Value of Serum Ferritin & Alpha Fetoprotein In The Diagnosis of Hepatocellular Carcinoma

Thesis
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By

Abeer Ahmed Abdalla
M.B., B.Ch.

Supervised By

Prof. Dr. Mohamed Awad-Alla Sallam
Professor of Internal Medicine
Faculty of Medicine-Ain Shams University

Prof. Dr. Tareef Hamza Sallam
Professor of Clinical Pathology
Faculty of Medicine-Ain Shams University

Dr. Samir Abdel-Hamid Ghait
Lecturer of Internal Medicine
Faculty of Medicine-Ain Shams University

Faculty of Medicine
Ain Shams University

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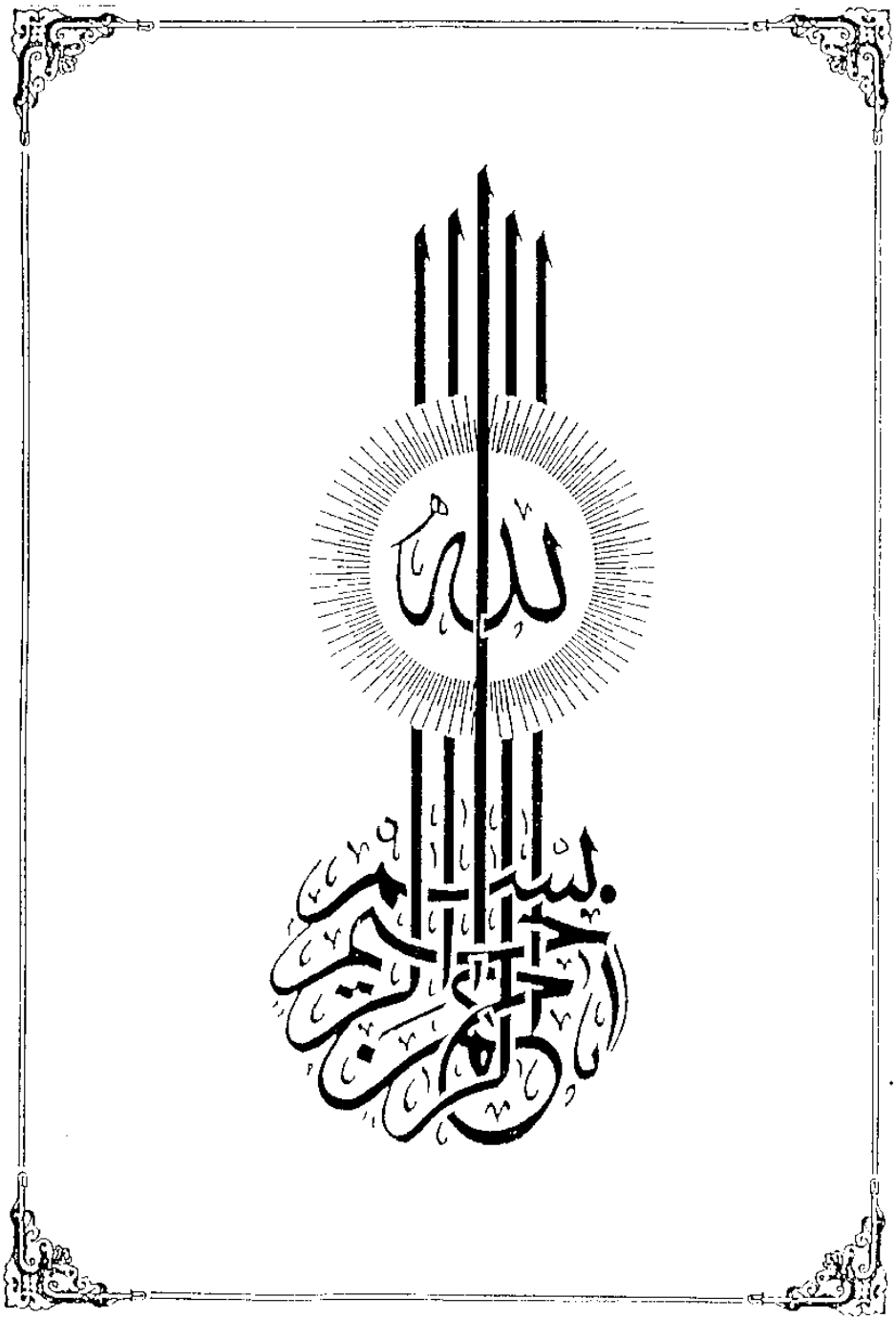

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Introduction & Aim Of The Work

Introduction

Liver cirrhosis is considered to be a premalignant condition of hepatocellular carcinoma (HCC). Approximately 10% to 30% of patient with liver cirrhosis are reported to have hepatocellular carcinoma ***(Sherlock, 1989)***.

Hepatocellular carcinoma is one of the most common malignancies in the world ***(Linsell et al., 1976)***, and there is frustration due to late diagnosis and bad therapeutic results. So, many clinical programs for its early detection have been developed ***(Kobayashi et al., 1985)***.

One of the most commonly used screening methods nowadays is the use of tumour markers although it is not a substitute for histologic or cytologic diagnosis ***(Laszlo, 1988)***.

Serum ferritin is a new tumour marker for diagnosis of hepatocellular carcinoma and it seems more specific (85% versus 68% for alpha fetoprotein) and more sensitive (88% versus 59% for alpha fetoprotein) ***(Giannoulis et al., 1984)***.

Aim of the work:

The aim of this work is to clarify the value of Serum ferritin as tumour marker in the diagnosis of hepatocellular carcinoma in patients

with liver cirrhosis in comparison with alpha fetoprotein, also to evaluate the value of combined assay of alpha fetoprotein and ferritin in the diagnosis of hepatocellular carcinoma and to find whether ferritin has a complementary value for alpha fetoprotein in the diagnosis or not.

Review Of Literature

Liver & Malignancies

The liver is affected by both simple and malignant growths. The simple ones are usually anatomical curiosities of no clinical importance. Malignant disease of the liver, however, is common, secondary deposits in the liver being much more common than primary cancers.

Primary Carcinoma of The Liver

Basically, there are 2 types of primary carcinoma arising from the liver. One of them from the hepatocytes and is called hepatocellular carcinoma (HCC) or liver cell carcinoma. The other arises from the bile duct and so, it is called cholangiocarcinoma.

Very infrequently a neoplasm appears to share characteristics of both lines. The hepatocholangiocarcinoma possibly because it arises in more primitive cells capable of differentiating in both directions.

Hepatocellular carcinoma, grievously sometimes still called a "hepatoma", accounts for about 90% of all primary liver cancers ***(Robbins et al., 1984)***.

Sherlock (1989) classified primary liver tumours according to their cell of origin into:

I. Hepatocellular:

A. *Benign:* adenoma "Liver cell adenoma".

B. *Malignant:*

- Hepatocellular carcinoma.
- Fibro-lamellar carcinoma.
- Hepatoblastoma.

II. Billiary:

A. *Benign:*

- Adenoma "Bile duct adenoma".
- Cystadenoma.
- Papillomatosis.

B. *Malignant:*

- Cholangiocarcinoma.
- Combined hepatocellular cholangio carcinoma.
- Cystadeno carcinoma.

III. Mesodermal:

A. *Benign:* Haemoangioma.

B. *Malignant:*

- Angio sarcoma (hemangio-endothelial sarcoma).
- Epithelioid hemangio-endothelioma.
- Sarcoma.

IV. Others:

- Mesenchymal haematoma.
- Lipoma.
- Fibroma.

Hepatocellular Carcinoma

Epidemiology:

Geographic distribution and incidence:

The disparity in the frequency of hepatocellular carcinoma between high-risk and low-risk countries can only be described as dramatic (30-40 fold). It is the most frequent type of cancer in many parts of Asia and Africa: Mozambique 70% of all carcinomas; Senegal 67%; Bantus in South Africa 50%; India, China, Taiwan and the Philippines each 20% ***(Neumayr and Weiss, 1981)***.

In the United States and Western Europe, hepatocellular carcinoma is increasing in incidence but remains relatively uncommon, accounting for less than 1 per cent of all causes of death at autopsy 2.5 per cent or less of all malignant growths. In certain other areas of the world, including parts of subsaharan Africa, South east Asia, Japan, Oceania and Greece, hepatocellular carcinoma is among the most frequent malignant tumour and is an important cause of overall mortality ***(Scharschmidt, 1988)***.

There is more than 250,000 new cases of liver cancer every year. The highest frequency is in Africa and Oriental races in whom there is nearly always an associated cirrhosis. The condition is increasing in the West and in California, the frequency had multiplied three times in the last twenty years ***(Peters et al., 1977)***.

In Egypt, ***Sorour (1930)*** at kasr El-Aini Hospital in an autopsy study, found only 15 cases of hepatocellular carcinoma among 365 cancers encountered all-over the body with a percentage frequency of 1.4 ***Barsoum (1938)*** recorded a percentage frequency of 1.5.

Abdel-Ghaffar (1979) estimated the frequency of hepatocellular carcinoma to account for 4.9 % of all chronic liver disease. Later, the annual reports of the Cancer Registry of the Metropolitan Cairo area have shown a rising incidence of primary hepatic malignancy from 1.5 to 2.6 % of the total cancer in Egypt during the years 1976 through 1980. ***Kamel (1983)*** found that hepatocellular carcinoma represents 7.2% of all cases of chronic liver disease.

Doll et al. (1966) had classified the countries according to the rate of development of primary liver cancer per 100,000 males per year, into 3 groups as shown below.

Table.(1): *Primary liver cancer reported by Cancer Registries.*

Area	Rate per 100,000 males per year
Group I:	
Mozambique	98.2
China	17.0
South Africa	14.0
Hawaii	7.2
Nigeria	5.9
Singapore	5.5
Uganda	5.5
Group II:	
Japan	4.6
Denmark	3.4
Group III:	
England and Wales	3.0
USA	2.7
Chile	2.6
Sweden	2.6
Iceland	2.5
Jamaica	2.3
Puerto Rico	2.1
Columbia	2.0
Yogoslavia	1.9

(Doll et al., 1966).

Age and sex:

In high-risk areas, markers of hepatitis B virus (HBV) are almost always present in patients with hepatocellular carcinoma. Moreover, the disease tends to be fulminant and to occur in those under the age of 40, and the male : female ratio is approximately 3 : 1. In contrast, in low-risk areas, such as the U.S. and Western Europe, markers for hepatitis B virus are found in less than half of the patients. The neoplasm runs a subacute course, and it tends to occur in cirrhotic elderly men with the male: female ratio approximately 9 : 1 ***(Sumithran***

and Mac Sween, 1979). However, *Schwartz (1990)* had reported that hepatocellular carcinoma affects all age groups.

The fibrolamillar variant of hepatocellular carcinoma occurs mainly in adolescent and in young adults, with mean age of 26 years and equally in both sexes *(Farhi and Shikes, 1983)*. In children, hepatocellular carcinoma accounts for 2 per cent of malignancies over half of the tumours become manifest between the ages of 5-15 years. Hepatoblastoma usually affects children under 2 years with a male : female ratio of 6 : 1 *(Dehner, 1978)*.

As noted previously, hepatocellular carcinoma is predominantly a disease of males *(Scharschmidt, 1988)*. The male : female ratio was, world wide, estimated to be 3 times more frequent in males than in females *(Sherlock, 1989)*. However, the sex ratio ranges from 2 to 6 males for each female patient *(Schwartz, 1990)*.

The reason for this male predominance remains speculative but the role of testosterone is evident on animal models. In animals, testosterone increases the incidence of, and castration affords protection against, spontaneous and chemically induced hepatic tumours *(Agnew and Gardner, 1952 and Reuber, 1959)*.

In human, the higher male predominance may partly be due to higher carriage rate of hepatitis B. Expression of androgen receptors