

RISK FACTORS FOR HEPATOCELLULAR CARCINOMA

Sonya Banova, Iskren Kotzev

Clinic of hepatogastroenterology, St. Marina University Hospital of Varna

ABSTRACT

Hepatocellular carcinoma (HCC) is the most common primary cancer of the liver and the third greatest cause of cancer-related death worldwide, incidence is increasing. The aim of this retrospective study is to estimate the incidence of HCC and to identify the risk factors for HCC in patients who have passed through the Clinic of Hepatogastroenterology, Varna. All they have serologic tests, imaging examinations (abdominal ultrasonography, CT, MRI) and fine needle biopsy. Men are 125 of pts. and women are 55 (2.3:1). The average age at diagnosis is 62 ± 9.44 (m) and 65 ± 12.02 (f) years. The majority of patients (68%) with HCC had cirrhosis. Viral infection was found in 54% of the cases: hepatitis C (HCV) – 46 pts. (26%), hepatitis B (HBV) - 52 pts (29%). Diabetes mellitus have 40 pts (22%). Alcohol abuse was observed in 38 pts. of the surveyed (21%). These study shows that the main risk factors for HCC are male gender, older age, viral hepatitis (HCV and HBV), alcohol intake, presence of cirrhosis and diabetes. Thus, the best strategy is eliminating modifiable risk factors (alcohol, diabetes) and to treat with viral infections (HBV, HCV).

Key words: *Hepatocellular carcinoma, risk factors, liver cirrhosis, viral hepatitis, alcohol abuse, background environment*

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary cancer of the liver (1). Incidence is increasing and HCC has risen to become the 5th commonest malignancy worldwide and the third leading cause of cancer related death, exceeded only by cancers of the lung and stomach. The most recent World Health report, indicated a total of 714 600 new cases of HCC worldwide (Table 1), with 71% among men (Fig. 1) (6).

MATERIAL AND METHODS

The aim of this retrospective study is to estimate the incidence of HCC in patients with chronic

liver diseases and to identify the risk factors for HCC in our group of in-patients. 17 450 adult in-patients have passed through the Clinic of Hepatogastroenterology, Varna, for the twelve-year period (Jan 2001- Dec 2012). HCC was established in 180 of them (1%). We interviewed all subjects regarding their alcohol consumption and background environment. All they have serologic tests, imaging examinations and fine needle biopsy.

RESULTS

Men are 125 of pts. versus 55 women (2.3:1). The average age at diagnosis is 62 ± 9.44 (m) and 65 ± 12.02 (f) years. The majority of patients (63%) with HCC had cirrhosis. Viral infection was found in 54% of the cases: hepatitis B (HBV) - 52 pts. (29%), hepatitis C (HCV) – 46 pts. (26%). Alcohol abuse was observed in 38 pts. of the surveyed (21%). Working with harmful substances was found in three patients, and two patients had Wilson's disease. The most frequent combinations of risk factors are: cirrhosis with viral etiology - 55%; cirrhosis with ethanol - 68%. From

Address for correspondence:

Sonya Banova, MD
Clinic of hepatogastroenterology
St. Marina University Hospital of Varna
1 Hristo Smirnenki Str., 9010 Varna, Bulgaria
e-mail: s_banova@abv.bg

Received: November 21, 2013

Accepted: December 2, 2013

Table 1. Global frequency of new cases of hepatocellular carcinoma

Year (reference)	Total number	Male	Females
1990	437 408	316 300	121 100
2000	564 300	398 364	165 972
2002 (The World health report, 2003)	714 600	504 600	210 000

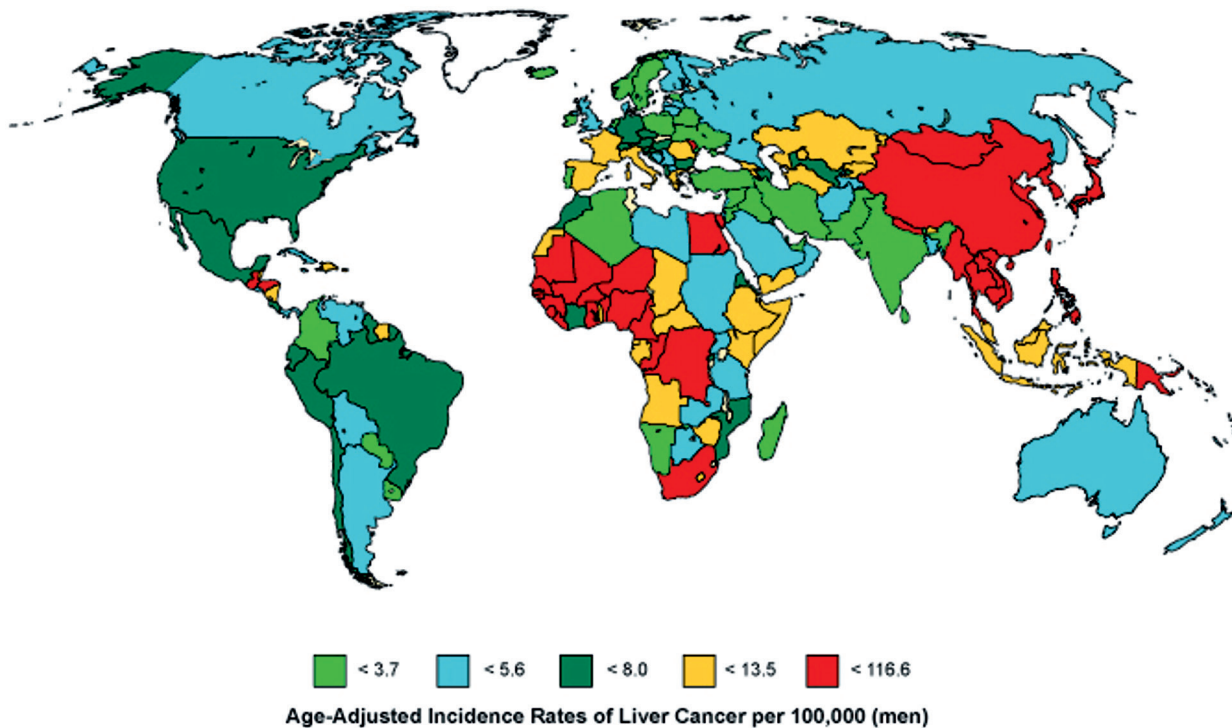


Fig. 1. Worldwide Incidence of Hepatocellular Cancer. Source: International Agency for Research on Cancer 2013

our data we can conclude that the main risk factors in this cohort of patients are:

- Male sex – 125 pts. (69%)
- Advanced age (> 60) – 116 pts. (64%)
- Cirrhosis of viral etiology -89 pts (50%)
- HBV - 52 pts. (29%)
- HCV – 46 pts. (26%)
- Diabetes mellitus - 40 pts. (23%)
- Alcohol abuse – 38 pts. (21%)
- Alcohol induced cirrhosis – 30 pts. (17%)
- HBV-infection (without cirrhosis) – 8 pts. (5%)

DISCUSSION

This pathology is associated with several risk factors, not only environmental but also genetic, generating an increasing interest in attaining a better

understanding of this disease, which is still associated with very late diagnosis and poor prognosis (4).

Major risk factors for HCC are viral (chronic hepatitis B and chronic hepatitis C), toxic (alcohol and aflatoxins), metabolic (diabetes and non-alcoholic fatty liver disease, Wilson's disease, hereditary haemochromatosis) and immune-related diseases. Most of these risk factors also lead to the formation and progression of cirrhosis, which is present in 80 to 90% of patients with HCC and it is a risk factor also itself - 68% in our study. Over 80% of primary liver cancer worldwide is attributable to the effects of chronic infection with hepatitis B or C virus (HBV or HCV) - 46% in our study. Hepatitis B is considered the strongest risk factor associated with HCC in the majority of countries, but more important in Asia and Africa. The annual incidence of HCC in hepa-

titis B patients with cirrhosis exceeds 2% (8). Hepatitis B virus is thought to be carcinogenic both directly and indirectly, because HBV DNA is integrated into cellular DNA of host and can be demonstrated in HCC cells in 95% of the cases (7). Hepatitis B infection is powerful oncogenic factor and may cause HCC without presence of cirrhosis - 5% in our study. That's why antiviral therapy can prevent HCC. Early treatment intervention is necessary to prevent damaging liver cells and decrease viral genome integration. Another important issue is that use of vaccines against HBV should eventually be of benefit, especially in endemic area (2).

Liver cancer has a higher prevalence in patients with HCV-associated cirrhosis than in non-viral etiologies of chronic liver disease, while only a few cases of HCV-associated HCC have been reported in the non-cirrhotic liver (1pts.), indicating that the virus possibly has a mutagenic effect.

Cirrhosis is the major risk factor for the development of HCC regardless of the cause. The annual incidence of HCC in patients of cirrhosis is about 3% (8). In our study we observed 123 patients with both cirrhosis and HCC - 68%.

In several studies conducted in Western countries, 30 to 40% of patients with hepatocellular carcinoma did not have chronic infection with HBV or HCV, suggesting the presence of other causes of disease - 44% in our study. Multiple non-viral factors have been implicated in the development of HCC. Increased body mass index and diabetes with subsequent development of non-alcoholic steatohepatitis represent significant risk factors for HCC. Moreover diabetes mellitus is identified as a negative prognostic indicator in hepatocellular carcinoma, though the basis for this is unknown (3,5). Other non-viral causes of HCC include iron overload syndromes, Wilson disease, α -1 antitrypsin deficiency, porphyrias, autoimmune hepatitis, alcohol abuse, tobacco, oral contraceptive, aflatoxin, pesticides exposure. Our study shows 21% alcohol abuse in patients with HCC.

CONCLUSION

Those results show that the most important risk factors for HCC are male gender, older age, viral hepatitis (HCV and HBV), alcohol intake, presence of cirrhosis and diabetes. Thus, the best strategy is eliminating modifiable risk factors (alcohol, diabetes) and to treat HBV and HCV infections with antiviral therapy.

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