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DIAGNOSTIC AND PROGNOSTIC VALUE OF
SEMIQUANTITATIVE ESTIMATION OF URINARY HUMAN
CHORIONIC GONADOTROPHIN (H.C.G.) IN THE FIRST
TRIMESTER BLEEDING

Thesis

Submitted in partial fulfilment for Requirement
Of Master Degree in Gynaecology and Obstetrics

By

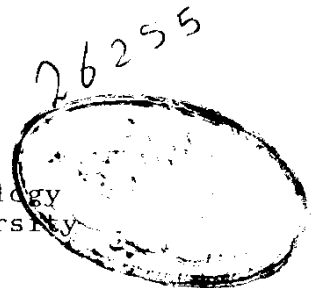
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INTRODUCTION

INTRODUCTION

Vaginal bleeding in early pregnancy is a common problem giving rise to much anxiety in patients and often presenting a dilemma to the clinician. Clinical examination, urinary pregnancy testing, and ultrasound scanning have been stated to give an absolute diagnosis in cases of missed abortion and hydatidiform mole and in more than half the cases of blighted ova. These results are necessarily very dependent on the skills of the observer. Biochemical tests can be subjected more readily to quality control and thus have advantage in certain centers (Masson et al., 1983).

Traditional differential diagnosis of the bleeding in the first trimester of pregnancy are uterine abortion, ectopic pregnancy, gestational trophoblastic disease and associated causes.

AIM OF WORK

AIM OF THE WORK

The objective of this study is to evaluate the utilization of semiquantitative estimation of urinary Human chorionic gonadotrophin "H.C.G." by Immunologic test of pregnancy in cases of the first trimester bleeding and to correlate the amount of urinary HCG with the outcome of pregnancy at the end of the first trimester.

REVIEW OF LITERATURE

HUMAN CHORIONIC GONADOTROPIN

CHEMICAL STRUCTURE

Physiochemical properties:

Human chorionic gonadotropin (HCG) is a glycoprotein hormone produced by the placenta during pregnancy. It's molecular weight is 36.700 daltons and it's isoelectric point is 4.5 (Birken and Canfield, 1978).

It consists of a hormone-non specific subunit α and a hormone specific β subunit. The α subunit contains 92 aminoacids, and the sequence is nearly identical to those of α subunits of the other glycoprotein hormones (Viz; human luteinizing hormone (hLH), human follicle-stimulating hormone (hFSH), and human thyroid-stimulating hormone (hTSH) (Saxena, 1983).

The complementary HCG- β subunit contains 145 aminoacids with several regions homologous to the glycoprotein hormones β subunits such as FSH- β and TSH- β and striking homology of 80 aminoacids of the initial 115 with hLH- β subunit, except that HCG- β subunit contains an additional 30 aminoacids 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 carboxy

terminus of the HCG- β subunit are O-glycosidically linked to serine instead of asparagine (Saxena, 1983).

Biologic Properties:

Owing to the structural similarities between hLH and HCG, the two hormones are very similar in their biologic and immunologic properties (Saxena, 1983).

The structural homologies between HLH, between hLH, hFSH and hTSH also explain an intrinsic fSH and TSH-like activity of HCG, the later explains hyperthyroidism in late pregnancy (Braunstein and Hershman, 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 Corpus Luteum of gestation. This is necessary for implantation the growth and preparation of the endometrium for implantation. It is very probable, but not conclusively proven, that HCG stimulates steroidogenesis in the early fetal testis. So that androgen production will ensue and masculine differentiation can be accomplished (Kaplan and Grumbach, 1978).

It also appears that the function of the inner fetal zone of the adrenal cortex may depend upon HCG for steroidogenesis early in pregnancy (Speroff et al., 1983).

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

Immunologic Properties:

HCG and its α and β subunits are highly antigenic and can produce antibodies of high titer, specificity, and affinity when injected into heterologous species such as Guinea pigs, rabbits, and sheep. It would appear that the antibodies against the α subunit cross-react with the α -subunit of the other glycoprotein hormones, 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 and hFSH and their β -subunits (Vaitukaitis et al., 1972).

Production and Secretion Sites:

Placenta:

HCG is produced by the syncytiotrophoblast of the placenta during pregnancy and secreted into the blood by both mother and fetus (Landesman and Saxena, 1976).

It has been used as an indicator of pregnancy and can be detected as early as 6 to 8 days following ovulation (Saxena et al., 1977). Plasma levels of HCG rise rapidly with doubling in concentration ranged from 1.4 to 3.5 days, which was not constant but increase with HCG concentration and gestational age (Donald et al., 1985).

Normal placenta also produces free α -HCG with the advancement of the pregnancy, the level of α -HCG exceeds that of HCG, and after the 8th to 10th weeks of pregnancy, the α -HCG subunit is detected in the peripheral blood and urine (Vaitukaitis, 1974).

The levels of β -HCG rise rapidly and in a manner similar to those of HCG, reaching maximum levels between the 8th to 12th week and subsequently decreasing to insignificant levels. The radioimmunoassays measure subunits of HCG as well as fragments of HCG, which are not detected by bio-or receptorassays. This is reflected in the varying ratio of biologic to immunologic activities of HCG throughout gestation and by the elevated levels of α -HCG and β -HCG during pregnancy (Vaitukaitis, 1974).

Fetus

The level of HCG in fetal serum, in amniotic fluid were clearly measurable prior to 12th week with level up to 550 ng/ml in serum and 7400 ng/ml in amniotic fluid (Clements et al., 1976).

The mean cord blood HCG concentrations from pooled data of both male and female newborn infants show a declining trend from 23 weeks of gestation to term, sex difference were observed for HCG, the mean concentration of HCG in the cord plasma of female newborn infants exceeded that of male newborn infants between 23 and 43 weeks of gestation; between 29 and 36 weeks of gestation, this difference was statistically significant (Yuen et al., 1987).

Kletzky et al., (1985) found that there is a similar qualitative and quantitative pattern of HCG secretion between maternal serum and amniotic fluid throughout pregnancy. The significant correlation ($r=0.85$, $p=0.001$) between the levels found in both compartments indicates that the secretion of HCG from the syncytiotrophoblast is evenly distributed. Since it has been found that the level of HCG in cord blood are extremely low, it can be suggested that its presence in amniotic fluid in concentration similar to that of serum is the result of direct diffusion from the placenta (Crosignani, 1972).

Normal Tissues:

Extracts from human testis, urinary concentration and pituitary extracts, as well as plasma obtained from non pregnant subjects contain a substance that is chromatographically and electrophoretically similar to HCG and exhibit in vitro biologic activity similar to HCG and hLH (Robertson et al., 1978).

A postmenopausal urinary gonadotropin preparation is also found to contain in vitro HCG-like biologic activity in the RRA. The source of HCG is assumed to be of pituitary in origin. A large concentration of immunoreactive α -Co-chromatographing with TSH- α , LH- α or FSH- α , has also been detected in extract of normal pituitary tissue (Kaplan et al., 1976, Kourides et al., 1975, Ractliff, 1974). An immunoreactive HCG-like substance has been identified in extract of liver and colon (Yashimoto et al. 1977).

Sperm:

An HCG like material has been detected in the sperm of various species including humans. The β subunit of HCG was demonstrated by a fluorescein-labeled double antibody technique in the spermatozoa of seven volunteers. The HCG-like substance is present in 5% to 7% of spermatozoa in all specimens analyzed. HCG like material in the sperm could provides the precursor for the production of a chorionic gonadotropin-like material by the conceptus prior to