بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

﴿ قـــسـم ﴾

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بالرسالة صفحات

لم ترد بالأصـــل

EFFECT OF ZINC SUPPLEMENTATION ON INSULIN LIKE GROWTH FACTOR-1 (IGF-1) SERUM CONCENTRATION IN CHILDREN WITH CHRONIC LIVER DISEASE

Thesis

Submitted For Partial Fulfillment For

The Master Degree In Pediatrics

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قالوا سبحانك

لا علم لنا إلا ما علمتنا
إنك أنت العليم الحكيم

صدق الله العظيم

(البقرة ٣٢)

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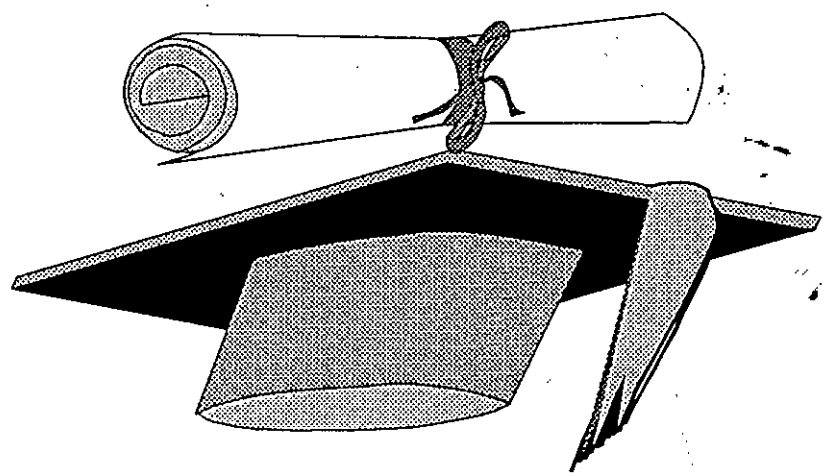

REVIEW OF LITERATURE

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CHRONIC LIVER DISEASE IN CHILDREN

Chronic liver disease encopasses a wide spectrum of disorders, including infectious, metabolic, genetic, drug–induced, autoimmune and idiopathic diseases [1].

CHRONIC HEPATITIS

Definition:

Chronic hepatitis is defined as a chronic inflammatory reaction in the liver continuing without improvement for at least 6 months. [1].

Causes of chronic hepatitis in children: [2]

I.Chronic Viral Hepatitis

Hepatitis B , C & D

II.Autoimmune Hepatitis

Anti-smooth muscle antibody positive .

Anti-liver – kidney microsomal antibody positive .

Antisoluble liver antigen antibody positive .

Others (includes antibodies to liver –specific lipoproteins)

Overlap syndrome with sclerosing cholangitis and auto antibodies

III.Drug – Induced Hepatitis

IV.Metabolic Disorders:

Alpha-1- antitrypsin deficiency .

Wilson disease

Tyrosinemia

Niemann-pick disease type 2

Glycogen storage disease type IV

Cystic fibrosis

Galactosemia.

Clinical features suggesting chronicity:

Chronic hepatitis should be suspected in the patients with hepatitis in the following circumstances:

(1) History of conjugated hyperbilirubinaemia in infancy .

(2) Family history of chronic liver disease, inherited or autoimmune disorders

(3) A relapse of an apparent acute hepatitis .

(4) Persistence of clinical features of acute hepatitis .

(5) Previous history of hepatitis B,C or D hepatitis .

(6) Clinical features of chronic liver disease at presentation such as: Small, hard or nodular liver, firm splemomegaly, ascites, cutaneous dilated abdominal veins, growth failure, muscle wasting, cutaneous features of chronic liver disease as facial telangiectasia, spider naevi and palmer erythema [2]

Pathological classification :

According to the histological features, chronic hepatitis can be classified into : [1,2]

Chronic Persistent Hepatitis (C.P.H.):

C.P.H. is marked by expansion of the portal zone by mononuclear cells and some fibrosis. The limiting plate of liver cells between portal zones and liver cell columns is intact. Piece-meal necrosis of liver cells is not seen. The liver architecture is preserved . C.P.H. is non progressive and, therefore , it is a benign form of chronic hepatitis .

Patients with C.P.H. are usually asymptomatic. Serum transaminases may be elevated two – to five folds, bilirubin, alkaline phosphatase, gamma globulin and albumin concentrations tend to be normal. The diagnosis of chronic hepatitis depends greatly on the results of serological tests and liver biopsy [3].

Chronic Active Hepatitis (C.A.H.):

C.A.H. is marked by the presence of an inflammatory infiltrate, primarily of lymphocytes and plasma cells, which greatly expands the portal areas. This inflammatory infiltrate extends into the liver lobule, causing erosion of the limiting plate and "piece –meal necrosis". The severe form is marked by fibrous septa extending from the portal zones into the liver columns with isolation of groups of liver cells in the form of "rosettes". Necrosis is

sometimes bridging the lobule between portal triads or hepatic veins "bridging necrosis", portal-central or portal-portal. The milder form of C.A.H. shows only slight erosion of the limiting plate with some piece-meal necrosis but without bridging or rosette formation. Patients with C.A.H. present with more prominent clinical features and greater abnormalities of liver function tests[4].

Chronic Lobular Hepatitis:

Chronic lobular hepatitis is sometimes termed prolonged or unresolved acute hepatitis. Many of the histological features resemble acute viral hepatitis as focal liver cell degeneration and necrosis maximal around the central veins with infiltration by inflammatory cells, but the duration is greater than 3 months. There is no piece-meal necrosis, or fibrosis. The course is characterized by remissions and relapses marked by elevations of transaminases [3].

Grading of Chronic Hepatitis Activity:

In chronic hepatitis, grading is a measure of the severity of necro-inflammatory process. Several grading systems have been used, the most important of which is the Knodell score or the histological activity index (HAI) [5]. This consists of three separate scores for different components of the lesion.

Table (1): Knodell score for grading of chronic hepatitis [5].

Component	Score
1.Periportal necrosis with or without bridging necrosis .	0-10
2.Intralobular degeneration and focal necrosis.	0-4
3.Portal inflammation.	0-4

With the HAI scoring, necro-inflammatory activity can be approximately equated with verbal grades or diagnosis[6,7].

Table(2): Chronic hepatitis: correlation of HAI score and diagnosis [7].

HAI	Brief description	Possible diagnosis in nomenclature
1-3	Minimal chronic hepatitis	Non specific reactive hepatitis - CLH - CPH
4-8	Mild chronic hepatitis	Severe CLH, CPH , mild CAH
9-12	Moderate chronic hepatitis	Moderate CAH
13-18	Severe chronic hepatitis	Severe CAH with bridging necrosis

NB: CLH = chronic lobular hepatitis
CPH = chronic persistent hepatitis
CAH = chronic active hepatitis .

LIVER CIRRHOSIS

Definition:

Cirrhosis is defined pathologically as a diffuse process affecting the whole liver in which the normal architecture is replaced by structurally abnormal nodules surrounded by prominent fibrous tissue [2].

Pathology :

The cardinal pathological features reflect irreversible chronic injury of the hepatic parenchyma and include extensive fibrosis in association with the formation of regenerative nodules. These features result from hepatocyte necrosis, collapse of the supporting reticulin network with subsequent connective tissue deposition, distortion of the vascular bed, and nodule regeneration of remaining liver parenchyma.The regenerating nodules disturb hepatic architecture and a full picture of cirrhosis develops[1].

Pathogenesis[8,9,10]

The process that leads to hepatic fibrosis results from the dynamic inter-action among extracellular matrix components (ECM) , several hepatic cell types and humoral mediators or cytokines. Formation of fibrous scar is the net result of increased formation and decreased degradation of ECM . When

hepatocytes are injured, a cascade of events is initiated that is mediated by the complex interplay of cytokines. The earliest response seems to be the release of factors such as interleukin-1 (IL1) , interleukin-6 (IL6) and tumour necrosis factor-α (TNFα) that stimulate the inflammatory response and exert mitogenic effects on mesenchymal cells .

Hepatocyte injury leads to activation of fat storing (Ito) cells in the space of disse by transforming growth factor-β (TGF-β) derived from kupffer cells and other initiating factors from hepatocytes, platelets and lymphocytes. These factors activate hepatocytes and endothelial cells to produce connective tissue proteins. They also activate Ito cells which are thought to proliferate as myofibroblasts . The early changes in matrix in the space of disse are associated with laying down of fibril-forming collagens (types I, III and V) and fibronectin.

Sinusoids are converted to capillaries (capillarization) and there is loss of endothelial fenestrae. Sinusoidal stenosis leads to an increased hepatic vascular resistance and to portal hypertension. Progression of fibrosis disrupts hepatic archietecture and leads to cirrhosis and portal hypertension.

Classification:

1. Morphological Classification[11]

Three anatomical types are recognized: micronodular, macronodular and mixed. Macronodular cirrhosis is characterized by nodules of various sizes (upto 5cm) separated by broad septae. Micronodular cirrhosis with nodules of uniform size (less than 1cm) separated by fine septae. Regeneration in micronodular cirrhosis results in a macronodular or mixed appearance.