MATERNAL SERUM COPPER AS AN INDICATOR FOR FETAL OUTCOME

THESIS

Submitted By

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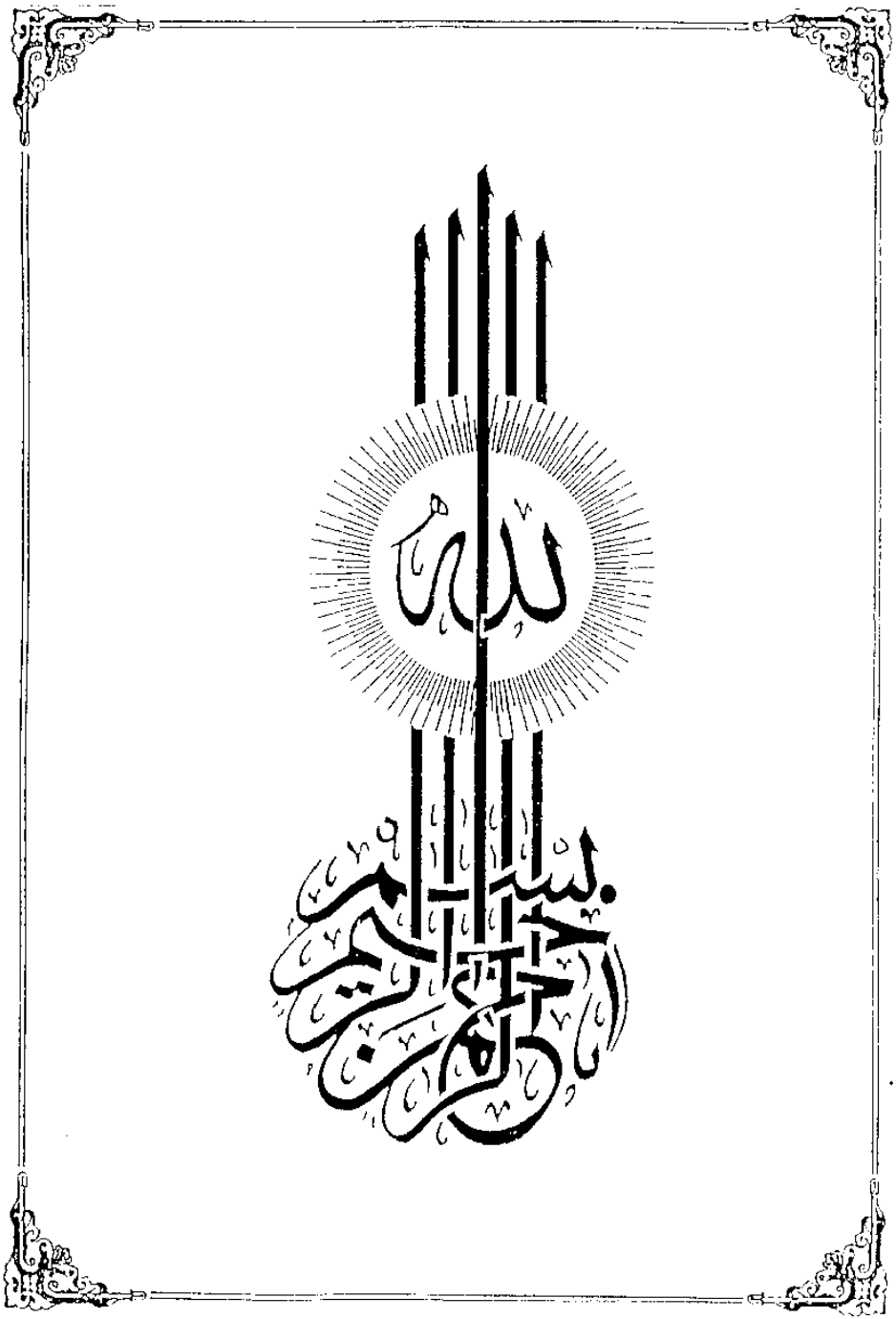

C O N T E N T S

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INTRODUCTION

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Estimation of serum copper during pregnancy was a point of interest for so many investigators. Now it is well known that maternal serum copper levels rise gradually with the advance of pregnancy reaching its maximum level at term.

The cause of this rise was explained by the increased endogenous oestrogen secretion during pregnancy. This explanation was strengthened by the elevation of serum copper following administration of oestrogen preparations to women.

This strong relation between serum copper and oestrogens raised the possibility of employment of maternal serum copper levels as a measure of placental function and as an indicator of fetal survival, instead of detecting urinary and serum oestrogens as copper estimation is much easier.

REVIEW OF LITERATURE

COPPER IN NATURE

The presence of copper in plant and animal tissues was recognized early in the nineteenth century, but general acceptance of its universal distribution in biological material developed only at the beginning of the twentieth century.

The first evidence that copper plays an important role in vertebrates was provided by Hart et al., 1928, who showed that it is required for prevention of anaemia. It was reported that copper is essential for synthesis of cytochrome oxidase, and thus copper was established as a biologically significant catalyst.

1. Animal and plant sources of copper:

Copper is widely distributed in foods; most diets provide the amount needed per day to maintain copper balance. Basic food staffs such as fresh vegetables, meats and refined cereals, provide two to four times the concentration in milk. The richest sources of dietary copper are nuts, some shellfish, liver, kidney, raisins

and dried legums. The mixed diet of the later period of infancy meets or exceeds the value of 0.05 mg/kg/day, suggested as needed by infants at this time.

Cow's milk is a poor source of copper (concentration of 0.015 - 0.18 mg/L.). Human milk ranges from 1.05 mg/L. at the beginning of lactation to 0.15 mg/L. at the end (Harper et al., 1979).

2. Distribution of copper in tissues:

Serum copper concentration at birth, as an average, 30 ug/dl, subsequently there is a gradual rise so that after eight months of age, the values range from 125 - 240 ug/dl (Krieger, 1966).

The average copper concentration in the liver after birth is about 20 ug/gram dry weight (Krieger, 1966).

Hair copper seems to reflect the total body copper but may be unreliable unless increasing concentrations in the shaft with distances from the scalp are taken in account (Hambidge et al., 1972).

The copper is widely distributed in the tissues with the highest concentration in the liver, kidney, bone marrow, hair, muscles and lung. The amounts in normal brain, C.S.F., heart and endocrine glands are normally very low.

The adult human body contains 100 - 150 mg of copper; about 64 mg are found in the muscles, 23 mg in the bones and 18 mg in the liver which contains a higher concentration of copper than that of any of the other organs studied. It is of interest that the concentration in the fetal liver is 5 - 10 times higher than that in the adult liver (Harper et al., 1979).

The young and newborn animals contain a higher tissue concentration of copper than older animals (Chou and Adolph, 1953). In most species, the copper content of the brain is not influenced, like other organs, by changes in dietary copper.

The copper content of the iris, choroid and retinal pigment of the eye, of most species, is very

high (Bowness and Morton, 1952).

The copper content of the hair is very high and is higher in pigmented than non pigmented hair. Depigmentation of hair is one of the signs of copper deficiency in many species (Kikkawa et al., 1955).

The copper is an essential component of a number of enzymes but in the serum and red cells, found firmly bound as ceruloplasmin and erythrocuprein respectively. In the serum, a small amount is loosely bound to albumin and very small amount is in the free state and is capable of diffusion through the semipermeable membranes like the blood-brain barrier, red cell memberane, the glomerular membrane and the placenta (Scheinberg and Sternlieb, 1960).

The loosely bound copper is known as "direct-reacting" copper because it reacts freely with copper complexing reagents (Harper et al., 1979).

3. The principal copper-proteins:

There are undoubtedly several forms in which copper may exist in vivo and these include free cupric, or cuprous ions, and combinations of copper with amino acids, purines, pyrimidines, nucleotides, DNA, RNA and proteins.

a. Ceruloplasmin:

It is an α_2-globulin present in the plasma in a concentration of 20-35 mg/100 ml, with a molecular weight of 151.000. It contains about 0.3% copper which corresponds to eight copper atoms per molecule.

About 90 - 96% of plasma copper is bound in the form of ceruloplasmin. Ceruloplasmin is deep blue and it contains hexosamin, hexose and neuraminic acid.

Ceruloplasmin is characterised by its oxidative activity toward certain polyphenols and polyamins; the reversibility of its copper-protein bond, in vitro, if the copper is first reduced by ascorbic acid, and also characterised by its heterogenicity and inherited

deficiency (Scheinberg and Sternlieb, 1960).

b. Tyrosinase:

It is a mammalian copper-protein with considerable resemblance to ceruloplasmin. Its molecular weight and copper content are not accurately known although the latter seems to be of the order of 0.1 to 0.2%.

It has oxidative activity toward poly-and mono-phenols. It has the reversibility of its copper-protein bond, possible heterogenicity and inherited deficiency (Brown et al., 1959).

c. Cerebrocuprein:

It is a copper-protein isolated from bovine and human brain. Its copper content of 0.29%, representing two atoms of copper per molecule, its bluish-green colour, and the relative stability of its copper-protein bond, are similar to properties of ceruloplasmin.

It differs from ceruloplasmin in having a molecular weight of only 30.000 to 40,000 and in lacking any enzymatic activity toward paraphenylenediamine.

d. Erythrocuprein:

It is a copper-protein isolated from human erythrocytes (Kimmel et al., 1959). At least 80% of the red blood cell copper is present as erythrocuprein. The copper content of the red blood cell is constant, while that of the serum is highly variable, averaging about 90 ug/dl. (Harper et al., 1979). The remainder of erythrocyte copper is more lossely bound to unidentified proteins and is much more labile than erythrocuprein (Prasad, 1978).

Erythrocuprein differs from ceruloplasmin in being only faintly greenish-blue, in having less than one-fourth the molecular weight, in possessing a different isoelectric point, in lacking oxidative activity toward paraphenylenediamine, in having different absorption spectra in both visible and ultraviolet light and in being present in its usual concentration in a patient with Wilson's disease.

Erythrocuprein is distinct from ceruloplasmin and from hepato-cuprein (Shapiro et al., 1961).

There are no data concerning copper in white blood cells nor platelets.

e. Cytochrome oxidase:

It has well-known importance in aerobic oxidation. One molecule of heme, one atom of iron and one atom of copper are present in each water - soluble monomer of the cytochrome oxidase. The copper of cytochrome oxidase is reduced specifically by cytochrome Č, and probably by ascorbate as well, and that this reduction may be connected with the function of the enzyme (Scheinberg and Sternlieb, 1960).

The cytochrome oxidase activity is markedly diminished in experimental and natural copper deficiency.

f. Copper-proteins in liver:

The functions of hepatocuprein and a copper-protein isolated from horse liver are unknown. It is possible that these are the same protein (Scheinberg and Sternlieb,1960).

The hepatic uricase, which catalyzes the oxidation of uric acid to allantoin, possesses enzymatic activity