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### جامعة عين شمس

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## Assessment of amniotic fluid insulin in pregnancies complicated by diabetes mellitus

#### Thesis

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Alexandria University
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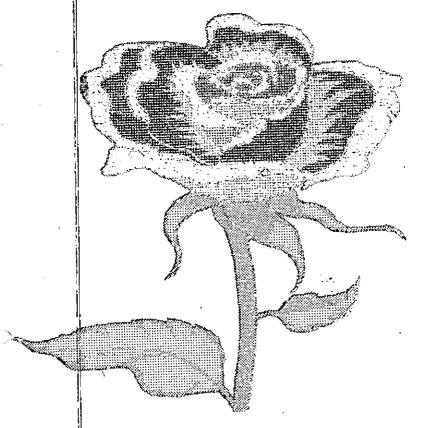
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To my lovely son Ezzat

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#### Introduction

Diabetes is a syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism, associated with absolute or relative deficiencies in insulin secretion and/or insulin action.

(1) When fully expressed, diabetes is characterized by fasting hyperglycemia. But the disease can also be recognized during less overt stages and before fasting hyperglycemia appears, most usually by the presence of glucose intolerance. Diabetes mellitus may be suspected or recognized clinically by the presence of characteristic symptoms such as excessive thirst, pruritis, unexplained weight loss, or one or more of the many complications associated with or attributable to the disease. (2)

Diabetes is one of the most common medical complications of pregnancy. Diabetic patients can be separated into those who were known to have diabetes before pregnancy (overt) and those diagnosed during pregnancy (gestational). (3)

Gestational diabetes mellitus is a clinical entity with short term and long term implications for both the mother and fetus. (4-7) When undiagnosed or treated inappropriately, Gestational diabetes mellitus

(GDM) is associated with maternal and fetal morbidity. <sup>(8, 9)</sup> There is evidence that mild degrees of hyperglycemia can be associated with complications to the mother and the fetus. These complications were significantly reduced with appropriate treatment of these women. <sup>(10-13)</sup>

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. (14) This definition applies regardless of whether or not insulin is used for treatment. Undoubtedly, some women with GDM have previously unrecognized overt diabetes. Because GDM is typically a disorder of late gestation, hyperglycemia during the first trimester usually means overt diabetes. (15)

#### Incidence of diabetes in pregnancy:

It has been estimated that diabetes mellitus complicates 2 to 3% of all pregnancies, and that 90% of these cases represent women with gestational diabetes mellitus (GDM). (3)

#### Maternal metabolism and pathophysiology of diabetes in pregnancy:

During normal pregnancy, maternal metabolism adjusts to provide adequate nutrition for both the mother and the growing fetoplacental unit.

Early in pregnancy, glucose homeostasis is altered by increasing levels of estrogen and progesterone that lead to beta cell hyperplasia and increased insulin response to glucose load. (16)

Pregnancy has been linked to a state of "accelerated starvation", characterized by a relative hypoglycemia in the fasting state. (17) This state is due to two major influences:

- 1- Glucose provides the major, although not the entire fuel requirement for the fetus. A difference in gradient causes a constant transfer of glucose from the mother to the fetus.
- 2- Placental hormones, specifically estrogen and progesterone, and particularly Human Placental Lactogen (HPL), interfere with the action of maternal insulin.

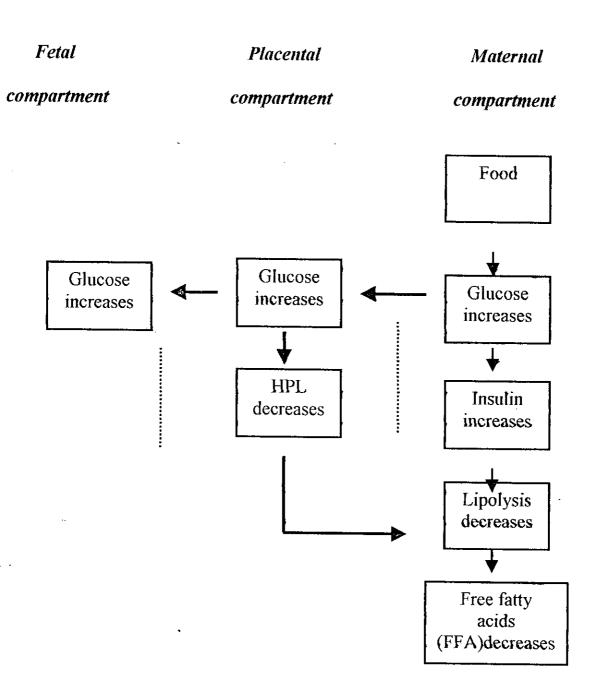
Despite the above processes, early and midpregnancy are periods of maternal anabolism marked by increasing maternal protein and fat stores.

The relative hyperinsulinemia observed in early pregnancy serves to promote lipogenesis and decrease lipolysis.

#### Metabolism of the second half of pregnancy and the role of HPL:

The metabolic role of HPL is to mobilize lipids as free fatty acids. In the *fed state*, there is abundant glucose available, leading to increased insulin levels, lipogenesis and glucose utilization. This is associated with decreased gluconeogenesis and a decrease in the circulating free fatty acid levels, because the free fatty acids are utilized in the process of lipogenesis to deposit storage packets of triglycerides. (17-23)

As glucose decreases in the *fasting state*, HPL levels rise. This stimulates lipolysis leading to increase in the circulating free fatty acids. Thus, a different fuel is provided for the mother so that glucose and amino acids can be conserved for the fetus. With sustained fasting, maternal fat is utilized for fuel to such an extent that maternal ketone levels rise. There is limited transport of free fatty acids across the placenta. Therefore, when glucose becomes scarce for the fetus, fetal tissues utilize the ketones that do cross the placenta.



HPL changes in the fed stage (17-23)