LIPOPROTEIN PATTERN
IN
NORMAL NEWBORNS

THESIS

Submitted in partial fulfilment of

Master Degree of Pediatrics

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1986

ACKNOWLEDGEMENT

I would like to express my deepest thanks, gratitude and appreciation to Prof. Dr. MOHAMAD AHMAD AWADALLA; Prof. of Pediatrics and Genetics, Ain Shams University, for his close supervision, valuable guidance, generous help and support all through this work.

I would like also to thank Dr. MOHSEN A. GADALLAH and Dr. MAHMOUD SAAD; Lecturers of Community, Environmental and Occupational Medicine, for their great help in doing the statistical analysis of this work.

My best and sincerest thanks are also due to all parents and the healthy adults whose help was essential to complete this work.

بسم الله الرحمن الرحيم

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INTRODUCTION

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Since Fredrickson and Lees proposed a system for phenotyping hyperlipoproteinemia in 1967, the concept of coronary heart disease detection and prevention utilizing lipoprotein electrophoresis has become a reality.

Epidemiologic studies have related dietary intake of fats, especially cholesterol and blood levels of lipids with the incidences of atherosclerosis and coronary heart disease (Henry et al., 1974).

Plasma lipids do not circulate freely in the plasma, but are transported bound to protein and can thus be classified as lipoproteins. The various fractions are made of different combinations of protein, cholesterol, glycerides, cholesterol esters, phospholipids and free fatty acids (Chin and Blankenhorn, 1968).

Several techniques have been employed to separate the plasma lipoproteins, including electrophoresis, ultracentrifugation, and thin layer chromatography. Electrophoresis and ultracentrifugation are two of the most widely used methods and each has given rise to its own terminology (Fredrickson et al., 1967).

Various types of support media have been used for the electrophoretic separation of lipoproteins. Cellulose acetate offers several distinct advantages over other media as agarose-gel, starch and polyacrylamide gel. Cellulose acetate does not require expensive, complicated and bulky equipment and the method is readily adaptable to broad scale screening programs (Chin and Blankenhorn, 1968).

Studies performed by many investigators revealed special lipoprotein pattern and lipid profile among healthy newborns. They detected increased alpha-lipoprotein values, decreased pre-beta, and beta lipoproteins and decreased total lipids, cholesterol and triglyceride values (Lerdo et al., 1976, Strobl et al., 1983; Skinner et al., 1983; Rosseneu et al., 1983 and Glueck et al., 1984).

However, as far as we know, no such studies have been done to assess lipoprotein pattern in the newborns among Egyptians.

AIM OF THE WORK

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An increasing amount of research has evaluated plasma lipoproteins as risk factor for coronary heart disease, the major emphasis had been made on very low density and low density lipoproteins (VLDL and LDL) levels (Sakurai et al., 1978 and Nikitin et al., 1981).

Recently it is proved at all ages that the high density lipoprotein (HDL) is an important index to the risk for coronary heart disease where healthy individuals proved to have higher levels of HDL than did individuals with coronary heart disease (Rosseneu et al., 1983 and Glueck et al., 1984).

Many investigators had found special lipoprotein pattern among newborns, characterized by elevated alpha lipoprotein, decreased pre-beta and beta lipoprotein values (Lerdo et al., 1976, Strobl et al., 1983 and Skinner et al., 1983).

The aim of the present work was to determine the lipoprotein pattern among Egyptian healthy newborns and to compare this pattern with that of Egyptian healthy adults, in a trial to search for any special pattern among newborns which may be considered as a risk factor for coronary heart disease necessitating special preventive dietetic measures.

REVIEW

OF

LITERATURE

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LIPIDS

The term "lipid" is applied to those fatty, oily and waxy substances of animal or vegetable origin that are practically insoluble in water, but dissolve freely in non-polar solvents such as chloroform, ether, benzene and hexane (Orten and Neuhaus, 1975).

In physiologic fluids and in most tissues, lipid molecules are present in combination with proteins forming lipoproteins. This promotes solubility of lipids in aqueous medium (Ellefson and Caraway, 1980).

Extraction of plasma lipids with a suitable lipid solvent and subsequent separation of the extract into various chemical classes of lipids demonstrate the presence of triglycerides, cholesterol, phospholipids and unesterified long chain fatty acids (free fatty acids) (Mayes, 1983).

TRIGLYCERIDES

Chemistry:

They are esters of fatty acids with glycerol, each molecule of glycerol is esterified with three fatty acids.

There is considerable disagreement over the normal values for serum triglycerides, in fasting state, values of 60-185 mg/100 ml in men, and 55-135 mg/100 ml in women, can be considered normal (Ramsay, 1980). In infants the range for triglycerides in serum is 10-140 mg/100 ml (Bhagavan, 1978).

Metabolism of Triglycerides:

Triglycerides may be exogenous (dietary fat) or endogenous (synthesized in the liver) in origin.

Exogenous triglycerides, in the lumen of upper intestine, are hydrolysed by pancreatic lipase, the major products of hydrolysis are B-monoglycerides and free fatty acids which form soaps and less than one fourth of ingested fat is completely broken down to glycerol and fatty acids (Mayes, 1983). Following hydrolysis, bile salts combine with free fatty acids and monoglycerides to form polymolecular aggregates, 3-10 nm in diameter, known as micelles. These are solubilized by the detergent action of bile salts, so that a clear aqueous solution rather than an emulsion is formed and becomes in close contact with mucosal cells (Ganong, 1977). Passive diffusion seems to be the mechanism by which micelles enter the mucosal cells (Cantarow and Trumper, 1975). Inside the mucosal cells, the fatty acids and monoglycerides are re-esterified to triglycerides. These are then coated with a carrier protein, phospholipids, free and esterified cholesterol to form chylomicrons, which serve as a carrier of exogenous triglycerides. The chylomicrons are released into the intercellular spaces, chylomicrons enter the lymphatic system and gain access to the systemic circulation via the thoracic duct (Bhagavan, 1978). Triglycerides that follow this route have predominantly long chain fatty acids (more than 10 carbon atoms), medium and short-chain fatty acids (10 carbon atoms or less) are absorbed directly into the portal blood as free fatty acids bound to albumin (Orten and Neuhaus, 1975).

Endogenous (hepatic) triglycerides are synthesized from two main sources (i) excess free fatty acids (FFA) reaching the liver from the circulation, and (ii) FFA synthesized de novo in the liver from dietary carbohydrate. The formed hepatic triglycerides are then incorporated into pre-beta lipoprotein (Zilva and Pannall, 1983).

In adipose tissue, which is metabolically highly active, the triglycerides are continually undergoing breakdown and resynthesis, the resultant of these two processes determines the magnitude of the FFA pool in adipose tissue, which in turn is the source and determinant of the level of FFA circulating in plasma. Triglycerides in adipose tissue are hydrolysed by a hormone sensitive lipase to form glycerol and FFA. Since glycerol cannot be utilized in this tissue, as it lacks the enzyme glycerokinase, glycerol diffuses to plasma where it is utilized by the liver and kidney which posses the active glycerokinase. The FFA formed by lipolysis are resynthesized in the tissue to acyl CoA by a thiokinase and re-esterified with glycerol-3-phosphate to form triglycerides (Mayes, 1983).

In general, glycerol-3-phosphate is obtained from two potential sources, one is glucose by reduction of dihydroxyacetone phosphate. The second is the phosphorylation of glycerol by glycerokinase at the expense of ATP (Orten and Neuhaus, 1975). In adipose tissue, which lacks the glycerokinase, glycerol-3-phosphate is derived from glucose. Conditions in which intracellular glucose is not available, as in fasting, starvation and diabetes mellitus, breakdown exceeds synthesis and FFA accumulate and pass into the blood stream (Zilva and Pannall, 1983).

Hormone-sensitive lipase is activated by cyclic adenosine monophosphate (cAMP) via protein kinase. ACTH (growth hormone), TSH, epinephrine, glucagon and vasopressin activate hormone-sensitive lipase, thus accelerating lipolysis and release of FFA from adipose tissue raising plasma FFA levels. Insulin exerts opposite effects (Ganong, 1977).

Recently, the atherogenic potency of triglycerides is much debated (Hulley et al., 1980).

CHOLESTEROL

Cholesterol is the most important compound of those classed as sterols, those that have perhydrocyclopentanophenanthrene nucleus, as a common structure (Bhagavan, 1978).

Cholesterol is distributed in all cells of the body, especially in the nervous tissue. It occurs in animal fat but not in plant fat (Bhagavan, 1978).

In plasma, cholesterol exists in two forms; (i) free cholesterol, and (ii) esterified cholesterol (combined with long chain fatty acids). Free cholesterol comprises about 20-40% and ester cholesterols about 60-80% of the total cholesterol. This ratio is usually preserved with remarkable constancy