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SOME ADRENAL ASPECTS IN PREGNANT DIABETICS

THESIS

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INTRODUCTION
AND
AIM OF WORK

I N T R O D U C T I O N

The incidence of preeclampsia is higher among pregnant diabetics . Hydramnios is also one of the commonest clinical findings found in pregnant diabetics .

AIM OF THE WORK

The aim of this work is to study some adrenal aspects in pregnant diabetics .

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Physiology of normal pregnancy

Many physiological changes in pregnancy affect the various organ systems . These changes are influenced by variations in maternal metabolic fuels which in turn are dependent on various hormones in the mother (Felig,1977).

I) Metabolic changes during pregnancy

Maternal and fetal fuel metabolism :

- Pregnancy in the fasted state :

In the fasted condition, there is a continuous transfer of glucose and amino acids from the mother to the fetus, while insulin does not pass. As a result of this, maternal blood levels of glucose and amino acids and consequently insulin will drop. Therefore, the mother is exposed to exaggerated and accelerated response to starvation and liable to starvation ketosis (Grasso et al., 1968; Freinkel, 1969; Adam et al., 1969; Obenshain et al., 1970; Felig and Lynch, 1970; Freinkel et al.,1974; Freinkel and Metzger, 1975; Felig, 1977 and Kolkhoff , Kissebah and Kim, 1978) .

MOTHER	PLACENTA	FETUS
Glucose	Diffusion	Glucose
Amino acids	Active Transport	Amino acids
Free Fatty Acids	Gradient Dependent Diffusion	Esterified to tri- glycerides by Adipocytes
Ketones	Diffusion	Ketones — Oxidation
Insulin	Binding Cleavage	
Lipolytic and anta- gonistic to insulin	Synthesis { HPL Oestrogen Progesterone }	

Maternal, placental and fetal integration of
fuels for the promotion of fetal growth .

HPL = Human Placental Lactogen .

Quoted from Hollingsworth , Am. J. Obstet. Gynaecol., 146:
420 , (1983) .

- Pregnancy in the fed state :

In the post - absorptive condition, blood glucose levels are elevated than that in non - pregnant condition (O'Sullivan and Mahan, 1964) . This hyperglycemic state was explained as a result of failure of glucose uptake by the liver (Felig, Wohren and Hendler, 1975) . The hyperglycemia is associated with an increase in insulin levels (Tyson and Merimee, 1970 and Van Aasche and Aerto , 1975) .

The hyperglycemia and hyperinsulinemia are attributed to liver and peripheral tissue resistance to insulin (Felig, 1977) . Gabbe (1981) explained hyperinsulinemia and insulin resistance by the increased levels of human placental lactogen which increases maternal lipolysis and utilization of fat for energy and spares glucose for fetal consumption . Other hormones as free cortisol and prolactin also contribute to the insulin resistance at the 3rd trimester . Oestrogen and progesterone may directly alter maternal islet cell function producing B-cell hyperplasia and hyperinsulinemia. Puavilai et al., (1982) reported that the impairment in insulin action is at a site distal to the insulin receptor i.e. a post - receptor defect .

II) Physiological changes during pregnancy

Many physiological changes have been noticed , meanwhile we will discuss briefly the much more important changes as regards our work .

Blood , it was found that an increase in the total blood volume occurs especially after 34 weeks of pregnancy, followed by a gradual fall until term . This is mainly due to the increase in plasma volume . This is associated with an increase in red cells, white blood cells and platelets (Dewhurst, 1981) .

A dilutional fall in plasma proteins and electrolytes have been noticed as well, although an increase in globulin levels is recorded (Dewhurst, 1981) .

A significant rise in cholesterol and triglycerides is noticed as well (Dewhurst, 1981) .

Cardiovascular system , early in pregnancy, a rise in the cardiac output occurs followed by a drop; reflecting changes on the glomerular filtration rate , occur respectively (Dewhurst, 1981) .

As regards the gastrointestinal tract , a reduction

in motility of the stomach and bowel peristalsis leading to constipation is sometimes recorded . This probably is due to progesterone effect during pregnancy (Dewhurst, 1981) .

III- Endocrine changes during pregnancy

It was believed that the endocrine changes in pregnancy do not manifest until after implantation of the blastocyst . From that time until delivery of the placenta, there is a progressive maternal hormonal changes, much of which are due to endocrine activity of the placenta and fetus . Now, it becomes apparent that even the pre-implantation blastocyst is endocrinologically active . The fetus in very early and late pregnancy plays an important role in the regulation of its own development and perhaps in the initiation of spontaneous labour (Dewhurst , 1981) .

As demonstrated before, placental hormones are effective in the endocrine changes in pregnancy , we will start our discussion by the placental hormones .

A) Placental hormones :

Placental hormones are categorized into :

✱ Peptide Hormones :

- Human chorionic gonadotrophins .
- Human placental lactogen .
- Human chorionic corticotrophin .
- Placental thyrotrophins .
- Relaxin .
- Other placental proteins .

✱ Steroid Hormones :

- Progesterone .
- Oestrogen .

1- Human chorionic gonadotrophin (HCG) :

HCG is secreted from the trophoblast before implantation and also before the first missed period (Mishell et al., 1974) . It rises rapidly in early pregnancy , reaching a peak between 8th and 10th week of pregnancy . Then there is a relatively rapid drop to 18th week and levels remain more or less constant until after delivery (Baunstein et al.,1976). Dewhurst (1981) believed that HCG has some control on steroid synthesis from the placenta and is responsible partly for morning sickness .

2- Human Placental Lactogen (HPL) or Human Chorionic Somatomammotropin :

Schneider, Kowalski and Sherwood (1975) declared that HPL is present in 2 molecular forms . The small molecule is a dominant one in body fluids and the big molecule is the active hormone secreted by the placenta.

Josimovich & Archer (1977) put a positive correlation between the rate of HPL secretion and placental weight during pregnancy . The investigator declared 3 main possible physiological functions of HPL :

- a) It is lactogenic .
- b) It is lipolytic, retains nitrogen, increases insulin resistance as well as its levels .
- c) A possible control on progesterone synthesis .

3- Human Chorionic Corticotrophin :

Rees et al., (1975) reported the existence of human chorionic corticotrophin with adrenocorticotrophic hormone (ACTH) like activity .

4- Placental Thyrotrophins :

Yamamoto et al., (1979) and Harada et al., (1979) declared the presence of thyroid stimulators in the placenta, but their nature is unknown .