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## Estimating the Risk of Hepatocellular Carcinoma in Developing Countries

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### Review Article

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#### ABSTRACT

Hepatocellular Carcinoma is otherwise known as Liver Cancer is the third most affecting cancer in the world. According to the Statistics, the treatment is available in developed countries. Most of the parts of Asia and Africa are majorly affected due to this disease. The disease is heterogenous and more likely to spread rapidly in the body. Due to the disease, cells divide repeatedly and affects the metabolic and immune functions of the liver. The spread of Hepatitis B and C can be controlled by Vaccination and awareness programs. The present review focuses majorly on treatment options, prevention and future prospects of prevention of disease. The disease shows progressive effects due to poor medical facilities, Changes in life style, Improper dietary management and Alcoholism.

#### INTRODUCTION

The cancer that affects liver is called Hepatocellular carcinoma.<sup>[1,2,3]</sup> Hepatocellular carcinoma otherwise known as Malignant hepatoma. It is the third leading cancer throughout the globe. It leads to the damage of hepatocytes which leads to the death of the individual within 6-20 months. This type of cancer is usually seen in men than in women.<sup>[2-7]</sup> The occurrence of this cancer is more than 80% in developing countries than in developed countries. More than 6,00,000 deaths occurring in Asia and Africa annually due to this cancer. Although Liver cancer is the sixth most occurring cancer in the world, due to its poor diagnosis it was detected as third<sup>[8,9]</sup>.

#### Anatomy of Liver

Liver is the largest organ in the human body. It performs a wide variety of functions namely metabolism, production of bile, carbohydrate synthesis, immune functions and urea formation<sup>[11-14]</sup>. The microscopic anatomy of liver contains parenchymal and nonparenchymal cells<sup>[12,13]</sup>. Parenchymal cells or hepatocytes comprise the bulk of the organ and carry out complex metabolic processes. Hepatocytes are responsible for the major role in metabolism<sup>[14,12]</sup>. The liver also aids in the detoxification of drugs and other foreign substances. Biliary passages begin as tiny bile canaliculi formed by hepatocytes<sup>[16-18]</sup>. These microvilli-lined structures progress into ductules, interlobular bile ducts, and larger hepatic ducts.

#### Causes of Liver Cancer

The major causes of this cancer are:

- Cirrhosis
- Hepatitis B and C infections<sup>[19,20]</sup>
- Other factors

#### Cirrhosis

The major and most common cause of Hepatocellular Carcinoma is Cirrhosis (Alcoholism). Most patients (90%) with this complication have underlying cirrhosis. The risk of developing hepatocellular carcinoma is 3-5 times more in alcoholic patients<sup>[19-21]</sup>. The most common causes of cirrhosis are alcoholism, fatty liver and Hepatitis C infection.

### **Hepatitis B and C Infections**

Hepatitis B is mainly caused due to virus. The virus can be transmitted in unhygienic conditions. The causes of both Hepatitis B and C are more likely similar. In China, the development of Hepatocellular carcinoma is mainly due to Hepatitis B virus (HBV)<sup>[22,23]</sup>. In USA and Europe, both Hepatitis B and C equally contribute to the disease whereas in Japan, Hepatitis C is the major risk factor in the development of carcinoma.

### **Other factors**

Diseases caused by abnormal liver function, such as hemochromatosis, a condition in which excessive iron is absorbed and deposited into the liver and other organs, and Wilson's disease, caused by the abnormal storage of copper in the liver. Prolonged exposure to environmental toxins and parasitic infections also causes Cirrhosis<sup>[23-25]</sup>.

### **Pathophysiology**

Body is composed of several cells. If there is an abnormal growth in the cells then it is termed as tumour. If there is abnormal growth in the cells of liver it is called hepatocellular carcinoma<sup>[26-29]</sup>. As the Hepatitis virus enters the liver cells, it multiplies more rapidly and inhibits the functioning of the liver.

As a result, the liver loses its normal functioning and enlarges in its size at the initial stage. The chronic stage of hepatocellular carcinoma leads to complete liver failure<sup>[31-34]</sup>.

The pathophysiology of hepatocellular carcinoma has not been definitively elucidated. In 1981, after Beasley linked HBV infection to hepatocellular carcinoma development, the cause of hepatocellular carcinoma was thought to have been identified<sup>[35]</sup>. However, subsequent studies failed to identify HBV infection as a major risk factor, and it became apparent that most cases of hepatocellular carcinoma developed in patients with underlying cirrhosis for HBV infection were found to have HBV DNA integrated in the hepatocyte genome<sup>[36-38]</sup>.

Inflammation, necrosis, fibrosis, and ongoing regeneration characterize the cirrhotic liver and contribute to hepatocellular carcinoma development<sup>[39,40]</sup>. In patients with HBV, in whom hepatocellular carcinoma can develop in liver that are not cirrhotic, underlying fibrosis is usually present, with regeneration. By contrast, in patients with HCV, hepatocellular carcinoma invariably present in the setting of cirrhosis. This difference may relate to the fact that HBV is a DNA virus that integrates in the host genome and produces HBV X protein that may play a key regulatory role in hepatocellular carcinoma development. HCV is an RNA virus that replicates in the cytoplasm and does not integrate in the host DNA<sup>[41,42,43]</sup>.

### **Symptoms of Hepatocellular Carcinoma**

Early stages of liver cancer do not show any symptoms. As the tumour grows and spreads larger, several symptoms can be noticed. They are :

- Pain in the upper abdomen in the right side
- Nausea and Vomiting
- Weakness
- Yellow colour of skin
- Loss of appetite
- Weight loss

## Diagnosis of Liver Cancer:

Different tests can be used to diagnose liver cancer. They are

Physical Examination

Blood tests

Liver function tests

CT and MRI scanning

Ultrasound examination

Liver Biopsy

### Physical Examination

An exam of the body to check general signs of health, including checking for signs of disease, such as lumps or anything else that seems unusual. A history of the patient's health habits and past illnesses and treatments will also be taken<sup>[45-48]</sup>.

### Blood tests

The procedure in which a sample of blood is examined to measure the amounts of certain substances released into the blood by organs, tissues, or tumour cells in the body. Certain substances are linked to specific types of cancer when found in increased levels in the blood.<sup>[45,46]</sup> These are called tumor markers. An increased level of alpha-fetoprotein (AFP) in the blood may be a sign of liver cancer. Other cancers and certain noncancerous conditions, including cirrhosis and hepatitis, may also increase AFP levels. Sometimes the AFP level is normal even when there is liver cancer.

### Liver function tests

A procedure in which a blood sample is checked to measure the amounts of certain substances released into the blood by the liver. A higher than normal amount of a substance can be a sign of liver cancer<sup>[46,47]</sup>.

### CT and MRI scanning

A procedure that makes a series of detailed pictures of areas inside the body, such as the abdomen, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography. A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body, such as the liver. This procedure is also called nuclear magnetic resonance imaging (NMR)<sup>[47-49]</sup>.

### Ultrasound imaging

A procedure in which high-energy sound waves (ultrasound) are bounced off internal tissues or organs and make echoes. The echoes form a picture of body tissues called a sonogram<sup>[50]</sup>.

### Liver Biopsy

Small cells or tissues are collected from the liver by means of a fine needle is called biopsy. It is the most accurate and final stage diagnosis of liver cancer<sup>[51]</sup>.

### Prevention of Hepatocellular Carcinoma

Liver Cancer can be prevented by vaccination. Hepatitis B is the major cause for liver cancer. Hence People in under developed and developing countries have to get awareness regarding the vaccination of Hepatitis B. Antiviral treatment helps in preventing cirrhosis in patients<sup>[52,53]</sup>.

## Treatment and Management

The treatment and Management of tumour depends on the size, number of tumours spread and the suitability of the patient for liver transplantation<sup>[54]</sup>. Some of the treatment options for patients affected with liver cancer are :

- Surgical resection
- Radiotherapy
- Chemotherapy
- Cisplatin gel injection
- Liver transplantation

### Surgical Resection

Surgical resection is the most common treatment for noncirrhotic patients. In this method, if a part of liver is damaged, this can be surgically removed and liver can regrow the missed part. If it is totally damaged, then liver transplantation is the only option<sup>[55,56]</sup>.

### Radiotherapy

The tumour or cancer cells can be killed by passing radiation. Advanced techniques have been developed such as Stereotactic body radiation therapy through which the radiologists can easily target the tumour cells without destroying the healthy tissues<sup>[56-58]</sup>.

### Chemotherapy

Chemotherapy is the treatment of tumour with the help of drugs. It is usually given through IV administration<sup>[58]</sup>.

### Cisplatin gel injection

The technique in which the gel of cisplatin is inserted into the liver cells by means of a fine needle. The method has promising results in initial stages of treatment but the treatment at advanced stages has to be still assessed. This treatment option is under clinical trials<sup>[59,60]</sup>.

### Liver transplantation

Liver transplantation can be done to the patient only if the tumour is less than 6 cm in size. It can be transplanted to the patients. It is the best option for the patients with acute liver failure<sup>[61-63]</sup>.

## CONCLUSION

Liver Cancer is mostly affected to people in Africa, Asia and some of the developing countries. Lack of awareness, Lack of dietary management, Poor Medical facilities are the major causes of this disease. As the disease is heterogenous, genetic factors also play a key role for its occurrence<sup>[64]</sup>. Liver transplantation and Hepatic resection remain as the corner stones for curative therapy of Liver Cancer. However, the success rate of these therapies are 5 years<sup>[64,65]</sup>.

### Future Prospects

The advancement of Medicine has developed new techniques to identify the tumour at early stage. Researches being carried out on immunotherapy and gene therapy to identify and target on specific gene and increase the mortality<sup>[64,68]</sup>. The major challenge is to develop a specific therapeutic modality for the patients with early diagnosis who could tolerate resection<sup>[66]</sup>. By developing these

techniques, the treatment should be made available to the common people and should be cost effective<sup>[66,67]</sup>.

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