

# The Prevalance of Anti-Hepatitis C Virus in Patients with Hepatocellular Carcinoma

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**Özet:** HEPATOSELLÜLER KARSİNOMALI HASTALARDA ANTI-HEPATİTİS C VIRUS PREVALANSI

Hepatosellüler karsinomada (HCC) Hepatitis C Virusunun (HCV) rolünü araştırmak amacıyla HCC'li 32 hastada HCV antikorları araştırıldı. 32 hastanın 4'ünde (%12.5) enzim immunoassay (EIA) yöntemi ile HCV antikorları saptandı. 115 volanter kan donörü kontrol grubu olarak çalışmaya alındı. Kontrol grubunda 1 olgu da (%0.8) HCV antikorları saptandı. HCC grubunda geri kalan 28 olguda Hepatitis B Virus (HBV) işaretleyicileri pozitif. HBsAg pozitiflik oranı ve anti HCV oranı HCC'li hastalarda kontrol grubuna göre anlamlı olarak yüksek bulundu ( $p < 0.001$ ). Ancak anti HCV prevalansı aynı oranda yüksek değildi. HBsAg (-) olan 12 HCC'li hastanın 3'ünde (%25) HCV antikorları saptandı. HCC'li hastalarda HCV antikor varlığının yaş, tümör büyüklüğü, tümör eko paterni ve kan transfüzyonu ile ilişkisi saptanmadı.

Bu sonuçlar, güneydoğu anadolu bölgesinde HCC patogeneğinde HCV enfeksiyonunun önemli rolü olmadığını göstermektedir.

**Anahtar kelimeler:** Hepatitis C virus, hepatosellüler karsinoma.

Hepatitis C Virus (HCV) is the main causative agent in parenterally transmitted non-A, non-B hepatitis (1). It can result in chronic hepatitis and liver cirrhosis and has been suggested to be an important factor in the pathogenesis of hepatocellular carcinoma (2-4). Based on the examination of anti-HCV (circulating antibody against

**Summary:** To evaluate the role of Hepatitis C Virus (HCV) in patients with hepatocellular carcinoma (HCC), the antibodies to HCV (anti-HCV) were detected by enzyme immunoassay in 4 patients of the 32 patients with HCC (12,5%). 115 volunteer blood donors were taken as control groups to study. 1 out of donors had anti-HCV (0.8%). The rest of 28 HCC patients had HBV serologic markers. The positive rates of hepatitis B surface antigen and anti-HCV in patients with HCC were significantly higher than in control subjects ( $p < 0.001$ ). But, the prevalence of anti-HCV was not also high in patients with HCC. In HBsAg (-) patients with HCC, anti-HCV was detected in 3 patients of 12 HCC (%25). In patients with HCC, the presence of anti-HCV was not related to age, tumor size, tumor echo pattern, and blood transfusion.

This result indicate that HCV infection may have not an important role in the pathogenesis of HCC in Southeast Turkey.

**Key words:** Hepatitis C virus, hepatocellular carcinoma.

C 100-3 antigen of HCV), a high association of HCV and HCC was reported in Western countries and Japan (5-7). However, the causative role of HCV seemed to be different in hepatitis B virus endemic areas. Turkey is an HBV endemic area. HBV was shown to be the major cause of chronic liver diseases in this country (8,9). To determine whether HCV infection also play an etiologic role in patients with HCC, we surveyed

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**Table I:** Results in study group.

	Case No	Frequency
Anti-HCV Positivity (total)	4	12.5%
Anti-HCV and HBsAg positive	1	3%
HBsAg	20	62.5%
IgG anti-HBc	28	87.5%
IgG anti-Delta	11	34.3%
HBeAg	3	9.3%
Anti-HBe	22	68.7%

**Table II:** Results in control group.

	Frequency
Anti-HCV positivity (Volunteer Blood Donors)	0.8%
HBsAg positivity (Healthy Group)	7.7%

the prevalence of anti-HCV in sera from 32 patients with HCC.

## MATERIALS and METHODS

Sera of 32 patients with histologically proven HCC were collected from the Division of Gastroenterology, Dicle University Hospital, Turkey. There were 23 male and 9 female patients, with a mean age of 49.4 years (range 37 to 66 years). In the control groups, sera also were collected from 115 volunteer blood donors (76 men and 49 women, mean age 37.6 years, range 24 to 61 years). All sera were tested for HBsAg, antibody to HBcAg, HBeAg, and anti-HCV antibodies. HBsAg and antibody to HBV (Abbott) were measured by commercially available radioimmunoassay kit. Serum anti-HCV (Ortho HCV antibody ELISA Test System) was measured by ELISA with a microplate technique.

## RESULTS

Of the 32 patients with HCC, 20 (62.5%) had positive results for HBsAg, 28 for antibody to hepatitis B core antigen, 11 for IgG anti-Delta Ag, 3 for HBeAg, 22 for anti-HBe and 4 for anti-HCV, 3 Anti-HCV cases were detected in patients with HBsAg negative HCC and 1 anti-HCV case was together with HBsAg positive HCC (Table 1,2). The prevalence of HBsAg was 7.7% in volunteer blood donors. The prevalence of anti-HCV was

not much higher in patients with HCC. The sex, age, tumor size distribution among both groups of patients did not exhibit a statistically significant difference, in HCC cases.

## DISCUSSION

After the discovery of the Australian antigen by Blumberg et al (10), in the 1970s and the later recognition of it to be the hepatitis B-associated antigen-HBsAg-many investigators began their epidemiologic studies on the possibility of an association between HBV and chronic liver diseases and HCC (11,12). Although most patients with HCC have positive results for HBsAg, a higher proportion have other HBV markers. Our recent study also demonstrates a high prevalence of HBV infection in patients with HCC; however, some patients seem to have no evidence of HBV infection. A small proportion of cases appear to be related solely to other etiologic factors. The relative importance of these factors seems to vary from one population to another. The development of commercial kits to detect serum anti-HCV allows us to begin an epidemiologic study of the possible association between HCV and HCC. The early reports from Spain (13) and Italy (14) showed that HCV may be associated more closely with HCC than with HBV. Reports from South Africa (15) showed that HCV is associated with HCC but HBV is still present in a higher proportion of South African patients. In Taiwan, in contrast to the high prevalence of HBsAg (15% to 20%) among the general population, the anti-HCV prevalence is low (0.8%) (16), however, the anti-HCV prevalence is relatively high in patients with HCC (13%). There is still a difference in the prevalence of anti-HCV in patients with HCC with HBsAg-positive as compared with HBsAg-negative results. This difference is more evident in Chinese patients than in European or African patients (14,10). In Italy, Spain, the United States, and Japan 40-75% of patients with HCC had positive results for anti-HCV (13,14,15). France has a lower detection rate, of 28% (17).

In Turkey, we found that 62.5% of patients with HCC were HBsAg positive and 12.5% were anti-HCV positive. Although these data indicate a

relatively minor impact of HCV infection on the prevalence of HCC in Turkey, the etiologic role cannot be discounted when only 0.8% of the controls had positive results for anti-HCV. The relative significance of HCV in the prevalence of HCC in various regions obviously will differ, depending on the importance of other possible carcinogenic factors in the locality. In areas with a high HBV infection rate, serologic evidence of past HBV infection does not necessarily exclude its possible role in causing HCC, and investigators became particularly interested when integrated HBV-DNA genome was reported in tumors from patients with no serologic markers of HBV (18). However, this was refuted by recent studies showing no detectable viral integration even in

the presence of anti-HBc or anti-HBs (19). The mechanism of carcinogenesis in HCV-associated HCC requires additional investigation. Currently, it is not possible to say whether the virus is directly carcinogenic or that it tends to malignant transformation indirectly by causing cirrhosis.

This study confirms that HBV is the main causal factor of HCC in Turkish patients, and HCV infection may play an etiologic role in patients with HBsAg-negative HCC. In addition more epidemiologic studies with greater details of risk factors for that population will further define the pathogenic role of HCV in HCC and its relative significance in different parts of the world.

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