

## The Prevalence of Thrombocytopenia in Patients with Chronic Hepatitis B and C

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**Background and Aims:** Thrombocytopenia is a relatively common extrahepatic manifestation of hepatitis C, even in the absence of cirrhosis. Also, thrombocytopenia has been reported in chronic HBV infection. The aims of present study were to evaluate the prevalence of thrombocytopenia in chronic HCV and HBV infection in the absence of cirrhosis and to assess the relationship between HBV and HCV infection and frequency of thrombocytopenia.

**Methods:** 438 patients (219 patients with chronic active hepatitis B and 123 inactive carriers of HBV and 96 patients with chronic HCV infection) were enrolled in this study. Thrombocytopenia was defined as platelet counts below 150,000/ $\mu$ l.

**Results:** The prevalence of thrombocytopenia was 17.7% in patients with chronic active hepatitis B and 10.6% in HBV inactive carriers, 13.3% in patients with chronic hepatitis C and 5.3% in control group. The prevalence of thrombocytopenia in chronic hepatitis B and C was significantly more than control group.

**Conclusions:** These results in Iran, with 2-3 million people with chronic HBV infection and around 400,000 with chronic HCV infection shows that HBV and HCV infections, even in the absence of cirrhosis, may be two causes of thrombocytopenia.

### Introduction

Extrahepatic manifestations are commonly observed in patients with chronic hepatitis C. One of these manifestations is thrombocytopenia. Several different mechanisms are reported to be related with this abnormality.

These mechanism include:

- 1) portal hypertension and hypersplenism in end stage liver disease (cirrhosis).
- 2) autoimmune reaction to platelets.
- 3) direct infection of platelets and megakaryocytes by HCV.

Several reports have shown that HCV infection even in noncirrhotic patients, is one of the causes of thrombocytopenia in different countries.

In addition, some reports have shown that thrombocytopenia is associated with chronic hepatitis B.

It is estimated that approximately 400,000 people in Iran are chronically infected with HCV and also more than 2,000,000 people are infected with HBV

There is no survey study association between thrombocytopenia.

The aims of present study were:

1) to assess the prevalence of thrombocytopenia in noncirrhotic patients with chronic hepatitis C and B in Iran.

2) to determine the relationship between the prevalence of thrombocytopenia with HBV infection, HCV infection, age and sex.

### Materials and Methods

From 2000 to 2002, all consecutive patients with chronic hepatitis B and C referred to Tehran Hepatitis Center were enrolled in to the study. Tehran Hepatitis Center is a referral specialized clinic for liver diseases where many patients

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suffering from liver diseases and hepatitis from around Iran are referred to in order to receive consultation and clinical care. Patients with evidence of cirrhosis according to the results of liver biopsy, splenomegaly, ascites, esophageal varices and liver function and also those who were on immunosuppressive therapy were excluded. All patients were treatment-naïve.

A total number of 438 patients who met the criteria were eligible to enter the study. These patients consisted of 219 patients with chronic active hepatitis B (170 males and 49 females, mean age =  $34/96 \pm 11/83SD$ ), 123 inactive carriers of HBV (78 males and 45 females, mean age =  $34/44 \pm 11/43SD$ ) and 96 patients with chronic hepatitis C (82 males and 14 females, mean age =  $35/41 \pm 11/58SD$ ).

Serving as controls, enrolled 131 healthy blood donors (66 males and 65 females, mean age =  $40/8 \pm 10/92SD$ ) in to the study.

Chronic hepatitis C was diagnosed on the basis of molecular assay by qualitative RT-PCR.

The diagnosis of chronic active hepatitis B was made on positive HBs Ag for more than six months in addition to: 1) Quantitative HBV DNA level more than 100,000 copies/ml and elevated liver enzymes or 2) Total score of more than 4 in liver biopsy. Histological scores were determined according to the modified Knodell, s scoring system.

Inactive carrier state of HBV was diagnosed on the basis of, the positive HBs Ag for more than six months in addition to quantitative HBV DNA level less than 10,000 copies/ml and normal liver enzymes.

Liver function tests and platelet count were recorded from the patients' files.

In this study, thrombocytopenia was defined as platelet counts below 150,000/ $\mu$ l

## Results

A total of 438 patients and 131 cases as control were included in this study. 396 (%69.1) subjects were men with a mean age of  $36.4 \pm 11/8$  (SD).

The prevalence rates of thrombocytopenia in various groups were summarized in Table 1

There was a significance difference in the prevalence of thrombocytopenia between groups ( $P=0.007$ ). The prevalence of thrombocytopenia in chronic hepatitis C and B were more than control subjects .

Males were 3.1 times more exposed to affecting thrombocytopenia than females ( $P=0.003$ ).

Chronic active hepatitis B patients were 3.5 times

more exposed to affecting thrombocytopenia than control cases ( $P=0.005$ ).

**Table 1.** Prevalence rates of thrombocytopenia in various groups of the study.

Hepatitis status	Prevalence of thrombocytopenia
Healthy blood donors	5.3%
Chronic active hepatitis b	17.7%
Inactive HBV carriers	10.6%
Chronic hepatitis C	13.1%

**Table 2.** Comparison of thrombocytopenia between patients regarding hepatitis status and sex.

	OR	CI 95%	P value
<b>Hepatitis status</b>			
Control (healthy blood donor)	1		
Active chronic hepatitis B	3.5	1.5-8.2	0.005
Inactive HBV infection	2.1	0.8-5.6	NS
Chronic hepatitis C	2.3	0.9-6.2	NS
<b>Sex</b>			
Female	1		
Male	3.1	1.5-6.6	0.003

## Discussion

Several studies have shown that thrombocytopenia is frequently observed in chronic hepatitis C (3-6) and a variety of pathogenic mechanisms are reported to be implicated in this abnormal finding.

In cirrhotic patients sequestration of platelets in the enlarged spleen secondary to portal hypertension can cause thrombocytopenia(7, 18).

However, thrombocytopenia also occurs in patients with chronic hepatitis C without cirrhosis.

Another mechanism is autoimmune reaction to platelets(8, 9, 15, 18).

Some reports indicated that HCV infection may reflect the expression of platelets-associated immunoglobulin G (PAIgG) leading to platelets destruction by reticulo-endothelial system(10, 15, 19).

In addition, several studies have suggested that HCV may have a direct pathogenic role in the process leading to thrombocytopenia (10, 20, 21).

The incidence of mild thrombocytopenia (defined as a platelet count under 150,000/ $\mu$ l) is between 41-50% in patients with HCV infection (10, 22, 23), while severe thrombocytopenia (defined as a platelet count of less than 50,000/ $\mu$ l as a reported incidence of %9 (12, 23).

Otherwise, several reports from different countries, confirmed the high prevalence of HCV infection in patients with chronic thrombocytopenia (11, 12, 14, 20, 24).

Furthermore, thrombocytopenia associated with PAIgG has been reported in chronic hepatitis B<sup>(15)</sup>.

In present study, thrombocytopenia was diagnosed in %10.6 of inactive carriers of HBV and %17.7 in chronic active hepatitis B that were significantly higher compared with control group.

The present study in Iran, with more than 2-3 million people with chronic HBV infection and approximately 400,000 patients with chronic HCV infection, shows that chronic HBV and HCV infections, even in the absence of cirrhosis, may have been two causes of thrombocytopenia. Therefore, we suggest checking HBV and HCV serologic tests in patients with thrombocytopenia even in the absence of signs suggesting cirrhosis.

Thrombocytopenia in patients with chronic viral hepatitis is often believed to be due to hypersplenism resulting from hepatic cirrhosis and portal hypertension.

We excluded cirrhotic patients from this study, thus thrombocytopenia in these patients is due to other mechanisms.

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