DIAGNOSTIC AIDS TO METABOLIC DISEASES OF THE NEWBORN

Thesis

Submitted for partial fulfilment
of Master Degree in Pediatrics

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1984

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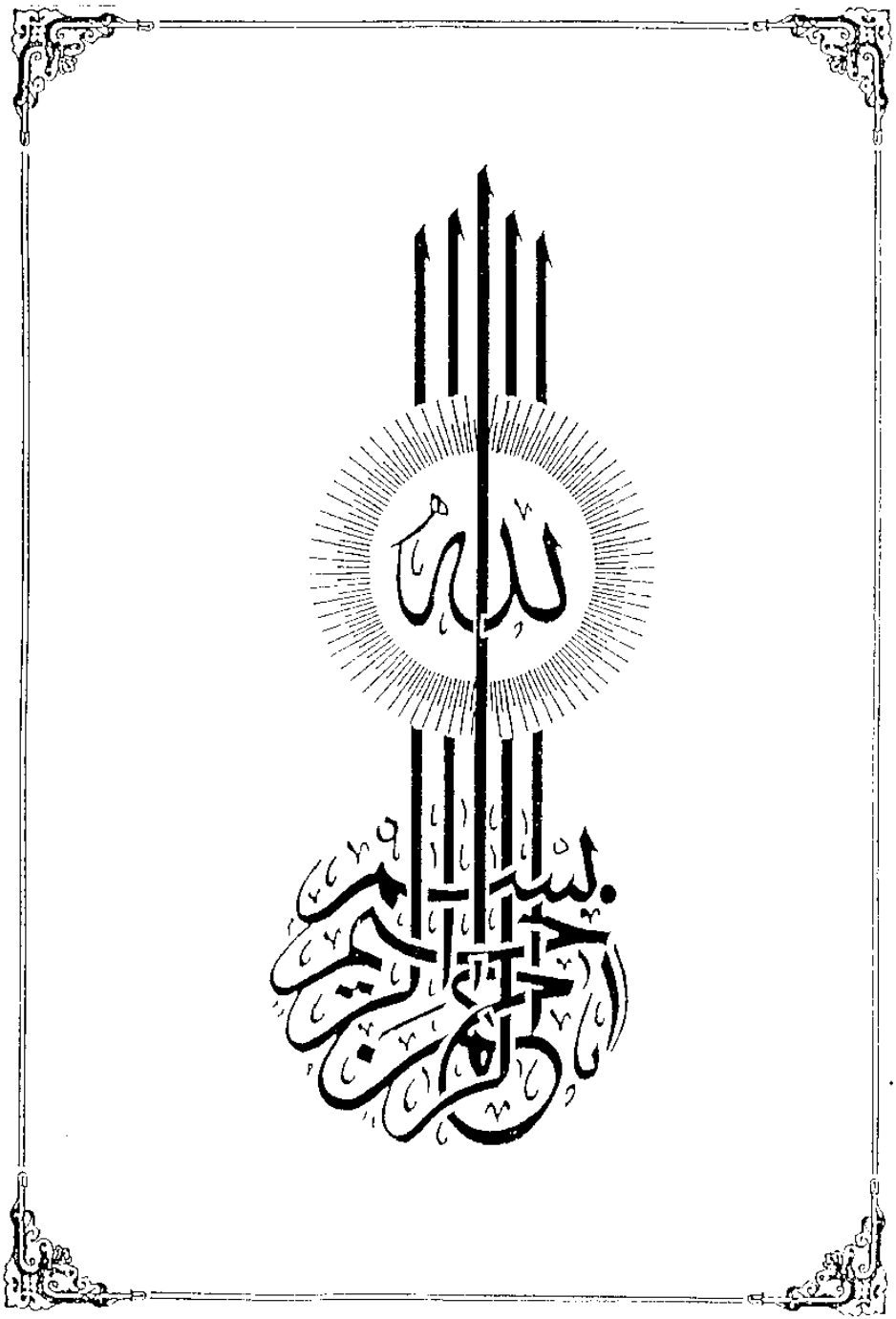

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ACKNOWLEDGEMENT

I would like to express my deepest gratitude to professor Dr. Yehia El Gamal, professor of Pediatrics, faculty of Medicine, Ain Shams University. His continuous encouragement, supervision and guidance were indispensible help to me during completion of this essay. I would like also to thank Dr. Galila M.Kamal,lecturer of Pediatrics, faculty of Medicine, Ain Shams University for her kind advice and valuable suggestions all through the time this work was under supervision.

Ahmed S. Ateek

INTRODUCTION AND AIM OF THE WORK

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The number of metabolic diseases in the newborn which pediatricians have to consider has greatly increased.

Some of these diseases are harmless, they are therefore of academic interest only, an example is pentosuria. The remainder like phenylketonuria can cause symptoms and serious effects. Some of these disorders can be treated simply and effectively, others can be only palliated by more complex treatment (Danks 1981).

The possibility of metabolic disease in the newborn should be considered when there is:

A) A history of unexplained neonatal deaths in the family (Cloherty 1982).

B) Suggestive dietetic history (Avery 1981).

C) Unexplained hypoglycemia, metabolic acidosis ketosis or hyperammonemia. (Packman et al 1978 & Hsia 1974).

D) Neonatal signs and symptoms of jaundice, hepatomogaly, weight loss, poor feeding, lethargy, coma, seizures, vomiting, diarrhea, rapid respiration, dehydration, unusual colour of urine, unusual odour to sweat or urine and coarse facial features.

E) Progression of these signs and symptoms with no evidence of infection,central nervous system hemorrhage or other congenital and acquired defects (Cloherty 1982).

F) Lack of relief of signs and symptoms with usual therapy. (Ampola 1976).

G) Abnormal metabolic screening test in a presymptomatic newborn.(Nyhan 1974,Buist and Shaver,1973).

The aim of this thesis is to offer the aids for early diagnosis of metabolic disorders in order to prevent their serious sequelae such as neonatal death, mental retardation,liver affection and jaundice by early and proper management.

Early diagnosis of such cases offers to the anxious parents logic explanation about the etiology,the nature of the disease and the proper way to avoid its complications as well as genetic counselling for the forth coming offspring.

REVIEW OF LITERATURE

Metabolic diseases which may produce acute illness in the newborn:

I) Urea cycle defects and other congenital hyperammonemic states:

This includes several diseases among which we can mention:.

- Carbamylphosphate synthetase deficiency.
- Ornithine transcarbamylase deficiency.
- Citrullinemia(argininosuccinic acid synthetase deficiency).
- Argininosuccinic aciduria(argininosuccinic acid lyase deficiency).
- Hyperargininemia (arginase deficiency).
- Syndrome of hyperammonemia,hyperornithinemia and homocitrullinuria).
- Periodic hyperlysinemia with hyperammonemia.
- Lysinuric protein intolerance with defective transport of basic amino acids(Stanbury et al 1978).

II) Disorders of amino acid metabolism:

The metabolism of several amino acids may be seriously deranged and in turn influences the child-health.Disorders of amino acid metabolism include:

- Hyper valinemia(Valine aminotransferase deficiency)

- Maple syrup urine disease (branched chain ketoacid dehydrogenase deficiency).

- Isovaleric acidemia (isovaleryl CoA dehydrogenase deficiency).

-B-keto-thiolase deficiency.

- Propionic acidemia(propyl CoA carboxylase deficiency).

- Methylmalonic acidemia(methylmalonyl CoA mutase deficiency,methylmalonyl CoA racemase deficiency or disorders of cobalamin metabolism).

- Glutaric acidemia(glutaryl CoA dehydrogenase deficiency).

- Non ketotic hyperglycinemia(defect in the glycine cleavage system).

- Hyper-B-alaninemia(B-alanine-α-ketoglutarate aminotransferase deficiency).

- Tyrosinemia(P-hydroxyphenyl pyruvic acid oxidase deficiency).-5-oxoprolinuria(glutathione synthetase deficiency)(Stanbury et al 1978).

- B-metlyl corotonic aciduria(B-methyl-corotonylCoA carboxylase deficiency or disorders holocarboxylase-synthetase.(Barlett and Gompertz 1976).

- Bhydroxy.B-methylglutaric aciduria(B-hydroxy-B methylglutaryl CoA lyase deficiency)(Schutgens et al 1979 Faull et al 1976).

- Homocystinuria (cystathionine synthetase deficiency (type I)-N-methyltetrahydrofolate methyltransferase deficiency (Type II)-N-Methylene-tetra hydrofolate reductase deficiency(type III).

- Histidinemia(histidase deficiency(Morrow and Auerbach 1983).

III)Disorders of carbohydrate metabolism:

These include avariety of disorders among which we mention:

- Galactosemia(galactose-1-phosphate uridyl transferase deficiency).

- Hereditary fructose intolerance (fructose-1-phosphate aldose deficiency).

- Fructse 1,6-diphosphatase deficiency.

- Neonatal hypoglycemia.

- Glycogenstorage disease type I (glucose-6-phosphatase deficiency).

- Glycogenstorage disease type II (α-1,4-glycosidase deficiency)(Stanbury et al 1978)-phosphoenolpyruvate carboxykinase(Whelan et al 1979;Gregersen et al 1977; Goodman et al 1975).

- Pyruvate carboxylase deficiency(Atkin et al 1979, Saudurbray et al 1976,Brunette et al 1972).

- Pyruvate dehydrogenase deficiency (Stromme et al 1976, Farrell et al 1975).

- Pyruvate dehydrogenase phosphatase deficiency (Robinson and Sherwood 1975).

IV) Disorders of lipid metabolism:

- Dicarboxylic aciduria(defect in fattyacid ω oxidation(Truscott et al 1978,Gregersen et al 1976).

V) Miscellaneous:

Other diseases not included in the above group should have an attention:

- Pyridoxine dependent convulsions(Glutamic acid decarboxylase deficiency (Lott et al 1978,Hunt et al 1954).

- Congenital adrenal hyperplasia with salt loss (21-hydroxylase deficiency 20,22-desmolase deficiency 3B-hydroxysteriod dehydrogenase deficiency).

- Menke's syndrome(defect in copper metabolism)(Stanbury et al 1978).

VI) Disorders diagnosed only by screening the newborn population:

- Phenylketonuria(phenylalanine hydroxylase deficiency) (Stanbury et al 1978).

- Dihydropteridine reductase deficiency & defects in biopterin synthesis(Curtius et al 1979,Danks et al 1978).

- Congenital hypothyrordism(Manunes 1981).

Clinical features of metabolic diseases in the neontal period:

A newborn is suspected to have a metabolic disease if one or more of the following clinical features exists in the neonatal period.

I)Feeding difficulties and vomiting:

They are associated with many metabolic diseases, but they are most prominent with:

1- Protein intolerance such as organic acidemias and urea cycle disorders.
2- Carbohydrate intolerance such as galactosemia and hereditary fructose intolerance.
3- A drenogenital syndrome(Cloherty 1982).

II) Hypoglycemia:

For inborn errors of metabolism,to be differentiated from other causes of hypoglycemia,attention must be paid to unusual pattern of onset or response and to association with other metabolic disturbances. For instance,in fructose intolerance,hypoglycemia presents only after fructose has been introduced into the diet which is rarely discovered in the neonatal period unless fruit juice is introduced in the infant's diet. The hypoglycemia of glycogenosis is associated with voracious appetite,poor-