DIAGNOSTIC AND PROGNOSTIC VALUE OF QUANTITATIVE ESTIMATION OF SERUM B-SUBUNIT HUMAN CHORIONIC GONADOTROPIN (HCG) AND PROLACTIN IN THE FIRST TRIMESTER BLEEDING

THESIS

Submitted In Partial Fulfillment for
Requirement of Master Degree
In
(GYNAECOLOGY AND OBSTETRICS)

Presented By

AFAF KHEDER SOUDY IBRAHIM

UNDER SUPERVISION OF

Prof.Dr. AMIN HASSAN EL ZENEINY

Professor of Obstetrics and Gynaecology

Faculty of Medicine, Ain Shams University

Dr. MOUNIR M. FAUZY EL-HHO

Assistant Professor of Obstetrics and Gynaecology

Faculty of Medicine, Ain Shams University

Dr. MOHAMED ABDEL HAMID MANSOUR

Head of the Radiation Research, Department for Health National Center of Radiation Research and Technology.

Faculty of Medicine
Ain Shams University

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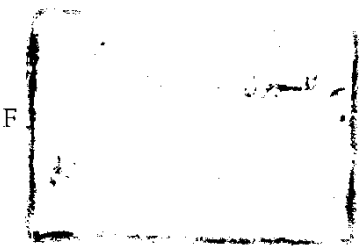

UNDER SUPERVISION OF

Prof. Dr. AMIN HASSAN EL ZENEINY
Prof. of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University

Dr. MOUNIR M. FAUZY EL-HAO
Assistant Professor of Obstetrics and Gynaecology
Faculty of Medicine, Ain Shams University.

Dr. MOHAMED ABDEL HAMID MANSOUR
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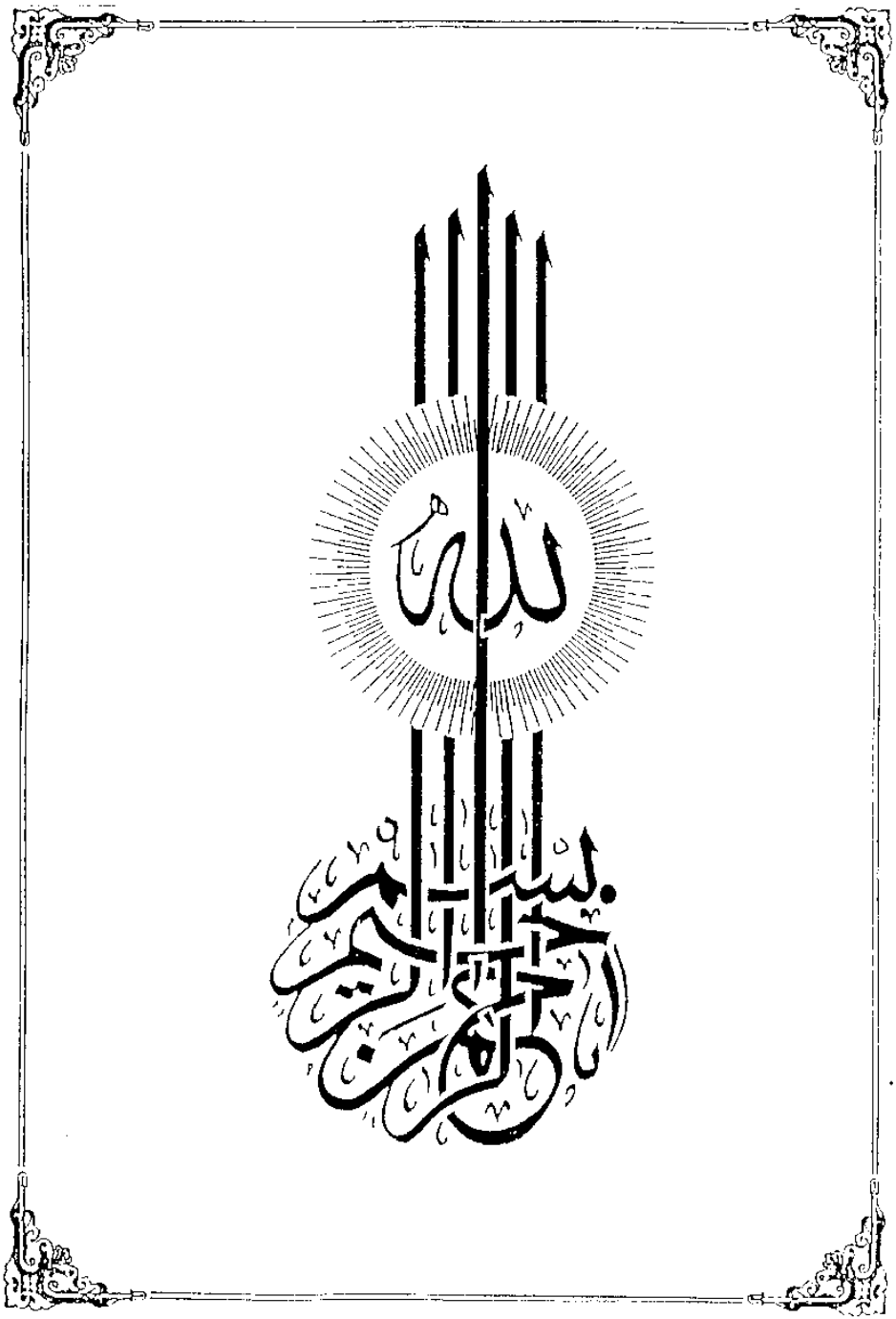

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

"اللَّهُ يَعْلَمُ مَا تَحْمِلُ كُلُّ أُنثَىٰ وَمَا تَغِيضُ الْأَرْحَامُ
وَمَا تَزْدَادُ وَكُلُّ شَيْءٍ عِندَهُ بِمِقْدَارٍ"

صَدَقَ اللَّهُ الْعَظِيمُ

سورة الرعد، آية "٨"

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INTRODUCTION

INTRODUCTION

Bleeding in the first trimester of pregnancy is a frequent serious complication. Traditional differential diagnosis are uterine abortion, ectopic pregnancy, gestational trophoplastic diseases and associated causes. The information obtained by the sensitive radioimmunologic assay of different trophoblastic markers including human chorionic gonadotropin (HCG) and prolactin, has significantly improved the diagnosis of common problems in early pregnancy. These methods have a distinct value in the diagnosis of pregnancy and its prognosis (Jouppila et al., 1984).

AIM OF THE WORK

AIM OF THE WORK

The objective of this study is to evaluate the utilization of quantitative estimation of serum β subunit HCG and serum prolactin by RIA. In cases of first trimester bleeding (6 weeks - 12 weeks)and to correlate the hormonal levels with clinical picture and outcome of pregnancy at the end of first trimester.

REVIEW OF THE LITERATURE

HUMAN CHORIONIC GONADOTROPIN

CHEMICAL STRUCTURE

Physiochemical properties:

Human chorionic gonadotropin (HCG) is a glycoprotein hormone, containing approximately 30% carbohydrate.

It is secreted by the syncytiotrophoblast cells of the placenta and is present in the blood and urine during pregnancy. Its molecular weight is 36.700 daltons and its isoelectric point is 4.5 (Birken and Canfield, 1978).

It consist of a hormone-non specific subunit α and a hormone specific β subunit of molecular weight of 14.500 and 22.200 daltons, respectively.

The α subunit contains 92 amino acid, and the sequence is nearly identical to those of the α subunits of the other glycoprotein hormones (Viz.,human Luteinizing Hormone (HLH), human follicle-stimulating hormone (HFSH), and human thyroid stimulating hormone(H-TSH) (Saxena, 1983).

The complementary HCG-β subunit contains 145 aminoacids with several regions homologous to the other glycoprotein β subunits such as FSH-β, TSH-β and a striking homology of 80 amino acids of the initial 115 with the HLH-β subunit, except that HCG-β subunit contains an additional 30-amino-acid sequence at the C-terminal which is rich in proline.

The α subunit contains two and the β subunit five carbohydrate moieties attached to the protein chain.

The monosaccharide sequence in contrast to all other oligosaccharide side chains, the three oligosaccharide units of the carboxyl terminus of the HCG-β subunit are O-glycosidically linked to serine instead of asparagine (Saxena, 1983).

Biological properties:

Owing to the structural similarities between hLH and HCG. The two hormone are very similar in their biologic and immunologic properties (Saxena, 1985). Since the 30-amino acid-carboxyl-terminal sequence is not present in the HLH-β molecule, it is reasonable to assume that this portion of the HCG molecule is not necessary for biologic activity (Lonvet et al., 1971).

This is further suggested by studies in which antibodies specific to the tail piece failed to neutralize the biologic activity of HCG. However in the case of macromolecules, the sequence specificity may be of lesser value than the conformational specificity in relation to a biologically meaningful interaction of the molecule with the antibody or the receptor. The structural homologies between HLH, HFSH and HTSH also explain an intrinsic FSH and TSH-like activity of HCG. The later has been implicated in hyperthyroidism in late pregnancy (Braunstein et al., 1976).

Ashitaka et al.,(1970) reported that a component with HCG-like activity distinct from HCG and HTSH has been identified in the extract of normal and molar pregnancies. Similary FSH and TSH like components have also been purified with HCG from placental extracts (Siris et al., 1977). During the peri-implantation phase, following the fertilization of the ovum, HCG acts as a stimulus to sustain the secretion of progesterone by the corpus lutum of gestation. This is necessary for implantation the growth and preparation of the endometrium for implantation. Human chorionic gonadotrophin also acts as a stimulus for the synthesis of fetal teticular androgens. The enormous production of HCG during pregnancy is apparently not a metabolic waste. Since a decreased production of HCG can result

in a spontaneous abortion. It has been shown that lower production of HCG. can be compensated for by enhanced corpus luteum and placental response (Saxena, 1978). The primitive trophoblast produces HCG early during normal pregnancy. Concentration of HCG rise to peak values by 8 to 12 weeks of gestation. There is a decrement in HCG levels to aplateau that is maintained throughout the remainder of the pregnancy (Rose et al., 1968).

The finding of HCG-specific adenyl cyclase stimulation in the placenta has suggested the possibility of autoregulation of the biosynthesis of steroid within the placenta (Hussa et al., 1974).

Immunologic proporties:

Human chorionic gonadotropine and its α and β subunit are highly antigenic and can produce antibodies of high titer, species such as guina pigs, rabbits and sheep. The antibodies against the α subunit cross-react with the α subunit of the other glycoprotein hormone, owing to the similarity in the aminoacids sequence. However, antibodies raised against the hormone specific β-subunit can discriminate HCG and its β-subunit from HLH, HLSH, HFSH and B subunit (Vaitukaitis et al.,1972).