FETAL CORD PROLACTIN CONCENTRATION IN DIABETIC PREGNANCIES

Thesis

Submitted For Partial Fulfilment Of The Master Degree In Paediatrics

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1989

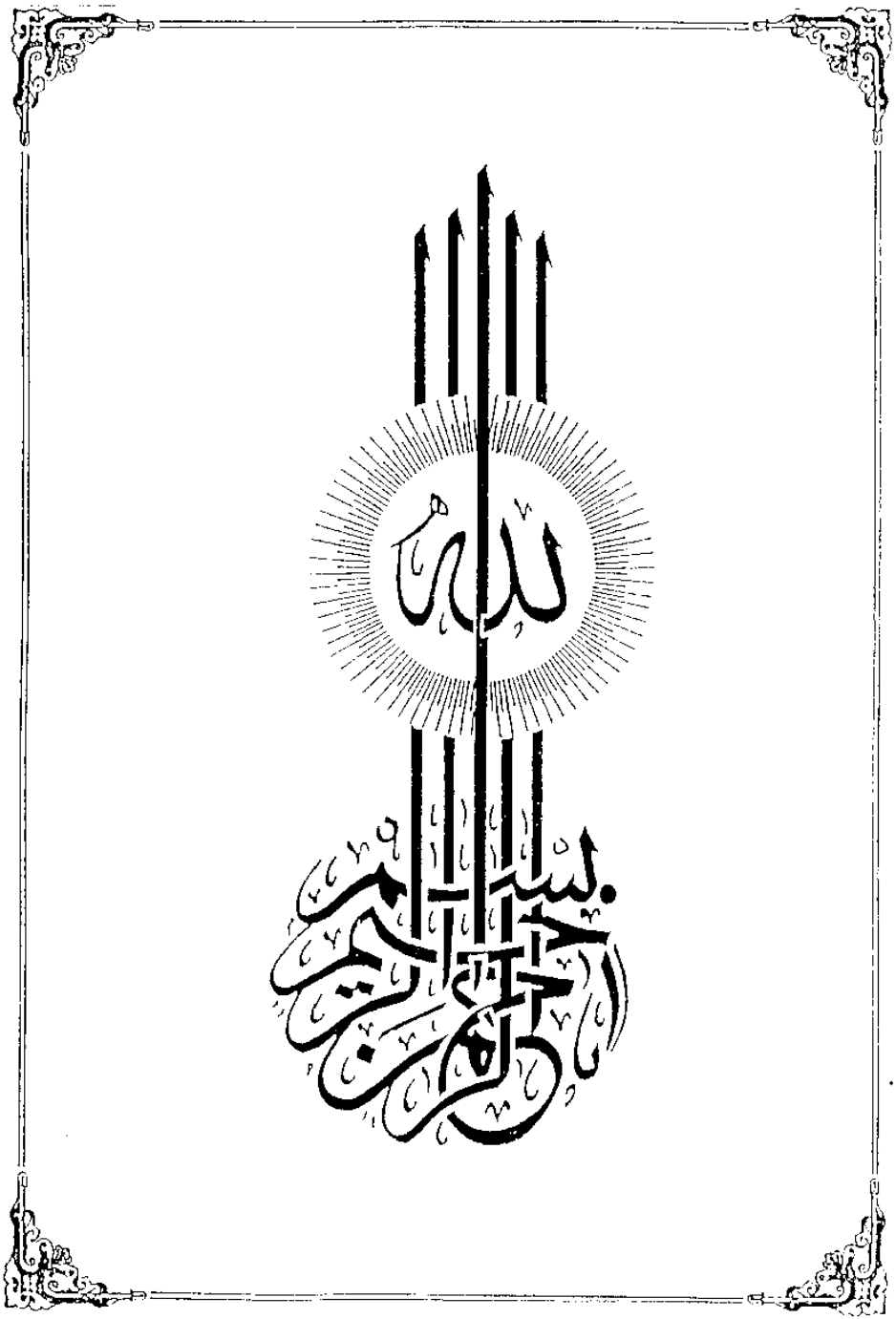
ACKNOWLEDGEMENT

First thanks to God, who gives every thing without return.

I would like to express my deep thanks and gratitude to my teacher and advisor Dr. *Hamed Ahmed El-Khayat*, Assistant professor of Pediatrics, Faculty of Medicine, Ain-Shams University, for his considerable help and support during this research in which it has been my good fortune to work under his supervision.

I am sincerely indebted to Dr. *Mohamed Nabegh Al-Mahalawi*, Assistant professor of Obst. & Gyn., Faculty of Medicine, Ain-Shams University, for his help and advice throughout the whole work.

I am extremely grateful for Dr. *Sanaa Youssef Shaaban*, lecturer of Pediatrics, Faculty of Medicine, Ain-Shams University, for her helpful guidance and unlimited support.



CONTENTS

ABBREVIATIONS USED

D.M.	:	Diabetes mellitus
I.D.Ms.	:	Infants of diabetic mothers
I.D.D.M	:	Insulin dependent diabetes mellitus
N.I.D.D.M.	:	Non-Insulin dependent diabetes mellitus
G.D.	:	Gestational diabetes mellitus
R.D.S.	:	Respiratory distress syndrome
PRL	:	Prolactin hormone

INTRODUCTION AND AIM OF THE WORK

Introduction And Aim of The Work

The contribution of the respiratory distress syndrome in the neonatal morbidity and mortality in infants of diabetic mothers is one of the main problems in the current pediatric practice (Robert et al., 1976).

The major etiologic factor in the development of respiratory distress syndrome is a deficiency of surfactant as a surface active material that lines the alveoli and reduces surface tension at the alveolar tissue air interphase, thereby prevents atelectasis during expiration (Adams et al., 1970 and Brumlety et al., 1976).

Various factors are affecting the surfactant synthesis and fetal lung maturation, different hormones such as insulin, cortisol, testosterone and thyroxine are known affecting fetal lung maturity (Mendelson et al., 1981).

Recently prolactin has been implicated as an additional factor controlling the maturation of the fetal lungs. Some studies reported significant decrease in the mixed-cord prolactin concentrations of infants of diabetic mothers (Saltzman et al., 1986). Others denied any change in prolactin concentration in diabetic pregnancy (Ballard et al., 1978).

Therefore, this study aimed to determine the fetal cord prolactin concentrations in newborns of diabetic mothers and the possibility of subsequent development of respiratory distress syndrome in these neonates.

REVIEW

Physiology of Prolactin Hormone (PRL)

PRL is a single chain polypeptide of molecular weight about 20000. The entire linear sequence of 198 aminoacids has been identified (Shome and Parlow, 1979).

PRL Secretion :

PRL is secreted by the lactotropic cells which coexist with growth hormone producing cells in the lateral wing of the anterior pituitary gland (Chang, 1978).

Electron microscopy and immunohistochemical staining techniques indicated that the PRL secreting cells possess distinct morphologic features, lamellar pattern of the rough endoplasmic reticulum, large secretory granules (400-900 μm in diameter) and polymorphism of their secretory granules (Hopkins et al., 1973).

In the lactotropic cells PRL is synthesized within the cisterns of the rough endoplasmic reticulum and packaged by the Golgi apparatus into small membrane-bound progranules, which are used to form large mature secretory granules.

These granules lie in the cytoplasm until their contents are secreted by exocytosis resulting from fusion of the granular membrane with the surface membrane of the cell itself (Chang, 1978).

Molecular Actions :

Most studies indicated that PRL acts on specific

receptors which are located on the outer membrane of the target cells (Fraser et al., 1979).

It is well known that the target organ for PRL is the mammary gland during pregnancy and lactation, however, a number of other organs are affected by this hormone (Hamosh and Hamosh, 1977).

Zinder et al., (1974) have shown that the adipose tissue becomes a target organ for PRL during late pregnancy and lactation.

In addition to the mammary gland, PRL binds specifically to a number of other tissues such as Liver, Adrenal cortex and Kidney (Ponser et al., 1974).

Control of PRL production :

Current investigative efforts indicate that prolactin secretion is regulated primarly by hypothalamic inhibitory factor called prolactin-inhibitory factor; PIF (Meites and clemens, 1972).

Dopamine is the major biogenic amine controlling basal secretion of prolactin (Birge et al, 1970; and Meties, 1973).

L'Hermite et al, (1978) found that dopamine and norepinephrine when injected into the third Ventricle of rats, lower serum prolactin levels were obtained.

Serotonin has also been implicated in mediating prolactin release (Zacur et al., 1976).

Control of prolactin release appears to be largely

inhibitory in nature, although prolactin-releasing activity has also been demonstrated in several animal species, furthermore thyrotropin-releasing hormone (TRH) in pharmacologic amounts has been shown to stimulate prolactin secretion in human (Meites and Clemens, 1972).

Factors affecting the secretion of human Prolactin :

According to Ganong (1983) and modified from Frantz (1978) the factors affecting Prolactin secretion include :

Factor	Change in PRL level
- Sleep	1^{+}
- Nursing	1^{++}
- Breast stimulation in non-lactating	1
- Stress	1^{+}
- Hypoglycemia	1
- Sternuous exercise	1
- Sexual intercourse in women	1
- Pregnancy	1^{++}
- Estrogens	1
- Hypothyroidism	1
- TRH	1^{+}
- Phenothiazines	1^{+}
- Opiates	1
- Glucose	N
- Somatostatin	N
- L-dopa	D^{+}
- Apomorphine	D^{+}
- Bromocriptin and related ergot derivatives	D^{+}

1, moderate increase & N, no change

1^{+}, marked increase & D, moderate decrease

1^{++}, very marked increase & D^{+}, marked decrease

Biological Activities of PRL :

The physiologic role of human PRL in both males and females is obscure, despite the fact that not less than 85 biological actions of PRL have been proposed (Saxena, 1977).

*** PRL and breast development :**

PRL is a lactogenic hormone and it also appears to induce mammotropic stimulation, at least in experimental animals (Sulman, 1970).

Its role in normal pubertal breast development of human female is only theoretic as there are no data in humans to support or deny its potential mammotropic role (Jacobs,1974).

Moreover, serum PRL level in Pubertal males with unilateral or bilateral gynecomastia have not been reported to be elevated (Jacobs, 1974 and Nicoll, 1974).

However, Thorner et al., (1977) reported that there is a small rise in PRL level in girls during breast development, and Archer, (1980) had suggested that a combined effect of estrogen and PRL on the breast tissue accounts for breast development that is recognized as thelarche.

*** PRL and lactogenesis :**

The principle physiologic role of PRL is initiation and maintenance of lactation (lactogenesis) and this is the only well documented effect of PRL in the human (Saxena, and Archer, 1980).

Changes in serum PRL levels will affect milk secretion.

Bromocriptin which inhibts PRL secretion will result in a decrease in milk secretion (Roland et al., 1973).

Prolactin can induce milk formation when added to explants of mammary glands from pregnant mice in vitro (Williams, 1974).

PRL increases the capacity of mammary tissue maintained in culture to synthesize fatty acids (Hollowes et al, 1973) and other milk constituents such as casein and lactose (Turkington et al., 1973).

In the syndrome of pituitary infarction (Sheehan's syndrome), failure to lactate in the postpartum period may be an early and valuable sign of partial or complete hypopituitarism or an isolated deficiency of PRL secretion (Turkington, 1972).

*** Prolactin and adrenal cortex :**

Posener et al., (1974) had demonstrated specific receptors for PRL in the adrenal cortex and suggested that PRL may affect its function.

Giusti et al., (1977) have been discovered that levels of plasma dehydroepiandrosterone sulphate (DHEAS) are much more elevated in non-pregnant women with hyperprolactinemia than in women with normal plasma PRL level.

However, Parker et al., (1978) had found in 30 patients with hyperprolactinemia as a result of pituitary tumour, normal levels of DHEAS. Also, Varma et al (1977) injected

Ovine PRL into normal men and noted no change in adrenal androgen.

*** Prolactin and Ovarian function :**

PRL may indirectly stimulate cholesterol synthesis from acetate and sensitize the ovary to the steroidogenic action of L.H. (Saxena, 1977).

It has been reported that short luteal phase and low progesterone secretion may be associated with elevated plasma PRL concentrations in some infantile women and that this condition may be corrected by bromocriptin (Deplozo et al, 1979).

*** Prolactin and Surfactant Synthesis :**

Discussed later with multihormonal regulation of surfactant synthesis.

INFANTS OF DIABETIC MOTHERS

(I.D.M.S.)

IDMs are considered high risk infants. Diabetic pregnancy is associated with higher fetal wastage and perinatal mortality owing to the increase in incidence of complications during pregnancy . Stillbirths, cesarean sections , and pre-maturity are common complications among diabetic pregnancies (Fletcher, 1981).

IDMs have an increased risk of many problems which include :

- Respiratory distress syndrome.
- Hypoglycaemia .
- Hypocalcaemia and hypomagnesaemia.
- Cardiomyopathy
- Polycythaemia and hyperviscosity.
- Renal vein thrombosis.
- Hyperbilirubinaemia.
- Congenital malformations.
- Macrosomia and less commonly intrauterine growth retardation.
- Prematurity.
- Other problems: which include poor feeding, poor suckling reflexes and high gastric residuals. (Fletcher, 1981).