PSYCHOLOGICAL AND BIOCHEMICAL ASPECTS OF LIVER CIRRHOSIS

Thesis

Submitted for Fulfillment of Phelosophy Doctorship in Midical Childhood Studies

By

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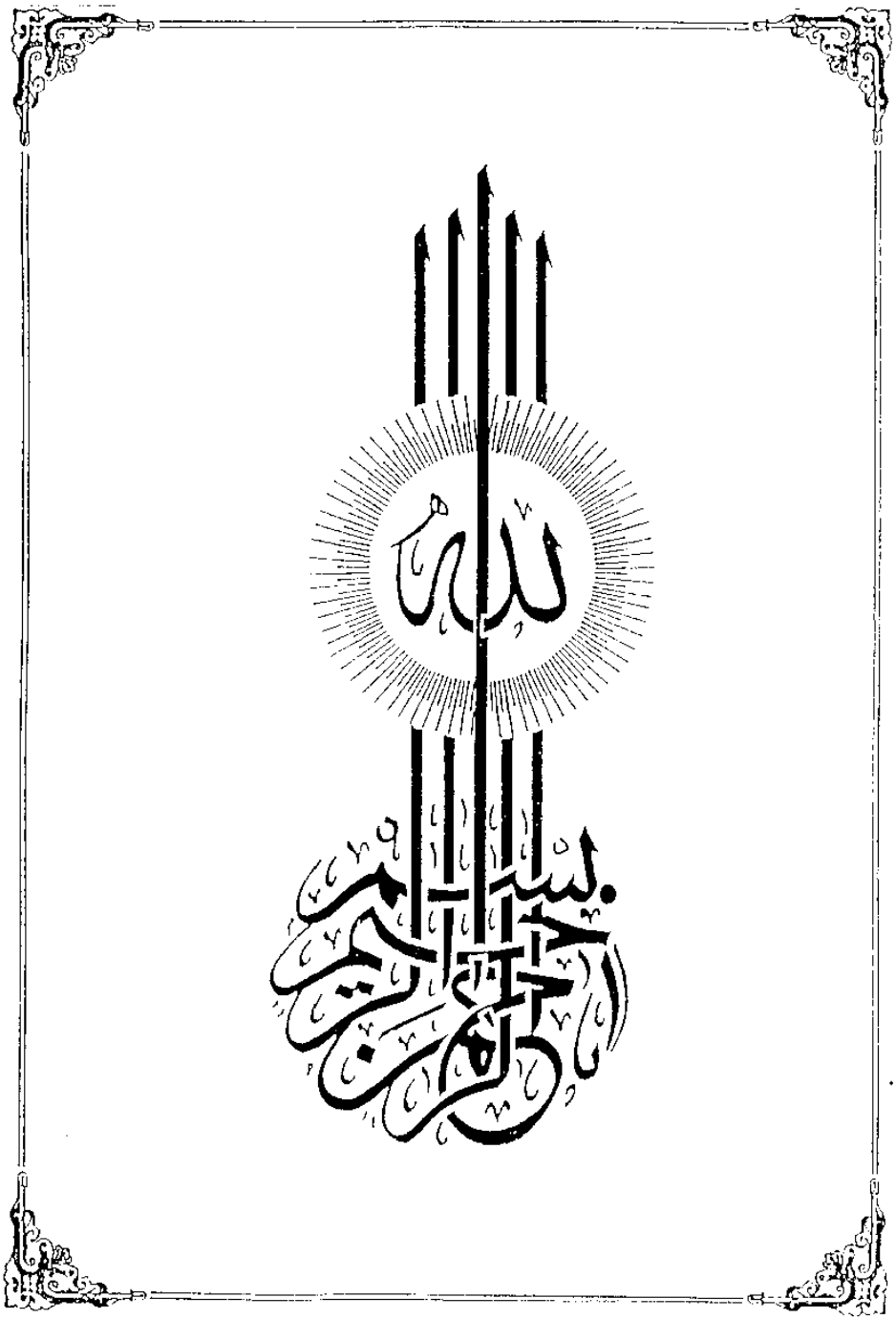

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INTRODUCTION AND AIM OF WORK

INTRODUCTION and AIM OF THE WORK

INTRODUCTION

Cirrhosis, is the end stage of many forms of liver injury. Although the diagnosis of cirrhosis implies an irriversible or even progressive pathological change, it is still compatible with growth and normal activity for many years ***(Sherlock, 1993)***.

Optimizing growth and development is a major goal in treating chronic pediatric disease. Some, but not all, children with chronic liver disease have been noted to have deficits in both growth and mental development ***(Stewart et al., 1988).***

The liver plays a crucial role in maintaining nutritional homeostasis of infant and adult ***(Watkins and glassman, 1985).***

Malnutrition in chronic liver diseases is due to several factors including anorexia with reduced caloric and nutrient intake, maldigestion, malabsorption and increased resting energy expinditure ***(Tanner and Lama, 1991).*** Micronutrient deficiencies during early life may negatively affect intellectual development in these children. Of the fat-soluble vitamins, vitamin E specifically has been found to relate to neurologic and mental function ***(Stewart et al., 1988).***

The prevalence of chronic illnesses in childhood and their association with mental health problems has been the subject of much research over many years. Many studies suggest that a chronic illness predispose to psychopathology, while others fail to find such a relationship. ***Pless and Pinkerton (1975)*** used a "noncategorical approach" which emphasizes that the chronicity of the disease and its impact of the child or family is more important than the specific character of the disorder ***(Weiland et al., 1992).***

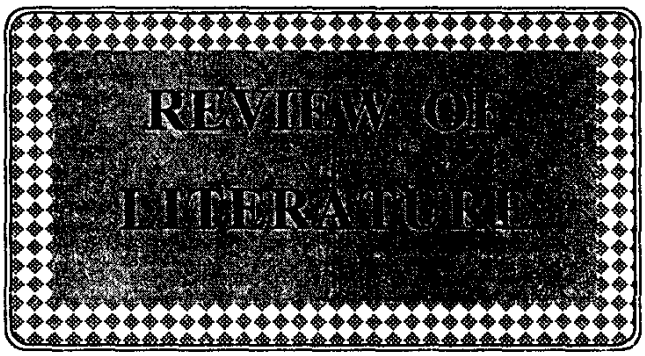
Emotional and behavioral problems affect 18% to 20% of children and the rates are higher in children with chronic illness. Despite the many years of research, methodologic variation and the lack of comparative studies across illness have led to contradictory findings about the psychologic correlates of chronic illness ***(Canning et al., 1992).***

AIM OF THE WORK

The aim of the work is :

1) To clarify how a specific disability may have serious repercussions on the child's personality, development, and family functioning and therefore on the whole society.

2) to present the results of nutritional assessment in cirrhotic patients and to suggest some interventional guidlines that may not only improve nutritional management but also decrease morbidity of these patients,



CIRRHOSIS IN CHILDREN

Definition:

Cirrhosis is a pathological term. A recent precise and generally accepted definition is: "a diffuse process characterized by fibrosis and a conversion of normal architecture into structurally abnormal nodules" ***(Tanner, 1989)***. Fibrosis and nodule formation are essential components of the definition but both occure in the abscence of cirrhosis, for example in congenital hepatic fibrosis and in focal nodular hyperplasia respectively.

Hepatic Necrosis: whilest not necessarily present at the time of diagnosis, must have occurred during induction of cirrhosis.

Hepatic regeneration: is implicit in nodule formation, but the histological features of regeneration are difficult to recognize because of the low rate of mitosis ***(Tanner, 1989)***.

The process of necrosis due to the persistence of the etiologic agent and the ischemic consequences of the tissue injury amplify the potential for nodular regeneration. Vascular and micro-environmental changes occure. The vascular changes that occur consists of fibrovascular septa with the formation of a peri-nodular plexus and shunts. The micro environmental changes include a loss of the normal lobular gradient and cell polarity, an uncoupling of liver cells, and the closure of gap junctions. These factors, together with capillarization of the sinusoids,

result in marked disturbances of intercellular connections, communications and interactions *(Callea et al., 1991)*.

The presence of liver plates more than one cell thick is a criterion used by adult hepatologists, but in infancy liver plates are frequently two cell thick. Binucleate or multinucleate cells are frequent in infantile hepatitis not progressing to cirrhosis. Regeneration may be implied by compression of surrounding parenchyma and reticulin by the nodule.

Inflammatory infiltration: may be present (active cirrhosis) or abscent (inactive cirrhosis) *(Tanner, 1989)*.

Classification:

Cirrhosis may be classified morphologically, aetiologically and clinically *(Millward - Sadler et al., 1986)*.

1) Morphological:

Three anatomical types of cirrhosis are recognized: micronodular, macronodular and mixed.

Micronodular cirrhosis: is characterized by thick, regular septa, by regenerating small nodules varying little in size, and by involvement of every lobule. The micronodular liver may represent impaired capacity for regrowth.

Macronodular cirrhosis: is characterized by septa and nodules of variable sizes and by normal lobules in the larger nodules, previous

collapse is shown by juxtaposition in the fibrous scars of three or more portal tracts. Regeneration is reflected by large cells with large nuclei and by cell plates of varying thicknesses ***(Sherlock, 1993)***.

Regeneration in a micronodular cirrhosis results in a macronodular or mixed appearance. With time, micronodular cirrhosis often converts to macrondoular ***(Fauerholdt, et al., 1983)***.

Tanner, (1989) added that the situation in which collagen surrounds small groups of hepatocytes as in Indian childhood cirrhosis, has been termed "micro-micro" nodular cirrhosis. he also stated that micro nodular cirrhosis (nodules < 3 mm in diameter) is obvious in a liver biopsy sample, whilest macrodular may be missed if the biopsy needle enters one large nodule or traverses nodules tangientially.

2) <u>Aetiological</u>:

According to ***Mowat and Brunt (1984)***, the causes of cirrhosis in childhood are perhaps most simply considered under two broad pathological headings: post-necrotic and biliary cirrhosis. Genetic causes contribute to both pathological varieties (Table 1).

Table (1): Causes of cirrhosis in childhood ***(Mowat and Brunt,1984)***.

I. Post-necrotic cirrhosis

- Post hepatitic:
  - = Hepatitis in infancy, especially in alpha -1- antitrypsin defeciency.
  - = Viral hepatitis, type B chronic active hepatitis.
  - = Hepatitis due to toxins: Aflotoxin.
  - = Hepatitis due to drugs: actinomycin D, Methotrexate.
- Venous congestion:
  - = Constrictive pericarditis.
  - = Budd-chiari syndrome.
  - = Congestive cardiac failure.
  - = Epstein anomaly.
- Veno occlusive disease.
- Indian childhood cirrhosis.
- Ulcerative colitis.

II. Biliary cirrhosis

- Extrahepatic biliary atresia.
- Intra hepatic biliary hypoplasia.
- Byler's disease.
- Cystic fibrosis.
- Biliary stenosis or obstruction.
- Choledocholithiasis.
- Ulcerative colitis.
- Familial intrahepatic cholestasis.

- Ascending pyogenic cholangitis.
- Primary sclerosing cholangitis.
- Cholangitis due to fasciola, ascaris.

III. Genetic causes

- Alpha-1-antitrypsin difficiency.
- Cystic fibrosis.
- Wilson's disease.
- Galactosaemia.
- Fructosaemia.
- Glycogen storage disease type III, IV.
- Tyrosinosis.
- Neimann - pick disease.
-Gausher's disease.
- A-Beta lipoproteinaemia.
- Sickle cell disease.
- Thalasaemia.
- Haemochromatosis.
- Zellweger's syndrome.
- Caprostanic acidemia.

Aetiological information is more likely to come from the recognition of accompanying histological features such as:

1) Features of biliary abstruction,

2) Piecemeal necrosis and inflammatory infiltration in chronic aggressive hepatitis;

3) Cytoplasmic orcein staining in hepatitis B;

4) Granular orcein staining, whether scanty and accompanied by fatty change as in Wilson's disease or copious and accompanied by hepatocyte necrosis and hyaline inclusions as in Indian childhood cirrhosis;

5) Iron deposition as in haemosiderosis,

6) Alpha-1- antitrypsin inclusions;

7) Storage cells;

8) Glycogen, as in type IV glycogenesis;

9) Centrilobular congestion and necrosis, as in hepatic venous out flow obstruction ***(Tanner, 1989)***.

3) Clinically:

Cirrhosis apart from other features peculiar to the cause, results in two major events: hepatocellular failure and portal hypertension. In clinical terms, the types are either "Compensated" or "Decompensated" ***(Sherlock, 1993).***

Functional categorization of patients with cirrhosis is often based upon Pugh's modification of Child's score (Table 2). This scoring system is of limited value in childhood, as it takes little account of growth, nutrition, or cause of cirrhosis ***(Tanner, 1989)***.