

CHOLELITHIASIS IN INFANCY AND CHILDHOOD

Essay

Submitted for partial fulfilment of the master degree of

General Surgery "M.Sc"

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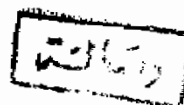
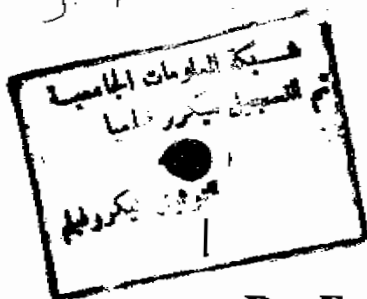
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ACKNOWLEDGMENT

I would like to express my profound gratitude and deepest respect to professor Dr. Ibrahim Bassiouny , Professor of Pediatrics Surgery, Faculty of Medicine, Ain Shams University, for giving me the privilege to work under his supervision, for his kind help, guidance and encouragement throughout this work.

I am also grateful to Dr. Tarek Hassan, Lecturer of Pediatric Surgery and Dr. Alaa Fayez, Lecturer of Pediatric Surgery, Faculty of Medicine, Ain Shams University, for their valuable suggestions, advices and supervision in this essay, I am very thankful for their critical time, encouragement, and kind support.



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Physiological And Pathological Review

Physiology of Bile

Bile Composition :-

Bile is a complex aqueous solution formed in the liver and containing electrolytes, conjugated bile salts, phospholipid "Primarily lecithin" cholesterol, fatty acids mucin, proteins and a variety of hepatic metabolites and bile pigments. The electrolyte content and osmolality of bile approach those of plasma, however, the bladder bile is more concentrated than hepatic bile (Furker 1977).

Biliary Lipids:

Lecithin and cholesterol comprise the majority of bile lipids. Lecithin is a phospholipid which is insoluble in water. Cholesterol being formed by the liver as well as being absorbed by the gastrointestinal tract. Cholesterol is either converted into bile salts or excreted directly into the bile. Bile salt micelles markedly increase the solubility of these lipids in the bile. In the intestine lecithin is hydrolysed to choline and fatty acid cholesterol is reabsorbed into an enterophepatic circulation and serves as a feed back mechanism in the control of cholesterol synthesis in the liver (Heubi et al 1982 and Vunbergmann et al 1975).

Bile Acids and Bile Salts:

The primary bile acids in human bile are cholic acid and chenodeoxycholic acid. These important compounds are synthesized in the liver from cholesterol by several intermediate steps. Cholic acid is the bile acid found in the largest amount in the bile itself. Both cholic and chenodeoxycholic acids are formed from a common precursor which is derived itself from cholesterol. "Danielsson 1975"

Bile acids are synthesized in a rate of 200-500 mg/d to replace the bile acids lost in feces. They represent the only significant way for elimination of cholesterol as the body tissues can't break down the steroidal nucleus. Bile acids enter the bile as glycine or taurine conjugates namely glycocholic or glycochenodeoxycholic and taurocholic or taurochenodeoxycholic acids in a ratio glycine:taurine of 3:1.

Since bile contains significant quantities of alkali cations "Na and K" .It is estimated that bile acids and their conjugates are actually in a salt form and hence the term bile salts is usually used to describe these compounds in the bile (Nair and Kritchevsky 1973).

- **Bilirubin Metabolism**

As a result of degradation of the red blood corpuscles in the reticuloendothelial system, haemoglobin is released and metabolised to biliverdin. This pigment is reduced to unconjugated water insoluble bilirubin "the so called indirect bilirubin measured by the Van den Bergh reactions", carried in the blood, bound to albumin, and extracted by the hepatocytes in the presence of glucouronyl transferase, bilirubin is conjugated with glucuronic acid and to a lesser extent with sulfate forming bilirubin glucuronide and bilirubins sulfate. This water soluble conjugated bilirubin "direct bilirubin" is then secreted in the bile canaliculi. The daily load of bilirubin for excretion is about 300mg. In the Gut Intestinal bacteria convert the bilirubin to urobilinogens. These urobilinogens are either extracted by the hepatocytes to enter the enterohepatic circulation or excreted in the urine (Suchy et al 1987, and Schmid McDonough 1978).

Functions of Bile:

The secretion of bile serves three major functions, first bile salts, phospholipids and cholesterol aggregate within the bile to form mixed micelles. By emulsification, the micellar complex allows enteric absorption of ingested

fats and the fat soluble vitamins "A,D,E,C,". Absorption of certain minerals "Calcium, Copper and iron" is also facilitated. Second, bile serves as the vehicle for enteral excretion of bilirubin. Third, in part by neutralizing gastric acid, bile helps to maintain the proper alkaline environment in the duodenum, that in the presence of bile salts, allows maximal activity of the post prandial digestive enzymes (Harper et al 1980).

Pathology of Gallstones

Compsition of Stones:

Most idiopathic gallstones in children and teenagers are composed of varying proportion of pigment "Calcium bilirubinate", cholesterol and calcium why stones form is not known one popular belief is that bile supersaturated with cholesterol is responsible for calculus formation (Macmillan et al 1974).

Cholesterol Stones:

The majority of these stones are mixed cholesterol stones that contain at least 75% cholesterol by weight and varying amounts of phospholipids, biliary pigments and other

organic and inorganic (Substances. pure cholesterol stones occur infrequently (Sabiston 1987).

* Pure cholesterol stones are soft, pale yellow, usually smaller in size. However most non-pigmented stones are of the mixed cholesterol variety and vary in size from a sandy concentration to aggregates up to 2.5 cm in diameter, while pigment calculi from hemolysis are composed largely of calcium bilirubinate usually shaped like mulberry and black in colour (Sabiston 1987).

* The physical process of cholesterol stone formation occurs in three stages:

- 1- Supersaturation of bile with cholesterol.
- 2- Crystallization/precipitation.
- 3- Growth of cholesterol stone.

Stone formation is a complicated process in which many poorly understood factors augment each of the three stages of stone formation (Welch et al 1986).

* **Pigment Stones:**

There are two forms, pure pigment stones and calcium bilirubinate stones. Pure pigment stones are smaller

biliary tree infested with the parasite *clonorchis sinensis* or *ascaris lumbricoids*. *Escherichia coli* makes A B-glucouronidase that is believed to deconjugate bilirubin in bile which may favour formation of insoluble calcium bilirubinate. The inflammed gall bladder or biliary radicals may play arole by elaborating organic substances, which by serving as anidus may increase the lithogenicity for pigment stones (Trotman and Soloway 1982 and Sabiston 1987).

Incidence And Aetiology

Cholelithiasis in infancy and childhood

Incidence

Until 1960 about 600 cases had been described with cholelithiasis in children. Since 1960 increasing number of children and adolescents have been described with cholelithiasis in individual reviews of which the largest single study being of 83 patient (Holcomb et al, 1980).

In adults cholelithiasis complicates cholecystitis in 93% of patients where as in children this percentage falls to about 57 to 69% (Ulin et al 1952).

However, cholecystitis in the children age group is usually related to several factors as spesis, anatomical anomalies metabolic disorders, hemolytic anemias, and hereditary disorders (Mac Millan et al, 1974).

The peak incidence of gallstones in children occurs between the age of ten to thirteen years of age (Brenner et al 1964).

The incidence of cholelithiasis in children is higher in females than in males in a range of 11:10 (Morales1, et al 1967), which rises to 19:1 with sederund 1962.

The incidence is equal in both races blacks and whites (Mac Millan et al, 1974).

Cholelithiasis occurs in infancy, childhood and adolescents in sufficient frequency to warrant its consideration in the differential diagnosis of upper abdominal pain and discomfort (Gravier et al, 1968).

Under lying aetiology of cholelithiasis in infancy and childhood

Cholelithiasis in infancy and childhood with hemolytic anemias is predominant, However an increasing number of children are developing gallstones after prolonged use of total parenteral Nutrition (TPN), following distal ileal bowel resection, or in association with adolescent pregnancy, the use of birth control pills and obesity. However in many children no aetiologic factors are identifiable (Rescorla and Grosfeld 1992).

Cholelithiasis in infancy and childhood and hemolytic anemias.

Traditionally, it has been emphasized that hemolytic anemias was the primary cause of gallstones in most young patients (Gravier et al 1968).

Also, most studies agreed that the most commonly associated condition with cholelithiasis in children was hemolytic anemia and was found in 71% of patients (Gleen 1959).

However, some studies reported that gall stones occur more frequently in patients with no hemolytic anemias as in the study of saulerlund and zetterstream on 57 children with gall stones among whom only three had hemolytic anemia, and the study of Brenner and Stewart on 244 children with cholecystitis where 60 % of them had gall stones but only 8.4% of them had hemolytic anemia (Soderlund and Zetterstrom 1962).

In the presence of heamolysis, the increased destruction of red blood cells releases excessive quantities of free hemoglobin, this is ultimately degraded into bilirubin and excreted in the bile and thus increased hemolysis might have led to stone formation (Mac millan et al 1974).

Cholelithiasis in childhood in association with some hemolytic discases has been well documented as in.

*** Heriditary spherocytosis:** The incedence of cholelithiasis in Heriditary spherocytosis ranges from 43% to 66% of patients. (Dewey et al 1970).

However others reported lower incidence as (30%). "Lawre 1979" and (26%) (Robert 1986 and Welch et al 1986).