Chronic HCV related HCC and its correlation with serum iron and gender

THESIS

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Abstract

The incidence of hepatocellular carcinoma (HCC) is rising, and it is currently the sixth most common malignancy worldwide. HCC carries a poor prognosis and is the major cause of liver-related death in patients with compensated cirrhosis.

Excess serum iron is common in patients with end-stage liver disease from aetiologies, such as hepatitis C or alcohol use.

Iron overload is one of most important risk factor of hepatocellular carcinoma in the patients with liver cirrhosis.

Assessment of iron studies (serum iron and ferritin) are simple and non invasive to detect iron overload.

The aims of this study were to determine the prevalence of serum iron overload in patients with end-stage liver disease caused by HCV and to examine the association of hepatic iron overload with hepatocellular carcinoma.

The study includes 50 HCV related HCC (25 females & 25 males) (group I) and 20 non-HCC liver cirrhosis as controls (group II).

Hemoglobin, Total, direct billirubin, Albumin, PC&INR, AST, ALT, ALP, Alpha fetoprotein, Serum iron& ferritin and Abdominal Ultrasound and Triphasic C.T Abdomen were determined.

Transaminases are higher in HCC patients than non HCC liver cirrhosis. (P-value: o.oo2 for AST) (P- value: 0.0001 for ALT)

Key Words:

The liver, Iron metabolism, Hepatitis C Virus(HCV), Hepatocellular carcinoma (HCC), HCC & its correlation with iron,

To my family & my wife for without their everlasting love,

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Content

No **Page**

Content cont.

No **page**

List of figures

No **page**

List of tables

No **page**

List of tables cont.

No **page**

List of tables cont.

No **page**

Introduction & aim of the work

Hepatocellular carcinoma is rapidly fatal tumour usually becomes symptomatic at stage beyond the reach of currently available treatments. The only hope for cure lies in early diagnosis. The annual incidence of HCC was 2.1% usually related to age – male sex –concurrent HBV- HCV- alcohol abuse (**Beaton & Adams, 2006).**

Mild to moderate Iron excess is found in patients with liver diseases unrelated to genetic hemochromatosis. In the course of chronic liver diseases may observe there is fluctuation in both serum Iron and ferritin especially with patients with liver cirrhosis (**Pirisi et al., 2004).**

Iron overload is risk factor for cancer in general and hepatocellular carcinoma in particular, this oncogenic effect could be explained by over production of reactive oxygen species and free radicals **(Fargion et al.,2000).**

The incidence of hepatocellular carcinoma in females less than males, this is explained by Iron overload in males with liver cirrhosis more than Iron overload in females with liver cirrhosis **(Fargion et al., 2000).**

Iron depletion therapy could interfere with fibrosis development and possible reduce the incidence of HCC (**Nahon etal. 2008).**

There is importance to follow Iron studies (serum Iron and ferritin) for patients with liver cirrhosis.

The aims of this study were to determine the prevalence of serum iron overload in patients with end-stage liver disease caused by HCV and to examine the association of serum iron overload with hepatocellular carcinoma.

The Liver

The liver is a vital organ present in vertebrates and some other animals; it has a wide range of functions, a few of which are detoxification, protein synthesis, and production of biochemicals necessary for digestion. The liver is necessary for survival; a human can only survive up to 24 hours without liver function. The liver plays a major role in metabolism and has a number of functions in the body, including glycogen storage, decomposition of red blood cells, plasma protein synthesis, hormone production, and detoxification. The liver is also the largest gland in the human body. It lies below the diaphragm in the thoracic region of the abdomen. It produces bile, an alkaline compound which aids in digestion, via the emulsification of lipids. It also performs and regulates a wide variety of high-volume biochemical reactions requiring very specialized tissues (**Maton et al., 1993)**.

Medical terms related to the liver often start in hepato- or hepatic from the Greek word for liver, hēpar (ήπαρ).[The Greek word "ήπαρ" was derived from hēpaomai (ηπάομαι): to mend, to repair, hence hēpar actually means "repairable", indicating that this organ can regenerate itself spontaneously in the case of lesion **(Maton et al., 1993)**.

Anatomy

An adult human liver normally weighs between 1.4-1.6 kg (3.1-3.5 lb) **(Ramzi et al., 2005),** and is a soft, pinkish-brown, triangular organ. Averaging about the size of an American football in adults, it is both the largest internal organ and the largest gland in the human body (not considering the skin).

It is located in the right upper quadrant of the abdominal cavity, resting just below the diaphragm. The liver lies to the right of the stomach and overlies the gallbladder.

Blood flow

The liver receives a dual blood supply consisting of the hepatic portal vein and hepatic arteries. Supplying approximately 75% of the liver's blood supply, the hepatic portal vein carries venous blood drained from the spleen, gastrointestinal tract, and its associated organs. The hepatic arteries supply arterial blood to the liver, accounting for the remainder of its blood flow. Oxygen is provided from both sources; approximately half of the liver's oxygen demand is met by the hepatic portal vein, and half is met by the hepatic arteries **(Shneider &Philip, 2008).**

Biliary flow

The bile produced in the liver is collected in bile canaliculi, which merge to form bile ducts. Within the liver, these ducts are called intrahepatic bile ducts, and once they exit the liver they are considered extrahepatic. The extrahepatic ducts eventually drain into the right and left hepatic ducts, which in turn merge to form the common hepatic duct. The cystic duct from the gallbladder joins with the common hepatic duct to form the common bile duct. The term biliary tree is derived from the arboreal branches of the bile ducts. The intrahepatic bile ducts form the most distant branches of this tree. Bile can either drain directly into the duodenum via the common bile duct or be temporarily stored in the gallbladder via the cystic duct**.** The common bile duct and the pancreatic duct enter the duodenum together at the ampulla of Vater **(Melissa, 2004)**.

Lobes

Traditional gross anatomy divided the liver into four lobes based on surface features. The falciform ligament is visible on the front (anterior side) of the liver. This divides the liver into a left anatomical lobe, and a right anatomical lobe.

If the liver flipped over, to look at it from behind (the visceral surface), there are two additional lobes between the right and left. These are the caudate lobe (the more superior), and below this the quadrate lobe.

From behind, the lobes are divided up by the ligamentum venosum and ligamentum teres (anything left of these is the left lobe), the transverse fissure (or porta hepatis) divides the caudate from the quadrate lobe, and the

right sagittal fossa, which the inferior vena cava runs over, separates these two lobes from the right lobe.

Each of the lobes is made up of lobules; a vein goes from the centre of each lobule which then joins to the hepatic vein to carry blood out from the liver.

On the surface of the lobules there are ducts, veins and arteries that carry fluids to and from them **(David et al., 2003).**

Table. I: Functional anatomy

Correspondence between anatomic lobes and Corinaud segments	
Segment*	**Couinaud segments**
Caudate	1
Lateral	2, 3
Medial	4a, 4b
Right	5, 6, 7, 8

* Or lobe in the case of the caudate lobe.
Each number in the list corresponds to one in the table.

1. Caudate
2. Superior subsegment of the lateral segment
3. Inferior subsegment of the lateral segment
4. a.Superior subsegment of the medial segment
   b.Inferior subsegment of the medial segment
   Inferior subsegment of the anterior segment
   Inferior subsegment of the posterior segment
   Superior subsegment of the posterior segment
   Superior subsegment of the anterior segment

The central area where the common bile duct, hepatic portal vein, and hepatic artery proper enter is the hilum or "porta hepatis".
The duct, vein, and artery divide into left and right branches, and the portions of the liver supplied by these branches constitute the functional left and right lobes.

The functional lobes are separated by an imaginary plane joining the gallbladder fossa to the inferior vena cava. This separates the liver into the true right and left lobes. The middle hepatic vein also demarcates the true right and left lobes. The right lobe is further divided into an anterior and posterior segment by the right hepatic vein.

The left lobe is divided into the medial and lateral segments by the left hepatic vein. The fissure for the ligamentum teres also separates the medial and lateral segments. The medial segment is also called the quadrate lobe.

In the widely used Couinaud (or "French") system, the functional lobes are further divided into a total of eight subsegments based on a transverse plane through the bifurcation of the main portal vein. The caudate lobe is a separate structure which receives blood flow from both the right- and left-sided vascular branches **(VanLeeuwen, 1994).**

Physiology

The various functions of the liver are carried out by (hepatocytes). Currently, there is no artificial organ or device capable of emulating all the functions of the liver. Some functions can be emulated by liver dialysis, an experimental treatment for liver failure **(Howard et al., 1999)**.

Synthesis

1) Proteins produced and secreted by the liver, large part of amino acid synthesis .The liver is responsible for the mainstay of protein metabolism, synthesis as well as degradation. The liver produces albumin, the major osmolar component of blood serum **(Howard et al., 1999)**.

2) The liver performs several roles in carbohydrate metabolism:

- Gluconeogenesis (the synthesis of glucose from certain amino acids, lactate or glycerol).

- Glycogenolysis (the breakdown of glycogen into glucose) (muscle tissues can also do this).