EVALUATION OF THE ANTI HEPATITIS C VIRUS SEROPOSITIVITY AND SERUM TRANSMANES IN OUR HOSPITALS

HASTANEMİZ ANTI HEPATITIS C VIRUS SEROPOZİTİLİĞİNİN VE SERUM TRASİMİNAZLARININ DEĞERLENDİRİLMESİ

HEPATIT C VIRUS

Aims: Hepatitis C Virus (HCV) is an important infectious disease agent that can cause chronic liver disease, cirrhosis, and hepatocellular carcinoma. It is necessary to follow the changes in incidence of HCV in order to determine the extent to which liver diseases caused by HCV will affect the population. Our study aimed to determine the anti-HCV seropositivity in the patients presenting to our hospital and to evaluate this in conjunction with serum transaminase levels. Material and Method: The anti-HCV seropositivity of blood samples of a total 131,851 patients presenting to various departments in our hospital between January 2012 and June 2015 was studied with spectrophotometric enzymatic methods by using chemiluminescence microparticle immunoassay technique. The samples with anti-HCV S/CO values ≥22651 were considered to be positive. Data were analyzed retrospectively. IBM SPSS Statistics 22 (IBM SPSS, Turkey) program was used for statistical analysis. Repeat specimens were excluded from the analysis. Results: Anti-HCV seropositivity was determined in 868 (0.65%) of the 131,851 patients in the study. Anti-HCV seropositivity was determined in 655 (0.49%) of 80,507 patients in whom anti-HCV alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were examined together. The mean age of the patients was 43.23±19.58 years (range: 0-115 years), of whom 45,293 (56.3%) were female and 35,214 (43.7%) were male. The prevalence rate of anti-HCV seropositivity was statistically significantly higher in the patients with higher levels of AST (p<0.01) and in the cases with higher levels of ALT (p<0.05) compared to the healthy individuals (p=0.007; p=0.01). There was no statistically significant difference between incidence rates of anti-HCV seropositivity in the patients according to AST/ALT distributions (p=0.05). Higher levels of AST and ALT were observed in 138 (21.06%) and 242 (36.94%) of 655 patients with anti-HCV seropositivity, respectively. The anti-HCV seropositivity was determined to be higher in patients in their 5th, 6th, and 7th decades. Discussion: The prevalence of HCV infection is approximately 2.8% worldwide; while the prevalence of HCV infection in Turkey varies between 1% and 2.4%. The prevalence of HCV infection was determined to be 0.65% in the patients presenting to our hospital, which is lower than the overall prevalence in Turkey. Elevated levels of AST and ALT were observed in 138 (21.06%) and 242 (36.94%) of 655 patients with anti-HCV seropositivity, respectively. Anti-HCV prevalence was determined to be 2% in those with elevated AST levels and 2.2% in those with elevated ALT levels.

Keywords: Hepatitis C Virus; Alanine Aminotransferase; Aspartate Aminotransferase

Öz
Amaç: Hepatit C Vırus (HCV), kronik kareçer hastalığı, siroz ve hepatoselüler karsinomaya yol açabilmektedir. HCV ve diğer kareçer hastalıklarını oluşturduğu nedenlerden biri de kareçer enfeksiyonu olabilir. HCV enfeksiyonunun ve kareçer enfeksiyonunun klinik ve biyolojik belirtileri bilinen her gün artan HCV prevalansı, kareçer enfeksiyonunun belirtilerinin ve sonlarına giren kareçer enfeksiyonunun belirtilerinin belirlenmesi ve öncü önlemlerin gerekliği ortaya çıkmıştır. Çalışmamızda, hastanemize başvuran hastaların anti-HCV seropozitifliği, ALT ve AST düzeyleri ile değerlendirilmiş, Türkiye geneline göre 0.65 olarak tespit edilmiştir. 

Materials and Methods: The prevalence of (C6 infection in Turkey varies between 1-2.4 percent according to the world Health Organization. In our hospital, the frequency of anti-(C6 seropositivity was determined to be 2.8 percent among patients above 40 years of age. The mean age of the patients was 43.23±19.58 years (range: 0-115 years), of whom 45,293 (56.3%) were female and 35,214 (43.7%) were male. The prevalence rate of anti-(C6 seropositivity was statistically significantly higher in the patients with higher levels of AST (p<0.01) and in the cases with higher levels of ALT (p<0.05) compared to the healthy individuals (p=0.007; p=0.01). There was no statistically significant difference between incidence rates of anti-(C6 seropositivity in the patients according to AST/ALT distributions (p=0.05). Higher levels of AST and ALT were observed in 138 (21.06%) and 242 (36.94%) of 655 patients with anti-(C6 seropositivity, respectively. The anti-(C6 seropositivity was determined to be higher in patients in their 5th, 6th, and 7th decades. Discussion: The prevalence of HCV infection is approximately 2.8% worldwide; while the prevalence of HCV infection in Turkey varies between 1% and 2.4%. The prevalence of HCV infection was determined to be 0.65% in the patients presenting to our hospital, which is lower than the overall prevalence in Turkey. Elevated levels of AST and ALT were observed in 138 (21.06%) and 242 (36.94%) of 655 patients with anti-HCV seropositivity, respectively. Anti-HCV prevalence was determined to be 2% in those with elevated AST levels and 2.2% in those with elevated ALT levels.

Keywords: Hepatit C Virüsü, Alanin Aminotransferaz, Aspartat Aminotransferaz

Oznachat Keyelmelar
Hepatitis C Virus; Alanin Aminotransferaz; Aspartat Aminotransferaz

DOI: 10.4328/JCAM-4955
Received: 18.02.2017 Accepted: 08.05.2017 Printed: 01.04.2017 J Clin Anal Med 2017;8(suppl 2): 105-8 Corresponding Author: Arzu İnrem, Mikrobiyoloji Bölüümü, Ummanıye Eğitim ve Araştırma Hastanesi, Elmalı, 34764 Ummanıye, İstanbul, Türkiye. T: +90 2166321818-4958 E-Mail: aruziinrem93@gmail.com

Journal of Clinical and Analytical Medicine I 105
Introduction
Hepatitis C virus (HCV) infection is an important public health problem that causes mortality and morbidity throughout the world [1]. It is estimated that, worldwide, approximately 185 million people (2.8% of the global population) are infected with hepatitis C [2]. Chronic HCV infection is the leading indication for liver transplantations [3]. The primary transmission route of HCV is transfusion of blood and blood products. A marked decrease has occurred in this route of transmission with the introduction of routine screening of HCV antibodies in the blood banks [4,5]. The diagnosis of chronic viral hepatitis is made during the investigation of elevated liver enzymes, which is determined incidentally in approximately half of the patients [6]. Fatty liver disease is the cause of elevated ALT (alanine aminotransferase) levels in more than half of the cases. The result is considered to be chronic viral hepatitis in approximately 5% of the patients with elevated ALT levels [7]. Enzymes are found to be within normal limits in one-third of the patients with chronic hepatitis C infection. Anti-HCV antibody is investigated serologically for the diagnosis of the infection and HCV RNA levels are examined using a molecular method for the detection of viremia. HCV RNA viral load is monitored with liver transaminases during treatment and follow-up, while the severity of inflammation and fibrosis in the liver is determined through biopsy. Although the serum level of liver transaminases is not specific for the disease, it may contribute to the diagnosis and follow-up of the infection. The ratio of AST (aspartate transaminase)/ALT (alanine transaminase), called the De Ritis ratio, is used to discriminate between acute and chronic forms of hepatocellular injury [8]. Our study aimed to contribute to the relevant literature on this subject by evaluating the incidence of anti-HCV seropositivity in our region together with elevated ALT, AST levels, and the AST/ALT ratio.

Material and Method
The blood samples of 131,851 patients (age range: 0-115 years) sent from various departments of our hospital between January 2012 and June 2015 were studied using the chemiluminescence immunoassay method (Advia Centaur CP Bayer-Siemens, Germany). Architect i1000 Abbott ABD autoanalyzer. According to the manufacturer’s instructions, specimens with an S/CO value of < 1 were considered to be negative and specimens with an S/CO value of ≥ 1 were considered to be positive. ALT level of 0-34 U/mL, AST level of 0-40, and AST/ALT ratio of < 1 were considered to be normal values. Data were evaluated regarding anti-HCV seropositivity. ALT, AST, AST/ALT ratio, and mean age. Statistical analysis was performed using the IBM SPSS Statistics 22 (IBM SPSS, Turkey) program. The Chi-Square test was used for comparison of qualitative data, in addition to descriptive statistical methods (mean, standard deviation, and frequency). Significance was evaluated at a level of p<0.05.

Results
Blood specimens of 131,851 patients were sent to the microbiology laboratory of our hospital. Of these, 868 (0.65%) were determined to be anti-HCV positive. Six hundred and fifty-five (0.8%) of 80,507 blood specimens examined simultaneously for anti-HCV, ALT, and AST were determined to be anti-HCV positive. There was no statistically significant difference between prevalence rates of anti-HCV seropositivity in the patients by gender (p=0.05) (Table I). Prevalence rates of anti-HCV seropositivity were higher in patients in their 5th, 6th, and 7th decades (Table II). Elevated levels of AST and ALT were observed in 138 (21.06%) and 242 (36.94%) of 655 patients with anti-HCV seropositivity, respectively.

The prevalence rate of anti-HCV seropositivity was statistically significantly higher in the patients with elevated levels of AST (2%) compared to the patients with normal levels of AST (0.7%) (p: 0.001; p<0.01). The risk for anti-HCV seropositivity was 0.34-fold greater in the patients with elevated levels of AST (OR: 0.340; 95% CI: 0.281-0.411). The prevalence rate of anti-HCV seropositivity was statistically significantly higher in the patients with elevated levels of ALT (2.2%) compared to the patients with normal levels of ALT (0.6%) (p: 0.001; p<0.01). The risk for anti-HCV seropositivity was 0.267-fold greater in the patients with higher levels of ALT (OR: 0.267; 95% CI: 0.228-0.313).

| Table I. Evaluation of Anti-HCV seropositivity according to gender distributions |
|---------------------------------|---------------------------------|
| Anti-HCV                       | Gender                          | p     |
|                                 | Female                          | Men   |       |
| Positive                        | 356 (99,8)                      | 299 (98,0) | 0,323 |
| Negative                        | 44937 (99,2)                    | 34915 (99,2) |       |

| Table II. Distribution of Anti-HCV according to the age groups |
|---------------------------------------------------------------|
| Anti-HCV | 0-9 years | 10-19 years | 20-29 years | 30-39 years | 40-49 years | 50-59 years | 60-69 years | 70-79 years | 80-89 years | 90-99 years | 100 years and over |
|----------|-----------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------------|
| Positive | 5 (0,2%)  | 12 (0,3%)   | 47 (0,3%)   | 67 (0,4%)   | 80 (0,7%)   | 127 (1,2%)  | 158 (1,8%)  | 101 (1,8%)  | 51 (1,6%)   | 6 (1,2%)    | 1 (5,9%)        |
| Negative | 6639 (99,8) | 3982 (99,7) | 14947 (99,7) | 18076 (99,6) | 11599 (99,3) | 10845 (98,8) | 8510 (98,2) | 5562 (98,2) | 3173 (98,4) | 503 (98,8)  | 16 (94,1)       |

| Table III. Evaluation of Anti-HCV seropositivity according to distributions of ALT, AST, AST/ALT |
|---------------------------------------------------------------|
| Anti-HCV | Positive | Negative | p     |
|----------|----------|----------|-------|
| AST      | Normal   | 517 (0,7%) | 73213 (99,3%) | 0.001** |
|          | High     | 138 (2%)  | 6639 (98%)    |       |
| ALT      | Normal   | 413 (0,6%) | 69048 (99,4%) | 0.001** |
|          | High     | 242 (2,2%) | 10804 (97,8)  |       |
| AST/ALT  | Normal   | 602 (0,8%) | 72829 (99,2%) | 0,527  |
|          | High     | 53 (0,7%)  | 7023 (99,3%)  |       |

Chi-Square Test **p<0.01

HEPATIT C VIRUS
The prevalence of HCV varies according to the geographical region and age. The prevalence of HCV infection is estimated to be 2.8% worldwide. It is estimated that approximately 185 million people are infected with hepatitis C throughout the world [2]. The regional prevalence of HCV in Africa, America, Asia, Australia and Oceania, Europe, and the Middle East are as follows: 3.2%, 1.5%, 2.1%, 1.2%, 2.3%, and 4.7% [9]. Japan, Taiwan, and Italy are among the countries with a higher prevalence of HCV infection. The prevalence of HCV infection is the lowest in North Europe, at less than 1% [10]. The prevalence of HCV infection is as high as 15-20% of the general population in Egypt [10,11]. Estimated the prevalence of HCV antibodies and HCV RNA, among the 15–59 year age group, to be 14.7 and 9.8% respectively in Egypt [11]. HCV prevalence rates are as follows in developed countries with lower prevalence rates but higher population: Germany 0.6%, Canada 0.8%, France 1.1%, and Australia 1.1%. HCV prevalence rates have been reported as follows in developed countries with larger populations and slightly lower prevalence rates: United States of America (USA) 1.8%, Japan 1.5–2.3%, and Italy 2.2% [10]. In the meta-analysis performed by Hanafi et al., higher prevalence rates (>3.5%) were observed in North Africa/Middle East, Central and East Asia; moderate prevalence rates (1.5–3.5%) in sub-Saharan Africa, Andean, South and Southeast Asia, Central and Southern Latin America, Caribbean, Oceania, Australasia, and Central, Eastern, and Western Europe; and lower prevalence rates (<1.5%) in Asia Pacific, Tropical Latin America, and North America [12]. HCV prevalence rates in Turkey vary between 1% and 2.4%. In our study, the HCV prevalence rate was found to be 0.65% in the general hospital population, which is lower than the overall HCV prevalence rate of Turkey. Although countries like the USA, Australia, Spain, Italy, Japan, and Turkey have similar mean HCV prevalence rates (1.1-1.9%), the age-specific HCV prevalence patterns of these countries are very different. The highest HCV prevalence in USA is between 30–49 years of age. The prevalence is lower under 20 years of age and after 50 years of age. Similar to Australia, HCV transmission during the past 2-4 decades has occurred predominantly in young adults [10]. There are large variations in prevalence between groups with different risk factors in countries with the epidemiological characteristics of the USA, Australia, and North and Western European countries. IV drug use has been the leading transmission route of HCV in the USA over the past 40 years and also accounts for most of the newly acquired infections in the west, north, and south European regions [10]. Most of the anti-HCV positive patients in Turkey are over 50 years of age, which shows us that risk of HCV infection was higher about 40-60 years ago. Age-specific prevalence gradually increases with population increase in countries such as Turkey, Spain, Italy, Japan, and China [10]. Studies investigating age-specific prevalence in Turkey have determined that the prevalence increases after 50 years of age [5,13]. Also in our study, anti-HCV seropositivity was observed to occur more frequently in the 5th, 6th, and 7th decades (Table II), consistent with the other studies performed in Turkey. HCV is most commonly transmitted with a percutaneous exposure to infected blood. The predominant route for transmission of HCV differs from country to country. Although blood transfusions are the most frequent route of transmission, intravenous drug use is also significant in developed countries. Transmission through sexual contact and vertical transmission are less seen routes [4,10,14]. Data from the blood center of the Turkish Red Crescent between 2008 and 2012 found that the rate of anti-HCV seropositivity in donors was between 0.02% and 0.004% [15,16]. The rate of anti-HCV seropositivity among hemodialysis patients and peritoneal dialysis patients in our country was reported as 9.8% and 4.7%, respectively [17]. Twenty-seven percent of cirrhosis and 25% of hepatocellular carcinoma (HCC) in the world is associated with HCV [10]. In the study performed by Ökten [18], while hepatitis B virus (HBV) infection still maintains its importance in the etiology, the contribution of HCV has risen from 23% to 38.1% during the last decade. Similarly, while the contribution of HBV in the etiology of cirrhosis decreased from 56.6% to 45.9%, the contribution of HCV rose from 25.2% to 45.9% [10]. Certainly, it is critically important to develop diagnostic tests for hepatitis C virus.

Due especially to the insidious subclinical anicteric course of HCV infection, it is highly difficult to diagnose in its acute phase. In healthy individuals, the transaminases ALT and AST are normally found in lower concentrations in the serum, due to normal cell cycle and regeneration. While ALT is relatively specific to the liver, AST is found in the skeletal muscle, myocardium, kidney, brain, pancreas, and erythrocytes other than hepatocytes. Therefore, ALT reflects hepatocellular injury more specifically than AST. An elevated ALT level suggests that elevated AST level is also hepatic in origin. In our study, we observed that elevated ALT and AST levels were significantly associated with anti-HCV seropositivity (Table III). However, the possibility of false anti-HCV seropositivity results or normal ALT levels in patients with chronic HCV infection should be considered. In published studies, 30% of the patients with chronic HCV infection had continuously normal ALT levels [19,20]. Many studies investigating the relationship between serum HCV RNA levels and ALT levels in patients with chronic HCV infection have yielded contradictory results [21]. In our study, higher levels of AST and ALT were observed in 138 (21.06%) and 242 (36.94%) of 655 patients with anti-HCV seropositivity, respectively. The relationship between elevated levels of ALT and AST and anti-HCV incidence was investigated. But it remained inconclusive due to the following difficulties in the diagnosis and follow-up of the disease: anti-HCV seropositivity and AST/ALT ratio alone is not sufficient for diagnosis; false negativity and false positivity may occur; ALT levels may be normal in patients with chronic HCV infection; and, despite being considered the gold standard in the diagnosis and follow-up of the disease, serum HCV RNA levels can have a fluctuating course. In our study, anti-HCV prevalence in the patients presenting to our hospital was found to be lower than the overall HCV prevalence rate throughout the world and in Turkey.
Competing interests
The authors declare that they have no competing interests.

References
1. Cooke GS, Lemoine M, Thurz M, Gore C, Swan T, Kamarulzaman A, et al. Viral hepatitis and the global burden of disease: a need to reframe. J Viral Hepat 2013; 20: 600-1.
2. Hanafiah MK, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013; 57: 1335-42.
3. Tabak F, Baik I, Tekel E. Viral Hepatitis. (Ed) Türkçülü S. Hepatitis C virusu viroloji ve seroloji 2007 (1): 228-45.
4. Wilke Topçu A, Süleyman G, Doğanay M. Hepatit C Virüsü. Ed. Alakan S. Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji . Nobel 2008 (3):1911-28.
5. Barut HÜ, Gündüz Y. Öğrenme ve profesyonel hepatit C epidemiolojisi. Klinik Dergisi 2009; 22(2): 58-43.
6. Sentürk H. Kronik viral hepatitler güncel durum. İç Hastalıkları Dergisi 2017.
7. Hatemi I, Barut G, Balık İ. A Population survey for screening chronic liver diseases in individuals from Turkey. J Hepatol 2003 (2):216.
8. Nafees M, Ditta A, Jaffer G. Clinical Significance of elevated serum aminotransferases levels in asymptomatic individuals with hepatitis C infection. Annals 2010;16(3):174-8.
9. Lauarchy D. Evolving Epidemiology of Hepatitis C virus. Clin Microbiol Infect 2011;17(2):107-15.
10. Alter MJ. Epidemiology of hepatitis C virus infection. World J Gastroenterol 2007; 13(7): 2456-41.
11. Kandee J, Gendry M, El-Refa A., L. Funk A., Fontanet A., Talata M. The prevalence of hepatitis C virus infection in Egypt 2015: Implications For Future Policy on Prevention and Treatment. Liver Int 2017; 37:45-53.
12. Hanafiah KM, Groeger J, Flaxman AD, Wiersma ST. Global Epidemiology of Hepatitis C Virus Infection: New Estimates of Age Specific Antibody to HCV Seroprevalence. Hepatology 2013;1535-42.
13. Simmonds P. Virology of hepatitis C virus. Clin Ther 1996;18(Suppl B):9-36.
14. Sheppard CW, Findlay L. Alter MJ. Global epidemiology of hepatitis C virus infection. Lancet Infect Dis 2005; 5(9): 588-67.
15. Tabak F, Baik I, Tekel E. Viral hepatit. Mstık R (Ed). Türkiye’de viral hepatit epidemiolojisi yayınınlari irdelenmesi. İstanbul, 2007:9-50.
16. Tosun S, Ayhan MS, İbır B. Hepatit B virüsü infeksiyonu ile savaşımızda ülke kaynaklarının ekonomik kullanımı. Viral Hepatit Dergisi 2007;12(5):137-41.
17. Şuleymanlar G, Seyahi N, Altıparmak MR, Serdengeçti K. Current Status of Renal Replacement Therapy in Turkey: A summary of Turkish society of Nephrology 2009 Annual Registry Report. Turk Neph Dial Transpl 2011; 20(1):1-6.
18. Okten A. Türkiye’de kronik hepatit, siroz ve hepatosellüler kanserona etyolojisi. Güncel Gastroenterol 2003;7(5):187-91.
19. Bacon BR. Treatment of patients with hepatitis C and normal serum aminotransferase levels. Hepatology 2002;36(5):179-84.
20. Puoti C, Bellis L, Guarniero D, DeFurto O, Spilabetti L, Cestanza OM. HCV carriers with normal alanine aminotransferase levels: healthy persons or severely ill patients? Dealing With An Everyday Clinical Problem. Eur J Intern Med 2010; 21:57-61.
21. Ghany MG, Chan TM, Sanchez Pescador R, Urdea M, Lok AS. Correlation between serum HCV RNA and aminotransferase levels in patients with chronic HCV infection. Dig Dis Sci 1996; 41:2214-8.

How to cite this article:
İrvem A, Özsil K. Evaluation of the Anti Hepatitis C Virus Seropositivity and Serum Transaminases in our Hospitals. J Clin Anal Med 2017;8(Suppl 2): 105-8.