DETERMINATION OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE IN THE NEONATES WITH HYPERBILIRUBINEMIA

Thesis

Submitted for partial fulfilment

of master degree in pediatrics.

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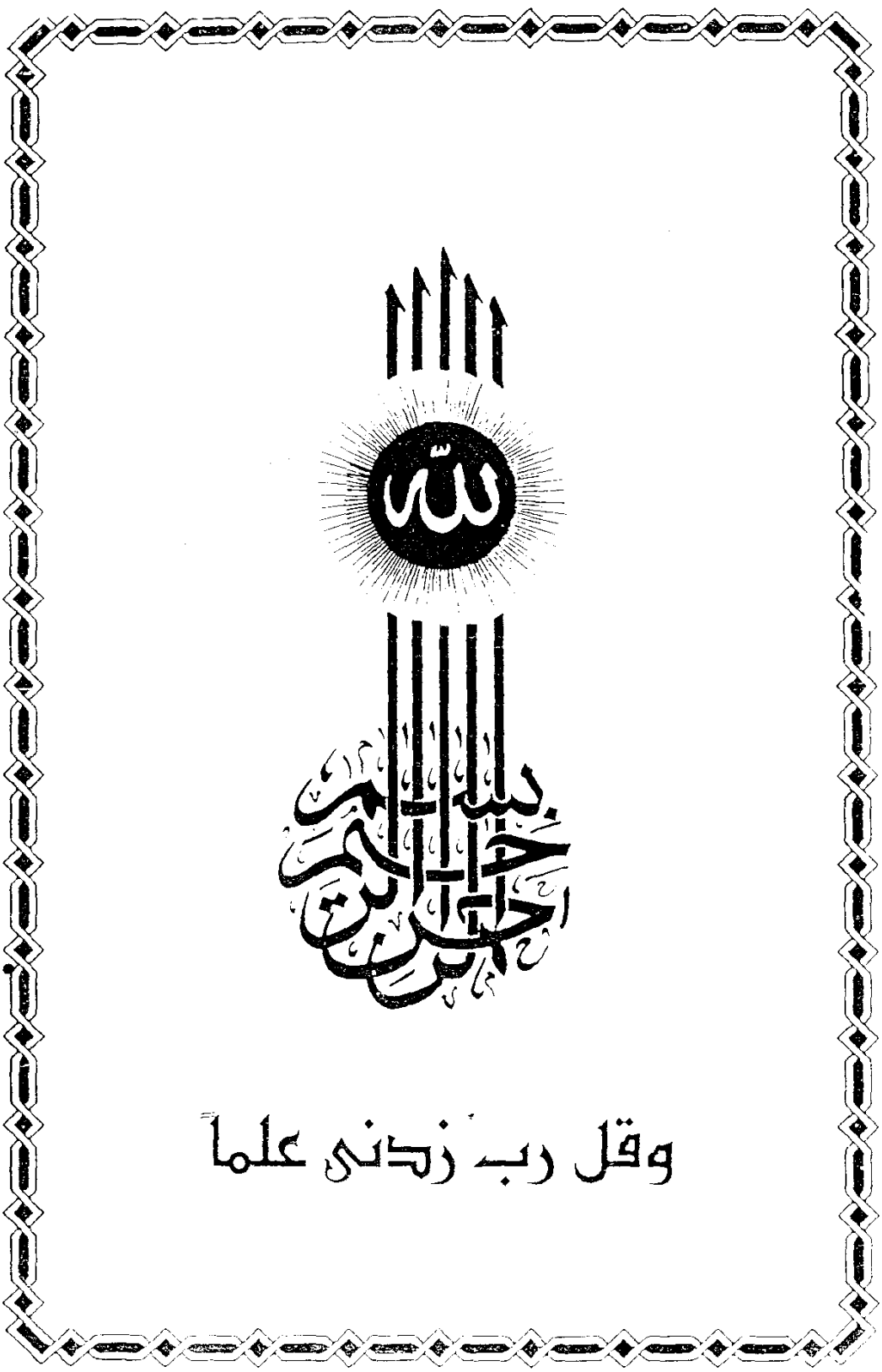
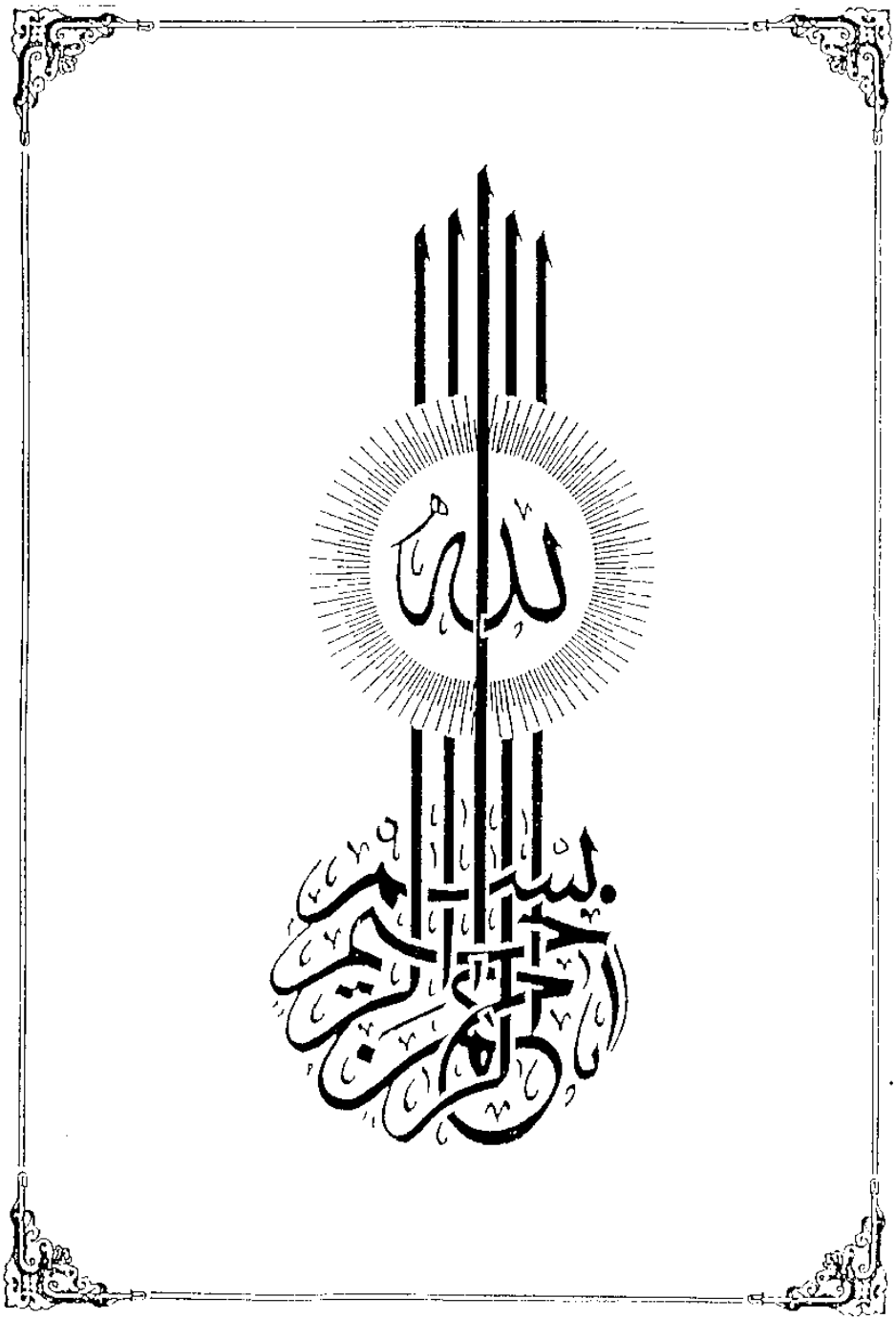
1994





ACKNOWLEDGEMENT

I am deeply indebted to Professor Dr. **ABDEL-KHALIK ABDEL-AZIZ KHATTAB**. Professor Of Pediatrics, Ain Shams University, I will always remember his kind help, and continuous support that always make me feel grateful to him.

My deep thanks are due to Professor Dr. **SAWSAN EL SOKKARY** Professor of Pediatrics, Ain Shams University for her great help, continuous encouragement and valuable advice.

I am greatly indepted to Dr. **MONA EL-SAMAHY**. Ass. Prof. of Pediatrics, Ain Shams University for giving me this precious opportunity of working under her supervision, her wast knowledge experience and guidance added much to this work.

I am grateful to Dr. **SAFINAS EL-HABASHY**, Lecturer of Pediatrics, Ain Shams University for her great help continuous encouragement and valuable support.

I am grateful to Dr. **LAILA ABDEL-GHAFFAR**, Lecturer of Pediatrics, Ain Shams University for her help and cooperation.

Last but not least, my deep appreciation is expressed to all staff members patients of the Pediatric Clinic of Ain Shams University.

Hanaa Saleh.

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INTRODUCTION

Glucose -6- phosphate dehydrogenase deficiency is frequently occuring X - linked enzymatic defect.

Phenomenon of Glucose -6- phosphate dehydrogenase deficiency associated with neonatal hyperbilirubinemia is prevalent especially within the geographic distribution of the Mediterranean type of the enzyme defect.

Jaundice may be severe and may lead to Kernicterus, spastic cereberal palsy or death.

Higher number of G.6.P.D. deficient neonates developed hyperbilirubinemia and required phototherapy.

Hematocrite values were slightly lower in the Jaundiced G.6.P.D. - deficient neonates than in jaundiced control neonates, while there was a tendency for the reticulocyte values to be somewhat higher in the studies neonates.

Jaundice in female neonates may have been due to a heterozygous state with marked expression of G.6.P.D. - deficient gene in the liver.

An alternative factor influencing the development of jaundice may be defective glucuronidation of bilirubin in the liver due to defective G.6.P.D. activity in the hepatocytes.

In support of this theory is the finding of decreased G.6.P.D. - activity in the liver biopsy tissue G.6.P.D.- deficient adults (Kaplan, and Abramov 1992).

The life span of the G.6.P.D.deficient RBC is shortened resulting in early destruction of these cells. The newborn's liver protiens and enzymes have a reduced ability to take up and glucuronidate bilirubin.

This will stress the inability of the G.6.P.D. -deficient newborn to clear excess bilirubin even if the increased RBC destruction is niminal. (Lopez, and Cooperman 1971).

It is indicated clearly that subjects who are genetically G.6.P.D. -deficient have as group lower levels of G.6.P.D. - in liver tissue than subjects who are G.6.P.D. - normal (Oluboyede, et al 1979).

AIM OF THE WORK

The aim of this study is to evaluate the level of G.6.P.D. - in the neonates with hyperbilirubinemia.

This hyperbilirubinemia is unexplai ned i.e neonates with known causes for hyperbilirubinemia will be excluded.

REVIEW OF LITERATURE

Bilirubin Structure

Bilirubin is derived from the catabolism of proteins that contain heme. The quantitatively most important source of bilirubin is the breakdown of hemoglobin from senescent erythrocytes, although the metabolism of other heme containing proteins e.g. cytochromes have a little contribution to the total bilirubin pool (Wolkoff 1983).

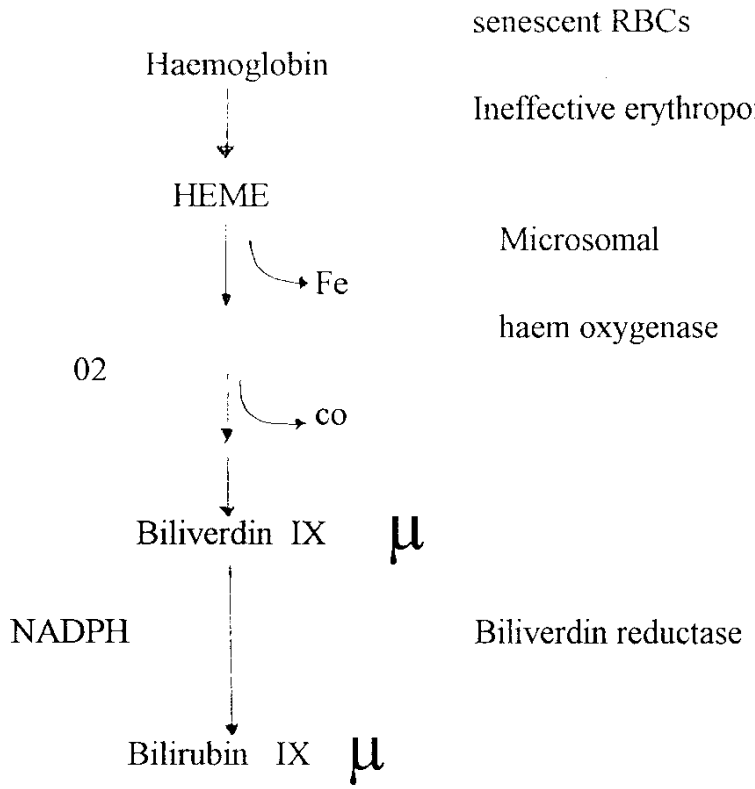

Figure 1 : Sources of bilirubin

Heme is oxidized by the enzyme heme oxygenase the products of this oxidation are biliverdin II, iron, and carbon monoxide. The iron is reused, the carbon monoxide is execreted by the Lungs, the biliverdin is rapidly reduced by the second

enzyme (biliverdin reductase) to bilirubin IX (The IX designation means that bilirubin is derived from protoporphyrin IX, which is the name of heme with out its iron and the designation is because the close ring of the protoporphyrin is opened at the carbon). The last step in which biliverdin is reduced to bilirubin takes a readily excretable and apparently non-toxic metabolite iebilirubin (Schmid and Mcdonagh, 1979)

The placenta is far more permeable to bilirubin Than to biliverdin, suggesting that the formation of bilirubin from biliverdin is required for placental clearance of heme catabolic products (Mcdonagh 1981).

In the plasma, the limited water solubility of bilirubin presents little problems because of Albumin's ability to serve as its transport protein (Brodersen, 1982).

The Lipid soluble bilirubin is difficult to excrete in its unmodified form, bilirubin can not be eliminated either in the urine or in the bile (Schmid and Mcdonagh 1979).

Normally, in the liver bilirubin is made more water soluble whereas a glucuronic acid is attached to one or both of the COOH groups, forming "Conjugated" or direct reacting bilirubin. Acommon detoxifying mechanism of the liver by adding a polar Sugar acid to solubilize a lipophylic molecule. In the neonates this hepatic detoxification mechanism does not have sufficient capacity for the bilirubin load (Kawade and Onishi, 1981).

Bilirubin Metabolism

Fetal biliruibin metabolism :

Bilirubin formed from catabolism of heme in utero disposal of bilirubin occurs by two mechanisms,

(a) Unconjugated bilirubin that enters the placental circulation is cleared into maternal circulation across the placenta. when conjugated bilirubin is formed it remains in the fetus and may accumulate in fetal plasma and other tissues.

(b) The fetal liver is the second route for bilirubin clearance in the fetus. This excretory pathway in fetus is limited as result of reduced hepatic blood flow, low level of hepatocyte Ligandin and limited UDP glucuronyl transferase activity.

Conjugated bilirubin that is excreted into the fetal gut is larg ly largly hydrolyzed and reabsorbed into the fetal circulation (Avery, etal., 1984).

Bilirubin can be found in normal amniotic fluid about the 12th week of gestation, and disappears by the 36 -37 wk of pregnancy. Increased levels of bilirubin has been found in the amniotic fluid of infants with severe hemolytic disease and in association with fetal intestinal obstruction. It has been suggested that bilirubin reaches the amniotic fliud from trachobronchial secretions, fetal urine, meconium, diffusion across the umbical vessles, diffusion from the Skin or direct transfer from maternal circulation (OSKI, 1984)

The only cell capable of removing significant quantities of unconjugated bilirubin from circulation is the hepatocyte which converts bilirubin by conjugation with other substance in to a form that either the liver cell or the kidney can excrete into bile or urine. Bilirubin enters the liver cell by a process of carrier-mediated diffusion with Ligandin (Y-protein) of the liver cell cytoplasm as the major intracellular transport protein, Z.protein