High Prevalence and Risk Factors of Significant Hepatic Fibrosis in Omani Patients with HBeAg-negative Chronic Hepatitis B Virus Infection: A Retrospective Study

Halima H. Al-Shuaili[1], Bushra Al Mashikhi[2], Ahmed Al Sinani[2] and Said A. Al-Busafi[3]*

[1]Department of Medicine, Armed Forces Hospital, Muscat, Oman

[2]College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

[3]Department of Medicine, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

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*Corresponding author: busafis@squ.edu.om

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Abstract

Objective: Hepatic fibrosis remains a potential complication for hepatitis B e antigen (HBeAg)-negative chronic hepatitis B virus (HBV) infection, also termed inactive HBV carriers, despite their generally favorable prognosis. This study aimed to determine the prevalence of significant fibrosis and associated risk factors among Omani patients with HBeAg-negative chronic HBV infection.

Methods: A retrospective study was conducted on 200 Omani inactive HBV carriers visiting a tertiary hospital in Muscat, Oman, between January 2017 and December 2018. Significant fibrosis (stage F2 or higher) was identified using two-dimensional shear-wave elastography, with baseline clinical, laboratory, and radiological data analyzed for associations.

Results: Among the total sample, 53% were male, with a mean age of 44.6 ± 9.3 years. The prevalence of significant fibrosis was 20% (n = 40), with male gender ($p = 0.007$), age ≥60 years ($p = 0.024$), and fatty changes in liver ultrasound ($p = 0.044$) identified as independent risk factors.

Conclusions: These findings underscore the importance of periodic assessment and monitoring of inactive HBV carriers, particularly those with risk factors such as male gender, older age, and the presence of fatty liver, for the progression of fibrosis.. Utilizing non-invasive tests for fibrosis can aid in early detection and management, thereby improving patient outcomes. Further research is recommended to validate these findings and explore the inactive HBV carrier stage and its complications in Oman.

Keywords: Hepatitis B e antigen-negative chronic hepatitis B virus infection, Inactive Hepatitis B Virus carriers; Hepatic Fibrosis; Prevalence; Risk Factors; Oman.

Introduction

Chronic hepatitis B Virus (HBV) Infection presents a pressing global health issue, leading to substantial morbidity and mortality.[1-3] Globally, an estimated 257.5 million individuals live with chronic HBV infection, constituting 3.2% of the population, with 555,000 deaths annually attributed to HBV-related sequelae.[2,3] The course of chronic HBV infection varies among patients, resulting in a wide spectrum of disease severity.[4] A large portion of HBV-infected patients are classified as inactive HBV carriers, also known as those with hepatitis B e antigen (HBeAg)-negative chronic HBV infection.[5]

According to the 2017 clinical practice guidelines of the European Association for the Study of the Liver (EASL), an inactive carrier state is identified by the absence of HBeAg and the presence of the HBe antibody (anti-HBe), along with consistently normal alanine aminotransferase (ALT) levels, coupled with low or undetectable serum levels of HBV DNA (<2,000 IU/mL). However, serum HBV DNA levels may fluctuate up to 20,000 IU/mL in some cases.[6] Inactive carriers generally have an excellent prognosis compared to other HBV-infected patients.[5,7] However, their evolving clinical profile necessitates regular monitoring for HBV reactivation. Additionally, although rare, life-threatening complications such as hepatocellular carcinoma (HCC) and cirrhosis can occur, underscoring the importance of frequent screening in this subset of patients.[8,9]

Furthermore, antiviral therapy is typically withheld from these individuals due to their ALT levels falling within the normal range and minimal hepatic damage being observed, leading to uncertainty regarding the appropriate timing for treatment initiation.[10,11] Consequently, untreated patients face an increased risk of progression to cirrhosis and HCC, highlighting the critical need for early identification of fibrosis and close surveillance of at-risk individuals, necessitating further studies.[12-16] While liver biopsy remains the gold standard for evaluating hepatic fibrosis, its invasive nature renders it suboptimal for routine monitoring of inactive HBV carriers.[14] Therefore, international guidelines recommend non-invasive techniques such as serum markers and elastography for the initial staging and monitoring of fibrosis.[16]

In Oman, where HBV endemicity ranges from approximately 2% to 7%, research on inactive HBV carriers and their associated complications is notably lacking.[1,17,18] This study aims to fill this gap by investigating the prevalence of significant hepatic fibrosis and its related risk factors among Omani inactive HBV carriers receiving care at Sultan Qaboos University Hospital (SQUH), a tertiary healthcare facility in Muscat, the capital of Oman. As one of the pioneering studies focusing specifically on inactive HBV carriers in this region, the findings from this research are anticipated to provide valuable insights into the prognosis of this population, potentially leading to improvements in overall patient care and outcomes.

Methods

This single-center study focused on 200 adult Omani patients (aged ≥13 years) diagnosed as inactive HBV carriers who underwent two-dimensional shear-wave elastography (2D SWE) at the adult hepatology clinic of SQUH between January 2017 and December 2018. According to the 2017 EASL guidelines, an inactive carrier state was defined by the presence of hepatitis B surface antigen (HBsAg) positivity, HBeAg negativity, anti-HBe positivity, persistently normal ALT levels (<40 IU/mL), and undetectable or low serum HBV DNA levels (<20,000 IU/mL).[6] Patients with major missing data, pregnant women, and those with concurrent chronic liver diseases such as hepatitis C, hepatitis D, human immunodeficiency virus infections, autoimmune hepatitis, cholesteric liver disease, alpha-1 antitrypsin deficiency, Wilson's disease, or hemochromatosis were excluded from the study.

The hospital's healthcare information system was utilized to gather data from the patients' electronic medical records (TrakCare, InterSystems Corp., Cambridge, Massachusetts, USA). Information was collected on potential risk factors for fibrosis development. Demographic and anthropometric factors included age, gender, marital status, place of residence, and body mass index (BMI). Family-related factors assessed the presence of a family history of HBV, HCC, or cirrhosis. Additionally, comorbidities such as type 2 diabetes mellitus (T2DM), sickle cell disease (SCD), thalassemia, dyslipidemia, renal disease, heart failure, fatty liver disease, and malignancy were considered. At the same time, nosocomial factors encompassed a history of hemodialysis, organ transplantation, surgery, and blood transfusions. Lastly, various biochemical parameters were assessed, including platelet and white blood cell counts, and levels of ALT, aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), albumin, total bilirubin, and alpha-fetoprotein.

All patients underwent simultaneous 2D SWE and liver ultrasound imaging under non-fasting conditions using the GE Logiq E9 2.0 with XDClear multi-purpose ultrasound system (GE Healthcare, Milwaukee, Wisconsin, USA). Changes in echotexture were assessed to diagnose cirrhosis and fatty liver disease and to classify the degree of hepatic fibrosis. Liver stiffness measurements (LSMs) of ≤7.1, >7.1–7.8, >7.8–8.0, >8.0–11.5, and >11.5 kPa corresponded to stages F0, F1, F2, F3, and F4, respectively, with stage F2 and higher indicating significant hepatic fibrosis.[19] Subsequently, depending on the presence or absence of significant hepatic fibrosis, the study population was divided into patients with or without significant hepatic fibrosis [Figure 1]. Comparisons between groups were conducted to determine potential risk factors for the development of significant hepatic fibrosis in inactive HBV carriers.

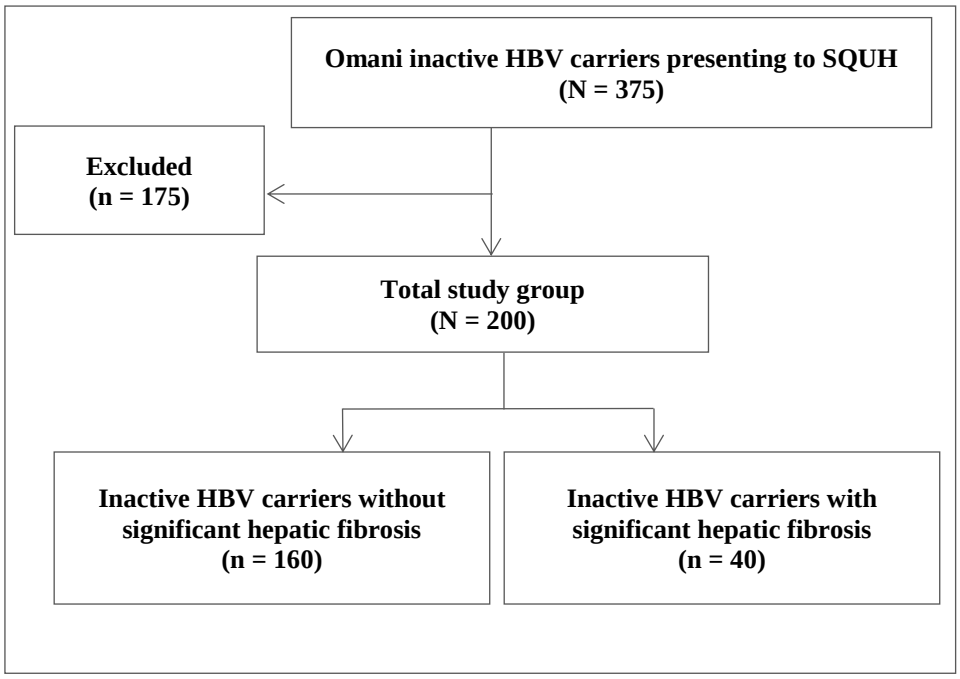


Figure 1: Flow diagram of the study population. HBV= hepatitis B virus; SQUH = Sultan Qaboos University Hospital.

Data analysis was performed using IBM SPSS Statistics software, version 26.0 (IBM Corp., Armonk, New York, USA). A Chi-squared test was performed to assess associations between significant hepatic fibrosis development and potential risk factors. The normality of data distribution for continuous variables was evaluated using the Kolmogorov-Smirnov test. Parametric variables were analyzed using a Student's t-test, while non-parametric variables were assessed using the Mann-Whitney U test. A p-value of <0.05 was considered statistically significant. Multivariate adjusted analysis utilized logistic regression, with variables exhibiting a p-value of <0.25 in the crude analysis included in the regression model.

Ethical approval for this study was obtained from the Medical Research and Ethics Committee of the College of Medicine and Health Sciences, Sultan Qaboos University (MREC #1548). Additionally, permission to access patients' medical records was granted by the Directorate of Hospital Information Systems at SQUH. All study procedures were conducted in accordance with the ethical standards outlined in the revised Declaration of Helsinki.

Results

A total of 200 out of 375 Omani inactive HBV carriers who were followed up at the SQUH adult hepatology clinic during the study period met the inclusion criteria [Figure 1]. Of these, 106 (53%) were male and 94 (47%) were female, and the mean age was 44.6 ± 9.3 years (range: 31–79 years). Most (61%) patients fell within the age group of 40 to 60 years, and there were no patients under 30 years of age in the cohort [Table 1]. No patients developed decompensated liver cirrhosis or HCC.

Table 1: Baseline characteristics of patients with HBeAg-negative chronic HBV infection and associations with significant hepatic fibrosis*.

Parameter	Total, n = 200 (%)	With significant hepatic fibrosis, n = 40 (%)	Without significant hepatic fibrosis, n = 160 (%)	OR (95% CI)	*p*-value
Age group in years					
30–40	63 (31.5)	9 (14.3)	54 (85.7)	5.618 (2.347–13.450)	0.003
40–60	122 (61.0)	23 (18.9)	99 (81.1)		

>60	15 (7.5)	8 (53.3)	7 (46.7)		
Gender					
Male	106 (53.0)	33 (31.1)	73 (68.9)	1.114 (0.451–2.755)	<0.001
Female	94 (47.0)	7 (7.4)	87 (92.6)		
BMI of >25 kg/m^2	117 (58.5)	22 (18.8)	95 (81.2)	0.786 (0.152–4.074)	1.0
T2DM	21 (10.5)	7 (33.3)	14 (66.7)	1.074 (0.336–3.432)	0.145
Dyslipidemia	19 (9.5)	4 (21.1)	15 (78.9)	-	1.0
HTN	17 (8.5)	9 (52.9)	8 (47.1)	5.516 (1.974–15.416)	0.002
NAFLD	115 (57.5)	29 (25.2)	86 (74.8)	2.268 (1.060–4.853)	0.049
Renal disease	5 (2.5)	3 (60)	2 (40)	6.405 (1.033–39.718)	0.056
Family history					
HBV infection	58 (29.0)	9 (15.5)	49 (84.5)	1.150 (0.230–5.762)	0.413
HBV-related cirrhosis	22 (11.0)	2 (9.1)	20 (90.9)	2.212 (0.828–5.911)	0.259
HBV-related HCC	9 (4.5%).	2 (22.2)	7 (77.8)	0.366 (0.082–1.635)	1.0
Hemoglobin in g/dL†	13.09 ± 1.81	13.76 ± 1.66	12.92 ± 1.81	-	0.009
Platelet count × 10^9/L†	243.5 ± 67.8	218.45 ± 70.19	249.73 ± 65.93	-	0.009
White blood cell count × 10^9/L†	5.50 ± 1.93	5.23 ± 2.06	5.56 ± 1.90	-	0.15
ALT in U/L†	22.5 ± 11.5	26.43± 13.7	21.52± 10.72	-	0.027
AST in U/L†	19.7 ± 6.2	20.95 ± 7.0	19.42± 5.95	-	0.079
ALP in U/L†	66.5 ± 19.2	73.22 ± 26.45	64.81 ± 16.59	-	0.061
Albumin in g/L†	44.9 ± 3.4	45.25± 3.44	44.8 ± 3.41	-	0.52
Total bilirubin in µmol/L†	9 ± 6.5	9.95 ± 5.62	8.84 ± 6.73	-	0.063
AFP in ng/mL†	2.52 ± 1.93	2.26 ± 1.70	2.59± 2.10	-	0.979
HBV DNA of <2,000 IU/mL	167 (83.5)	34 (20.4)	133 (79.6)	-	0.775

HBeAg = hepatitis B e antigen; CHB = chronic hepatitis B; HBV= hepatitis B virus, OR = odds ratio; CI = confidence interval; BMI = body mass index; T2DM = type 2 diabetes mellitus; HTN = hypertension; NAFLD = nonalcoholic fatty liver disease; HBV = hepatitis B virus; HCC = hepatocellular carcinoma; ALT = alanine transaminase; AST = aspartate aminotransferase; ALP = alkaline phosphatase; AFP = alpha-fetoprotein.
**Defined as liver stiffness measurements of >7.8 kPa. †Expressed as mean ± standard deviation.*

The distribution of patients across liver fibrosis stages, as determined by LSMs, was as follows: 142, 18, three, 31, and six patients were classified as stage F0, F1, F2, F3, and F4, respectively. Overall, a total of 40 patients (20%) developed significant hepatic fibrosis, defined as stage F2 fibrosis or higher [Figure 2].

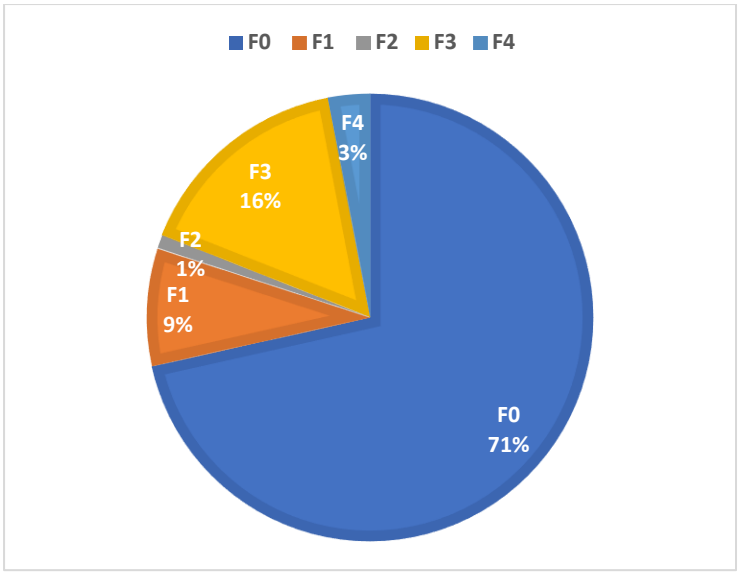
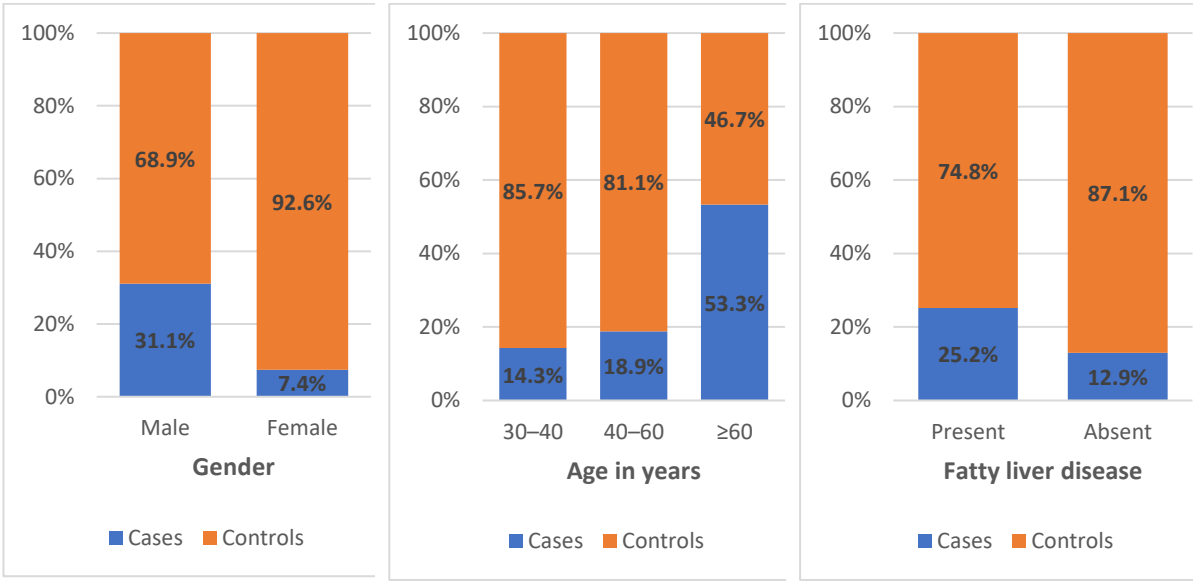


Figure 2: Fibrosis staging among Omani patients with HBeAg-negative chronic HBV infection (n = 200). *HBeAg = hepatitis B e antigen; HBV = hepatitis B Virus.*

Approximately 58.5% of the cohort were classified as overweight, denoted by a BMI exceeding 25 kg/m^2. Furthermore, 21 subjects (10.5%) presented with a diagnosis of T2DM, while 115 individuals (57.5%) had received a diagnosis of non-alcoholic fatty liver disease (NAFLD) [Table 1]. Several risk factors were significantly associated with the presence of significant hepatic fibrosis in the studied population [Table 1 and Figure 3].



(A) **(B)** **(C)**

Figure 3: Associations between significant hepatic fibrosis* and **(A)** gender (p <0.001), **(B)** age (p = 0,003), and **(C)** fatty liver disease (p = 0.049) among Omani patients with HBeAg-negative CHB infection (n = 200). HBeAg = hepatitis B e antigen; CHB = chronic hepatitis B. **The case group included those with significant hepatic fibrosis (defined as stage F2 or higher; n = 40), while the controls included those without significant fibrosis (n = 160).*

Male patients exhibited a higher prevalence of significant fibrotic changes than females, with 31.1% of males and 7.4% of females affected [Figure 3A] The likelihood of significant fibrosis development was significantly greater in males than females (odds ratio [OR] = 5.618, 95% confidence interval [CI] = 2.347–13.450; p <0.001). Similarly, patients aged ≥60 years showed a higher prevalence of stage F2 or higher fibrosis (53.3%) compared to those aged 30–40 years (14.3%) and 40–60 years (18.9%) [Figure 3B]. Univariate analysis revealed that patients aged ≥60 years had a five-fold increased risk of developing significant fibrosis compared to other age groups (OR = 5.618, 95% CI = 2.347–13.450; p = 0.003) [Table 1]. Hypertension (OR = 5.516, 95% CI = 1.974–15.416; p = 0.002) and NAFLD (OR = 2.268, 95% CI = 1.060–4.853; p = 0.049) were significantly correlated with significant liver fibrosis [Figure 3C]. Notably, 52.9% of hypertensive patients and 25.2% of those with NAFLD developed stage F2 or higher fibrosis [Table 1].

Certain biochemical parameters displayed significant associations with significant fibrosis. Specifically, patients with hepatic fibrosis exhibited higher hemoglobin levels than those without fibrosis (13.76 ± 1.66 vs. 12.92 ± 1.81 g/dL; p = 0.009). Moreover, ALT levels positively correlated with fibrosis (p = 0.027). Conversely, patients with stage F2 or higher fibrosis had a notably decreased mean platelet count compared to those without (218.45 ± 70.19 vs. 249.73 ± 65.93 × 10^9/L; p = 0.009) [Table 1] The multivariate regression analysis involving all participants unveiled independent associations of gender, age, and NAFLD with significant hepatic fibrosis as determined by LSMs [Table 2].

Table 2: Multivariate analysis of risk factors for the development of significant fibrosis among Omani patients with HBeAg-negative chronic HBV infection (n = 200).

Risk factor	OR (95% CI)	*p*-value
Age group in years	-	0.072
Age 40–60 years	1.329 (0.478–3.695)	0.585
Age >60 years	10.900 (1.371–86.631)	0.024
Gender	6.568 (1.673–25.785)	0.007
HTN	1.659 (0.248–11.093)	0.601
NAFLD	2.650 (1.025–6.855)	0.044
T2DM	0.360 (0.066–1.977)	0.24
Chronic kidney disease	6.538 (0.499–85.592)	0.152
Hemoglobin level	0.939 (0.678–1.300)	0.703
Platelet count	0.993 (0.986–1.000)	0.06
ALT level	1.016 (0.979–1.055)	0.404
ALP level	1.016 (0.996–1.037)	0.117
Total bilirubin level	0.989 (0.927–1.054)	0.728

HBeAg = hepatitis B e antigen; CHB = chronic hepatitis B; OR = odds ratio; CI = confidence interval; HTN = hypertension; NAFLD = nonalcoholic fatty liver disease; T2DM = type 2 diabetes mellitus; ALT = alanine transaminase; ALP = alkaline phosphatase.

Males exhibited a sixfold higher likelihood of significant fibrosis (OR = 6.568, 95% CI = 1.673–25.785; p = 0.007), while participants aged over 60 years were at a tenfold increased risk compared to those aged 30–40 years (OR = 10.900; 95% CI = 1.371–86.631; p = 0.024). Moreover, NAFLD emerged as an independent risk factor for hepatic fibrosis (OR = 2.650, 95% CI = 1.025–6.855; p = 0.044).

Discussion

Our study aimed to evaluate the prevalence of and associated factors for the development of significant hepatic fibrosis using non-invasive methods in individuals with HBeAg-negative chronic HBV infection (formally referred to as inactive HBV carriers). Among our cohort, a total of 40 patients, constituting 20% of the total sample size, were observed to manifest significant hepatic fibrosis, characterized by stage F2 fibrosis or advanced stages, as determined by LSMs. In the multivariate analysis, we identified male gender, age ≥60 years, and the presence of NAFLD as independent factors associated with significant fibrosis.

Previous studies from countries with low HBV endemicity have indicated that inactive HBV carriers generally demonstrate good prognoses, with a minimum prevalence of HBV-related hepatic fibrosis.[20-22] However, in high and intermediate endemic regions, the incidence of such complications tends to increase.[23-25] For example, a longitudinal, cross-sectional study from Taiwan, a country with an intermediate-to-high HBV prevalence, found that 16.1% of inactive HBV carriers experienced viral reactivation, while 15% developed hepatic fibrosis over the 25-year study period.[15] Another study from Egypt, an intermediate HBV prevalence country, reported that 20%

of inactive HBV carriers exhibited significant fibrotic changes as determined by liver biopsy.[24] To the best of our knowledge, the present study is the first to shed light on inactive HBV carriers and the prevalence of significant fibrosis, an important HBV-related complication, using non-invasive measures in Oman. The results, therefore, provide essential baseline data regarding the prevalence of and possible contributory risk factors for developing significant fibrosis in this subpopulation, which could help ensure early detection and optimal patient management.

The overall prevalence of significant fibrosis (20%) among Omani inactive HBV carriers identified in the current study aligns with findings reported in similar research conducted in intermediate HBV endemic areas (15–20%).[15,24] In contrast, studies from Saudi Arabia and Hong Kong have reported considerably higher prevalence rates for this complication (30.9% and 33.3%, respectively).[26,27] These variations in findings may be attributed to the use of liver biopsies instead of 2D SWE for hepatic fibrosis staging in the latter two studies. However, a study from Spain, another intermediate HBV-endemic country, indicated a prevalence rate of 25% using a non-invasive elastography technique similar to that utilized in the present study.[28] In this case, the discrepancy in findings might be explained by differences in the LSM criteria (>7.5 vs. >7.8 kPa), ultrasound equipment used, or the study duration.

The present study also investigated possible risk factors contributing to the development of significant fibrosis. Significant associations were observed between stage F2 or higher fibrosis and gender and age. Such findings are consistent with those reported in previous research from Taiwan and Bangladesh, in which both male gender and advanced age were significantly linked to the development of hepatic fibrosis in inactive HBV carriers.[15,29] On the other hand, studies from Spain and Hong Kong did not find significant associations with these two factors.[27,28] Moreover, while age was associated with the development of significant fibrosis in another Taiwanese study, the highest risk presented for patients aged 40–60 years rather than those aged ≥60 years.[30] Based on these findings, male and elderly patients with inactive HBV infections should be closely monitored to ensure early detection of hepatic fibrosis.

In a recent study conducted in Oman, intra-familial transmission emerged as the predominant mode of HBV transmission, while nosocomial transmission was found to be relatively uncommon.[18] Nonetheless, given the highly infective nature of HBV, both nosocomial and family-related factors were explored as possible risk factors for fibrotic changes in the present study. Although none of the family-related factors exhibited statistically significant associations, it is noteworthy that a quarter of inactive HBV carriers with stage F2 fibrosis or higher had a family history of either chronic HBV infection, HCC, or cirrhosis. The precise relationship between family history of HBV-related conditions and the development of significant fibrosis is uncertain; however, the frequency of the latter complication might be related to the fact that individuals with a family history of HBV are prone to infection earlier in life, resulting in a longer duration of infection and, consequently, an increased risk of advanced liver scarring.[18,24]

In the current study, among all evaluated comorbidities, only hypertension and fatty liver disease exhibited statistically significant associations with significant fibrosis. Notably, there is a paucity of research exploring the association between hypertension and its impact on inactive HBV carriers. Following a literature review, only one study from Spain was identified assessing these factors, reporting non-significant associations with both of these comorbidities.[28] The coexistence of fatty liver disease and chronic HBV infection has been studied extensively; however, except for the aforementioned Spanish study, there is a dearth of studies illuminating the prevalence of these conditions, specifically among inactive HBV carriers. A recent review highlighted the synergistic escalation of liver fibrosis risk when fatty liver disease coexists with chronic HBV infection, consistent with the observations of the present study.[30] The mechanism behind this is multifactorial, encompassing genetic, metabolic, and immune factors.[30]

Interest in non-invasive diagnostic tests for hepatic fibrosis in chronic liver diseases has grown considerably in recent decades. Such tests would mitigate the need for invasive procedures like liver biopsy and their associated complications, making regular follow-ups more convenient. As a result, researchers have explored the potential of different biochemical parameters as risk factors for fibrosis development and their efficacy in predicting such complications.[31,32] In particular, ALT stands out as a notable example, with previous research revealing a significant correlation between elevated ALT levels and fibrosis development, establishing it as a reliable predictor for such complications in inactive HBV carriers.[32,33] In contrast, conflicting findings have been reported in other research suggesting that ALT does not accurately predict significant liver injury.[24,27]

Nonetheless, ALT also demonstrated a positive significant correlation with significant fibrosis in the present study, as did hemoglobin level, while a negative correlation was observed for platelet count. A negative correlation with platelet count has also been reported in Chinese and Iranian populations, suggesting the potential utility of this factor for predicting hepatic fibrosis.[27,34] The association of hemoglobin with significant fibrosis lacks prior investigation, and the reasons for this association remain unclear. A recent study also identified a negative correlation between platelet count and the development of significant fibrosis in chronic Hepatitis B patients, supporting the current study's findings of this variable as an independent predictor of fibrosis.[35] Such findings support the effectiveness of implementing non-invasive biochemical parameters—especially platelet count—in the Omani population.

This study has several strengths. Firstly, it marks the first documentation in Oman of the prevalence of liver fibrosis among inactive HBV carriers. Additionally, it assessed a diverse array of risk factors, thereby providing a more holistic understanding of this particular subset of patients. However, we encountered certain limitations. The primary constraint stemmed from the restricted timeframe, which necessitated recruiting a limited sample size. A larger sample would have enhanced patient representation, thereby bolstering the reliability of comparisons between the case and control groups. Additionally, the retrospective nature of the study resulted in missing data related to crucial biochemical parameters, such as high-density and low-density lipoproteins, thyroxine, and thyroid-stimulating hormone. Consequently, analysis of these variables as potential risk factors was not possible. Finally, the current research focused on a single center in Muscat, potentially leading to an underestimation of the prevalence of significant fibrosis in the broader Omani population of inactive HBV carriers. Additional prospective studies in Oman, including a larger sample size, are recommended to address these limitations, further investigate the inactive HBV carrier stage and its related complications, and confirm causality for the associations identified in the present study.

Conclusion

In conclusion, this study highlights the high prevalence of significant hepatic fibrosis among Omani patients with HBeAg-negative chronic HBV infection. Our findings indicate that 20% of Omani inactive HBV carriers exhibit significant fibrosis, with male gender, age ≥60 years, and the presence of fatty liver on ultrasound being independent risk factors. These results underscore the critical need for periodic assessment and monitoring of inactive HBV carriers, particularly those with these risk factors. Utilizing non-invasive tests for fibrosis can help detect disease progression early, allowing for timely intervention and better patient outcomes. Routine biochemical parameters such as platelet count, hemoglobin, and ALT levels could serve as useful predictors of disease prognosis. The study provides valuable baseline data for understanding and managing significant fibrosis in this subpopulation, potentially aiding in early detection and optimal patient care. However, further research, including larger prospective studies, is recommended to validate these findings and comprehensively explore the inactive HBV carrier stage and its related complications. Addressing identified limitations, such as the restricted timeframe and single-center focus, will strengthen future investigations and enhance their applicability to the broader Omani population.

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