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The Role of Quantitative HBsAg Levels in Chronic Hepatitis B Infection

Kılıç Tekin et al. Evaluation of quantitative HBsAg

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ABSTRACT

Introduction: Chronic Hepatitis B (CHB) infection is essential for patient management, including treatment and follow-up. Therefore, qHBsAg may help physicians to reveal the stages of HBV infection. This study aimed to examine the variances in quantitative hepatitis B surface antigen (qHBsAg) levels across various stages of viral infection.

Methods: In this cross-sectional study, 183 patients who attended the Infectious Diseases outpatient clinic at xxx Hospital between July and December 2020, tested positive for HBsAg, and had not undergone prior treatment were included.

Results: Of 183 patients, 54.1% were male. The mean quantitative HBsAg (qHBsAg) level was 2.155 IU/ml (interquartile range: 625-12.759). Correlation analysis revealed that qHBsAg was significantly associated with age, laboratory results, and hepatitis B virus (HBV) DNA. In Receiver Operating Characteristic (ROC) analysis, which evaluates the predictive power of qHBsAg for chronic hepatitis, the AUC was 0.749 and the optimal cut-off value for qHBsAg was 3.081 IU/mL. The cut-off value for 95% specificity of qHBsAg in predicting chronic hepatitis was 38.641 IU/mL.

Conclusion: Quantitative HBsAg is an easily applicable and relatively inexpensive test for distinguishing different stages of chronic hepatitis. Therefore, qHBsAg can help clinicians in assess liver injury and plan treatment at the most appropriate time in patients with CHB infection. In patients with HBV DNA levels of exceeding 2,000 IU/mL, commencement of treatment without the necessity of liver biopsy may be considered when the quantitative HBsAg (qHBsAg) surpasses 38,000 IU/mL.

Keywords: HBeAg, HBV-DNA, chronic hepatitis B, qHBsAg, liver biopsy

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Introduction

Hepatitis B virus (HBV) is a member of the Hepadnaviridae family, characterized by its double-stranded DNA structure (1). Hepatitis B surface antigen (HBsAg) is secreted into circulation in tubular or spherical forms by hepatocytes infected with the (HBV). Quantitative HBsAg (qHBsAg) levels serve as reflection of the transcriptional activity originating from both closed circular DNA (cccDNA) and integrated DNA within hepatocytes. Therefore, qHBsAg levels can be used as an auxiliary indicator in the course of chronic hepatitis B (CHB) (2).

The standardization of HBsAg quantification has been achieved, leading to an increased utilization of this method in current practice. HBsAg Quantitation is a valuable parameter that can guide the staging and follow-up of CHB infection and can be used to predict complications of CHB infection and the decision of treatment initiation and cessation (3,4). This does not necessarily indicate that patients with infection have CHB. Hence, the identification of individuals with chronic hepatitis B and persistent HBV infection holds significant importance in patient management, encompassing treatment decisions and subsequent follow-up protocols. In this respect, qHBsAg can help physicians identify the stages of HBV infection (3). The main objective of the study was to examine variations in qHBsAg levels among distinct stages of infection. Additionally, the relationship between qHBsAg and the tested parameters was investigated.

Methods

Patients

In this single-center and cross-sectional study, a total of 183 patients with Hepatitis B who applied to the Department of Infectious Diseases and Clinical Microbiology, xxx Hospital between July and December 2020 were included.

The inclusion criteria cover patients aged 18 years and older, with confirmed HBsAg positivity for a minimum duration of one year, and no history of prior treatment for HBV. The exclusion criteria encompassed coinfection with HIV (human immunodeficiency virus), HCV (hepatitis C virus), hepatitis D virus (HDV) and hepatocellular carcinoma (HCC), pregnancy, findings suggesting alcoholic hepatitis.

We recorded the following data for each patient: age, gender, HBsAg, HBeAg hepatitis B envelop antigen (HBeAg), anti-HBe, HBV DNA levels, anti-HDV, anti-HCV, anti-HIV, biochemical values such as ALT (alanine aminotransferase), AST (aspartate aminotransferase) total bilirubin, alkaline phosphatase, gamma-glutamyl transferase, albumin, globulin, alpha-feto protein, hemogram, prothrombin time, INR (International Normalized Ratio) values, and abdominal ultrasonography findings. The biopsy findings (fibrosis and histological activity index) of patients who underwent liver biopsy in the last 1 year were also recorded.

The qHBsAg levels were correlated with biochemical results and HBV DNA levels obtained concurrently, whereas liver biopsies were performed within one year of blood sample collection.

According to the 2017 Classification by the European Association for the Study of the Liver (EASL), patients were categorized into four groups: HBeAg-positive chronic infection (HBV DNA > 10^7 IU/mL, normal ALT); HBeAg-positive chronic hepatitis (HBV DNA 10^4-10^7 IU/mL, elevated ALT); HBeAg-negative chronic infection (HBV DNA < 2000 IU/mL, normal ALT); and HBeAg-negative chronic hepatitis (HBV DNA > 2000 IU/mL, elevated ALT) (3).

An informed consent was obtained from patients before participating in the study.

Definitions and Reference Ranges

In the present study, biochemical analyses such as serum urea, serum creatinine, AST, and ALT levels were measured using kits applied to the Beckman AU2700 auto analyzer devices of the Biochemistry Laboratory of xxx Hospital.

Serological and virological tests were performed with the Abbott Architect I-2000 Device and the Architect Alinity Kit in the microbiology laboratory of xxx Hospital.

For HBsAg quantification, serum samples obtained from patients were stored at -40 °C, and qHBsAg levels were measured with Chemiluminescent Microparticle Immunoassay (CMIA) technique using the Elecsys HBsAg II (Roche Diagnostics, Indianapolis, USA) kit.

Statistical Analysis

For statistical analyses in this study, SPSS 15.0 for Windows (SPSS Inc., Chicago, Illinois, USA) was utilized. The Chi-square test was used for categorical variables. Mann-Whitney U test was used for subgroup analyses and interpreted with Bonferroni Correction. Kruskal Wallis test was used to compare the continuous variables in the four groups. The relationships between numerical variables were analyzed with Pearson Correlation Analysis when the parametric test conditions were met, and with Spearman's Correlation Analysis (Spearman's RHO Test) when the parametric test conditions could not be met. Statistical significance was given as $p < 0.05$.

ROC analysis was performed with reference to HAI, fibrosis, and chronic hepatitis classifications, and ROC graphs were shown to determine the diagnostic performance of the qHBsAg variable, which is clinically predicted to be effective in determining the risk group. Variables with an area under the curve (AUC) of > 0.500 that had a certain sensitivity and specificity in determining chronic hepatitis, HBV DNA levels, liver fibrosis, and HAI were also calculated.

Results

A total of 183 patients were included in this study, 84 (45.9%) of them were female. The patients' median age was 40 years (range: 30-48).

Liver needle biopsy was performed in 77 patients in the last 1 year. There were 64 (83.1%) patients with fibrosis between 0-2, and 13 (16.9%) with fibrosis 3-4 among patients who underwent biopsy. Fibrosis 5 or 6 was not detected in any of the patients. There were 58 (75.3%) patients with HAI between 0-6, and 19 (24.7%) with HAI > 6.

According to the Hepatitis Classification, 13 (7.1%) patients had HBeAg (+) chronic infection, 40 (21.9%) HBeAg (+) chronic hepatitis, 96 (52.5%) HBeAg (-) chronic hepatitis infection, and 34 (18.6%) were in the HBeAg (-) chronic hepatitis group.

The demographic characteristics and fundamental test outcomes presented in Table 1.

The comparison of the patient groups in terms of clinical and demographic characteristics, such as gender, age, laboratory results, HBV DNA, qHBsAg, fibrosis, histological activity index (HAI) scores, and hepatosteatosis are given in Table 2, and The subgroup analyses performed according to Bonferroni Correction for these features are given in Table 3.

In the correlation analysis, qHBsAg was significantly ascociated with age, ALT, AST, albumin, PTZ, AFP, and HBV DNA in the general study group. Furthermore, notable correlations were observed between qHBsAg and factors such as age, total protein, albumin, and HBV DNA among HBeAg-positive patients. Similarly, significant associations were identified between qHBsAg and the fallowing variables; age, ALT, and HBV DNA among HBeAg-negative patients (Table 4).

A moderate positive correlation was detected between qHBsAg and HBV DNA in the cohort ($r=0.626$, $p<0.001$) and HBeAg (+) group ($r=0.602$, $p<0.001$). A weak positive correlation was detected between qHBsAg and HBV DNA in HBeAg (-) group ($r=0.375$, $p<0.001$). In

HBeAg (+) and HBeAg (-) patient groups, as the HBV DNA value increased, the qHBsAg value also increased in Table 4.

The power of qHBsAg to predict fibrosis and HAI in patients with biopsy results was calculated using an ROC curve. In the ROC analysis, in which the predictive power for fibrosis ≥2 was evaluated, qHBsAg was insufficient to evaluate fibrosis ($p > 0.086$) (Figure 1).

In the ROC analysis, it was found that AUC for HAI ≥6 was not statistically significant (AUC=0.611, p=0.15). The AUC for HAI ≥9 was statistically significant (AUC=0.742, p=0.008).

In the ROC analysis performed to predict chronic hepatitis in patients, the AUC for qHBsAg was statistically significant (AUC=0.749, $p<0.001$). The cut-off point of qHBsAg in determining chronic hepatitis was determined as 3.081 IU/mL. The sensitivity was calculated to be 70.3% and specificity 70.6% for qHBsAg ≤ 3.081 IU/mL. In recognizing chronic hepatitis, the limit value was 38.641 IU/mL for 95% specificity, and the sensitivity was 18% for this value in Figure 2.

In the ROC analysis to evaluate the power of qHBsAg for HBV DNA >2.000 IU/mL in patients, the AUC for HBV DNA >2.000 IU/mL was statistically significant (AUC= 0.790, $p<0.001$) in Figure 3. For HBV DNA >2.000 IU/mL, the cut-off of the qHBsAg was found to be 1.924.5 IU/mL. The sensitivity was 72.3% and specificity was 70.4% for qHBsAg ≥1.924.5.

In the ROC analysis made to evaluate the predictive power of qHBsAg for HBV DNA >20.000 IU/mL in patients, the AUC was found to be statistically significant (AUC=0.814, $p<0.001$) in Figure 4. For HBV DNA >20.000 IU/mL as the reference, the cut-off point for the qHBsAg was determined to be 3.081 IU/mL. The sensitivity was 75% and specificity was 71.3% for qHBsAg ≥3.081.

No significant cut-off values were detected for qHBsAg to predict HBV DNA between 2.000-20.000 IU/ml (AUC = 0.475, p = 0.615).

Discussion

A total of 183 naive patients diagnosed with CHB were evaluated in this study. Upon evaluation of the correlation analyses, a positive association was identified between qHBsAg levels and ALT, HBV DNA, and HAI. Consequently, we deduced that employing qHBsAg could prove efficacious in determining the necessity for treatment initiation and in monitoring patient follow-up.

Quantitative HBsAg is one of the factors affecting the prognosis of the disease such as HBeAg positivity, HBV DNA elevation, and genotype. Previous studies have showed that qHBsAg level >1000 IU/mL in HBeAg-negative CHB patients was found to be associated with disease progression and development of HCC (5,6). Also, the EASL and American Association for the Study of Liver Diseases (AASLD) guidelines that the most important determinant of the decision to treatment cessation is HBsAg loss. There is an annual average loss of HBsAg of 0.4-2.3% depending on the stage of liver disease and the age of the patient. Given that most strategies targeting functional cure of HBV infection involve combination therapy with nucleos(t)ide analogues (NA), monitoring HBsAg becomes crucial for assessing response to novel therapeutic approaches. In addition to HBsAg loss, the degree of HBsAg decline or specific cutoff values could serve as secondary endpoints in early clinical trials. However, the precise magnitude of HBsAg reduction or the threshold indicating treatment success remains uncertain (3,7). This is often difficult to achieve, and requires long-term treatment. Some studies have examined that whether monitoring the qHBsAg level is a predictive value indicating HBsAg loss in the natural course of the disease. It was concluded that if qHBsAg levels were low before treatment (<1.000 IU/mL) and decrease in the early

stages of the treatment (e.g. 1-2 log IU/mL) were indicative for the development of HBsAg loss, but the limit value was not determined clearly (5,6).
Many studies conducted on HBsAg quantification emphasized that qHBsAg measurement is a dynamic parameter and may differ in the natural course of the disease (8,9). However, it was also shown that qHBsAg can be used as a reference to determine the severity of the disease, evaluate compliance with treatment, and decide on ending the treatment (10,11). In this respect, it is considered that qHBsAg may be a reliable marker that can be used in patient follow-up.
HBsAg seroclearance and anti-HBs formation are seen as the ultimate target to be called functional cure and to discontinue treatment in patients who receive treatment. For this reason, the quantitative measurement of HBsAg level plays important roles in patient follow-up (12). HBsAg seroclearance is an important parameter in predicting decreased HBsAg titer (especially HBsAg <10 IU/mL) and spontaneous HBsAg loss, which is used in treatment follow-up. Other markers were reported to be advanced age, low ALT, high platelet, and leukocyte count (13).
There are many studies reporting that quantitative HBsAg can be used in the differentiation of chronic infection and hepatitis (8,9). In a study of Brunetto et al., it was reported that a qHBsAg value of 1000 IU/mL is an appropriate limit value to differentiate between active and inactive Hepatitis B in genotype D patients (14). Unlike this, in our study, the sensitivity was calculated to be 86.5% and specificity 45.9% for qHBsAg 1000 IU/mL in predicting chronic hepatitis. In the present study, the AUC was statistically significant as a result of the qHBsAg with reference to chronic hepatitis (AUC=0.749) ($p<0.001$). The cut-off of the qHBsAg in determining chronic hepatitis was 3.081 IU/mL. The sensitivity was calculated as 70.3%, and the specificity 70.6% at this cut-off point. The limit value for 95% specificity of qHBsAg in recognizing chronic hepatitis was determined to be 38.641 IU/mL. Initiation of antiviral treatment without liver biopsy may be considered because of the high specificity values at this and above qHBsAg levels.
Different qHBsAg results were found in different stages of the disease because of the qHBsAg dynamism. In a study conducted in China, in which 623 people with different stages of Hepatitis B were examined, the patients were evaluated in 5 stages, and the disparities in qHBsAg levels throughout the natural course of disease were examined. In the study, it was found that median qHBsAg levels were different in each stage of CHB, and statistically significant differences were observed between them ($p < 0.001$). Also, HBsAg titers were found to be at the highest level in immune tolerants and lowest in inactive carriers. In addition, serum HBsAg level had a positive and strong correlation with HBV DNA in the immune clearance stage ($r=0.683$, $p<0.001$) (15). Similarly, in the present study, the qHBsAg median values were found to be different in all four groups, and there was a statistically significant difference between them ($p<0.001$). Also, similarly, the median value was found to be at the highest level in the HBeAg (+) chronic infection group, and the lowest in the HBeAg (-) chronic infection group. In the present study, similarly, the total patient group ($r=0.626$, $p<0.001$), HBeAg (+) patient group ($r=0.602$, $p<0.001$), and HBeAg (-) patient group ($r=0.375$, $p<0.001$) had varying degrees of positive correlations between qHBsAg and HBV DNA. In this respect, qHBsAg can provide us with an idea about the stage of the disease in its natural course.
qHBsAg level can provide information on disease activation in patients who did not or could not undergo a biopsy. However, current literature shows that qHBsAg is insufficient to evaluate significant fibrosis. For this reason, using non-invasive fibrosis tests (elastography, etc.) can be considered as an alternative to liver biopsy to show significant fibrosis.
In many studies that were conducted in recent years, it was shown that qHBsAg is useful in predicting the stage of liver damage (16,7). In a prior investigation, a robust and positive

correlation was identified between ALT, HBV DNA, HAI scores, and qHBsAg levels (8). In the present study, as in this study, it was shown that there is a positive correlation between the quantitation of HBsAg in the entire patient group and ALT ($p<0.001$) and HBV DNA ($p<0.001$). These findings may enable us to assess whether qHBsAg indicates a low or high risk of progressive liver damage, akin to ALT and HBV DNA levels. Moreover, they may offer guidance for physicians in the timing of treatment planning for patients.
The study had some strengths. First, we evaluated a homogenous group including only treatment-naive patients. Second, we performed various analysis methods including correlation and ROC curve analysis. Third, we could perform HBeAg subgroup analysis.

Study Limitations

There were several limitation points in this study. First t was conducted as a single-center, potentially limiting the generalizability of the findings. Second the sample size was relatively modest, this situation may potentially impact the statistical power and reliability of the findings. Third, liver biopsy outcomes were assessed retrospectively over a one-year period and were not conducted concurrently with other assessments. Additionally, due to budget constraints, genotype determination was not feasible for patients. Lastly, qHBsAg measurements relied on a single assessment, precluding a longitudinal analysis.

Conclusion

The quantitative HBsAg is an easily applicable and relatively inexpensive test, which can be used to differentiate between different stages of CHB. In this respect, qHBsAg may help to stratify patients with CHB as chronic infection and hepatitis, and to manage treatment decision. If qHBsAg is >38.000 IU/mL in patients with CHB, initiation of treatment may be considered without a liver biopsy.

Ethics Approval

The ethical commite of University of Health Sciences Turkey, Haseki Training and Research Hospital (approval number: 2020-111, date: 08.07.2020) approved the study protocol. Also, this study was supported financially by xxx Hospital (Protocol number:126, date: 20.04.2020).
There is no personal or financial conflict of interest in this study.

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Table 1. Demographic characteristics, laboratory parameters, and liver biopsy findings of patients

Characteristics	**Median (IQR)**
Age (years)	40 (30-48)
Gender	
Female (n, %)	84 (45.9)
Male (n, %)	99 (54.1)

ALT (IU/L)	28 (19-49)
AST (IU/L)	26 (20-38)
Total Bilirubin (mg/dl)	0.50 (0.40-0.70)
Direct Bilirubin (mg/dl)	0.10 (0.10-0.14)
Total protein (g/dl)	72.2 (70-75.8)
Albumin (g/dl)	42 (40-45)
INR	1 (0.90-1)
Prothrombin time (sec)	11.2 (11-12)
AFP (IU/mL)	2.83 (1.9-4)
HBeAg	
Positive	53 (29.0)
Negative	130 (71.0)
HBV DNA (IU/mL)	5.271 (623-444.240)
qHBsAg (IU/mL)	2.155 (625.1-12.759)
Fibrosis in biopsy	
0-2	57 (74.0)
≥2	20 (26.0)
HAI in biopsy	
0-6	48 (62.3)
≥ 6	29 (37.7)
Hepatosteatosis	
Grade-1	38 (67.9)
Grade-2	18 (32.1)
HBeAg + Chr. Infection	13 (7.1)
HBeAg + Chr. Hepatitis	40 (21.9)
HBeAg – Chr. Infection	96 (52.5)
HBeAg – Chr. Hepatitis	34 (18.6)
IQR: Interquartile Range; n: number of data; ALT: Alanine aminotransferase; IU/L: İnternational Unit /Liter; AST: Aspartate aminotransferase; mg/dl: miligram/deciliter; g/dl: gram/deciliter; INR: International Normalized Ratio (International Standardized Ratio); sec: second; AFP: Alfa fetoprotein; HBeAg: Hepatitis B envelop antigen; HBV DNA: Hepatitis B virus deoxyribonucleic acid; qHBsAg: quantitative Hepatitis B surfey antigen; HAI: Histologic Activity Index; Chr.hepatitis: chronic hepatitis; Chr.infection: chronic infection	

Table 2. Comparison of clinical and demographic characteristics according to EASL Classification

Characteristics	**HBeAg (+) Chr. Infection (n=13)**	**HBeAg (+) Chr. Hepatitis (n=40)**	**HBeAg (–) Chr. Infection (n=96)**	**HBeAg (–) Chr. Hepatitis (n=34)**	***p* value**
Gender					
Female n (%)	10 (76.9%)	15 (37.5%)	51 (53.1%)	8 (23.5%)	0.002
Male n (%)	3 (23.1%)	25 (62.5%)	45 (46.9%)	26 (76.5%)	
Age (years)					

Median	26	31	42	40	<0.001
IQR	20-31	27-47	37.25-50.75	32-47.25	
ALT (IU/L)					
Median	23	62.5	20	43.5	<0.001
IQR	17-29.5	43.5-93.5	16.25-26	33.75-85.75	
AST (IU/L)					
Median	24	43.5	20	36.5	<0.001
IQR	19-27.5	30.25-62	18-25.75	27-56	
Tot. bilirubin (mg/dl)					
Median	0.45	0.535	0.5	0.625	0.002
IQR	0.325-0.525	0.4925-0.7875	0.4-0.7	0.5-0.9	
Total protein (g/dl)					
Median	74.7	72	72.25	72.95	0.205
IQR	68.7-75.9	67.9-75	69.525-75.175	71-77.05	
Albumin (g/dl)					
Median	41	40.5	43	44	<0.001
IQR	40-43.5	37-43	41-45	42-46.25	
INR					
Median	0.9	0.995	0.9	1	0.048
IQR	0.9-1	0.9-1.1	0.9-1	0.975-1	
Prothrombin time (sec)					
Median	11.2	11.15	11.2	11.3	0.197
IQR	11.15-12.55	11-12.175	10.9-11.875	11-12.025	
AFP (IU/mL)					
Median	3.41	3.275	2.525	2.575	0.092
IQR	1.33-3.815	2.555-4.5375	1.9-3.645	1.875-4.17	
HBV DNA (IU/mL)					
Median	146.861	20.000.000	739.5	36.557	<0.001
IQR	3.464-92.645.057	182.179.8-486.041	107-2.921	11.893.25-758.476.5	
qHBsAg (IU/mL)					
Median	37.510	20.717	874.1	2.506.5	<0.001
IQR	24.742.5-170.410	11.789.5-143.825	275.325-2.172.25	1082.75-6.708.75	

EASL: European Association for the Study of the Liver; HBeAg: Hepatitis B envelop antigen ; Chr.infection: chronic infection; Chr.hepatitis: chronic hepatitis; ; n: number of data; *p: p* value; IQR: Interquartile Range; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; IU/L: İnternational Unit /Liter; mg/dl: miligram/deciliter; g/dl: gram/deciliter; qHBsAg: quantitative Hepatitis B surfey antigen;; INR: International Normalized Ratio (International Standardized Ratio); sec: second; AFP: Alfa fetoprotein; HBV DNA:Hepatitis B virus deoxyribonucleic acid; qHBsAg: quantitative Hepatitis B surfey antigen

Table 3. Sub-group analyses in which the clinical and demographic characteristics of patient groups are compared

Characteristics	HBeAg (+) Chr. vs. Infection		HBeAg(+) vs. Chr. Hepatitis		HBeAg(-)vs. Chr. Infection	
	HBeAg(+) Chr. Hepatitis	HBeAg(-) Chr. Infection	HBeAg(-) Chr. Hepatitis	HBeAg(-) Chr. Infection	HBeAg(-) Chr. Hepatitis	HBeAg(-) Chr. Hepatitis
	p	p	p	p	p	p
Gender	0.031	0.185	0.002	0.097	0.196	0.002
Age (years)	0.006	<0.001	0.001	0.001	0.252	0.084
ALT (IU/L)	<0.001	0.381	<0.001	<0.001	0.045	<0.001
AST (IU/L)	<0.001	0.209	<0.001	<0.001	0.237	<0.001
Total Bilirubin (mg/dl)	0.014	0.225	0.006	0.056	0.198	0.003
Direct bilirubin (mg/dl)	0.061	0.268	0.026	0.057	0.153	0.001
Albumin (g/dl)	0.355	0.187	0.019	0.001	<0.001	0.047
INR	0.338	0.728	0.200	0.053	0.649	0.013
HBV DNA (IU/mL)	0.077	<0.001	0.739	<0.001	<0.001	<0.001
qHBsAg (IU/mL)	0.148	<0.001	<0.001	<0.001	<0.001	0.001

HBeAg: Hepatitis B envelop antigen; Chr.hepatitis: chronic hepatitis; Chr.infection: chronic infection; *p: p* value; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; IU/L: İnternational Unit /Liter; mg/dl: miligram/deciliter; g/dl: gram/deciliter; INR: International Normalized Ratio (International Standardized Ratio); ; HBV DNA:Hepatitis B virus deoxyribonucleic acid; qHBsAg: quantitative Hepatitis B surfey antigen
Bonferroni Correction $p<0.0083$ (the significance value of *p* value was evaluated according to Bonferroni Correction)

Table 4. The correlation of quantitative HBsAg level with other parameters

Characteristics	Total qHBsAg		HBeAg (+) qHBsAg		HBeAg (-) qHBsAg	
	r	*p*	r	*p*	r	*p*
Age	-0.397	<0.001	-0.342	0.012	-0.259	0.003
ALT (IU/L)	0.386	<0.001	-0.213	0.125	0.236	0.007
AST (IU/L)	0.354	<0.001	-0.208	0.135	0.151	0.086
Total bilirubin (mg/dl)	0.050	0.503	-0.216	0.120	0.120	0.172
Direct bilirubin(mg/dl)	-0.001	0.988	-0.221	0.112	0.038	0.670
Total protein (g/dl)	0.021	0.780	0.300	0.029	0.060	0.498
Albumin (g/dl)	-0.158	0.032	0.315	0.022	-0.011	0.905
INR	0.106	0.153	-0.133	0.341	0.119	0.177
PT	0.152	0.040	-0.115	0.411	0.120	0.172
AFP (IU/mL)	0.155	0.036	0.058	0.681	0.110	0.212
HBV DNA (IU/mL)	0.626	<0.001	0.602	<0.001	0.375	<0.001

HBsAg: Hepatitis B surfey antigen; HBeAg: Hepatitis B envelop antigen; qHBsAg: quantitative Hepatitis B surfey antigen; r: correlation coefficient; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; IU/L: İnternational Unit /Liter; mg/dl: miligram/deciliter; g/dl: gram/deciliter INR: International Normalized Ratio (International Standardized Ratio); PT :prothrombin time; AFP: Alfa fetoprotein; HBV DNA:Hepatitis B virus deoxyribonucleic acid

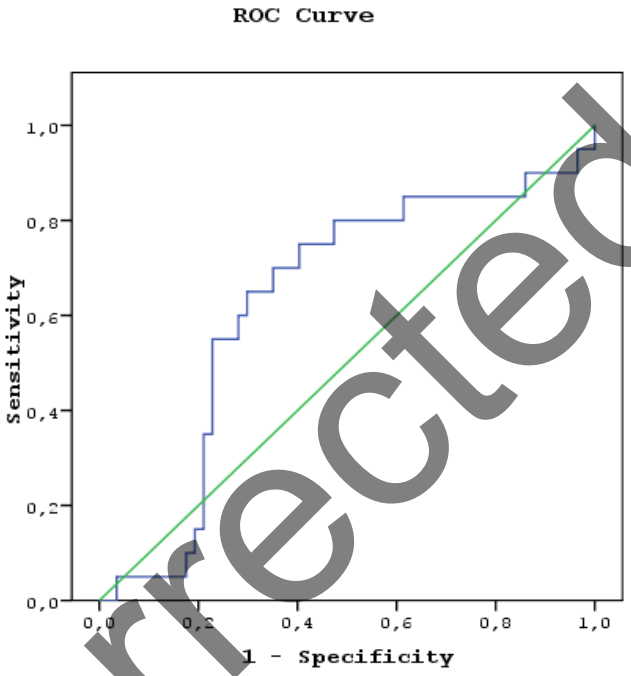

Figure 1. Examining the predictor power of qHBsAg Fibrosis 2 and over with ROC curve

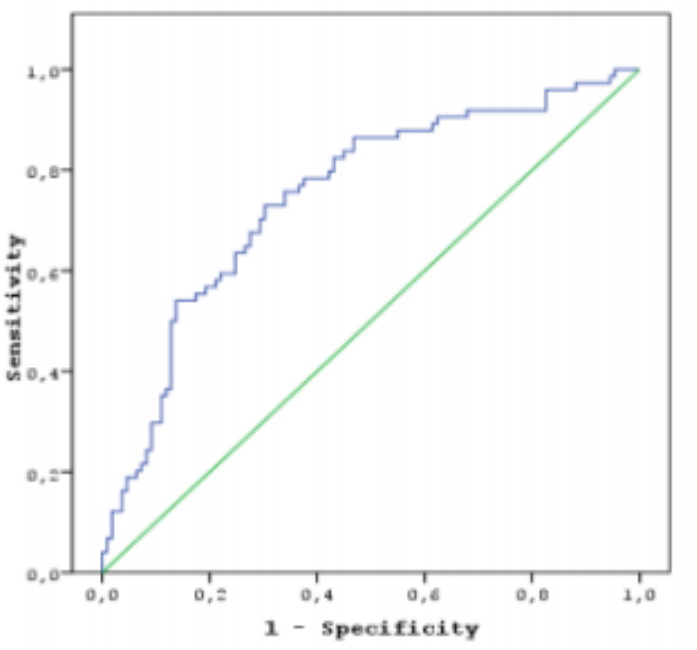

Figure 2. Examining the predictor power of qHBsAg for chronic hepatitis with ROC curve

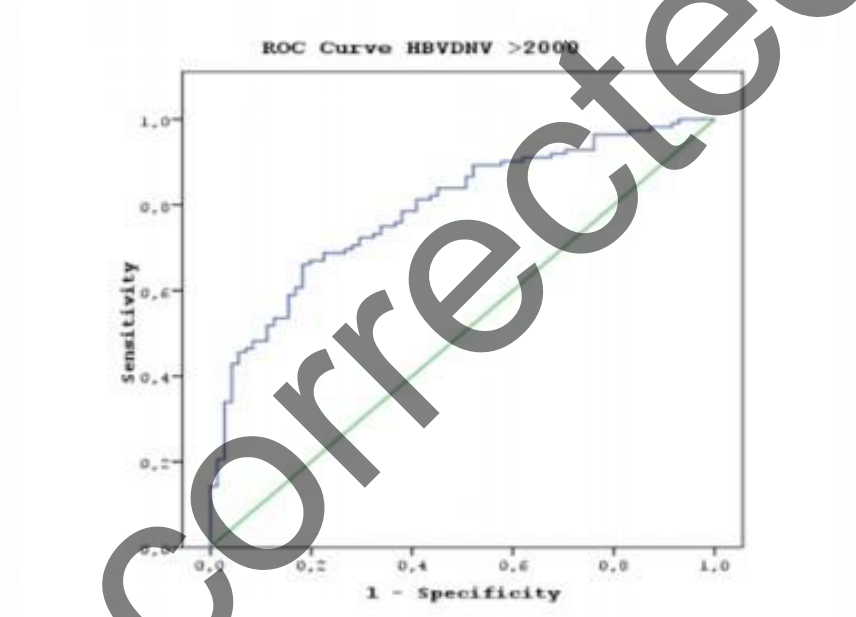

Figure 3. Examining the predictor power of qHBsAg for HBV DNA>2.000 IU/Ml with ROC curve

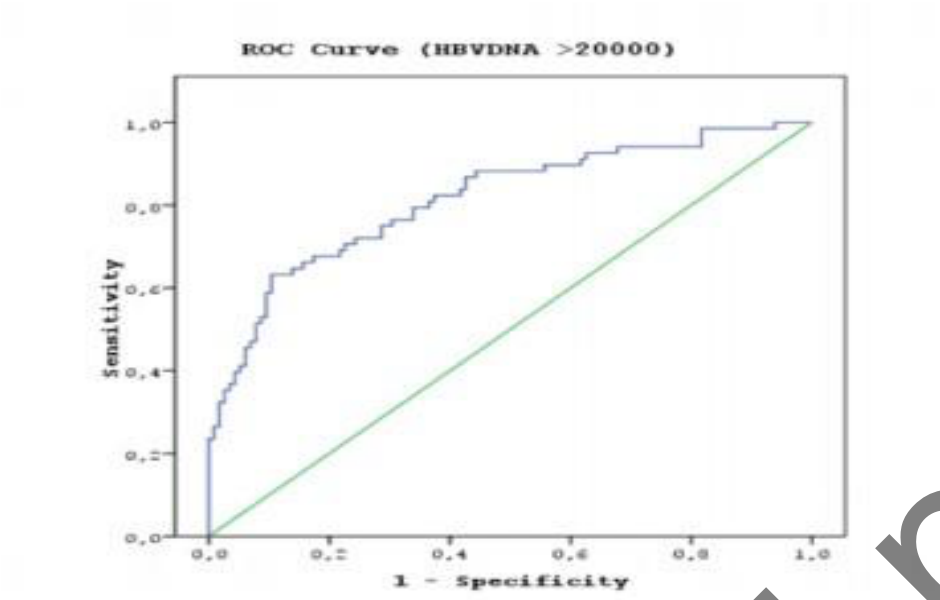

Figure 4. Examining the predictor power of qHBsAg for HBV DNA>20.000 IU/Ml with ROC curve