RELATION BETWEEN GROWTH HORMONE, RENAL SIZE BY ULTRASONOGRAPHY AND GLOMERULAR FILTRATION RATE IN DIFFERENT STAGES OF PREGNANCY



THESIS

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Sometimes, the truest feelings are those we keep inside, and though not often mentioned, they are the most sincere

To my very dear brother Ramzy, with all my love and respect

And to my children, Mohamed & Maya, they are my life



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LIST OF ABBREVIATIONS

anti-HGH : Antihuman growth hormone.

bGH : Bovine growth hormone.

CGP : Chorionic growth hormone-prolactin.

D.M. : Diabetes mellitus.

ELISA : Enzyme-linked immunosorbent assay.

ERPF : Effective renal plasma flow.
GFR : Glomerular filtration rate.

GH : Growth hormone.

GHRF : Growth hormone releasing factor.
hCS : Human chorionic somatomammotropin.
hCS-A : Human chorionic somatomammotropin A.
hCS-B : Human chorionic somatomammotropin B.

hCS-L : Human chorionic somatomammotropin pseudogene.

HGH : Human growth hormone.

HGH-N : Normal human growth hormone.

HGH-V : Human growth horomone variant.

hIGF-I : Human insulin-like growth factor I.

hPGH : Human placental growth hormone.

hPL : Human placental lactogen.
IGF-I : Insulin-like growth factor I.

KD : Kilo Dalton.

MAB : Monoclonal antihuman antibodies.
MABP : Mean arterial blood pressure.
mRNAS : Messenger ribnonucleic acids.

NSB : Nonspecific binding.
OD : Optical density.
PAH : Para-aminohippurate.

PGH : Placental growth hormone.

PRL : Prolactin.

RPF : Renal plasma flow.

RVR : Renal vascular resistance.

S.D. : Standard deviation.

SHR : Spontaneously hypertensive rat.

SM : Somatomedins.

SNGFR : Single nephron glomerular filtration rate.

Introduction & Aim Of The Work

INTRODUCTION & AIM OF THE WORK

Human pregnancy is characterized by a dynamic change in a variety of metabolic functions. The regulatory mechanisms responsible for these changes in maternal protein, carbohydrate and lipid metabolism have traditionally been ascribed to the dramatic increase in circulating steroid and peptide hormones. Pituitary growth hormone (HGH), a major regulatory protein, has anabolic effects and stimulates protein synthesis in many tissues including bone, muscle, connective tissue and visceral organs. HGH also has profound effects on carbohydrate and lipid metabolism (Merimee, 1979).

Increased concentrations of HGH and its variants were recorded from midpregnancy until full-term (Kaplan and Grumbach, 1964; Katz et al., 1969; Kletzky et al., 1985; Frankenne et al., 1988), and placental GH (PGH) behaves as a strong agonist to pituitary GH in binding to hepatic and other HGH receptors (Frankenne et al., 1988).

Furthermore, during normal pregnancy, glomerular filtration rate (GFR) and renal plasma flow (RPF) were recorded to increase by 30-50% above the pre-gravid values starting early in pregnancy and reaching maximum levels in the last trimester (Dignam et al., 1958; Lindheimer and Katz, 1970;

Dunlop, 1981; Ronco et al., 1988). Also, kidney length was reported to increase approximately one cm during normal pregnancy (Lindheimer and Katz, 1990; Kincaid-Smith, 1991).

On the other hand, more than forty years ago, it was noticed that increased HGH levels in patients with acromegaly were associated with an increase in renal size and function (Barnett et al., 1943) and the administration of HGH to normal human subjects led to a significant increase in GFR and RPF (Corvilain and Abramow, 1962).

Recently, much argue arose regarding the effect of increased GFR and RPF on the kidney function and morphology. Some investigators attributed glomerular injury to the increase in glomerular pressure (Brenner, 1983) and correlated the increased glomerular size with mesangial sclerosis (Doi et al., 1990). However, this effect was denied by other workers (Baylis and Rennke, 1985).

So, it became the aim of the present work to study the relationship between renal size, GFR and growth hormone (or its variants with similar activity in maternal serum) during different stages of pregnancy in comparison to non-pregnant women, and to compare the results of multiparae with those of primigravidae.

Review Of Literature

HORMONAL CHANGES IN PREGNANCY

HORMONAL CHANGES IN PREGNANCY

(A) Growth Hormone (And Its Variants) During Pregnancy

In 1956, Contopoulos and Simpson investigated the presence of growth-promoting activity in the plasma of normal and pregnant rats. They found that the plasma from pregnant rats at the sixteenth to twentieth days of gestation contained three times the amount of growth activity present in normal rat plasma. This growth promoting activity was not decreased by hypophysectomy of the mother at the twelfth day of pregnancy. So, the investigators suggested a foetal origin of the growth-promoting factor (Contopoulos and Simpson, 1956).

Later, Josimovich and MacLaren (1962), described that the placenta produced a substance which was immunochemically closely related to human pituitary growth hormone (HGH). This substance, which was isolated in relatively large amounts and purified form, from full term human placentas, was called "human placental lactogen" (hPL) due to its highly lactogenic properties in the pseudopregnant rabbit. However, this substance was devoid of the growth-promoting activity in the hypophysectomized rat tibial plate growth assay at the dose levels tested.