

# Seroprevalance of the Hepatitis B and C in Patients with Chronic Kidney Disease without History of Renal Replacement Therapy

## *Renal Replasman Tedavisi Almamış Kronik Böbrek Hastalarında Hepatit B ve C Seroprevalansı*

### ABSTRACT

**OBJECTIVE:** Hepatitis B (HBV) and hepatitis C (HCV) viruses are significant causes of morbidity and mortality in patients with chronic kidney disease (CKD). There is insufficient data on seroprevalence of HBV and HCV in CKD patients without renal replacement therapy (RRT).

**MATERIAL and METHODS:** Patients diagnosed as having CKD without RRT were analyzed. Seven hundred and eighty cases included study.

**RESULTS:** The seroprevalence of HbsAg and Anti-HCV were 3.5% and 1.3%, respectively. The seroprevalence of Anti-HBsAb analyzed in 456 (58.4%) patients was 39.3%. The seroprevalence of HBsAg and Anti-HCV did not differ between the patients in early stage (stage 3) and advanced stage CKD (Stage 4 and 5) ( $p=0.26$  and  $p=0.88$ , respectively). Seropositivity of Anti-HBsAb was 41.9% in early stage and 33.6% in advanced stage CKD ( $p=0.88$ ). No difference was detected in seroprevalence of HbsAg and Anti-HCV when patients were grouped regarding the underlying disorders of CKD ( $p=0.95$  and  $p=0.25$ , respectively).

**CONCLUSION:** Higher seroprevalence of Anti-HCV in hemodialysis patients, according to studies carried out in our country, may be secondary to the exposure to HCV during hemodialysis procedure. High seropositivity of Anti-HBsAb in early stage CKD, although not statistically significant, may point out the necessity of hepatitis B immunization earlier in the course of CKD. Screening the patients with CKD without RRT for HBsAg and Anti-HCV serologies would be applicable although there is no established consensus in guidelines.

**KEY WORDS:** Chronic kidney disease, Hepatitis B virus, Hepatitis C virus, Seroprevalance

### ÖZ

**AMAÇ:** Hepatit B (HBV) ve hepatit C (HCV) virüsleri, kronik böbrek hastalarında önemli bir morbidite ve mortalite nedenidir. Renal replasman tedavisi (RRT) almamış kronik böbrek hastalarında HBV ve HCV seroprevalansı için yeterli veri bulunmamaktadır.

**GEREÇ ve YÖNTEMLER:** RRT almamış kronik böbrek hastalıklı (KBH) olgular retrospektif olarak analiz edildi. Yedi yüz seksen olgu çalışmaya dahil edildi.

**BULGULAR:** HBsAg ve Anti-HCV seroprevalansı sırasıyla %3,5 ve %1,3 olarak saptandı. Anti-HBsAb seroprevalansının 456 (%58,4) hastada değerlendirildiği ve %39,3 olduğu tespit edildi. Olgular, KBH evreleri açısından değerlendirildiğinde, erken evre (evre 3 KBH) ile ileri evre (evre 4 ve 5 KBH) KBH grupları arasında HBsAg ve Anti-HCV seroprevalansı açısından istatistiksel anlamlı fark bulunmadı (sırasıyla  $p=0,26$  ve  $p=0,88$ ). Anti-HBsAb seropozitifliği erken evre KBH'da %41,9, ileri evre KBH'da %33,6 olarak tespit edildi ( $p=0,88$ ). Kronik böbrek hastalığı etiyojisi açısından altta yatan hastalıklarda, HBsAg ve Anti-HCV seroprevalansı benzer sıklıkta saptandı (sırasıyla  $p=0,95$  ve  $p=0,25$ ).

**SONUÇ:** Ülkemizde daha önce yayımlanan çalışmalar ışığında hemodiyaliz hastalarında, RRT almamış KBH hastalarına göre daha yüksek Anti-HCV seroprevalansı, hemodiyaliz prosedürü sırasında HCV maruziyeti ilişkili olabilir. Erken evre KBH'da Anti-HBsAb seropozitifliğinin istatistiksel anlamlı olmasa da daha fazla olması, KBH erken evrelerinde hepatit B aşılmasının daha etkin olabileceğini düşündürmektedir. RRT almamış KBH olgularında HBsAg ve Anti-HCV serolojik değerlendirmesi, kılavuz düzeyinde fikir birliği bulunmamakla birlikte uygun olabilir.

**ANAHTAR SÖZCÜKLER:** Hepatit B virüs, Hepatit C virüs, Kronik böbrek hastalığı, Seroprevalans

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## INTRODUCTION

Chronic kidney disease (CKD) is an important public health problem leading to end stage renal disease and cardiovascular disease (1,2). Increase in the prevalence of diabetes and hypertension, prolongation of average life expectancy brings about a rise in the prevalence of CKD in our country, as in throughout the world (1-5). According to 2008 data of Turkish Society of Nephrology, compared to 2000's, the prevalence of end stage renal disease increased two fold (756 vs. 358 per million population) (4,5). In addition to concomitant metabolic problems, cardiovascular diseases and infections are important causes of morbidity. Liver diseases are another important cause of morbidity and mortality accompanying CKD (6,7). Especially, in developing countries, viral hepatitis is the most important cause of liver diseases (7,8). Hepatitis B (HBV) and Hepatitis C viruses (HCV) may lead to some renal diseases (membranous nephropathy, membranoproliferative glomerulonephritis, mesangioproliferative glomerulonephritis, cryoglobulinemic membranoproliferative glomerulonephritis) as well (9,10). Although the prevalence of HBV and HCV infections has decreased recently with the measures taken in CKD population receiving hemodialysis and peritoneal dialysis, in renal transplantataion, which is the renal replacement therapy with best survival, it is important for patient selection and management. According to the reports of the Turkish Society of Nephrology, in CKD patients receiving hemodialysis and peritoneal dialysis, the seroprevalence of HBsAg and Anti-HCV were 3.9% and 8.5% for hemodialysis and 1.8% and 0.9% for peritoneal dialysis respectively (11). In patients with renal transplantation, these rates are reported to be respectively 2.9% and 8.4% (11). It is suggested that the increase in risk of being exposed to HBV and HCV infections in CKD may be related to impaired humoral and cellular immune response, blood transfusion, immunosuppressive drug use and inadequacy of basic protection methods in hemodialysis units (7,12).

In the CKD population without renal replacement therapy (RRT) (predialysis period), there is insufficient data on the prevalence of HBV and HCV infections. As far as we know, there

are few studies on this subject (13-15). It is not clearly known whether high HBV and HCV seroprevalance in CKD population receiving RRT stems from predialysis or pretransplantation period. The aim of the present study was to determine HBsAg and Anti-HCV seroprevalance in CKD populations who did not receive RRT.

## PATIENTS and METHODS

Adult patients diagnosed with CKD in the nephrology clinic of our hospital between January 2005 and December 2011 were identified retrospectively. CKD patients who had a glomerular filtration rate (GFR) below 60 mL/min/1.73 m<sup>2</sup> for three months and did not receive RRT were included in the study. Medical records of the patients from hospital files and hospital automation system were evaluated. Of 1715 patients who were identified, those without HBsAg and Anti-HCV serological tests were excluded from the study. Of the remaining 780 patients, age, sex, etiological causes of CKD, serum creatinine, alanine transaminase (ALT), aspartate transaminase (AST) values, HBsAg, Anti-HBsAb and Anti-HCV serological results were recorded. GFR was calculated with MDRD (Modification of Diet in Renal Disease Study) method (16), and patients were divided into two groups according to their GFRs (early stage CKD, GFR 30-59 mL/min/1.73 m<sup>2</sup>; and advanced stage CKD <30 mL/min/1.73 m<sup>2</sup>) (6). HBsAg, Anti-HBsAb and Anti-HCV were evaluated with chemiluminescence immunassay (Architect-Abbott) method. The study was approved by the local ethics committee (date:14.12.2011, No: 2011-283).

### Statistical analysis

Distribution of the variables was checked using the Kolmogorov-Smirnov test. Continuous variables with normal distribution were presented as mean ± SD. Variables with unequal distribution were expressed as medians (interquartile ranges: Q1-Q3). Categorical variables were presented as percentages and numbers. Student's t test (if normally distributed), or Mann-Whitney U test (if not normally distributed) were used to compare the continuous variables between the two groups. Categorical variables were compared with chi-square test.

**Table I:** Characteristics of the patients included the study.

	HBsAg (-) and Anti-HCV (-) n=743	HBsAg (+) n=27	Anti-HCV (+) n=10
Age	59.8±15.6 (16-92)	58.5±16.3	57.1±13
Male sex, n (%)	430 (55.1)	16 (59.3)	6 (60)
ALT (IU/L)	21.7±9.8 (5-65)	36.8±8.0	34.1±12.2
AST (IU/L)	22.4±9.4 (5-75)	38.0±11.1	35.7±12.6
GFR* (mL/min/1.73 m <sup>2</sup> )	30.9±14.4 (2-59)	33.2±11.6	32±14.6

\*ALT: alanine transaminase; AST: aspartate transaminase; GFR: glomerular filtration rate

Pearson correlation analysis was used to evaluate the relationship between variables. Binary logistic regression analysis was used for multivariate analysis. The odd ratios (OR) and 95% confidence intervals (CI) were calculated. Statistical significance was considered at a 2-tailed value of  $p < 0.05$ . Statistical analyses were performed using SPSS software (Statistical Package for the Social Sciences, version 18.0, SPSS Inc, Chicago, Ill, USA).

### RESULTS

A total of 780 patients who were diagnosed as CKD without RRT were evaluated. Mean age of the cases was  $59.8 \pm 15.6$  years (range, 16-92) and the proportion of males was 55.1%.

**Table II:** Etiological distribution of chronic kidney disease.

Etiology	n (%)
Diabetic nephropathy	237 (30.4)
Hypertensive nephropathy	149 (19.1)
Chronic glomerulonephritis	137 (17.8)
Urological causes	66 (8.5)
Secondary amyloidosis	45 (5.8)
Chronic tubulointerstitial diseases	41 (5.3)
Unknown	103 (13.2)
<b>Total</b>	<b>780 (100)</b>

**Table III:** Serological test results of Hepatitis B and C.

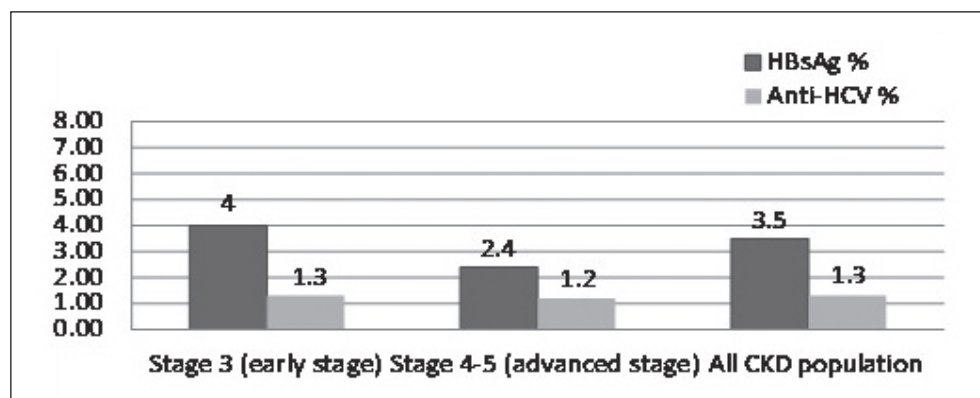
	n (%)
HBsAg (+)	27 (3.5)
Anti-HBsAb (+)*	179 (39.3)
Anti-HCV (+)	10 (1.3)
HBsAg (+) and Anti-HCV (+)	0 (0)

\* Anti-HBsAb serology was analyzed for 456 patients.

Demographic characteristics of the patients and laboratory results are demonstrated in Table I. The most common cause of CKD was diabetic nephropathy (Table II). Among the patients, HBsAg seroprevalence was 3.5% and Anti-HCV seroprevalence 1.3% (Table III). Anti-HBsAb seroprevalence was evaluated in 456 patients (%58.5) and was found to be 39.3%. No relation was found between age and sex and HBsAg, Anti-HCV seropositivity (for age  $p=0.78$  and  $p=0.83$ ; for sex  $p=0.66$  and  $p=0.33$  respectively). When patients were evaluated according to the stages of CKD, no statistically significant difference was found between early and advanced stage CKD groups in terms of HBsAg and Anti-HCV seropositivity ( $p=0.26$  and  $p=0.88$  respectively, Figure 1). Anti-HBsAb seropositivity was found to be 41.9% in early stage CKD and 33.6% in advanced stage CKD ( $p=0.88$ ). HBsAg and Anti-HCV seroprevalence was similar in patients with different etiological causes of CKD ( $p=0.95$  and  $p=0.25$  respectively, Figure 2).

### DISCUSSION

Hepatitis B and C viruses are the most frequent causes of infection in our country, as in the rest of the world. It is thought that chronic viral hepatitis influences around 500 million people throughout the world (17,18). Increase in the prevalence of CKD, and high rates of HBsAg and Anti-HCV seropositivity seen in hemodialysis patients have rendered these infections important in CKD population. It is known that, in CKD, especially in patients receiving dialysis, and in renal transplant patients, HBV and HCV infections are independent causes of morbidity and mortality (17-21). The risk of the development of cirrhosis and hepatocellular carcinoma due to chronic HBV and HCV infections, the risk of transmission to the other patients and medical personnel in hemodialysis centers, and the necessity for close follow up in renal transplant patients during immunosuppressive treatment are the major problems associated with HBV and HCV infections. It is suggested that, in patients undergoing renal transplantation, Anti-HCV positivity is associated with decreased graft and patient survival and HBsAg positivity associated with decreased patient survival



*Figure 1: Seroprevalence of HBsAg and Anti-HCV in CKD stages.*

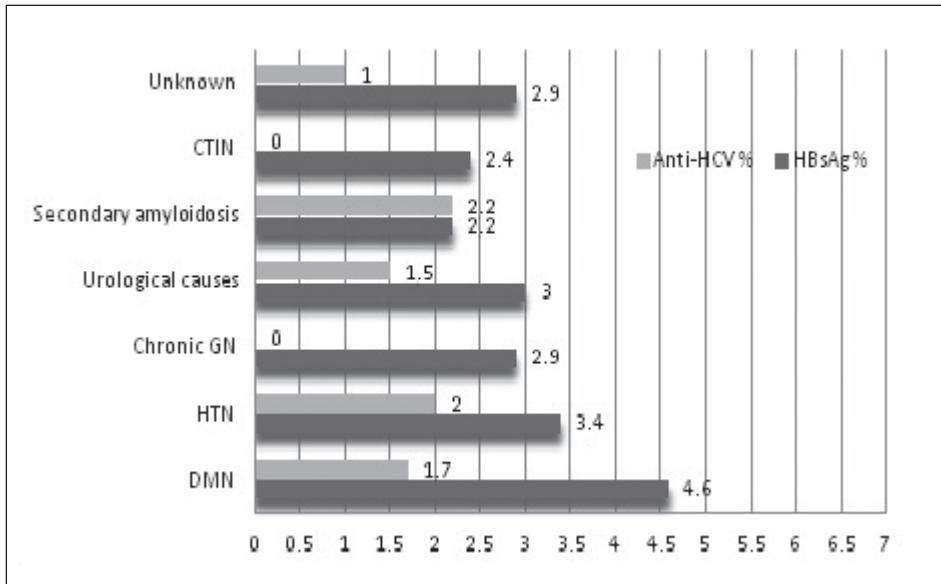


Figure 2: Seroprevalence of HBsAg and Anti-HCV in CKD etiologies.

**CTIN:** chronic tubulointerstitial nephritis, **Chronic GN:** chronic glomerulonephritis, **HTN:** hypertensive nephropathy, **DMN:** diabetic nephropathy)

(19,20). In addition, it is known that, HCV infection occurs more commonly in CKD and is associated with an increase in the risk of end stage renal disease (15,22). It is proposed that the risk of exposure to HBV and HCV increases in CKD due to impaired humoral and cellular immune response, blood transfusion, immunosuppressive drug use and inadequacy in basic protection measures in hemodialysis units (7,12-14). Through measures taken in recent years (serological virus screening in patients, evaluation of viral serology in blood product donors, decreasing the need for transfusion by using erythropoiesis stimulating agents, vaccination against HBV and basic infection control precautions) a decrease in HBV and HCV prevalence was reported in patients receiving renal replacement therapy in our country, and in the rest of the world (11). In our country, HBsAg and Anti-HCV seropositivity rates among hemodialysis patients were 11.1% and 54.6% respectively in 1997, whereas they were only 3.9% and 8.5% respectively in 2010 (11). However, particularly in hemodialysis and renal transplant patients, HCV seroprevalence is still quite high compared to that in normal population (11,21,23). It has been reported that in developed countries, the rates of HBsAg and Anti-HCV seropositivity among hemodialysis patients are between 0-4% and 2.6-22.9% respectively (24-26).

Whether the high HBV and HCV seroprevalence found in CKD population receiving RRT originates from predialysis or pretransplantation period is not clearly known. There are few studies evaluating HBV and HCV seroprevalence in CKD patients without RRT (13,14). In the study by Şit et al., HBsAg and Anti-HCV seroprevalences were found to be 10.5% and 7% respectively in 171 CKD patients in predialysis period (13). Their study was carried out in Southeastern Anatolia region,

where HBV and HCV infections occur more frequently (13). In the study by Fabrizi et al., in Milano, Italy between 1995-1999, HBsAg and Anti-HCV seroprevalence in CKD patients without RRT were found to be 3.7% and 11.5% respectively (14). The corresponding rates in those receiving hemodialysis were 8.7% and 29.2% (14). In the present study, HBsAg and Anti-HCV seroprevalence in CKD patients without RRT were established to be 3.5% and 1.3% respectively. According to 2010 data of Turkish Society of Nephrology, HBsAg seroprevalence in patients receiving RRT were found to be 3.95%, 1.9% and 2.9% respectively in hemodialysis, peritoneal dialysis and renal transplant patients. In the Türkiye Hepatitis Prevalence (TURKHEP) Study which has been recently carried out, HBsAg seroprevalence was reported to be 3.99% (23). Results obtained in the present study demonstrate that HBsAg seroprevalence in CKD patients who did not receive RRT is similar to that in the community and in CKD population receiving RRT (11,23). According to 2010 data of Turkish Society of Nephrology, among patients receiving RRT, Anti-HCV seroprevalence was found to be 8.5%, 0.9% and 8.4% respectively in hemodialysis, peritoneal dialysis and renal transplant patients. In TURKHEP Study, Anti-HCV seroprevalence was reported to be 0.95% (23). In the present study, anti-HCV seroprevalence was found to be similar to that in the community and in CKD population receiving peritoneal dialysis treatment and lower than that in CKD population receiving hemodialysis and renal transplantation treatment (11,23). Considering that hemodialysis treatment is preferred at the rate of 87.3% while initiating RRT in our country, it can be proposed that the increased Anti-HCV seropositivity in hemodialysis patients compared to CKD patients without RRT may be associated with the hemodialysis modality.



There is no established opinion in guidelines on whether the investigation of HBV and HCV serological markers is necessary in CKD patients without RRT. In K/DOQI (Kidney Disease Outcome Quality Initiative) issued Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification, there is no positive or negative opinion on that issue (6). In American Society of Transplantation's 'The Evaluation of Renal Transplantation Candidates: Clinical Practice Guidelines' it is recommended that all CKD patients considered for transplantation should be investigated in terms of HBV and HCV (27). In AASLD (American Association for the Study of Liver Diseases) Hepatitis B and C Guidelines, it is recommended that HBV and HCV should be investigated in patients undergoing hemodialysis treatment (28,29). In the same guide, HBV screening is recommended in countries with an intermediate (2-8%) prevalence. The data obtained in the present study indicate that HBsAg seroprevalance is over 2% in CKD patients who did not receive RRT. In addition, given the fact that our country is a middle level endemic region for HBV infection (23), and HBV and HCV infections are common in patients receiving RRT, there is an increased risk of mortality-morbidity with these infections. Also, considering the fact that Hepatitis B vaccination has a higher probability of success at early periods of CKD, it may be reasonable to investigate HBsAg and Anti-HCV serology in CKD patients who did not receive RRT.

In the present study, Anti-HBsAb seroprevalance was found to be 41.9% in early stage CKD group and 33.6% in advanced stage CKD group. In view of low efficiency of HBV vaccination in patients undergoing dialysis treatment (30), and of the immunosuppressive effects of the CKD itself, it may be judicious to carry out HBV vaccination starting from early stage CKD (24).

The present study has some limitations due to retrospective evaluation. HBV and HCV risk factors in patients were not determined, other serological markers including HBV DNA and HCV RNA, which are important markers in the evaluation of viral hepatitis were not evaluated, and the status of HBV vaccination and natural immunity status were not investigated.

In conclusion, HBsAg and Anti-HCV seroprevalance was found to be 3.5% and 1.3% respectively in CKD patients who did not receive RRT in our center. Hepatitis B and C viruses, which can lead to significant morbidity and mortality, may not have been investigated adequately among this patient population. As there is no recommendation in guidelines on whether HBV and HCV serological evaluation should be carried out in CKD population who did not receive RRT, studies with proper design are required in order to evaluate the necessity.

**DISCLOSURE:** The authors declare that they have no conflict of interest.

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