PERINATAL MORBIDITY AND MORTALITY AMONG INFANTS OF DIABETIC MOTHERS

THESIS

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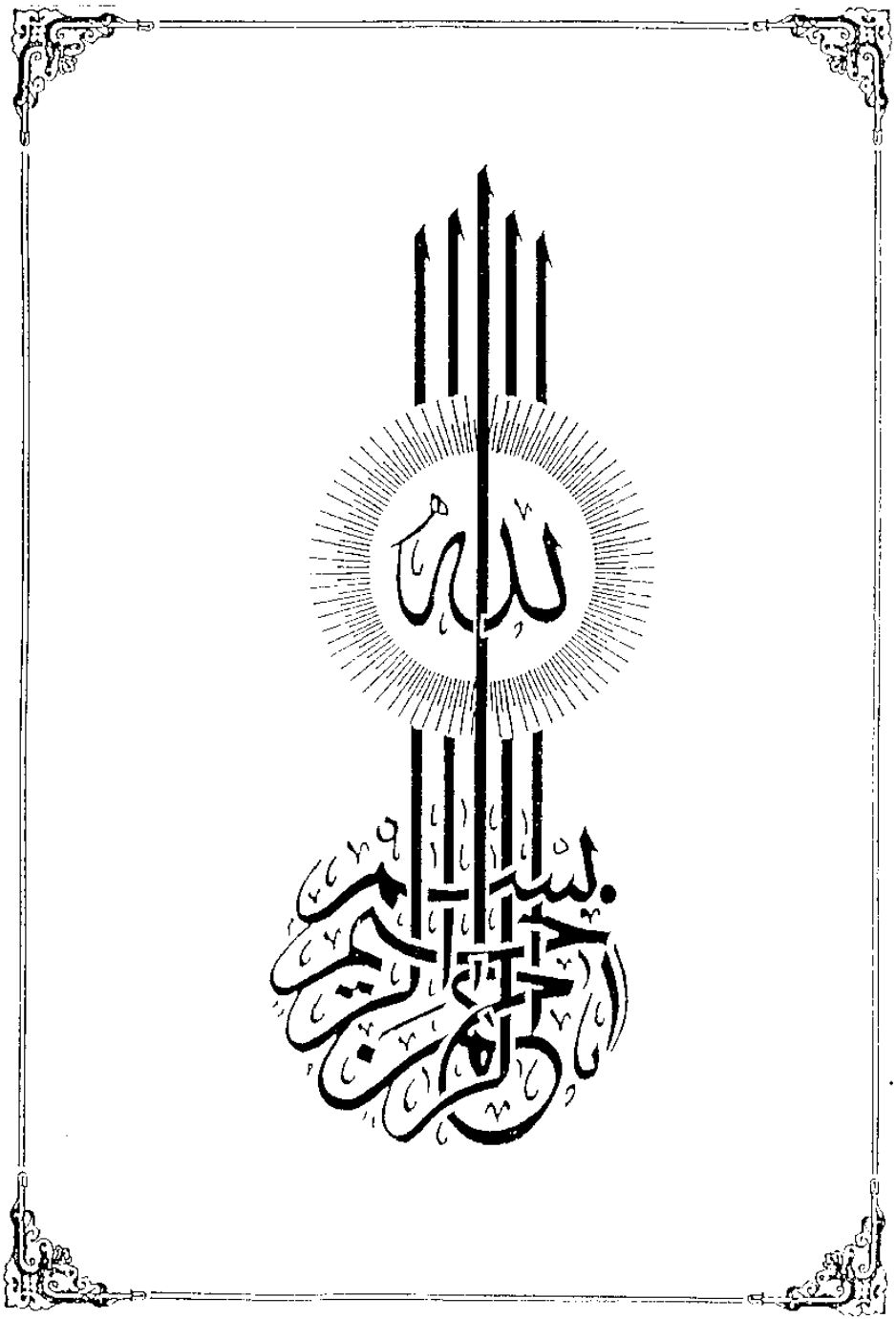
DEDICATION

TO DR. KAY F. MC FARLAND, WITH ALL THE LOVE,
RESPECT AND APPRECIATION THAT I HAVE.

EZZAT Y. HEMAYA



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I. INTRODUCTION

PERINATAL MORBIDITY AND MORTALITY AMONG INFANTS OF DIABETIC MOTHERS

I. INTRODUCTION

The recognized incidence of diabetes mellitus during pregnancy has increased since the discovery of insulin and its widespread use to control the disease.Before the discovery and use of insulin, diabetic women who were ketoacidosis-prone were unlikely to live long enough to become pregnant. Now, with the use of insulin , diabetes became easier to control than before, and many diabetic women have a good chance of becoming pregnant.Also, the prevalence of diabetes in the general population has increased, probably due to better detection. Consequently, diabetes during pregnancy has also become a more common medical problem. Prior to pregnancy, the incidence of diabetes is 0.1 % to 0.5 %.[1] During pregnancy, this incidence is much higher, ranging between 1.4 % and 2.6 %.[2] This is attributed to increased emphasis on detection and the diabetogenic effect of pregnancy. Thus, gestational diabetes occurs about ten times more frequently than diabetes diagnosed before the onset of pregnancy.[1]

Diabetes in pregnancy may have serious effects on both the baby and the mother.The diabetic pregnant woman has a high predilection for developing pre-eclampsia and eclampsia. Also, the incidence of hydramnios increases in pregnant women with diabetes. At the same time,the pregnant diabetic woman is more liable to suffer from postpartum hemorrhage.[3]

Among the infants of diabetic mothers, there is an increase in both perinatal morbidity and mortality. The most important causes of increased perinatal morbidity include hypoglycemia, hypocalcemia, hyperbilirubinemia, respiratory distress (due to respiratory distress syndrome or cardiomyopathy), macrosomatia, prematurity and/or congenital malformations.[4] Other problems include asphyxia neonatorum, birth injuries, heart failure, hypomagnesemia, increased blood volume, neurologic instability, polycythemia, hyperviscosity and transient hematuria. Perinatal mortality is most commonly related to congenital malformations and intra-uterine fetal death, especially toward the end of pregnancy.[2] In addition, a child of a diabetic mother or father has a higher likelihood of developing diabetes later on in its life.[5]

Some of the complications of pregnancy and perinatal morbidity and mortality can be reduced through meticulous care of the diabetic mother and her newborn infant. In general, pregnancy complications and perinatal morbidity and mortality increase with the increase in maternal blood glucose level. Metabolic changes that accompany the elevation in blood sugar level may explain many of the fetal and neonatal problems. For example, the first few weeks of pregnancy represent the critical time of organogenesis; maternal hyperglycemia during this period may be responsible for the development of fetal congenital malformations. The effect of maternal hypoglycemia during this period is unclear. Also, fetal macrosomia may be explained as a secondary effect of maternal hyperglycemia which in turn can lead to fetal hyperglycemia and hyperinsulinemia. Fetal macrosomia is associated with increased incidence of stillbirths and neonatal deaths. When diabetic ketoacidosis occurs during

the second trimester of pregnancy, fetal loss may be as high as 50 %.[5]

Meticulous management of the diabetic mother includes early detection and diagnosis of diabetes in pregnancy, control of blood sugar and management of labor. Early detection depends upon screening of pregnant women,especially those at high risk, with a blood sugar obtained one-hour after an oral glucose load. Estimation of glycosylated hemoglobin is not a sensitive method for detection of glucose intolerance.The criteria for diagnosis of diabetes in pregnancy differ from those used in the diagnosis of diabetes in nonpregnant women.

Diet and insulin therapy are the main methods used to control blood sugar during pregnancy.Special problems in the management of labor include the need to accurately assess gestational age and fetal pulmonary maturity as well as manipulation of insulin therapy during and after labor.

The most important test for estimation of fetal lung maturity is the amniotic fluid lecithin/sphingomyelin (L/S) ratio. Ultrasonography is used to evaluate fetal growth and thus estimate gestational age. Estriol excretion in urine is an indirect measure of fetal well-being; this hormone is produced by the fetoplacental unit and passes through the maternal circulation before being excreted. The non-stress test and oxytocin challenge test are other methods of fetal assessment. The non-stress test measures changes in fetal heart rate in response to fetal movement, whereas heart rate changes during

uterine contractions are measured by contraction stress test. Oxytocin may be used to stimulate uterine contractions and this test is referred to as oxytocin challenge test.

In addition, careful neonatal supervision may further reduce infant morbidity and mortality. The role played here by the Neonatal Intensive Care Unit (NICU), especially when the infant is premature, deserves special mention. The infant born of a diabetic mother, although large for gestational age, may be physiologically premature. Intensive medical care may be essential to save its life. The incubator represents one of the crucial methods for neonatal resuscitation ; it can offer for the infant an atmosphere with relatively high humidity, a suitable temperature and oxygen if necessary. Also, early correction of neonatal hypoglycemia and hypocalcemia is very important.

II. REVIEW OF THE LITERATURE

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A. Management of the Diabetic Mother

1. Screening and Diagnosis

Early detection of diabetes during pregnancy is the first step in obtaining good control of blood sugar and consequently, the best possible outcome. There are a number of recommendations regarding methods to optimize detection of diabetes. In some medical centers, all pregnant women, particularly those at high risk, are screened for diabetes toward the end of the second trimester or the beginning of the third trimester .[6] This period between 24-33 weeks of gestation denotes the time during which the insulin resistance induced by gestational hormones and enzymes increases dramatically.[7]

A number of factors may increase the likelihood of the pregnant woman becoming diabetic. Such risk factors include obesity, a positive family history of diabetes and previous development of gestational diabetes. Also, the risk is increased with advancing maternal age, and parity more than four.[8] Other risk factors include a previous abnormal glucose tolerance following stress such as surgery, infection, emotional trauma or use of some medications, e.g. cortisone.

It seems that obesity, per se, does not carry a significantly increased risk for the pregnant woman of developing diabetes in the absence of other risk factors.[9] However, it has been found that among patients with a previous history of glucose intolerance during pregnancy, about 47 % of the obese while

only about 26 % of the non obese pregnant women developed gestational diabetes.[9] In the absence of a previous abnormality of glucose tolerance during pregnancy, obesity alone does not increase the risk of diabetes mellitus. Consequently, overweight pregnant women can be divided into two categories depending upon the presence or absence of a gestational diabetic history, with previous gestational diabetes carrying a much higher risk than obesity. At the same time that obesity predisposes to gestational diabetes in high risk women, obesity may be a marker of the prognosis of the disease.[9]

Some similarities exist between pregnancy and obesity regarding their role in inducing glucose intolerance.[9] Both conditions may lead to metabolic changes causing an elevation in blood glucose after carbohydrate intake. Also, hyperinsulinemia and an increase in insulin resistance occur in pregnancy and obesity. There is also hyperplasia in islet cells, and glucose tolerance may normalize after pregnancy or with weight reduction.[9]

Once a woman is diagnosed as having gestational diabetes, she becomes more liable to develop diabetes again in subsequent pregnancies or even " non-gestational diabetes" later on. After pregnancy ends, the woman with gestational diabetes may become normal, may have impaired glucose tolerance or may become diabetic. Therefore, she should be re-classified after the end of pregnancy. In fact, about 20 % to 30 % of gestational diabetic patients may develop " permanent " diabetes during a period of 5 years.[10]

Genetic factors may play a role in the development of type I diabetes. This is indicated by the prevalence of certain histocompatibility antigens (HLA) on chromosome number 6. [6] In type II diabetic patients, a more clear hereditary association exists. An autosomal dominant genetic factor has been detected in some cases.[11] In general, there is a 10 % probability of developing diabetes when only one parent has diabetes.[6] If both parents have diabetes, the risk increases.

A blood sugar obtained one hour after taking an oral solution of glucose can be considered the most common method used for screening of pregnant women.[6-7] The patient drinks a 50 gm glucose solution and the serum or plasma glucose level is measured after one hour. A full 3-hour oral glucose tolerance test (OGTT) is recommended when the screening glucose level exceeds 150 mg/dl.[6] It has been found that a screening glucose level equal to or exceeding 150 mg/dl exists in 4 % of women below 20 years, 9 % of those between 20-30 years and 33 % of those above 30 years.[12] Other indications for OGTT include fasting glycosuria and previous occurrence of gestational diabetes or intrauterine fetal death.

One study shows that in a 50 gm, one-hour glucose screening test, a plasma glucose level of less than 135 mg/dl carries a probability of only 1 % for diabetes.[7] On the other hand, with a plasma glucose level over 182 mg/dl, the chance of having diabetes is 95 %. Therefore, the authors recommend no further tests for women with levels below 135 or above 182 mg/dl.