A SURVEY OF PREGNANT DIABETIC WOMEN TREATED AT AIN SHAMS UNIVERSITY HOSPITALS FROM JANUARY 1982 TO JANUARY 1983

THESIS

SUBMITTED FOR PARTIAL FULFILMENT
OF
M.S. DEGREE IN
OBSTETRICS & GYNAECOLOGY

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ACKNOWLEDGEMENT
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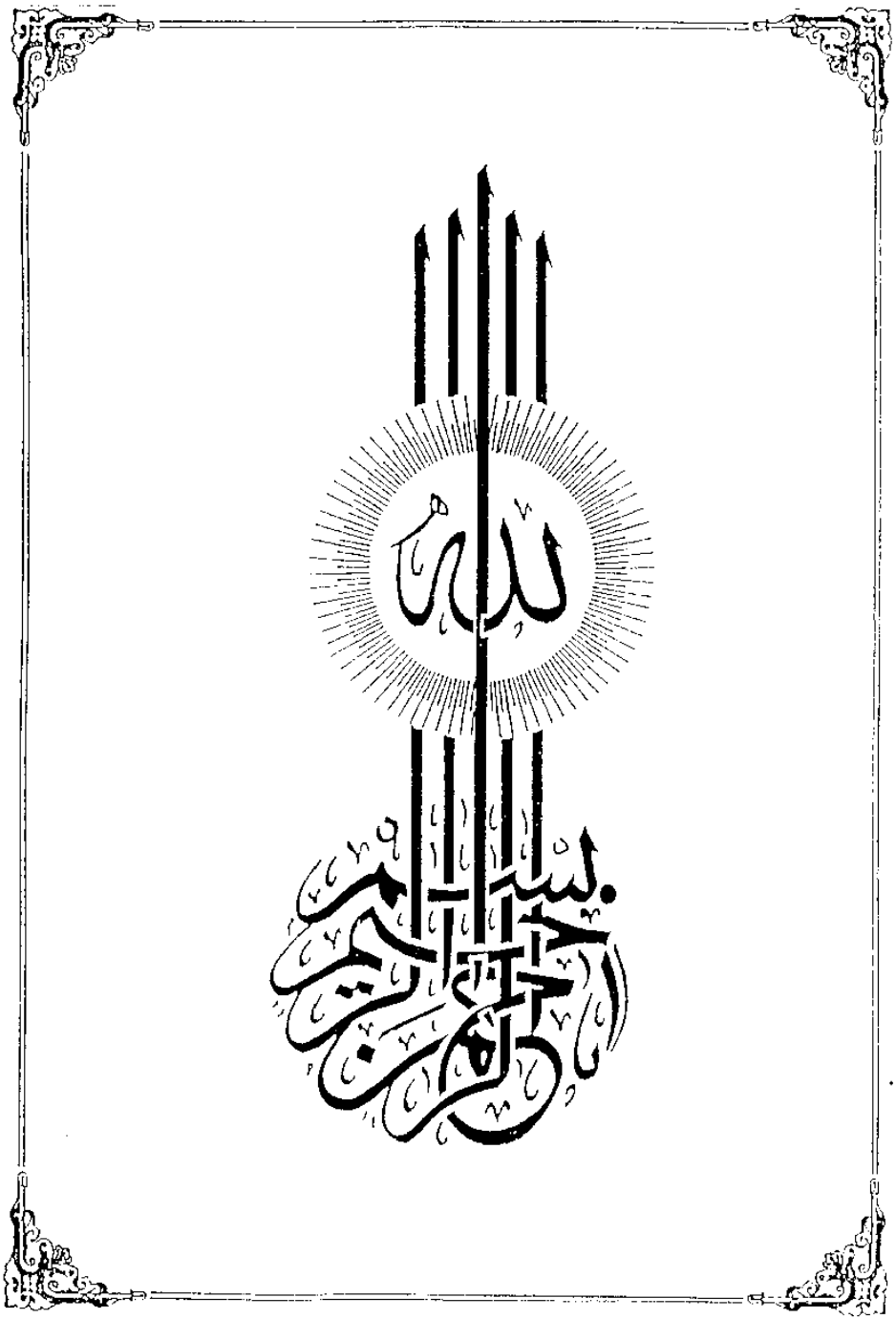
I wish to express my deep thanks and gratitude to Prof.Dr. Ali Marei Makhlouf, Professor of Obstetrics and Gynaecology, for giving me the privelage to work under his supervision, for his encouragement and eminent guidance and support.

I would like also to express my gratitudes and thanks to Dr. Abbas Ghazi for his kind supervision and help.



Contents
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INTRODUCTION

Introduction

Diabetes mellitus antedating pregnancy is recognized as an important cause of maternal morbidity, birth defects, intrauterine fetal death,and neonatal morbidity and death. An increased incidence of these complications has been associated with duration of diabetes, the presence of vascular lesions, and the degree of control of the diabetic state during pregnancy. Patients with poor control of diabetes have a higher risk of fetal or neonatal death, and the occurence of ketoacidosis in particular carries an excessive rate of fetal loss (Pedersen J., 1977),(White P., 1974), (Tyson J.E., et al. 1971).

Although mortality statistics of the diabetic mother's infant have shown marked improvement since the advent of insulin, the outlook for these infants and their mothers is still less than optimal. Mortality of the infants ranges from 0 to 21 percent in series reported in the last 10 years(Karlsson J., et al. 1972), (Sack R.A., 1969), (Adashi E. Y., et al. 1979), (Roversi G.D., et al. 1980).

Morbidity is such that congenital malformations are reported to occur in 5-8 percent of cases (White P., 1974),(Gabbe S.G., et al. 1977),(Kitzmiller J. L., et al. 1978), Cerebral dysfunction in 20 to 36 percent (Stehbens T. A, et al. 1977), macrosomia in 16 to 40 percent, (Kitzmiller J.L., et al.1978), (Gamsu H.R., 1979), (Soler N.G , et al. 1978),hypoglycemia in 16 to 76 percent (Kitzmiller J.L., et al. 1978),(Gamsu H.R., 1979), hypocalcemia in 8 to 22 percent (Kitzmiller J.L, et al. 1978),(Soler N. G., et al. 1978), hyperbilirubinemia in 19 to 35 percent (white P., 1974), (Kitzmiller J.L., et al. 1978),(Soler N.G., et al. 1978), and respiratory distress in 2 to 9 percent of cases studied (Adashi E.Y., et al. 1979),(Kitzmiller J.L., et al. 1978), (Soler N.G., et al. 1978).

Recently, the importance of tight control during diabetic pregnancy in producing better results has been stressed (Essex N.L., et al. 1973),(Gugliucci C.L., et al. 1976).

There are many other factors, however, in the modern management of the diabetic pregnancy that may result in the low perinatal mortality rates recently reported by several centres (Essex N.L.,

et al. 1973), (Gabbe S.G., et al. 1977), (Gugliucci C.L., et al. 1976), (Pedersen J., 1977).

Availability of elective abortion for unwanted pregnancies, the application of fetal monitoring tests for the detection of fetal distress, the prediction and prevention of respiratory distress syndrome (RDS) by the lecithin/sphingomyelin (L/S) ratio, and the tendency to perform delivery around term are examples of measures that may reduce perinatal deaths, independent of glucose control of the diabetic pregnant patient.

The dilemma of traditional management of pregnancy in the diabetic patient has been to time delivery to balance the risk of still birth late in gestation with that of neonatal death from pulmonary immaturity earlier in gestation. Recent conceptual and technologic advances in the realm of fetal assessment have offered the opportunity of individualized management for each diabetic pregnant woman.

Review Of Literature

Metabolic Control of diabetic pregnancy

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Perinatal mortality rates of 4-5% have recently been reported (Kitzmiller J.L., et al. 1978) for insulin-dependent diabetic pregnancies (class B-RF) managed in university centers. These out comes represent a vast improvement in the management of this high-risk pregnancy condition,which in the past accompanied by a 15-20% perinatal mortality rate.

Recent authers (Karlsson J., et al. 1972),(Essex N.L., et al. 1973), (Persson B., 1975),(Gabbe S.G., et al. 1977), (Kitzmiller J.L., et al. 1978),(Adashi E.Y., et al. 1979), have emphasized the beneficial effect of careful control of maternal blood sugar levels on diabetic pregnancy outcomes, thereby generating considerable interest in this aspect of management. In fact, Karlsson J., et al. 1972 reported that mean daily maternal blood sugar concentrations below 100 mg/dl in the third trimester of pregnancy were associated with perinatal mortality of approximately 4% compared to threefold to fourfold higher mortality rates when the mean third-trimester blood sugar levels were above 100 mg/dl. Since the frequencies of certain maternal (Pedersen J., et al. 1974)(preeclampsia, pyelonephritis, hydramnios, ketoacidosis) and

fetal (hypoglycemia, hypocalcemia, hyperbilirubinemia, respiratory distress, Congenital anomalies)complications are directly related to an increased risk of poor perinatal outcome and mortality, occurrence of such complications presumably was reduced by careful maintenance of maternal blood sugar levels below 100 mg/dl.

A direct cause-effect relationship between maternal euglycemia and reduction in maternal and fetal complication and perinatal mortality rates has been claimed; however, the role of metabolic control in itself in decreasing fetal wastage and neonatal mortality has not been proved. Much of the improved perinatal outcome may have resulted from other significant advances over the past decades in maternal and neonatal high-risk care, in assessment of placental function and fetal maturity, and in treatment of maternal and fetal complications.However, the high (20-30%) fetal mortality associated with severe maternal hyperglycemia and ketoacidotic coma (Pedersen J., 1977) and the reported associations between pregnancy ketosis and reduction in intellectual development (Stebbens T.A., et al. 1977) of the newborn have led to widespread belief that maternal ketoacidosis should be avoided in pregnancy. In addition, although not proved, many clinicians believe that careful regulation of maternal blood sugar levels does indeed

reduce the risks of preeclampsia, hydramnios, and urinary tract infection in the mother and thus improves perinatal outcome. Thus, at this time, controversy appears to involve the proper target level for maternal euglycemia in this conditon and not whether good metabolic control is of benefit (Leveno K.J., et al. 1979). Optimal maternal metabolic control in the insulin-dependent pregnant diabetic is a complex topic and involves consideration of several interrelated factors:

1) measurement or definition of maternal euglycemia.
2) regulation of dietary intake, i.e., proper distribution and division of intake of foodstuffs.
3) regulation of insulin, i.e., timing and dosage of exogenous insulin.

Definition of good metabolic control:

Careful metabolic supervision of insulin-dependent pregnant diabetics has been associated with good perinatal outcome in all reported studies. A major problem arises, however, when one attempts to define "good control" since criteria for documentation differ broadly. Moreover, all of the studies have involved women hospitalized in the third trimester, and many additional components of high-risk care, e.g., palcental function, fetal maturity studies, and bed rest in lateral recumbent position, undoubtedly contributed to the improved perinatal survival.

The (Karlsson J., et al. 1972) series reported a markedly low perinatal mortality rate ($<$ 4%) when the mean blood sugar level was $<$ 100 mg/dl. This "mean" value was obtained from the average of three daily determinations (at unspecified times in relation to meals) from 30-32 weeks' gestation untill delivery. Gillmer et al (Gillmer M.D.G., et al.1975) measured maternal plasma sugar every hour from 8:00 AM to 8:00 PM and every 2 hours at night in a carefully documented study of diurnal metabolic control of normal pregnant women in the third trimester and those with insulin-dependent diabetes in the third trimester. Although data were obtained on only 13 insulin-dependent pregnant diabetics, the patients had been hospitalized in the third trimester for at least 2 weeks and were under "optimal diabetic control" in a university center providing excellent documentation of well-defined "good metabolic control". The diurnal profile provided by these around-the-clock maternal plasma sugar measurements enables one to quantitate euglycemia in the normal nondiabetic third-trimester pregnancy and to arrive at therapeutic objectives in the insulin-dependent pregnant diabetic. The points to be noted are :

1) The relatively low maternal plasma sugar levels in the non diabetic pregnancy,
2) The significantly higher range of euglycemia or maternal plasma sugar values obtained in the well-

controlled insulin-dependent pregnant diabetic (mean daytime plasma sugar-117 mg/dl versus 88 mg/dl in normal group).

3) The far wider daily swings of plasma glucose levels in the insulin-dependent pregnant diabetic,

4) Much lower minimal plasma sugar levels (at night) and

5) Much higher maximum plasma sugar levels(in daytime).

Persson and Lunell (Persson B., 1975)(Persson B., et al. 1975) also reported carefully documented metabolic control in a series of 107 insulin-dependent pregnant diabetics. There was an acceptably low overall perinatal mortality rate of < 5% in these studies associated with "pregnancy glucose levels" or an average mean daily blood sugar level (average of determinations at 7:00 AM, 10:00 AM., noon, 4:00 PM, 7:00 PM during last 28 days of pregnancy) of approximately 120 mg/dl.

Adashi and Co-workers(Adashi E.Y , et al. 1979) strongly recommend stringent metabolic control of the insulin-dependent pregnant diabetic, reporting a perinatal mortality rate "approaching zero" and advocating that maternal plasma glucose concentration be maintained below 100 mg/dl throughout pre-

gnancy. However, this very low perinatal mortality rate results from a series containing mostly gestational diabetics with only 32 insulin-dependent diabetics of undescribed severity.

Criteria for "good metabolic control" vary widely, and one must evaluate each report carefully to compare different studies using differing endpoints. Several factors should be stressed:

1) Plasma sugar values are 15% higher than whole blood sugar determinations because of the lower red blood cell concentration of glucose;
2) timing of blood sugar determinations in relation to meals is essential to assessing mean daily values. Thus, Adashi et al., who recommend maternal plasma glucose concentrations below 100 mg/dl throughout pregnancy, appear in fact to be referring only to fasting plasma glucose, Karlsson and Kjellmer (Karlsson J., et al. 1972) reported improved perinatal outcome with mean blood sugar levels below 100 mg/dl, obtained from an average of three daily values at unspecified intervals from meals. Persson and Lunell (Persson B., et al. 1975), who reported good metabolic control with mean glucose levels in pregnancy of 120 mg/dl,