MATERNAL GLYCOSYLATED HEMOGLOBIN CORRELATION WITH BIRTH WEIGHT

THESIS

SUBMITTED FOR PARTIAL FULFILMENT
OF
MASTER DEGREE OF OBSTETRICS GYNECOLOGY

BY

NADIA MAHMOUD ATIA ZAITOUN

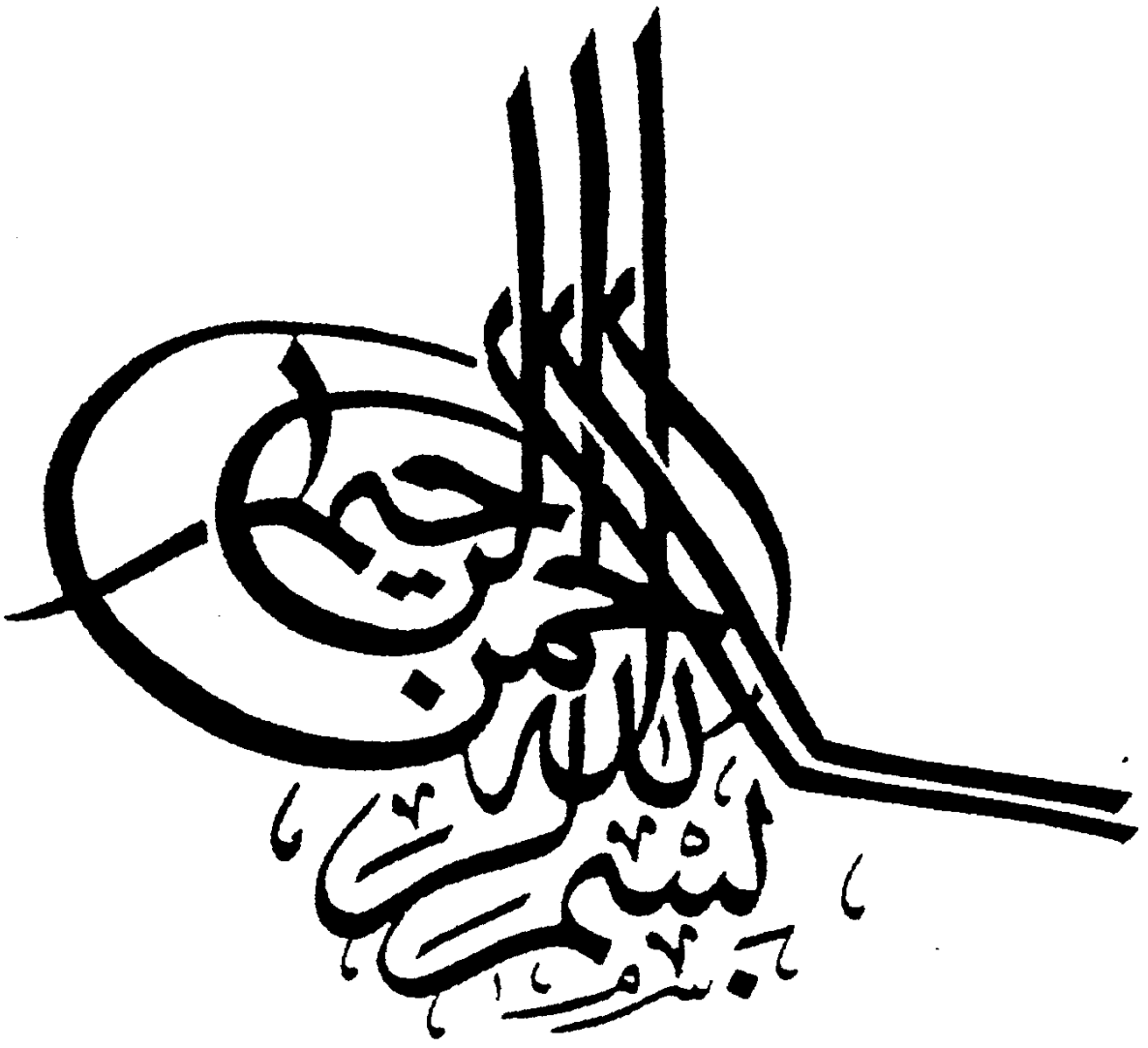
UNDER SUPERVISION
OF

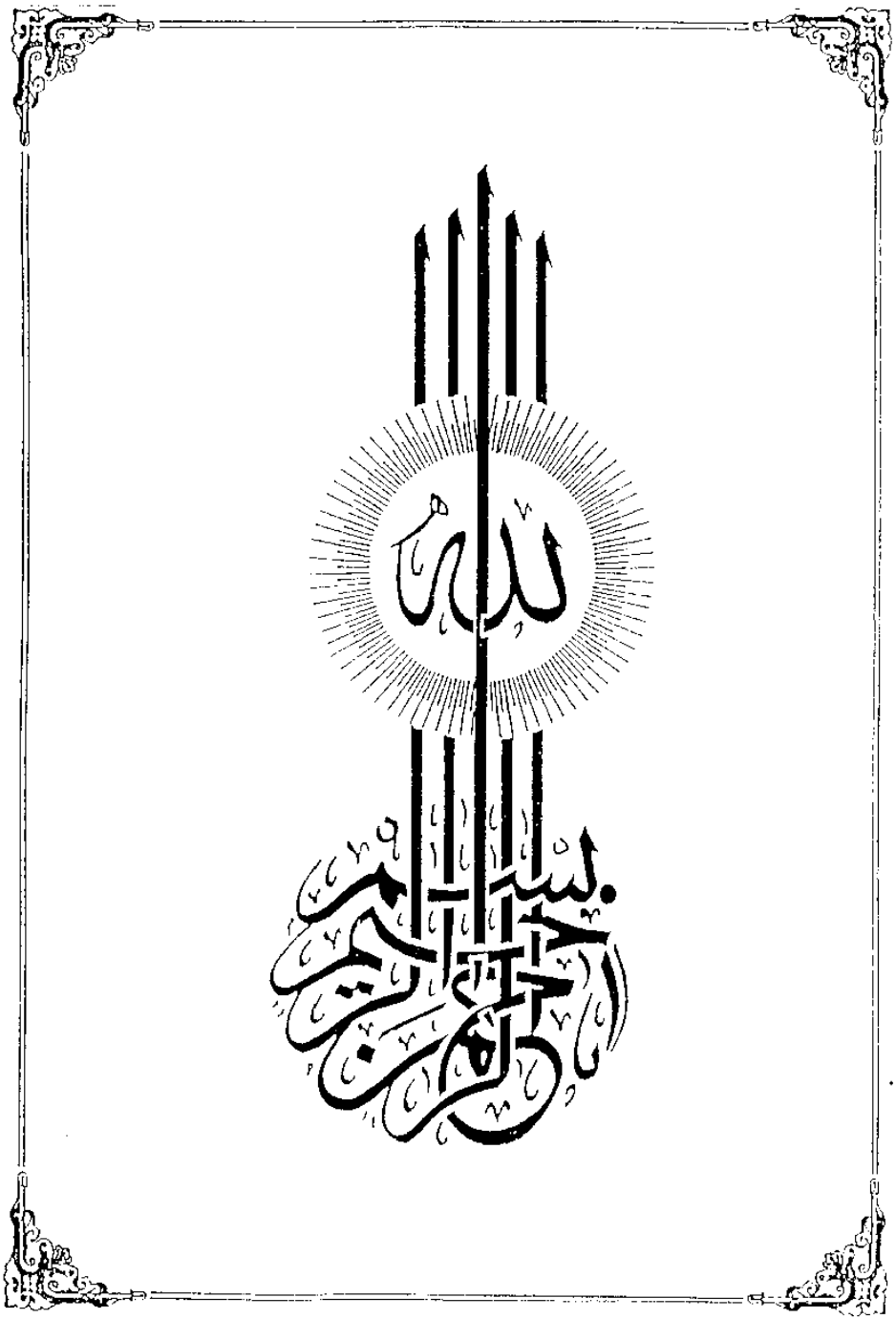
DR. HASSANEIN ALY MAKHLOUF
M.D. M.R.G.O.G
ASSISTANT PROFESSOR OF OBSTETRICS. GYNECOLOGY
FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

DR. MOHAMED ALY IBRAHIM
LECTURER OF OBSTETRICS. GYNECOLOGY
FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

DR. SAWSAN SAIID HAFEZ
LECTURER OF CLINICAL PATHOLOGY
FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

CAIRO
1988





ACKNOWLEDGEMENT

I would like to express my deepest gratitude and thanks to Dr. HASSANEIN ALY MAKHLUF, Assistant Professor of Obstetrics and Gynecology, Ain Shams University for his most guidance and assistance.

I would like to express my thanks to Dr. SAWSAN SAID HAFEZ, Lecturer of Clinical Pathology Faculty of Medicine, Ain Shams University, for her honest assistance for giving very possible help and follow up of the work.

I would like to express may thanks and deepest gratitude to Dr. ADEL SABBAQH, Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his advice, guidance and continuous encouragement throughout the whole work.

I am particularly indebted to Dr. MOHAMED ALY IBRAHIM, Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University for his honest assistance, fruitful suggestions, and who worked a great deal to bring this work to light.

Lastly, I would like to offer a special gratitude to Dr. SAID EL-TOUHAMY, Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University for giving every possible help, advice and guidance in performing the tedious task of statistical analysis of the results of this thesis.

CONTENTS

INTRODUCTION

INTRODUCTION

The effect of diabetes on pregnancy has been extensively studied. It is thought that maternal hyperglycemia passively produces foetal hyperglycemia wich induces fetal hyperinsulinemia (Pedersen. 1977)

The functional hyperinsulinaemia has been proposed to account for many of the complication observed in newborn infants of diabetic mothers such as hypoglycemia, hypocalcemia, respiratory distress syndrome, macrosomia and congenital abnormalities of the spine, and the skeletal genitourinary and cardiovascular system, (Pedersen et al., 1974)

The diagnosis of gestational diabetes is of prime importance since it has been shown that proper metabolic control during pregnancy can reduce the incidence of such anomalies. (Pedersen. 1977).

Gestational diabetes may remain undetected throughout pregnancy because of normal glucose tolrance tests with the only indication of such an abnormality being the delivery of a large for gestational age infant. (Pedersen. 1977)

Many retrospective studies have been performed on mothers of macrosomic infants to screen for gestational diabetes. The measurements of maternal glyeosylated hemoglobins have been shown to reflect the level of

glycemic control during the preceeding two to three months. (Widness et al. 1978) (Mayer and Freedman.1983).

Pollock et al (1981), reported a significant increase in the level of glycosylated hemoglobin in the mothers of large for gestational age infants compared to appropriate control women. Others have also shown similar increases in cord glycosylated hemoglobin levels in diabetic patients (Feldman. et al. 1994; Hall et al., 1983. and Worth et al., 1983).

AIM OF THE WORK

AIM OF THE WORK

The purpose of this study is to determine whether glycosylated hemoglobin concentration at time of delivery is related to birth weight and perinatal outcome in non diabetic pregnancy and in pregnancy complicated with diabetes mellitus.

REVIEW OF LITERATURE

3-1. GLYCOSYLATED HEMOGLOBINS

Human hemoglobin has probably been studied more extensively than any other macromolecule. Its structural and functional characterization has been simplified by the fact that human hemolysate contains one major hemoglobin component HbA (∂_2 β_2) which comprises over 90% of the total hemoglobin which is present in adult and children above the age of 6 months (O'shaughnessy et al. 1979). Besides HbA, two types of minor hemoglobin components in human hemolysate HbA2 ($\partial_2\Omega_2$) and fetal hemoglobin ($\partial_2\mp_2$) comprise about 2.5% and 0.5% of the total respectively.

The synthesis of these minor components is controlled by 8 and 7 chain genes. (Bunn et al. 1976). The minor hemoglobin components found in normal adult hemolysate may be post translation modifications of hemoglobin A When human hemolysate is chromatographed on cation exchange resins, three negatively charged minor hemoglobin components are eluted before the main hemoglobin A peak (Allen et al. 1958 and Huisman, et al. 1960). Heomoglobins A_{1a}, A_{1b} and A_{1c} comprise approximately 1.6%, 0.8% and 4% of the total hemoglobin of adult erythrocytes, respectively, thus hemoglobin A_{1c} is the most abundant minor hemoglobin component. (Bunn et a. 1976)

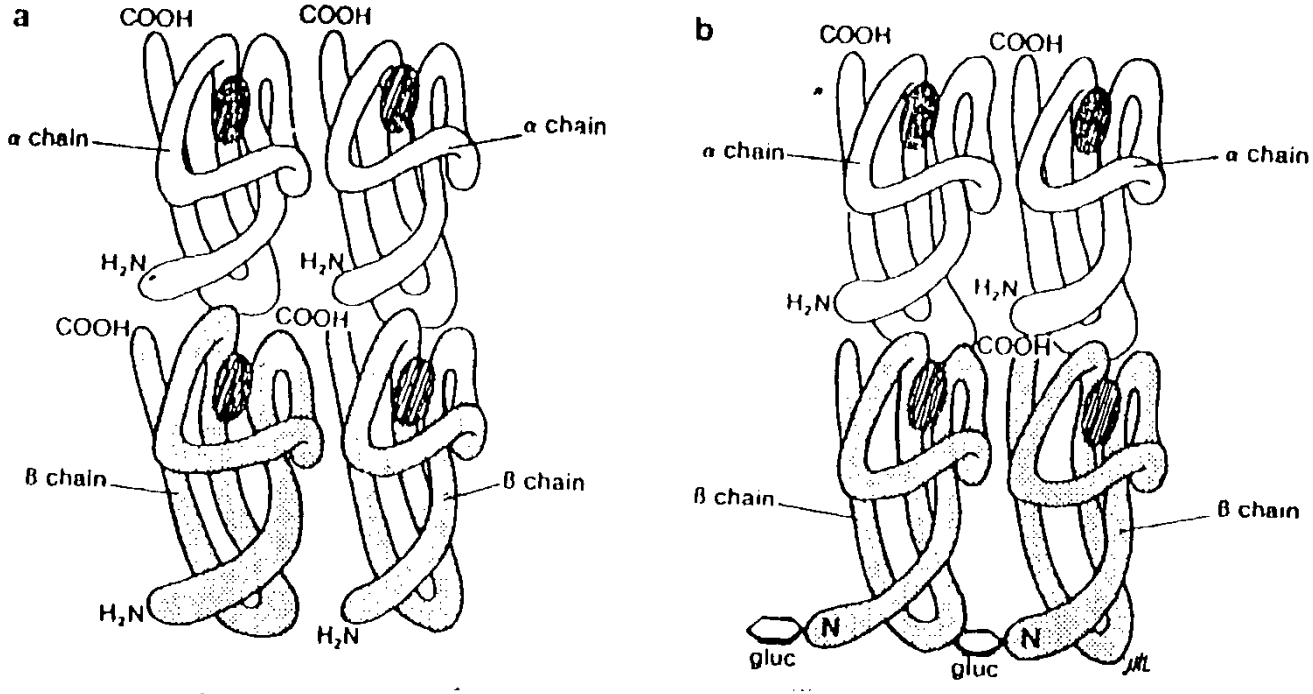
Homquist and Schroeder (1966) showed that hemoglobin A_{1c} is structurally indentical to hemoglobin A except that an unidentified group was linked to the terminal amino group of the B-chain means of a shiff

base. The glycosylation of hemoglobin takes place under physiologic conditions at a specific site on the hemoglobin, normally about 5 percent of hemoglobin in a population of normal human red cells is covalent linked to glucose resulting in the formation of a chromatographically distinct minor component (Allen et al., 1985). Hemoglobin A_{1c} was considerably enhanced by the discovery that there is a two to three fold increase in patients with diabetes mellitus. (Rahbar. 1968).

Rahbar and his colleagues (1969) survyed 1200 patients at Tehran Hospital and found two patients who showed abnormal pattern on ager- gel electrophoresis, both patients were diabetic. They examined another 47 diabetic patient and detected the some abnormal pattern in each case. Paulsen. (1973), had found similarly increased amounts of hemoglobin A_{1c} in children with overt insulin-dependent diabetes and normal amounts in nine children with asymptomatic hyperglycemia and suggested that these alteration may be specific genetic markers for diabetes mellitus.

Structural studies of HbA_{1c} :-

Hemoglobin A_{1c} is formed by condensation of glucose with the N-terminal amino groups of the beta chain of hemoglobin A. This reaction is slow non specific, non enzymatic, post translation and essential irreversible because the glucose attaches to the N-terminal groups of valine or lysine and spontaneously undergoes an amadori re-arrangement in which the unstable aldamine linkage becomes a stable ketoamine linkage



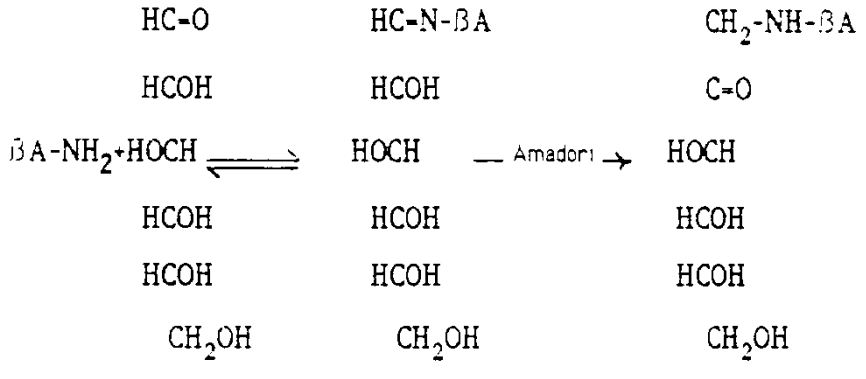
The nonenzymatic production of HbA_{1c} (b) from HbA (a) requires the formation of a Schiff base between the aldehyde of the glucose and the amino-terminal valine of the β-chain followed by an Amadori rearrangement to the relatively more stable ketamine. (Adapted from Jovanovic and Peterson. *1978*.

resulting of formation of HbA_{1c} (Koenig et al. 1977; Bunn et al., 1975; Fluckiger and Winterhalter, 1976).

Jovanovic and Peterson. (1978) had found that the non enzymatic of hemoglobin A_{1c} from hemoglobin A requires the formation of shiff base between the aldhyde of glucose and the amino terminal valine of the B. chain followed by an amadori rearrangement to the relatively more stable ketoamine.

Glucose is also linked in the same way to other sites on the hemoglobin molecule, such as the N. terminus of the ∂ chain and certain lysine residues (Bunn et al. 1979 and Shapiro. 1980)

Steps of glycosylation :-



Glucose — rapid → Aldamine (schiff base) — slow → Ketoamine

(Bunn et al. 1976)