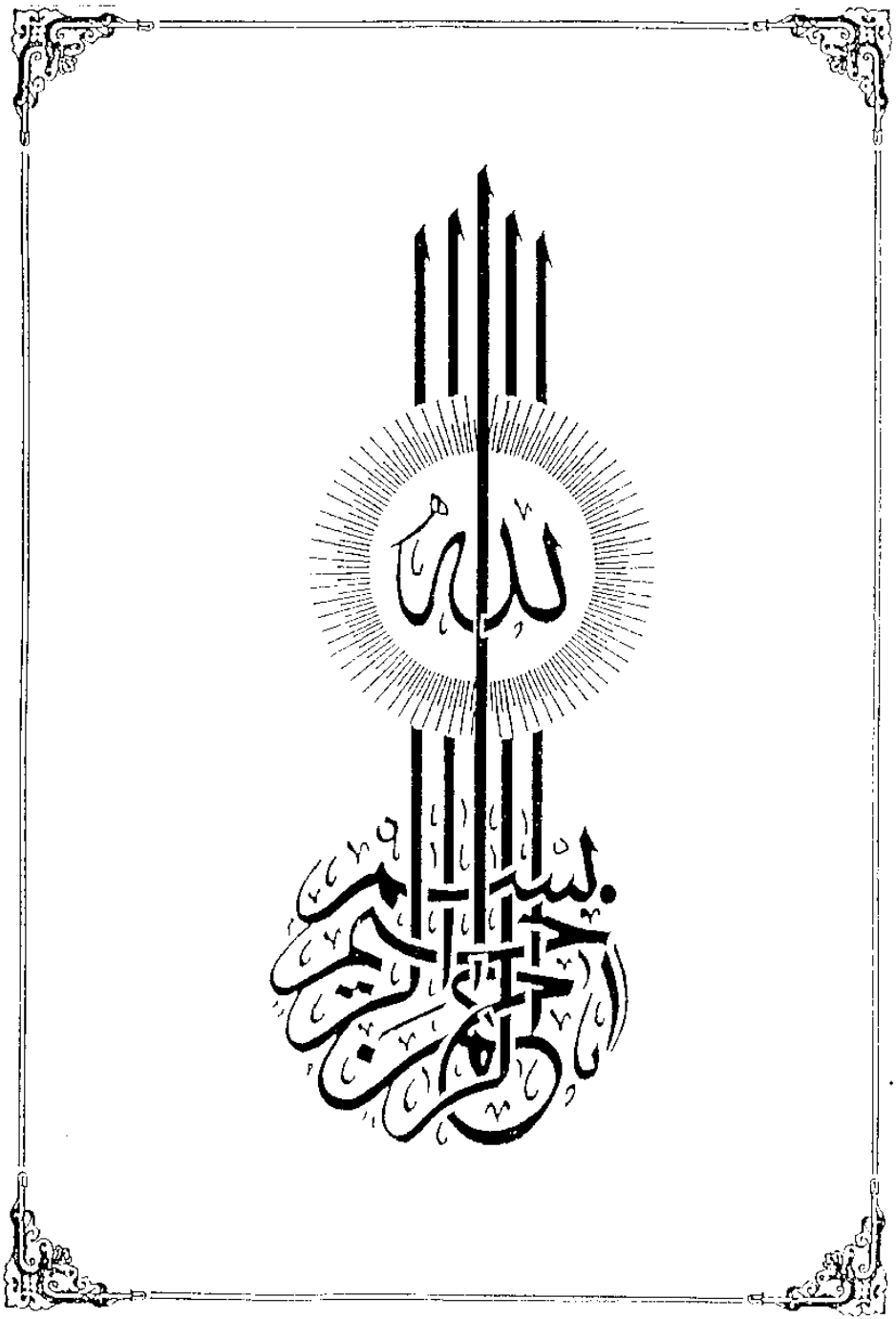

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Aim of the Work

Toxaemia is still the major cause for both the maternal and perinatal mortalities in obstetric practice.

For centuries many workers have been concerned with the etiology, diagnosis, prevention and treatment of the various forms of toxaemia. But the pathogenesis of such a specific disease of pregnancy is still unanswered.

The present study is concerned with the effect of normal pregnancy and pregnancy complicated by pre-eclampsia on the biochemical evaluation of certain enzyme levels in the serum as compared to their levels in the placenta.

We tried to answer the question whether the serum levels of these enzymes were contributed to by the placental enzyme levels and if there is a correlation between the serum and placental enzymes.

The study also included the estimation of total protein concentrations and the total amino acids contents in the serum and in the placenta of both normal and preeclamptic pregnant women. The idea of doing such estimation is based

on the fact that proteins are the main nutrient material transferred across the placental barrier. Impaired placental function can alter the rate of total amino acid transport to the foetus or it might be a selective inhibition of individual or groups of amino acids, thus interferring with the foetal protein synthesis and its growth and development.

The work was also extended to include the study of the effect of 5-hydroxytryptamine (Serotonin) in the development of toxaemia, by its determination in the blood and in the placenta of normal pregnancy and in preeclampsia.

INTRODUCTION

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Toxaemias of pregnancy are frequent complication of gestation, occuring in 6-7 percent of late pregnancies. Toxaemias of pregnancy are one of the three main complications responsible for the vast majority of maternal deaths i.e. Toxaemias, sepsis and haemorrhage.

Toxaemia of pregnancy account for about one third of the maternal fatalities. They are characterised by hypertension, oedema, and proteinuria separately or together and may culminate in convulsions and coma.

Classifications

The signs and symptoms of various toxaemias are non specific. Although many schemes of classification have been adopted.

In the United States of America toxaemia of late pregnancy have accounted for about 20 percent of maternal and faetal deaths (Eastman, 1950).

In England and Wales, a careful analysis was made by Bound et al. (1956-1960) in which they concluded that toxaemia and hypertension were a major cause of maternal death. In Egypt, Samour et al. (1969) reported that 20 percent of the maternal deaths were caused by toxaemia of pregnancy.

The classification which is in common use is that introduced by the American Committee on Maternal Welfare (1952). It includes the following:

I- Acute toxaemia of pregnancy (onset after the twenty-fourth week).

A) Preeclampsia:

1- Mild.

2- Severe.

B) Eclampsia (convulsions or coma, usually both, when associated with hypertension proteinuria, or oedema).

II- Chronic hypertensive vascular disease with pregnancy.

A) Without superimposed acute toxaemia.

1- Hypertension known to have antedated pregnancy.

2- Hypertension discovered in pregnancy (before twenty-fourth week and with post partum persistence).

B) With superimposed acute toxaemia.

III- Unclassified toxaemia.

The aetiology of preeclampsia:

The aetiology of preeclampsia remains unknown. Many facts have been discovered and many theories are suggested, based mainly upon modern ideas in treatment. The most important theories are:-

1- Uterine and placental ischaemia:

In this theory it was claimed by Page (1948) that there was a release of metabolic toxins into the maternal blood. Such toxins were claimed to be due to relative ischaemia and cellular anoxia of the uterus and placenta. In this way the occurence of toxaemia in primigravidae twins, hydromnios and concealed accidental haemorrhage can be explained on the assumption of an increased intra-uterine pressure precipitating uterine ischaemia. Walker and Turnbull (1953) measured the oxygen saturation in the cord blood of foetuses born by caesarean section or hysterotomy. They found that the oxygen saturation in the cord blood was less in cases of preeclampsia than in the normal pregnancy at the same stage of gestation. His observation explained both intrauterine faetal death and faetal distress during labour in preeclampsia.

Assali et al (1954), Morris et al,(1955), Johnson and Clayton (1957), Weis et al. (1958) found that hypotensive drug therapy in preeclampsia would increase the effective blood flow in the uterine wall.

Beinarz(1958), Muresan et al. (1959), Clemetson (1960), had suggested that downward venous drainage in placenta praevia is so efficient that toxaemia was not likely to occur. Also severe toxaemia was more likely

when the aorta was hypoplastic. But in preeclampsia it is still uncertain whether the ischaemia with reduced uterine blood flow is the cause of the toxaemia, or it is merely the result of the underlying hypertension.

2- Placental infarcts, toxins and enzymes:

Young (1914) had suggested that ischaemic placental infarcts might liberate certain toxins. An attempt to isolate the toxins was conducted by Wislocki (1948) and Russel (1957). They showed that the process of aging in the placenta with progressive thinning of the sycitium and a gradual thickening of the villous blood vessels was accelerated in essential hypertension and toxaemia.

Bartholomew et al. (1957), Shanklin (1959), Scott and Jeffcoate (1959) had produced evidence that toxaemia occured more frequently in the presence of an over active placenta, as in diabetes mellitus, hydrops foetalis and hydatidiform mole. In these abnormal placentae there was persistence of the trophoblastic activity and the gonadotrophin output was high.

Attempts were made to isolate such circulating toxins arising from placental infarcts. Schneider (1947) and Smith (1948) isolated Thromboplastin and menotoxin. Ahlmark (1950), Thompson and Thickner (1950), Sandler and Covency (1962), Lindberg and Westling (1962) had suggested

that the placenta contained a high concentration of histaminase and monoamine oxidase which would lead to the placental ischaemia. Poulson (1960), Oates (1960) found that a decrease in palecental monoamine oxidase had lead to the decreased inactivation of endogenous amine which inturn produced vasoconstriction and anoxia which could be the cause of the toxins released into the material circulation.

Certain enzymes were detected in high levels in toxaemias of pregnancy. Dawkins et al.(1959) found an increase in the serum isocitric dehydrogenase enzyme, Crisp et al. (1959) found that serum transaminase level was raised in toxaemic women. Neale (1965), Tennant (1970) found that serum alkaline phosphatase was high during preeclampsia and it was started that the serum alkaline phosphatase was of placental origin. It is not clear whether the toxaemic placenta actually secretes a toxic substance or whether the placenta did not function normally due to inactivation of its enzymes.

3- Renal ischaemia:

Chesley et al. (1940), Kenney (1950), Werko (1953), Alvarez (1959), Assali et al. (1960) studied the renal ischaemia in toxaemia of pregnancy and they suggested that both the renal blood flow and the glomerular filtration rate in toxaemia of pregnancy were diminished when compared to

those of normal pregnancy at the same period of gestation. Another factor which might play a role in the renal ischaemia was the renin-angiotensin-aldosterone system. In acute toxaemia renin secretion was stimulated and converted into angiotension which had dual roles, i.e. to aggrevate vaso-constriction, and to stimulate aldosterone secretion. This latter hormone increases sodium reabsorption through the renal tubules. Sodium reabsorption is already elevated because of the decrease in the glomerular filtration rate. The increased sodium reabsorption leads to oedema and renal ischaemia.

4- Chronic hypertensive vascular disease:
(Essential hypertension)

Brown (1933), Barnes (1945) had suggested that toxaemia was particularly more likely to occur in patients who had a familial tendency to hypertension. Such a pre-existing tendency to hypertension may be revealed by a rise in blood pressure which could result in recurrent toxaemia in subsequent pregnancies. Chronic hypertensive vascular disease or essential hypertension can present by a wide variety of clinical pictures depending upon the stage of the arteriolar scleroses and the effects on the heart, kidneys and brains.

5- Endocrine theories:

Colvin and coworkers (1942) had suggested hypothyroidism could cause toxaemia of pregnancy. But, Dexter and Weiss (1941) claimed that the clinical picture did not suggest hypothyroidism levels and the protein content of the oedema fluid is very low and the basal metabolic rate is not at the myxaedamatous level, there is no valid evidence that points to hypothyroidism as a cause.

Hofbauer (1926) had postulated that eclampsia is caused by hyperfunction of the posterior lobe of the pituitary. Hoffman and Anselmino (1936) had attempted to show that preeclampsia and eclampsia are dependent upon an increased amount of circulating antidiuretic and vasopressor hormones. Excessive chorionic gonadotropic hormone in the blood and urine of patients with toxaemia was first reported by Smith (1939) who demonstrated also that the placenta of toxaemic patients contained more of this hormone than could be recovered from the placenta of normal pregnancy. Taylor and Scardon (1939), as well as Cohen and coworkers (1943) had only found a slight correlation. Smith and Smith (1940) found a prog-ressive defficiency of progesterone and estrogen before and during toxaemia.

They postulated senility of the placental syncytium and premature withdrawal of the steroidal hormones. They

believed that the disturbances must be affected by means of the primary etiologic factor which probably involved either an intrinsic metabolic abnormality or a decrease in the blood supply to the placenta or both.

6- Disturbances in salt and water metabolism:

In some cases of pre-eclampsia and eclampsia there is retention in the body of an abnormal quantity of water, probably due to an increase in the retention of sodium chloride. These changes may be due in turn to the increase secretion of posterior pituitary antidiuretic hormone.

Also a raised concentration of oestrogen, progesterone and adrenal cortico steroids may result in increased intracapillary pressure, decreased plasma oncotic pressure or increased capillary permeability. Clinical oedema is a common but not invariable physical sign of preeclampsia. The fluid which can be detected clinically is interstitial and become apparent in the legs due to the upright position and a raised intravenous pressure from the enlarging uterus.

7- Dietary alterations:

It was established that certain gross dietetic deffi-ciencies such as vitamins A, B, C, D and minerals especially calcium and iron might cause toxaemia by an adverse effect on the endocrine glands. The balanced inactivation of hormone,