RESEARCH COMMUNICATION

Hepatocellular Carcinoma and its Early Detection by AFP Testing in Mongolia

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Abstract

Liver cancer is one of the leading causes of cancer death in Mongolia. Since 1982-1986 , when HCC became the most frequent cancer among the Mongolian population, the rate has been increasing continuously. In the period 2000-2005 years 35.3%of all newly registered cancer cases were liver cancers, with an incidence rate of 51.3 per 100,000 population. Compared to the previous 5 year period, the rate increased by 11%. The objective here was to analyze hepatitis B (HBV) and C virus (HCV)-related HCC cases and to evaluate the possibility of tumor marker (AFP) testing for early detection in Mongolia. Sera from a total of 513 patients with chronic liver diseases, liver cirrhosis and HCC were analyzed for liver function (ALAT, ASAT) and hepatitis virus markers (HBsAg, anti-HCV). Sera from 316 patients were also examined for alpha-fetoprotein (AFP) levels. The overall incidence of HBsAg or anti-HCV were very high (95.3%) among all patients. Some 33.5% (66/197) of patients with HCC were positive for HBsAg and 45.2% (89/197) for anti-HCV. Moreover, 17.3% (34/197) of HCC patients demonstrated co-infection with HBV and HCV. AFP levels were elevated in 4.6% (11/238) and 29.5% (23/78) of chronic hepatitis and cirrhosis patients, respectively. In HCC cases, 84.3% (166) of patients had increased level of AFP ranging from 32ng/ml to more than 400 ng/ml. We conclude that HBV/HCV infection is the main factor related to development of HCC in Mongolia and that testing for AFP serum levels is a useful tool for early detection and diagnosis.

Key Words: Hepatocellular carcinoma - HBV/HCV - AFP - Mongolia

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Introduction

Liver cancer is one of the frequent cancers in worldwide (Parkin et al., 2001), with hepatocellular carcinoma (HCC) above all the main cause of cancer death, especially in Mongolia. During last years the rate of HCC has been increasing continuously and at present HCC is the most common cancer in the country. Chronic infection with hepatitis B (HBV) and/or hepatitis C viruses (HCV) is a well known risk factor and the most influential determinant for development of HCC. A high prevalence of HBV and HCV in Mongolia has been reported previously (Oyunsuren et al, 1996). Since 1983, HCC leads cancer incidence among all registered cancer cases and at present prevalence rate of HCC is 51.3 per 100,000 population (Health Indicators, 2004).

Unfortunately, only 12.5% of HCC are being diagnosed in I and II stages and treatment effectiveness in late stages is very low. It is well known that detection of cancer at early stage decreases an incidence of cancer related death or prolongs age of patients. The most commonly used serum tumor marker, alpha-fetoprotein (AFP) is a fetal antigen produced by 50%--90% of HCC cases (Abelev et al, 1982). and at present it is useful tool for screening of chronic liver patients and early diagnosis of HCC (Fujiyama et al, 2002).

The aims of the present study were: 1) to analyze HCC cases of last 30 years period, related to hepatitis B (HBV) and C viruses (HCV) and 2) to study possibility of use of sera AFP test as tumor marker for early detection of HCC in Mongolia.

Materials and Methods

In total sera of 513 patients with chronic liver diseases, liver cirrhosis and HCC were analyzed for liver function (ALAT, ASAT) and hepatitis virus markers (HBsAg, anti-HCV). Sera of 316 patients were examined for alpha-fetoprotein (AFP) quantity. ALAT and ASAT analysis were made by the Raitmana Frenkle kinetic method on a WOHBC-100 photometer (China). ALAT up to 37 IU/l, ASAT 32 IU/l for females and ALAT 42 IU/l, ASAT 32 IU/l for males were considered to be normal.

HBV surface antigen (HBsAg) (Fujirebio Co Ltd, Japan)

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and hepatitis C virus antibody (anti-HCV) (Human GmbH, Germany or Ortho Clinical Diagnostics, Japan) were detected by ELISA or PHA assay. For the AFP test we used ELISA (ASIA Biotechnology CO.LTD, China) and Radioimmunoassay (RIA) kits (CIAE, China). Obtained values were assumed normal if less or equal to 10 ng/ml.

Confirmation of HCC diagnosis was based on ultrasound, computer tomography, and histopathological investigations. 12.1 % cases were diagnosed as in I and II stages, and the remaining 87.9% was diagnosed as in later stages (III and IV).The ages of patients were from 22 to 81 years old and 53.8% (276) of the total were males.

For statistical analysis were used data taken from the National Cancer Center, the National Center for Health Development, Ministry of Health (Health Indicators, 2004) and other resources (Nyamdavaa 1984, Dorjgotov, 1987).

Results

I. HCC

Cancer cases have increased among the Mongolian population during the last decades. The incidence of newly registered cancer cases per 100,000 population increased from 130.9 to 138.1 in last 5 years comparing to previous years. The five most frequent cancers, which make up about 85%-95% of all cancer cases are HCC, and stomach, lung, esophagus, and cervical cancer, in that order. It was estimated that a prevalence of HCC increased nearly 5 times during last 30 years and it has the leading position among 5 frequent cancers in Mongolia. Since period of 1982-1986 years, when HCC became the most common cancer among mongolian population, the rate of HCC has been increasing continuously (Figures 1 and 2).

In 2000-2005 years from all newly registered cancer cases, 35.3% belonged to liver cancer, with rate of 51.3. per 100,000 population. Figure 2 shows the rate of HCC among all cancer cases in last 3 decades. In 2005 among all cancer cases, HCC rates in male and female were about 46% and 35%, respectively. HCC prevalence increases with age of 40-49 in both males and females, and over 60 years reaches the highest value. The prevalence of HCC differs by geographical regions and has the highest rate in the eastern part of the country.

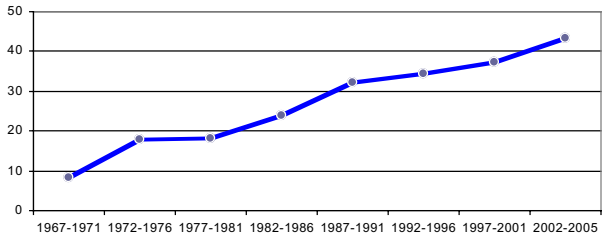

Figure 1. Increase of HCC Cases Over Time in Mongolia (per 100,000 population)

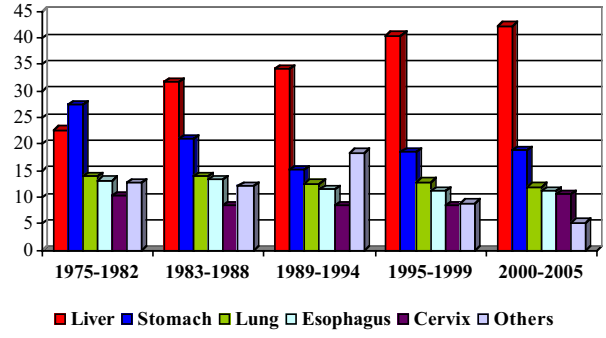

Figure 2. Prevalence of HCC Among Different Cancers (%) in the Period from 1973- 2003

Table 1. Viral Hepatitis Incidences in Liver Diseases

	Total (n=513)	Chronic (n=238)	Cirrhosis (n=78)	HCC (n=197)
M/F	276/237	131/107	35/43	110/87
Average age	51	40	53	61
HBsAg	35.9%	34.9%	44.9%	33.5%
anti-HCV	43.3%	48.3%	23.1%	45.2%
Coinfected	16.2%	12.2%	25.6%	17.3%
Overall infected	95.3%	95.4%	93.6%	95.9%
Not infected	4.7%	4.6%	6.4%	4.1%

II. Hepatitis viruses

The overall incidence of hepatitis infection was 95.3% with either HBsAg (35.9%), HCV (43.3%) or coinfection (16.2%) among all studied subjects. Table 1 shows the very high incidences of HBV and HCV in all 3 studied groups (93.6%-95.9%). HBsAg and anti-HCV prevalence in HCC patients were 33.5% (66/197), and 45.2% (89/197), additionally 17.3% (34/197) were coinfected. In other words, 95.9% of HCC patients had chronic hepatitis virus infection. In all HCC cases ALAT and ASAT levels were elevated compared with the normal values.

From statistical data it was clarified that HCC prevalence is higher in area where the incidence of hepatitis infection was high in period of 1958-1990 years (see Figure 3). High rates of HCC patients aged 50 and over were positive for HBsAg (44.4%) and anti-HCV (50.4%) (Figure 4).

III. AFP tests for early detection of liver cancer

Sera of 316 patients from 4 different hospitals, from those 197 (62.3%) with HCC, were examined for AFP level test. The result showed that AFP level were elevated in 4.6% (11/238) and 29.5% (23/78) of chronic hepatitis and cirrhosis

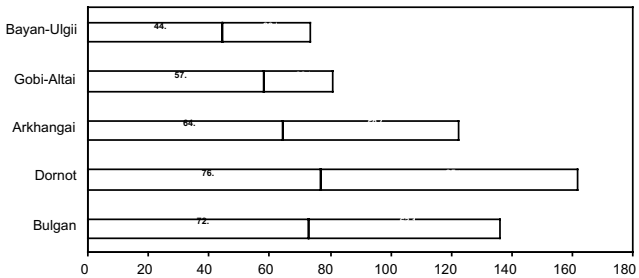

Figure 3. Comparative Incidences of Hepatitis (1958-1990) (left) and of HCC (2000-2004) (right) per 100,000 Population, in some Provinces (Aimaks)

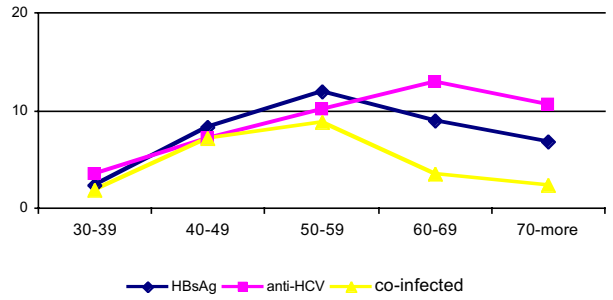

Figure 4. Age-specific Prevalence (%) of HBsAg and-anti-HCV among HCC Patients

patients, respectively. In HCC cases, 84.3% (166) had increased level of AFP ranging from 32ng/ml to more than 400 ng/ml. In all patients ALAT and ASAT levels were elevated about 8-230 times above normal value.

Sera of 11 liver cirrhosis and 15 HCC patients with elevated AFP level were examined again for AFP after 6 weeks from the first test time. In 3/11 (27.2%) cirrhosis and 9/15 HCC (60%) cases AFP levels had increased 0.3-1.1 and 1.1-3.1 times, respectively. These elevations might be correlated to HCC development (in cirrhosis cases) or progression (HCC cases).

Discussion

In the present study, all study groups (chronic hepatitis, liver cirrhosis and HCC) demonstrated very high HBV and HCV incidences (93.6%-95.4%). Overall, 95.9% of HCC patients were attributed to hepatitis infection with either single (HBsAg -33.5%, anti-HCV - 45.2%) or double (17.3%) infections.

We analyzed HCC statistical data covered a time period about last 30 years in the country. Okuda et al (1999) showed that when the geographical pattern of HBV prevalence was referred to, high prevalence region for HBV coincided well with high incidence areas for liver cancer. High prevalence of HBV and HCV infections in Mongolia were reported previously by Dashnyam et al (1993) and Oyunsuren et al (1996).The WHO weekly epidemiology record (2000) reported geographical differences in HCV prevalence with extremely high rates fro Mongolia. Results of our research showed that HCC prevalence is higher in area where the incidence of hepatitis infection was high in period of 1958-1990 years. Of interest, the prevalence of HCC differs by geographical regions, it has the highest rate in eastern part of the country. It might be correlated to past hepatitis infections, lifestyle habits (alcohol uptake, fatty meal etc) of people and environmental factors.

In Mongolia the incidence of HCC increased 5 times in 30 years period. Our result showed that the mean age at onset of HBV-related HCC is 10 years younger than the average age at onset of HCV related HCC cases. Age-specific trends of HCC incidence seem to be well understandable in terms of past hepatitis infection.

It is well established that AFP levels in blood sera is one of methods can be used for detection of liver cancer and prognosis. Elevated level of AFP might be correlated to other diseases, but in mostly, it increases (>10ng/ml) in HCC cases. By some authors (Tangkijvanich et al., 2000) an increase of AFP level was described as abrupt, reflecting level of HCC progression. Elevation of AFP level in 4.6%, 29.5% and 84.3% of our chronic hepatitis, cirrhosis and HCC patients, respectively showed the importance of AFP test for HCC detection. It is known that AFP test is useful tool not only for early detection of HCC, also for clinical follow-up of the patients (Fujiyama, 2002). In our case in those 9 HCC patients whose AFP was increased after 6 weeks, in some patients an enlargement of size of HCC was observed by ultrasound and other analysis.

In conclusion, HBV and HCV incidence is very high among liver patients including HCC in Mongolia and it is the most influential determinant for HCC development. For early detection and diagnosis of HCC it is needed to introduce AFP screening method, given the expected increase in hepatitis-associated HCC in the next decades.

Acknowledgement

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