ORIGINAL RESEARCH PAPER

Medicine

IMPORTANCE OF PROLIDASE ACTIVITY FOR DIFFERENTIAL DIAGNOSIS BETWEEN ASYMPTOMATIC HEPATITIS B CARRIERS AND HBEAG NEGATIVE CHRONIC HEPATITIS B PATIENTS

KEY WORDS: Chronic hepatitis B, HBeAg-negative, differential diagnosis, prolidase enzyme, asymptomatic HBV carriers

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ABSTRACT

Background: Prolidase is an enzyme that breaks down the iminodipeptides that occur after collagen destruction.
Aim: In this study, we aimed to investigate the importance of serum prolidase enzyme level in the differential diagnosis of asymptomatic CHB and HBeAg-negative CHB patients.
Patients and methods: Biochemical analyses, serological parameters associated with HBV, and serum prolidase levels were measured in asymptomatic HBV carriers (n=65), active CHB patients (n=60), and healthy controls (n=27). Liver biopsies were performed on asymptomatic HBV carriers and active CHB patients.
Results: Serum prolidase level was significantly higher in active CHB patients (819.92 ±123.74 IU/L) compared to asymptomatic HBV carriers (732.99 ±124.70 IU/L) and was higher in asymptomatic HBV carriers compared to healthy controls (529.4 ±74.73 IU/L) (p=0.001). The diagnostic efficiency of serum prolidase level was found to be strong in asymptomatic HBV carrier and HBeAg-negative CHB patient groups (c-statistics: 0.707). The diagnostic cut-off value of prolidase level was determined as 751.15 U/L (specificity: 63%, sensitivity: 72%, positive likelihood ratio: 1.97, and negative likelihood ratio: 0.43) by this analysis. A strong positive correlation was observed between serum prolidase level and the severity of fibrosis in asymptomatic HBV carriers (r=0.603, p=0.000). A positive correlation was determined between serum prolidase level and histological activity index (HAI) scores in patients with active CHB and asymptomatic HBV carriers.
Conclusions: Serum prolidase levels are associated with fibrosis in CHB patients. Hence, prolidase may be a useful test for differentiating between asymptomatic HBV carriers and HBeAg-negative CHB patients.

INTRODUCTION

A large population of chronic hepatitis B (CHB) infection, which is one of the most widespread causes of chronic liver disease worldwide, consists of asymptomatic carriers [1]. Previously, it was considered that this hepatitis B virus (HBV) carriers are clinically asymptomatic since the virus is dormant in these patients and thus the risk of developing cirrhosis is low. However, has been recently observed that the disease at the carrier stage is not dormant [2]. Because fibrotic activity has been found to be increased in patients with HBeAg-negative CHB, it is important to discriminate between asymptomatic HBV carriers and patients with HBeAg-negative CHB [3]. This discrimination is being made by determining serum ALT and HBV-DNA levels and performing liver histopathology. Liver needle biopsy is an invasive and costly method. Serum ALT and HBV DNA levels are a part of analyses that are used for estimating the stage of chronic hepatitis but their ideal limit values and certainty have not been clear yet [4].

Prolidase is an enzyme that breaks down iminodipeptides generated after collagen destruction and is a rate-limiting enzyme in the last stage of collagen degradation pathway. Increased production and destruction of collagen causes an increase in prolidase activity [5]. Several studies have demonstrated that serum prolidase activity is a useful marker for evaluating liver fibrosis and prolidase enzyme level also increases in parallel with higher stages of fibrosis [6-8]. Therefore, serum prolidase level has been considered to be a useful marker in patients with chronic liver disease for whom long-term follow up is important [9].

The aim of this study was to investigate the importance of prolidase level in the differential diagnosis of asymptomatic and HBeAg-negative CHB patients.

MATERIAL AND METHODS

Patients

The study was performed at the Gaziantep University Medical Faculty Hospital between September 2011 and June 2012. A total of 65 asymptomatic HBV carriers, 60 patients with CHB who were being followed up in the Gastroenterology Outpatient Clinic for three years, and 27 healthy volunteers were enrolled in the study. The written informed consent was obtained from all the participants. The study was performed in accordance with the principles of the Helsinki Declaration of 1975 as revised in 2008 and with the approval numbered 07.2011/39 of the University of Gaziantep Faculty of Medicine Clinical Research Ethics Committee.

The patients with positive anti-HCV, anti-HDV, and anti-HIV antibodies and those with positive antinuclear antibodies (ANA), anti-smooth muscle antibodies (ASMA), and anti-mitochondrial antibodies (AMA) were excluded.

Moreover, patients who had received antiviral therapy or immunomodulatory therapy within the last 12 months, those with decompensated liver cirrhosis, those with cancer, and those with inadequate liver biopsy were also excluded. Abdominal ultrasonography was performed on all patients. Body mass index (BMI) of the patients were calculated. After documenting their medical history in detail and conducting a comprehensive physical examination, complete blood count (CBC), serum hepatic function tests [aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total bilirubin, direct bilirubin, and albumin)], triglyceride level, total cholesterol level, fasting blood glucose (FBG) level, presence of anti-HIV, anti-HCV, anti-Delta, HBsAg, anti-HBs, HBeAg, anti-HBe, anti-HBc-IgM, and anti-HBcIgG antibodies, HBV-DNA, and prolidase levels were analyzed. The characteristics of asymptomatic HBV carriers were defined as follows: the presence of HBsAg in the serum for >6 months, HBeAg negative, anti-HBe positive, HBV DNA level of <2000 IU/mL, and persistently normal ALT/AST levels (<40 U/L). Asymptomatic HBV carriers were followed up for at least one year by analyzing their HBV-DNA and ALT levels every three months. From the group of patients with documented evidence of HBsAg positivity for >6 months and HBeAg (–) or (+), those with normal (<40 U/L) or high ALT levels and an HBV-DNA level of >2000 IU/mL were considered to have CHB infection.

HEALTHY CONTROL SUBJECTS

Prolidase level was determined using the serum samples of 27 normal healthy individuals. ANA, AMA, ASMA, HBsAg, anti-HCV, anti-HIV, and anti-HDV results of the control group were negative, and hepatic function tests, FBG, total cholesterol, triglyceride and CBC values were within normal ranges.

PROLIDASE ANALYSIS

Collection of blood samples and liver biopsy were performed on the same day for the patients. The blood samples were kept at room temperature for 30–60 min, centrifuged at 3000–5000 rpm for 10–15 min to obtain the serum samples, and stored in a freezer at –80°C for prolidase analysis. Approximately six months later, the serum samples were removed from the freezer. Prolidase level was measured using ELISA as described earlier in the literature [10].

HISTOLOGICAL EXAMINATION

Both asymptomatic HBV carriers and patients with CHB underwent ultrasonography-guided percutaneous biopsy of the right lobe of the liver. A quick-cut and 16-gauge cutting needle (GALLINI, Italy) was used for this procedure. The lengths of the biopsy samples were 1.5–2.0 cm with 7 or more available portal areas. Liver biopsy samples were examined in a pathology laboratory by a single pathologist. Histopathological examination was performed in accordance with the modified Ishak scoring system. It was agreed that samples with a histological activity index (HAI) of <4 and a fibrosis score of <2 would be considered as a mild histological lesion; HAI = 4–8 and fibrosis score = 2–3 would be considered as a moderate histological lesion; and HAI >8 and fibrosis score >3 would be considered as severe histological lesion.

SEROLOGY

In all the patients, anti-HCV, anti-HDV, anti-HIV, HBsAg, HBeAg, and anti-HBe tests were performed using ELISA, whereas HBV-DNA tests were performed using quantitative polymerase chain reaction (Amplicor HBV Monitor test, Roche Diagnostic Systems, Inc., Branchburg, NJ) (sensitivity 60 IU/mL).

STATISTICAL ANALYSIS

Statistical analyses were performed using a Statistical Package for the Social Sciences (SPSS) software [SPSS V16.0 (Inc., Chicago, IL, USA)]. For comparing normally distributed variables in two independent groups, we used Student's t-test, and for comparing abnormally distributed variables in two independent groups, we used the Mann–Whitney U test. Numerical data from more than two independent groups were analyzed by the Kruskal Wallis test. A cut-off value was determined for numerical variables using Receiver Operating Characteristic (ROC) curve analysis. Spearman's rho test was used to identify the relationship between serum prolidase level. Descriptive statistics were presented as mean ±standard deviation. A p-value <0.05 was considered statistically significant.

RESULTS

PATIENT CHARACTERISTICS

Demographic information and laboratory results of 152 cases were analyzed. The cases were divided into three groups: healthy volunteers (n = 27), asymptomatic HBV carriers, (n = 65) and active CHB patients (n = 60). Liver biopsy and histopathological examinations were performed in asymptomatic HBV carriers and patients with CHB.

We have evaluated some information regarding the groups such as; age, gender, CBC, total bilirubin, direct bilirubin, total cholesterol, triglyceride, FBG and urea, however we didn't observe any differences. There was no difference in asymptomatic HBV carriers and active CHB patients, in the abdominal ultrasonography in terms of steatosis grade. HBV-DNA levels were significantly lower in asymptomatic HBV carriers compared to active CHB patients (p=0.001). AST and ALT levels were significantly higher in active CHB patients than in asymptomatic HBV carriers and in healthy controls (p = 0.001). Albumin levels were significantly higher in healthy controls than in asymptomatic HBV carriers and in active CHB patients (p = 0.001). The results are presented in **Table 1.**

Serum prolidase level was significantly higher in active CHB patients compared to that in asymptomatic HBV carriers and significantly higher in asymptomatic HBV carriers compared to that in healthy controls (p=0.001) Figure 1.

Liver histology in asymptomatic HBV carriers and patients with chronic hepatitis B

While evaluating histopathological findings in asymptomatic HBV carriers and patients with chronic hepatitis B, the patients were classified according to HAI scores and degree of fibrosis.

The number of patients with moderate and severe HAI scores (≥4/18) was 13 (20%), and the number of patients with moderate and severe fibrosis (≥2/6) was 10 (15%) in asymptomatic HBV carriers. Serum prolidase level was significantly lower in asymptomatic carriers with mild fibrosis compared to those with moderate-to-severe fibrosis (p=0.001).

The number of patients with moderate and severe HAI scores (≥4/18) was 38 (63%), and the number of patients with moderate and severe fibrosis (≥2/6) was 52 (86%) in active CHB patients. Serum prolidase level was significantly lower in active CHB patients with mild fibrosis compared to those with moderate-to-severe fibrosis (p=0.001) **Table 1.**

Effectivity of prolidase in differentiating asymptomatic HBV carriers from patients with HBeAg- negative CHB

Patients with active CHB were divided into two groups: HBeAg-negative (n=45) and HBeAg-positive (n=15). Hundred and ten patients with HBeAg-negative were divided into 2 groups as asymptomatic HBV carriers (n=65) and HBeAg-negative CHB patients (n=45). Patients in these 2 groups were compared. Prolidase level was significantly lower in asymptomatic HBV carriers compared to that in HBeAg-negative CHB patients (p=0.001) **Table 2.**

Serum prolidase level and its diagnostic efficiency in differentiating asymptomatic HBV carriers and HBeAg-negative CHB patients were investigated. ROC analysis was performed. The diagnostic efficiency of serum prolidase level was found to be strong in asymptomatic HBV carrier and HBeAg-negative CHB patient groups (0.707, 95% CI (0.612 – 0.790). The cut-off value of prolidase level was determined as 751.15 U/L by this analysis. When prolidase level reached 751 U/L, sensitivity was found to be 72%, specificity to be 63%, positive likelihood ratio to be 1.97, and negative likelihood ratio to be 0.43. The diagnostic efficiency of serum prolidase level in asymptomatic HBV carrier and HBeAg-negative CHB patient groups is shown in **Figure 2.**

PROLIDASE IN HBEAG- NEGATİVE CHB

In our study, 45 patients with HBeAg-negative CHB were divided into two groups according to low and high prolidase levels in relation to 751 U/L after the cut-off value of serum prolidase level was determined as 751 U/L. There was no difference between the two groups in terms of age, gender, BMI, ALT, AST, HBV-DNA, albumin, FBG, triglyceride levels. HAI scores and fibrosis stage was significantly lower in patients with a prolidase level of <751 U/L (p=0.02, p=0.004) **Table 3.**

Correlation between serum markers of liver inflammation and histopathological findings with prolidase

Correlation analyses were performed between serum prolidase levels, levels of ALT and HBV-DNA; HAI; and the severity of fibrosis in asymptomatic HBV carriers and CHB patients in this study. A strong positive correlation was observed between serum prolidase level and the severity of fibrosis in asymptomatic HBV carriers (r=0.603, p=0.000) **Figure 3**. İn asymptomatic HBV carriers, there was no correlation between serum prolidase levels and ALT (r=0.109, p=0.30), however, a moderately positive correlation was noted between serum --prolidase levels and HAI scores (r=0.483, p=0.00). A weak positive correlation was determined between serum prolidase levels and HBV DNA in asymptomatic HBV carriers (r=0.26, p=0.8).

A moderately positive correlation was observed between serum prolidase level and the severity of fibrosis in the active CHB patients

(r=0.428, p=0.001) **Figure 4**. A weak positive correlation was determined between serum prolidase level and ALT levels and HAI scores in patients with active CHB [(r=0.335, p=0.009), (r=0.269, p=0.003)]. A moderately positive correlation was determined between serum prolidase levels and HBV DNA in patients with active CHB (r=0.424, p=0.001).

DISCUSSION

Majority of patients with CHB are asymptomatic and several recent studies have shown that being an asymptomatic HBV carrier is not harmless as presumed earlier [11]. A recent study has demonstrated that active disease and even cirrhosis may be observed in patients although their ALT and HBV-DNA levels are normal [12].

The current problem related to asymptomatic HBV carriers is how they can be identified successfully and followed up. Chu et al. [5] followed up 1965 asymptomatic HBV carrier patients for an average of 11.5 years and determined that reactivation had developed in 314 (15%). Cirrhosis developed in subsequent years in 47 of these patients, and without reactivation in 10 of 1651 patients who remained as carriers [5]. In a study performed by Yu et al. [13], 1506 asymptomatic HBV carrier patients were followed up for an average of 7.1 years, and cirrhosis was determined in 89 cases and HCC in 16 cases. Ter Borg et al. [14] performed liver biopsies in 174 asymptomatic carrier patients in Holland and determined cirrhosis in 10% of those patients. Al-Mahtab et al. [15] in their study recently performed liver biopsies on 141 patients who were followed up for being asymptomatic carriers and determined severe hepatic fibrosis (fibrosis score >3) in 12%. In their study including 95 asymptomatic carriers, Ikeda et al. [16] determined ≥2/6 fibrosis in 35% patients, ≥3/6 fibrosis in 12%, and cirrhosis in 6%. In our study, the ratio of moderate-to-severe fibrosis (≥2/6) in asymptomatic HBV carriers was determined to be 15% and HAI (≥4/18) to be 20%. These results are in accordance with the literature and prompted us to conclude that the disease in asymptomatic HBV carriers is not dormant or harmless, and either a non-invasive method determining fibrosis or histopathological examinations should be performed in carriers with a certain disease age.

Prolidase is involved in breaking down iminodipeptides formed after collagen degradation. Several studies have shown that there is an association between prolidase enzyme level and fibrotic activity. First, Myara et al. [5] determined high plasma prolidase activity in chronic liver disease patients and reported that serum prolidase activity increases in parallel with the degree of fibrosis [6-8,17]. In our study, serum prolidase level was significantly higher in CHB patients compared to asymptomatic carriers and was significantly higher in asymptomatic carriers compared to healthy volunteers. Serum prolidase level was significantly higher in CHB patients with moderate-to-severe fibrosis and asymptomatic carriers compared to patients with mild fibrosis. These results have helped us conclude that prolidase, due to its effects on collagen degradation and direct association with fibrotic tissue development, may be valuable in the long-term follow-up process of chronic liver patients and in monitoring their response to treatment.

In three separate studies supporting this opinion, it has been shown that serum prolidase activity is a useful marker in evaluating liver fibrosis and prolidase level increases in parallel with the increase in the stage of fibrosis [6-8]. The difference between our study and previously performed studies is the performance of liver biopsy of asymptomatic carriers and their comparison with the biopsy results of CHB patients and healthy volunteers. In our study, prolidase level was significantly higher in patients with HBeAg-negative CHB patients compared to asymptomatic HBV carriers. The diagnostic efficiency of serum prolidase in differentiating HBeAg-negative CHB patients from asymptomatic HBV carriers was also examined in our study. Accordingly, the diagnostic efficiency of prolidase was found to be strong, and 45 patients with HBeAg-negative active CHB were divided into two groups according to their low and high prolidase value of 751 U/L after determining the cut-off value of prolidase as 751 U/L. HAI and the stage of fibrosis were significantly higher in patients with a prolidase level of >751 U/L.

Kayadibi et al. [18] investigated the diagnostic value of serum prolidase activity by determining the histological changes in the liver in patients with non-alcoholic steatohepatitis (NASH) and their results are comparable with those reported by us. In their study, the serum prolidase level of patients with steatohepatitis was significantly increased compared to that in the control group and the group with simple steatosis and it correlated with the stage of fibrosis and the enzyme activity score [18]. Another study investigating the association between prolidase activity and ultrasonic staging in patients with NASH, it was determined that as the grade of steatosis on ultrasonography increases, serum prolidase activity also increases, and this condition has been linked to the possibly increased fibrotic activity [19].

All these studies have demonstrated that determining prolidase level may be an important test for diagnosing fibrosis. However, none of the non-invasive tests is a safe indicator as histological evaluation. Today, liver biopsy is still the gold-standard method for the evaluation of necroinflammation and liver fibrosis. However, in cases where a biopsy cannot be performed and where repeated biopsy is required, the use of these non-invasive tests may be useful.

In conclusion, the serum prolidase level is associated with fibrosis in CHB patients. It may be a useful non-invasive test in discriminating asymptomatic HBV carriers and HBeAg- negative CHB patients. Prospective studies with large populations requiring long-term follow up are required to determine whether prolidase, which has been determined to exhibit high sensitivity for being an indicator of fibrosis, can be a serum marker.

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Conflict of Interest: No conflict of interest was declared by the authors.

Disclosure: We have no relevant financial or nonfinancial relationships to disclose.

Tables (1-3) Table 1 Clinical and demographic information of asymptomatic HBV carriers, active CHB patients, and healthy

Variables	Healthy Volunteers (n=27)	Asymptomatic HBV Carriers (n=65)	Active CHB patients (n=60)	P Values
Age (years)	36.81 ±10.70	34.38±9.64	35.23±12.22	NS
Gender, female (%)	16 (59)	34 (52)	28 (46)	NS
BMI,(kg/m^2)	25.00 ± 1.83	23.26 ± 2.07	24.43± 3.53	**0.001**^{a,b}
WBC,x10ł/µL	6.53 ± 1.6	6.86 ± 1.75	6.83 ± 1.53	NS
Platelet,×10ł/µL	221.40±44.08	235.60 ± 60.22	230.05 ± 59.46	NS
ALT, U/L	29.33±15.23	24.78±12.20	65.10±65.15	**0.001,**^{b,c}
AST, U/L	21.18±5.83	21.64±7.02	41.10±35.80	**0.001**^{b,c}
ALP, U/L	48.88±25.48	76.47±29.42	86.25±31.53	**0.001**^{a,c}
GGT, U/L	27.11±12.40	22.55±12.52	37.96±28.25	**0.001**^{b,c}
Total bilirubin, mg/Dl	0.55 ± 0.24	0.64 ± 0.38	0.72 ± 0.51	NS
Total bilirubin, mg/dL	0.25 ± 0.16	0.25 ± 0.19	0.30 ± 0.33	NS
Albumin, g/Dl	4.18 ± 0.31	3.94 ± 0.42	3.96 ± 0.36	**0.001**^{a,c}
FBG, mg/dL	88.70 ± 11.49	90.93 ± 12.08	91.21 ± 13.63	NS

HBV DNA, ×10ł IU/mL		0.561±0.554	31256±888088	**0.001**
Serum Prolidase, U/L	529.40±74.73	732.99±124.70	819.92±123.74	**0.001**[a,b]
HAI, (mild/moderate/severe)		52/13/0	22/36/2	**0.001**
Fibrosis, (mild/moderate/severe)		55/9/1	8/42/10	**0.001**
USG,hepatosteatoz, (N/G1/G2/G3)		49/10/6/0	49/8/3/0	NS

Data are presented as mean ± standard deviation, number and percentage, and number, where appropriate.
CHB, chronic hepatitis B; **HBV**, hepatitis B virus; **NS**, not significant; **BMI**, body mass index, **FBG**, fasting blood glucose; **WBC**, White blood count; **ALT**, alanine aminotransferase; **AST**, aspartate aminotransferase; **ALP**, alkaline phosphatase; **GGT**, gamma-glutamyl transpeptidase; **G**, grade, **HBV-DNA**,hepatitis B virus deoxyribonucleic acid; **HAI**, histological activity index. **a**: Comparison of healthy volunteers with asymptomatic HBV carriers. **b**: Comparison of asymptomatic HBV carriers with chronic HBV patients. **c**: Comparison of healthy volunteers with chronic HBV patients

Table 2 Clinical and laboratory data of asymptomatic HBV carriers and HBeAg-negative with active CHB patients.

Variables	Asymptomatic HBV carriers (n=65)	HBeAg-negative CHB patients (n=45)	P values
Age	34.38±9.64	35.20±12.25	NS
Gender, woman (%)	34 (52)	21 (46)	NS
BMI, (kg/m¸)	23.26±2.07	24.46±3.70	0.03
ALT, U/L	24.78±12.20	58.82±59.99	0.001
AST, U/L	21.64±7.02	36.37±28.18	0.001
GGT, U/L	22.55±12.52	38.13±29.01	0.001
Albumin, g/dL	4.18±0.31	4.00±0.38	0.007
HBV DNA, ×10ł IU/mL	561.66 ±554.48	15758±53677.72	0.001
Serum Prolidase, U/L	732.99±124.70	824.32±115.06	0.001
HAI,(mild/moderate/severe)	52/13/0	20/23/2	0.001
Fibrosis,(mild/moderate/severe)	55/9/1	7/33/5	0.001

Data are presented as mean±standard deviation, number and percentage, and number, where appropriate. **CHB**, chronic hepatitis B; **HBV,** hepatitis B virus; **NS**, not significant; **BMI**, body mass index, **FBG**, fasting blood glucose; WBC, White blood count; **ALT**, alanine aminotransferase; **AST**, aspartate aminotransferase; **ALP**, alkaline phosphatase; **GGT**, gamma-glutamyl transpeptidase; **G**, grade, **HBV-DNA**,hepatitis B virus deoxyribonucleic acid; **HAI**, histological activity index.

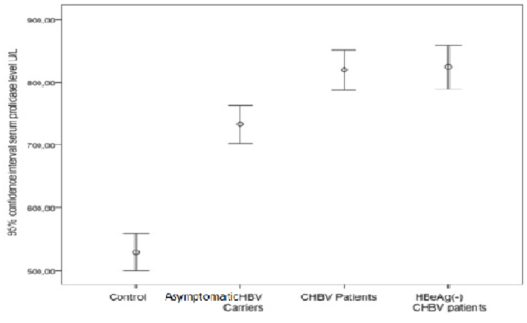
Table 3 Clinical and laboratory characteristics of patients with HBeAg-negative active CHB according to serum prolidase levels

	Serum Prolidase level		
Variables	**<751 U/L (n=12)**	**>751 U/L (n=33)**	**P values**
Age	31.91±10.84	36.39±12.66	NS
Gender, female (%)	5 (41)	16 (48)	NS
BMI, (kg/m¸)	24.83±2.75	24.33±4.02	NS
HBV DNA, ×10ł IU/mL	16416.16±4848.43	19891.52±5585.07	NS
ALT, U/L AST, U/L HAI,(mild/moderate/severe)	58.25 ± 72.57 33.00 ± 26.60 4/7/1	59. 03± 56.01 37.60 ± 29.03 4/18/11	NS NS 0.025
Fibrosis,(mild/moderate/severe)	5/6/1	2/12/9	0.004

Data are presented as mean±standard deviation, number and percentage, and number, where appropriate.
CHB, chronic hepatitis B; **HBV**, hepatitis B virus; **NS**, not significant; **BMI**, body mass index, **FBG**, fasting blood glucose; **WBC**, White blood count; **ALT**, alanine aminotransferase; **AST**, aspartate aminotransferase; **ALP**, alkaline phosphatase; **GGT**, gamma-glutamyl transpeptidase; **G,** grade, **HBV-DNA**,hepatitis B virus deoxyribonucleic acid; **HA**I, histological activity index.

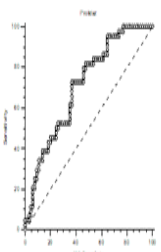
FIGURES (1-4)

Figure 1. The serum prolidase level in experimental groups (control group (n=27), asymptomatic HBV carriers (n=65), HBeAg-negative CHB patients (n=45), and active CHB patients (n=60)



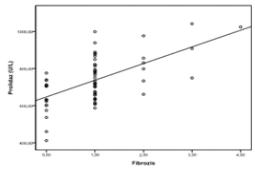
CHB: chronic hepatitis B; HBV: hepatitis B virus

Figure 2. The diagnostic efficiency of serum prolidase value in asymptomatic HBV carriers and HBeAg-negative CHB patients. The area under the curve is 0.707, %95 CI (0.612 – 0.790), in receiver operating characteristic analysis.



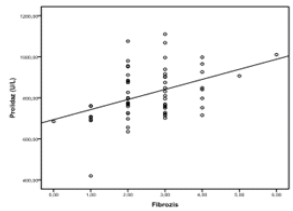
CHB: chronic hepatitis B; HBV: hepatitis B virus

Figure 3. Correlation between serum prolidase and fibrosis in asymptomatic HBV carriers



HBV: hepatitis B virus

Figure 4. Correlation between serum prolidase and fibrosis in CHB patients.



CHB: chronic hepatitis B

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