USE OF PLASMA PROLIDASE ACTIVITY IN EARLY DIAGNOSIS OF COLLAGEN CATABOLISM IN HEPATIC SCHISTOSOMIASIS

Thesis Presented By

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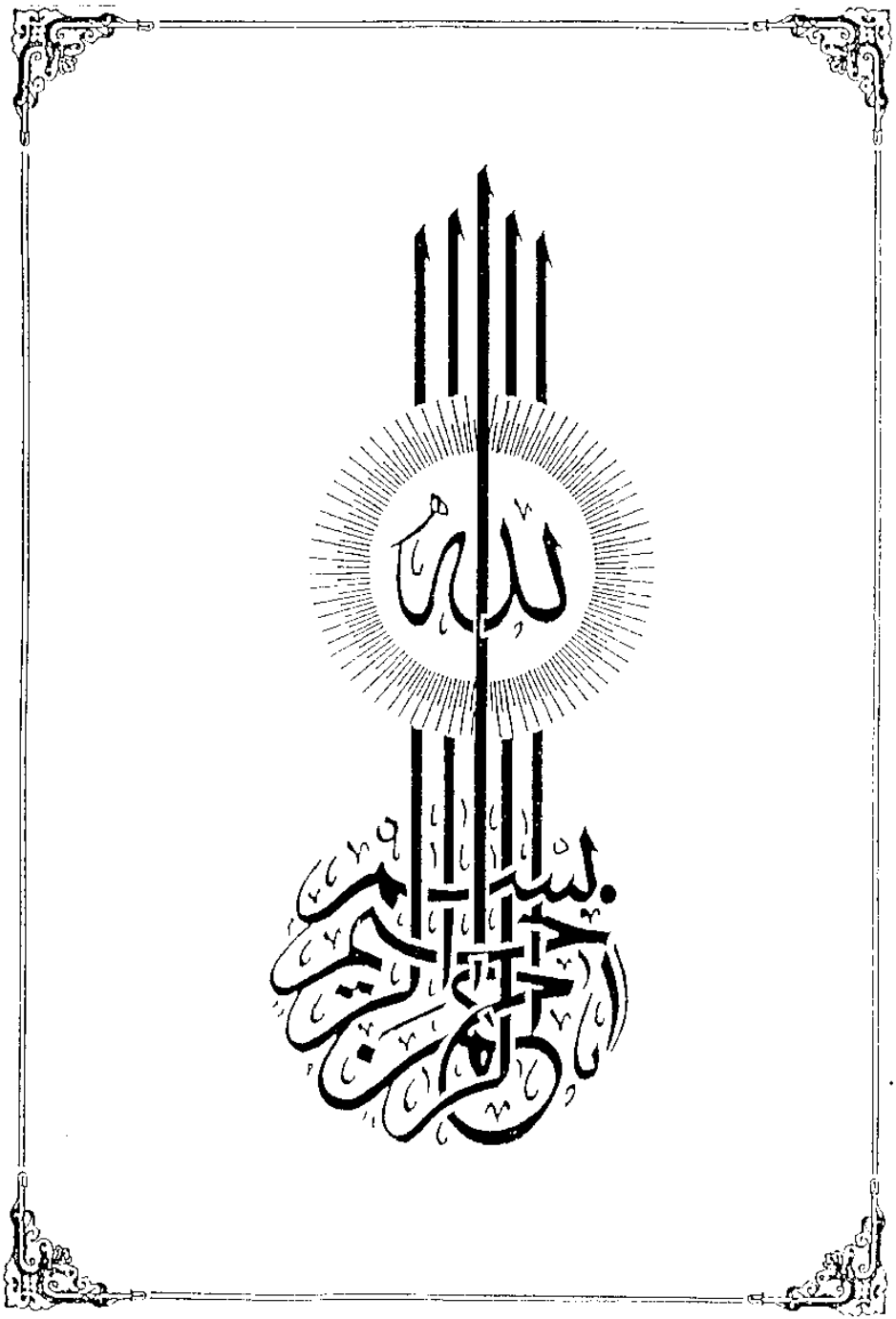

C O N T E N T S

INTRODUCTION

I N T R O D U C T I O N

Bilharziasis is the most prevalent disease in Egypt affecting 20 million population and reducing the total economic output by one third (Ayad , 1974) .

The main pathological feature and the occurrence of endstage pipestem fibrosis in hepatic schistosomiasis are determined by the competing process of collagen synthesis and collagenolysis which are both stimulated by liver injury in schistosomiasis (Popper , 1977) .

Hepatic fibrosis may be represented as a morphologic manifestation of little functional significance but it may represent a serious problem not only from compromising the hepatic function, but because of the possibility of progression of the fibrosis into a crippling life threatening disorder, cirrhosis . This dynamic aspect is related to the metabolism of collagen as one main and characteristic components of the connective tissue (Popper , 1975) .

Early diagnosis of hepatic fibrosis, inhibition of its formation and acceleration of the resorption of the newly formed collagen would lead to the amelioration of metabolic disorder and circulatory disturbance (Sambe et al., 1974) .

AIM OF WORK

THE AIM OF WORK

The aim of the present work was to study the correlation and availability to use plasma prolidase activity in early diagnosis of Collagen Catabolism in hepatic schistosomiasis .

REVIEW OF LITERATURE

C H A P T E R (I)

HEPATIC SCHISTOSOMIASTS

Introduction :

Hepatic schistosomiasis is propably the world's most prevalent chronic liver disease (Dunn and Kamel, 1981).

Schistosomiasis is a disease of the portal system, so the liver is expected to be affected in nearly every case. The various reaction of this organ depends on the intensity of hepatic invasion which may pass from a preclinical stage to the advaced firbrotic liver which may lead to death (Saleh, 1962).

Liver involvement in schistosomiasis was first described in Egypt by Kartulis (1885), but Symmers(1904), was first to notice that extensive scarring and thickening of the large portal tracts occured in response to the deposition of Schistosoma mansoni eggs in these sites and he used the term " clay-pipe stem cirrhosis " Sorour(1928) used the term periportal cirrhosis and Hashem (1947),adopted the term "coarse periportal fibrosis" on this basis that schistosomiasis does not cause necrosis of liver cells followed by regeneration as in other types of cirrhosis.

cases of portal hypertension caused by schistosomiasis. Schistosoma eggs were found concentrated in areas of portal fibrosis of cases with Symmer fibrosis in the absence of Symmer's fibrosis, egg did not concentrate in large portal areas regardless of the intensity of infection or the presence of lesser degrees of portal fibrosis.

Cheever (1968) and cheever et al. (1977) predicted that the extent and severity of chronic disease should be correlated with the intensity and duration of egg production by fertile worm pairs. This had been validated by quantitative postmortum study of patients with S. mansoni infection.

(2) Role of worm toxins.

Meleney et al. (1952) described foci of liver necosis in mice with unisexual Schistosoma mansoni, Schistosoma japonicum and Schistosoma haematobium infections and they supported the view that necrosis lesion are caused by the toxic products of worms.

Dewitt and Warren (1954) however, did not accept the toxin theory claming that this would attack the liver cells more diffusely and would be associated with sever derangment of liver function.

Electron microscopy of the liver in murine hepato-splenic schistosomiasis mansoni revealed in the cells adjacent to granulomatous or portal areas, some

disorganization of the rough endoplasmic reticulum(RER), depletion of glycogen, prominence of smooth endoplasmic reticulum (SER), hypertrophy of Golgi complex and increased numbers of mature lysosomes and autophagic vacuoles(Stenger, et al., 1967). These changes could be possible attributed to the mechanical pressure from expanding granuloma rather than true toxic changes.

(3) Role of dead schistosomes .

Menezes (1967) reported that portal fibrosis is mainly due to the inflammatory reaction induced by the dead adult parasites and to the proliferation of the connective tissue. Deposition of ova in newly opened capillaries only contributed in his opinion to increased fibrosis.

Elwi (1976) comment on these views that such events as they describe are certainly not commonly observed in practice and can hardly explain the uniform thickening of the whole of the intrahepatic course of the large portal tracts. Moreover, other observers provided a different opinion.

Warren (1962) found that his murine schistosomiasis model could not support the worms theory because treatment that killed the mature worms just prior to the onset of ovi-position did not result in the development of hepato-splenic diseases. But, the untreated counterparts of the

mice in which there was the usual outpout of eggs by the worms, all developed hepatosplenomegaly and hypertesion.

Cheever et al. (1965) reported that repeated cycles of Schistosoma mansoni infection of mice, resulting in an average of more that 100 dead worms entering the livers of these animals (equivalent on weight basis to several hundred thousand worms in a human liver), did not induce overt disease of the liver.

(4) Role of malnutrition .

Dewitt (1957a) mentioned that hepatosplenic schistosomiasis develops in well nourished animals in which there is little if any impairment in the absorption of fats and that malnutrion does not seem to be necessary for its development.

DeWitt (1957b) found also that a poor diet may in fact protect the animals as it had been shown to limit the worms production of eggs which are the major cause of the disease.

Hashem (1962) studied the effect of various deficient diets on the evolution of the hepatic schistosomiasis in animal and concluded that dietary deficiency may make the liver more vulnerabled to schistosomal infection in its earliest stages. In later stages deficiency of

diet creates an unfavourable medium for the proper development and reproduction of the worms during the infection.

(5) Role of hypersensitivity :

Andrade (1967) had an extrem point of view that considered the portal fibrosis in hepatic schistosomiasis result from a delayed hypersensitivity reaction to schistosomes antigen and not from the confluent of numerous tinny ova granulomes. The main excuse for this assumption is the scarcity of ova among the residual fibrous tissue in the portal tracts. Such a view does not take in consideration the fact that during the prolonged course of schistosomiasis a large number of ova laid in tissue is removed by tissue reaction.

However, there is a place for the assumption that some of the portal fibrosis may be related to the inflammtory reaction which occur in the liver before oviposition and which may become more intensified afterwards. (Raslavicus, 1965).

Warren et al. (1972) found that sensitization could be transferred between histocompatible mice with lymph nodes or splenic cells, but not with sera. These results strongly suggested that the schictosome egg granuloma is essential or cell-mediated type of immunological response as a manifestation of delayed hypersensitivity. Madwar and Voller (1975) was able to prove the presence of soulbe circulting schistosomal antigens in the blood of schisto-somal patients.

(6) Role of auto immunity .

Nairn et al. (1960) showed that liver cell bounderies and cytoplasmic membrane contain a specific liver antigen, and the antibodies shown by the complement fixation and the fluourecent techniques are produced as a result of tissue damage caused by the worms and their eggs.

Abdin (1963) put the auto immune theory as the only satisfactory explanation for the marked and diffuse portal thickening where ova are few or absent.

Shamma et al. (1965) reported that 26% of sera from patients with S. haematobium infection had circulating antibodies that fix complement in the presence of normal lung or liver homogenate.