# BONE CHANGES IN CHILDREN WITH POST HEPATITIC CIRRHOSIS

## THESIS

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By
Ali Abdel Hady Hassan Mourad
( M. B., B. Ch. )

Supervisors

Dr. SAZDIA ABDEL FATTAH
Prof. of Pediatric Department

Dr. NAWAL ZAKARIA
Prof. of X-ray Department

Dr. SAWSAN EL SOKARY
Assist. Prof. of Pediatrics



Faculty of Medicine
Ain Shams University

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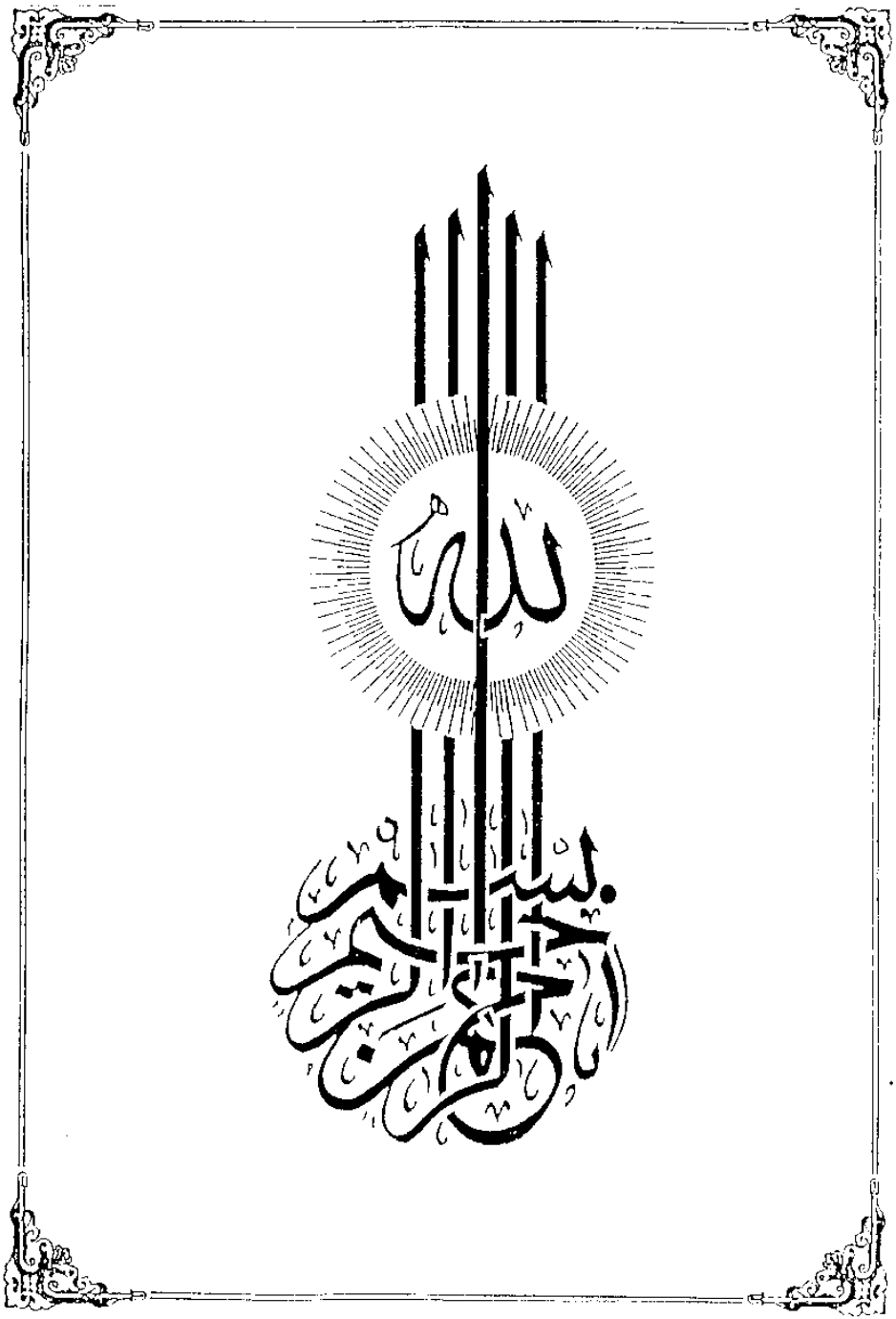

CONTENTS

# INTRODUCTION

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The range of hepatic functions is diverse and includes metabolic homoeostasis (e.g. of carbohydrate metabolism); storage and intermediate steps in fat and protein metabolism, an excretory function necessitated by the kidney's inability to handle non-polar (i.e. insoluble) substances such as bilirubin and numerous drugs (a function it subserves by conversion to polar form by conjugation, hydrolysis, oxidation, and reduction); a digestive function-production and secretion of bile salts, production of albumin and several factors essential for coagulation (Porfar 1978).

Bile, because of its bile salt content, is important of the intestinal absorption of calcium and magnesium, and this has been found both in experimental animals, (Lengmann and Dobbing, 1958, Kehayoglou et al., 1968), and in human subjects (Keboyoglou et al., 1968a, Whelton et al., 1971). Deficiency or absence of bile flow into the intestines may result in malabsorption of these elements.

1. Bile salts are essential for absorption of vitamin D (Schacter et al., 1964) which enhances the intestinal absorption of calcium (Schacter and Rosen, 1959, Sallis and Holdsworth, 1962) and magnesium (Meintzer and Steenbock, 1955; Hanna, 1961; Kobayashi et al., 1974, Miller et al., 1965, Kobayashi et al., 1974).

2. Bile salts are also important in the process of emulsification and micells formation in fat absorption (Borgstrom, 1967). Deficiency in the secretion of bile salts would adversely affect fat absorption, and formation of insoluble calcium soaps of unabsorbed fatty acids in the samll intestine would reduce calcium absorption (Staggreda and Mitchell, 1951; Kehayoglou et al., 1968b). In addition, bile salts may directly increase calcium absorption (Webling and Holdsworth, 1965).

Haymann (1937) reported that vitamin D disappeared from the serum of dogs when the bile duct was ligated. Furthermore, vitamin D that is absorbed from the gastrointestinal tract via the lymphatics transported from

there to the liver in the chylomicron of the plasma is hydroxylated in the liver microsomes to a more potent metabolite, 25-hydroxycholecalciferol (25-Hcc) Lund and De Luca, 1966; Ponchon et al., 1969, which is thought to be converted to more active forms, 1, 25 - or 21, 25-dihydroxycholecalciferol (1, 25 - or 21, 25-DHcc) in the renal tubule metachondria faciliated by parathyroid hormone. (Fraser and Kodicek, 1970).

Heptatic osteodystrophy has been recognized in patients with various liver diseases in infancy and childhood (Stamp, 1974, Harrison et al., 1973, Jung et al., 1978). The cause of hepatic osteodystrophy may be in part due to lack of vitamin D or disturbance of vitamin D metabolism in the liver.

# AIM OF THE WORK

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Infective hepatitis is an uncommon condition in infants and children. In the majority of cases complete recovery is the rule. However in 2% of cases, post hepatitic cirrhosis occurs (Shpylock, 1971).

Since liver is the site of initial activation of vitamin D and bile is essential for its absorption from the intestines, there may be a failure to metabolise the vitamin adequately in liver cirrhosis. Consequently, bone changes are liable to occur in post hepatitis cirrhosis.

The aim of the present study is to determine the bone changes which might possibly occur in Egyptian children with post hepatitic cirrhosis.

# REVIEW OF LITERATURE

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### Cirrhosis of the liver:

The term cirrhosis of the liver indicates varying degrees of fibrosis. In cirrhosis, the normal hepatic lobular architecture is deranged with nodular regeneration of liver cells surrounded by variable amounts of fibrous tissue that compress blood vessels. Compression impairs the blood flow more in the low pressure portal and hepatic veins than in the high pressure arteries. These cause further hepatocellular death and deposition of more collagen (Forfar, 1978; Nelson, 1975).

### Types of cirrhosis:

Cirrhosis is of two main types portal (or Laennec's cirrhosis) and biliary cirrhosis. In portal cirrhosis, bands of fibrous tissue radiate from the portal vein (in the portal triad) and surround the hepatic lobules.

Biliary cirrhosis occurs secondary to obstruction of the distended bile ducts (Abbassy, 1977).

Etiology of cirrhosis:

Cirrhosis of the liver may be caused by number of different agents. The following types can be recognised in infancy and childhood:

1. Cirrhosis following acute infectious hepatitis.
2. Chronic infections as bilharziasis and sometimes syphilis and kalaazar.
3. Cirrhosis following chronic biliary obstruction.
4. Autoimmune diseases e.g. plasma cell hepatitis.
5. Metabolic disorders and galactosemia Wilson's disease.Fanconi syndrome and rarely glycogen storage disease.
6. Sometimes cirrhosis may occur after recovery from carbon tetrachloride poisoning.
7. Cirrhosis may occur in long standing chronic hemolytic anemia partly due to repeated blood transfusion.

Disturbed liver functions in hepatobiliary disease.

Disturbed carbohydrate metabolism:

Abdel-Aal et al. (1971) found that in bilharzial liver fibrosis, the level of blood pyruvate and lactate showed some elevation which is more prominant in lactate than pyruvate. Keys and Snell (1938) found that the arterial $O_2$ saturation in hepatic disease is reduced. This anoxia may help lactic acid production by tissues and hence, high levels of blood lactic acid.

Disturbed protein metabolism:

In liver hypofunction, lowered levels of serum albumin is a common finding and serum gamma globulin is increased. Since serum albumin is mainly synthesised in the liver, it is conceivable to refer such decrement to diminished liver synthesising ability and dysfunction (Abdel Aal et al., 1971).

A diminished serum albumin/total globulin ratio in evident in most cases of liver cirrhosis.

Several factors may contribute to the striking hypergamma globunemia, viz hyper plasia of the reticuloendothelial system under the effect of the parasitic antigens with a consequential immunological response, (Moore et al., 1956, Magalhaes et al.,1965), or inability of the liver to rid itself of the gamma globulin. Besides, the hypergamma globunemia may be a compensatory phenomenon for the existant hypo-albuminemia as a trial to maintain a constant plasma osmotic pressure.

Disturbed Metabolism of Vitamin D, Calcium, Magnesium and Phosphorus:

Since the initial step of transformation of vitamin D to its active form. (25, hydroxy cholecalciferol) may take place in the liver (Lund and De Luca, 1966,Ponchon et al., 1969), there may be a failure to metabolise the vitamin adequately in hepatic cirrhosis (Ponchon and De Luca, 1969). This mechanism may participate in causing malabsorption of calcium and magnesium in hepatobiliary disease.