

# A Comprehensive Analysis of Inactive Hepatitis B Infection in a Cohort of Omani Patients

Halima H. Al Shuaili<sup>1</sup>, Bushra Al Mashikhi<sup>2</sup>, Ahmed Al Sinani<sup>2</sup>,  
and Said A. Al Busafi<sup>3\*</sup>

<sup>1</sup>Department of Medicine, Armed Forces Hospital, Muscat, Oman

<sup>2</sup>Medical Student, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

<sup>3</sup>Department of Medicine, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

Received: 24 April 2024

Accepted: 27 June 2024

\*Corresponding author: [busafis@squ.edu.om](mailto:busafis@squ.edu.om)

DOI 10.5001/omj.2024.104

## Abstract

**Objectives:** Inactive hepatitis B carriers constitute a considerable proportion of chronic hepatitis B virus (HBV)-infected patients. Understanding the clinical features of this often-overlooked population is essential to inform patient management strategies. Accordingly, this study aimed to describe the sociodemographic and clinical features of inactive hepatitis B carriers presenting to a tertiary center in Muscat, Oman.

**Methods:** A retrospective, descriptive study was conducted among 375 adult Omani patients with inactive HBV infections presenting to the Sultan Qaboos University Hospital between January 2017 and December 2018. Relevant data were collected from electronic patient records. Liver fibrosis status was determined using two-dimensional shear-wave elastography.

**Results:** A total of 200 patients met the inclusion criteria and were included in the analysis. Of these, 53% were male, and the mean age was  $45 \pm 9.3$  years. Most (77.5%) were aged 32–50 and were therefore born before 1990, the year of initiation of the national HBV vaccination program. A family history of HBV infection was reported in 29%, while 25% were obese. Significant fibrosis and advanced fibrosis/cirrhosis were observed in 16% and 3% of the cohort, respectively.

**Conclusion:** A large number of inactive Omani HBV carriers were born before the implementation of the national HBV vaccination program in Oman, and just under one-third had a family history of HBV infection. Importantly, despite being considered inactive carriers, 20% displayed radiological features of severe fibrosis. Screening for high-risk inactive HBV infection is essential to ensure early management and improved patient outcomes.

**Keywords:** HBV inactive carriers; Obesity; Significant Fibrosis; Elastography; Oman.

## Introduction

Chronic hepatitis B virus (HBV) infection persists and has a global impact, affecting approximately 292 million individuals worldwide.<sup>1</sup> The repercussions of HBV infection are profound, significantly contributing to the development of life-threatening conditions such as cirrhosis and hepatocellular carcinoma (HCC).<sup>2,3</sup> In 2019 alone, chronic HBV infections caused 820,000 deaths globally, placing a substantial burden on healthcare systems.<sup>4</sup> In Oman, precise data on the prevalence of HBV infection remain elusive.<sup>5,6</sup> However, estimations suggest a moderate prevalence of 2–5%, highlighting the need for ongoing vigilance and surveillance.<sup>1,6</sup>

Most global HBV infections involve inactive CHB, with individuals in this phase of infection known as inactive carriers.<sup>7,8</sup> According to the 2017 clinical practice guidelines of the European Association for the Study

of the Liver (EASL), inactive carriers are individuals who test negative for hepatitis B e-antigen (HBeAg), positive for HBe antibody (anti-HBe), and consistently exhibit normal alanine aminotransferase (ALT) levels (<40 IU/L) and low or undetectable serum levels of HBV DNA (<2,000 IU/mL).<sup>9</sup> However, the EASL also acknowledges a subgroup of inactive carriers with HBV DNA levels of 2,000–20,000 IU/mL, along with normal ALT levels and minimal hepatic necroinflammatory activity. Regular monitoring is essential for inactive HBV carriers to detect any reactivation or potential disease progression, including routine assessment of liver fibrosis status.<sup>10</sup>

Compared to other subgroups of HBV-infected patients, individuals in the inactive carrier phase generally have a reasonably favorable prognosis.<sup>7,11</sup> Nevertheless, the clinical profile and long-term effects of inactive infection can vary widely. For instance, some patients may have inactive infections for life, while others may experience HBV reactivation, reported in 9.4–15.9% of inactive carriers with a history of previously resolved HBV infections.<sup>7,12,13</sup> Additionally, although uncommon, the development of HCC and liver fibrosis remains possible.<sup>7,10,14</sup>

The significant proportion of inactive HBV carriers in the population makes this demographic particularly intriguing for research purposes, especially given that such patients often do not receive prompt medical attention.<sup>10</sup> Furthermore, research on this specific subgroup of patients is notably limited in Oman, an area characterized by an intermediate frequency of HBV infection.<sup>1,5,6</sup> Therefore, this study aimed to describe the sociodemographic and clinical features of a cohort of adult Omani inactive hepatitis B carriers presenting to a tertiary center in Muscat, Oman. This research represents the first attempt in Oman to characterize the epidemiological and clinical presentations of individuals with inactive HBV infections.

## Methods

This single-center, retrospective, descriptive study was conducted at the Sultan Qaboos University Hospital (SQUH), a tertiary care hospital in Muscat, the capital city of Oman, from January 2017 to December 2018. The hospital serves patients referred from primary or secondary centers nationwide. Our target population comprised all adult Omani inactive HBV carriers who visited the adult hepatology clinic at SQUH, received a diagnosis of inactive chronic HBV infection, and underwent follow-up during the study period.

Inclusion criteria included adult Omani patients (aged  $\geq 13$  years old) diagnosed with inactive HBV infections who had undergone two-dimensional (2D) shear-wave elastography. According to the EASL criteria, inactive HBV carriers were defined as patients positive for HBsAg, negative for HBeAg, and positive for anti-HBe, with normal ALT levels and HBV DNA levels of <20,000 IU/mL.<sup>9</sup> Excluded from the study were patients with missing data, pregnant women, and those with chronic liver diseases such as hepatitis C, hepatitis D, HIV infection, autoimmune hepatitis, cholesteric liver disease, alpha one antitrypsin deficiency, Wilson's disease, or hemochromatosis.

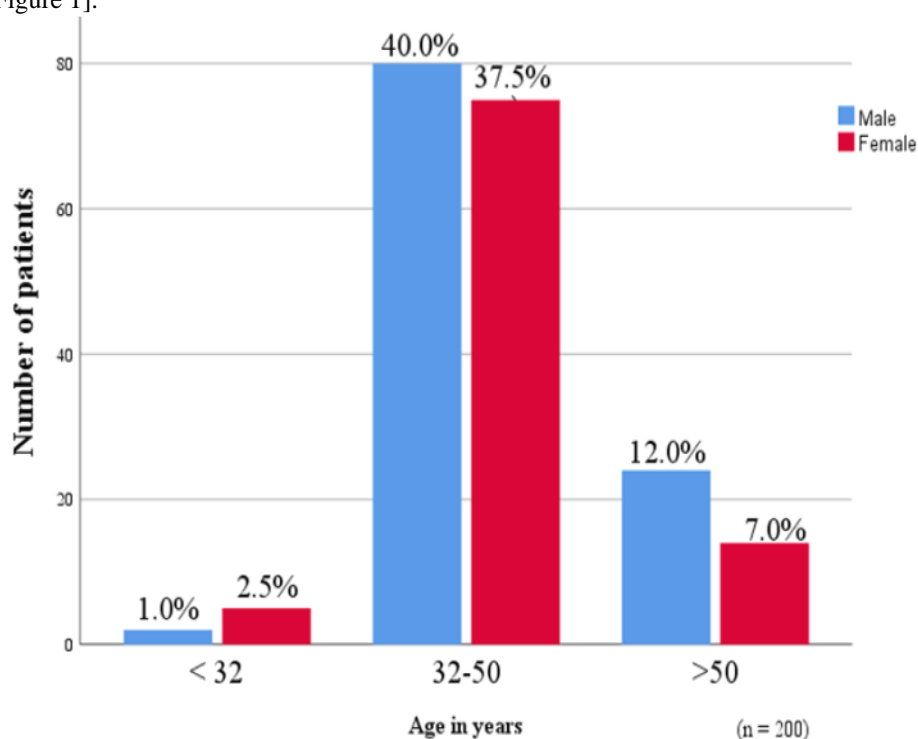
Relevant demographic, clinical, laboratory, and radiographical data were extracted from the patients' electronic medical records using the hospital's healthcare information system (TrakCare, InterSystems Corp., Cambridge, Massachusetts, USA). Additionally, information regarding anthropometric parameters, comorbidities, and family and personal history of HBV-associated risk factors was collected. As per the World Health Organization's body mass index (BMI) cut-off points, patients were classified as underweight (<18.5 kg/m<sup>2</sup>), normal weight (18.5–24.9 kg/m<sup>2</sup>), overweight (25.0–29.9 kg/m<sup>2</sup>), or obese ( $\geq 30.0$  kg/m<sup>2</sup>).<sup>15</sup> Liver stiffness measurements from ultrasonography and 2D shear wave elastography imaging were used to categorise liver fibrosis status as follows: (1) F0: no fibrosis ( $\leq 7.1$  kPa); (2) F1: minimal scarring (7.1–7.8 kPa); (3) F2: significant fibrosis (7.8–8.0); (4) F3: severe fibrosis (8.0–11.5 kPa); and (5) F4: cirrhosis or advanced scarring (>11.5 kPa).<sup>16</sup>

The Statistical Package for the Social Sciences (SPSS) software, version 27.0 (IBM Corp., Armonk, New York, USA), was utilised for data analysis purposes. Categorical variables were presented as frequencies and percentages, while continuous variables were presented as means and standard deviations. Data were visually presented using frequency tables, pie charts, or bar charts.

Ethical approval for the study was obtained from the Medical Research and Ethics Committee of the College of Medicine and Health Sciences at Sultan Qaboos University. Authorisation to review patients' medical records was granted by the relevant authorities from the Directorate of Hospital Information Systems at SQUH.

## Results

A total of 375 patients with inactive HBV infections presented to the clinic during the study period; however, 175 (46.7%) did not meet the inclusion/exclusion criteria. Thus, the analysis ultimately included 200 patients. Of these, 106 (53%) were male, and the mean age was  $45 \pm 9.3$  years, with most (77.5%) aged between 32 and 50 years [Figure 1].



**Figure 1:** Age and gender distribution of adult Omani inactive hepatitis B carriers (N = 200).

Patients reported a family history of chronic hepatitis B, cirrhosis, and hepatocellular carcinoma (HCC) in 58 (29%), 22 (11%), and nine (4.5%) cases, respectively. Moreover, 40 (20%) had undergone surgical procedures, and five (2.5%) had received blood transfusions. No patient reported alcohol consumption. The most common comorbidities were type 2 diabetes (10.5%), dyslipidemia (9.5%), and hypertension (8.5%). Nearly half of the patients (48.5%) had a body mass index (BMI) of 25 or above. The majority hailed from Muscat Governate, representing 38% of the cohort [Table 1].

**Table 1:** Sociodemographic and clinical characteristics of adult Omani inactive hepatitis B carriers (N = 200)

| Characteristic                  | n (%)        |
|---------------------------------|--------------|
| <b>Age in years</b>             |              |
| Mean $\pm$ SD                   | 45 $\pm$ 9.3 |
| <b>Gender</b>                   |              |
| Male                            | 106 (53)     |
| Female                          | 94 (47)      |
| <b>BMI &gt;30</b>               | 50(25)       |
| <b>Relevant family history</b>  |              |
| Chronic HBV infection           | 58 (29)      |
| Cirrhosis                       | 22 (11)      |
| HCC                             | 9 (4.5)      |
| <b>Relevant medical history</b> |              |
| Blood transfusions              | 5 (2.5)      |
| Surgeries                       | 40 (20)      |
| Alcohol consumption             | 0 (0)        |
| <b>Comorbidities</b>            |              |
| T2DM                            | 21 (10.5)    |

|                              |          |
|------------------------------|----------|
| Dyslipidaemia                | 19 (9.5) |
| Hypertension                 | 17 (8.5) |
| Renal disease                | 5 (2.5)  |
| Malignancy                   | 5 (2.5)  |
| SCD                          | 3 (1.5)  |
| Heart failure                | 1 (0.5)  |
| Thalassaemia                 | 1 (0.5)  |
| <b>Governate destitution</b> |          |
| Muscat                       | 76(38.0) |
| Ad Dakhilyia                 | 36(18.0) |
| Al Batina South              | 31(15.5) |

*SD = standard deviation; HBV = hepatitis B virus; HCC = hepatocellular carcinoma; T2DM = type 2 diabetes mellitus; SCD = sickle cell disease.*

HBV DNA levels ranged from 2,000 to 20,000 IU/mL in 33 patients (16.6%), while 132 (66.3%) had levels below 2,000 IU/mL. Thirty-four patients (17.1%) had undetectable HBV DNA levels. According to shear-wave elastography, most patients (71.5%) showed no fibrosis (stage F0); however, 32 (16%) and six (3%) exhibited severe fibrosis (stage F3) and cirrhosis (stage F4), respectively [Table 2].

**Table 2:** Biochemical, viral, and radiological features of adult Omani inactive hepatitis B carriers (N = 200)

| <b>Feature</b>                            | <b>n (%)</b>   |
|---|----------------|
| <b>Liver function</b>                     |                |
| Mean ALT level in U/L ± SD                | 22.5 ± 11.5    |
| Mean AST level in U/L ± SD                | 19.7 ± 6.2     |
| Mean ALP level in U/L ± SD                | 66.5 ± 19.2    |
| Mean total bilirubin level in µmol/L ± SD | 9 ± 6.5        |
| Mean albumin level in g/L ± SD            | 44.9 ± 3.4     |
| <b>Viral load*</b>                        |                |
| Median HBV DNA level in IU/mL (IQR)       | 139.5 (20–779) |
| Not detected                              | 34 (17.1)      |
| 0–2,000 IU/mL                             | 132 (66.3)     |
| 2,000–20,000 IU/mL                        | 33 (16.6)      |
| <b>Liver fibrosis stage†</b>              |                |
| F0: No fibrosis                           | 143 (71.5)     |
| F1: Minimal scarring                      | 17 (8.5)       |
| F2: Significant fibrosis                  | 2 (1)          |
| F3: Severe fibrosis                       | 32 (16)        |
| F4: Cirrhosis or advanced scarring        | 6 (3)          |

*ALT = alanine aminotransferase; SD = standard deviation; AST = aspartate aminotransferase; ALP = alkaline phosphatase; HBV = hepatitis B virus.*

*\*Percentages for this variable are calculated out of the total number of patients for whom data were available (n = 199). †As determined by shear-wave elastography.*

## Discussion

This retrospective cohort study aimed to identify the demographic and clinical characteristics of Omani patients with inactive HBV infections at a tertiary hospital in Muscat, Oman. The cohort exhibited a 1:1 gender ratio. Some studies reported a similar gender distribution among inactive HBV carriers, while others noted a male predominance, which may result from estrogen's protective effect against chronic liver disease development.<sup>17-19</sup> However, the intensity of male predominance in chronic HBV infection escalates with disease progression, peaking in HCC cases.<sup>19</sup> Additionally, the reported gender differences might relate to the higher risk of bloodborne infection transmission among men due to behaviours like unprotected sex and intravenous drug use, potentially less common in highly conservative, religious countries like Oman.<sup>20</sup>

The mean age of the cohort was 45 years, with the majority (77.5%) born before 1990—the year Oman included the HBV vaccination in its national childhood immunization program.<sup>21</sup> Previous reports among Omani chronic HBV patients have made similar observations.<sup>5</sup> Notably, most female patients were of childbearing age, increasing the risk of mother-to-child transmission. Indeed, a significant portion of chronic HBV patients in Oman reports a positive family history, with 8.8% noting a maternal link.<sup>6</sup> Correspondingly, nearly one-third of the

study's cohort had a positive family history of HBV infection, underscoring the role of vertical transmission and intra-familial contact in spreading HBV within the Omani population. Globally, especially in regions with moderate-to-high HBV incidence, vertical transmission remains the predominant method of HBV spread.<sup>22</sup>

In the present study, 20% of the patients had undergone surgical procedures. We did not assess the timing of these procedures relative to the diagnosis of HBV infection; therefore, we could not determine any correlations between these factors. However, a previous case-control study from Iran—which has a hepatitis B incidence comparable to Oman's—identified a history of surgery as an independent risk factor for chronic HBV transmission.<sup>23</sup> Similarly, a study among Bahraini patients with chronic HBV infections highlighted dental treatments, surgical procedures, and blood transfusions as significant transmission routes.<sup>24</sup> Conversely, a systematic review found that surgical operations have a minimal impact on maternal HBV transmission in various Arab and African countries.<sup>25</sup> Thus, assessing the exact impact of surgical treatments on HBV transmission remains difficult. However, the risk of this transmission route could be substantially reduced by implementing preoperative screening and rigorous sterilization and disinfection practices.

In this cohort, 71.5% of the patients hailed from the Muscat, Ad Dakhiliyah, and Al Batinah Governorates of Oman. Previous research shows that 81.6% of HBV patients reside in the northern parts of Oman.<sup>26</sup> These findings make sense given that Muscat is the capital and most populous governorate of Oman. Therefore, one would expect a higher representation of patients in Muscat and its neighboring regions due to their greater population density. Moreover, more than two-thirds of the patients in this study were obese or overweight according to BMI metrics, aligning with the prevalence of these nutritional states in Oman's general population.<sup>27</sup> Other studies also report high rates of obesity and metabolic syndrome among inactive HBV carriers.<sup>28,29</sup> This observation is crucial because researchers have noted that elevated BMI levels might increase the prevalence of steatohepatitis and accelerate liver fibrosis development.<sup>30</sup>

In our study, most patients either had undetectable HBV DNA levels or levels below 2,000 IU/mL, consistent with findings from other studies on patients with inactive HBV infections.<sup>29</sup> Moreover, inactive HBV carriers commonly exhibit an average ALT level of  $22.5 \pm 11$  U/L, which can indicate liver damage and is, therefore, a crucial metric for guiding follow-up and treatment decisions.<sup>14,31</sup> Although inactive HBV infections were traditionally associated with lower rates of liver fibrosis, recent evidence suggests that some patients may indeed develop liver fibrosis. Transient elastography, a non-invasive method, has emerged as a promising tool for assessing fibrosis without the need for a liver biopsy.<sup>16,32</sup>

Contrary findings exist in the literature regarding the prevalence of histological liver changes in inactive HBV carriers. Reports range from moderate liver fibrosis in 10% to up to 20% of patients showing significant fibrosis.<sup>33,34</sup> In this study, 71.5% of patients exhibited no evidence of liver fibrosis (stage F0) according to two-dimensional shear-wave elastography. However, 1% and 16% of patients displayed significant fibrosis (F2) and severe/advanced fibrosis (stage F3), respectively, while 3% had developed cirrhosis (stage F4). Although the proportion of patients with significant fibrosis (stage F2) was notably lower compared to other studies using transient elastography (14–25%), the rate of stage F4 cirrhosis aligned with previously reported rates (5–6%).<sup>28,29</sup> This discrepancy in findings might stem from the absence of reported alcohol consumption history in this cohort or the exclusion of patients with co-infection history with hepatitis C, human immunodeficiency virus co-infection, and steatohepatitis—all of which pose a significant risk of liver fibrosis among inactive HBV carriers.<sup>29</sup>

This study illuminates the sociodemographic and clinical features of inactive hepatitis B carriers in Oman, a previously unexplored area of research. The findings could guide future investigations into related research avenues, including causal relationships. Additionally, the results facilitate differentiation between healthy inactive carriers and those requiring additional medical attention due to significant fibrosis. However, it's important to acknowledge certain limitations of this study, including potential missing or inaccurate data inherent in retrospective studies reliant on existing medical records. Furthermore, although the study was conducted at a single center, the sample size should be deemed representative of the Omani population given that SQUH serves as one of only four tertiary care hospitals in Oman and receives patients from across the country.

## Conclusion

This study aimed to describe the sociodemographic and clinical profile of a sample of inactive hepatitis B carriers who presented to a tertiary hospital in Oman. It is notable that a significant proportion of patients were born before the integration of the HBV vaccine into the national immunization program in 1990. This underscores a heightened

risk of vertical transmission, further supported by the presence of a family history of HBV infection, which was reported in nearly one-third of the participants. While the majority of patients showed either no or minimal fibrosis, a substantial subset (20%) exhibited significant or advanced fibrosis and cirrhosis, highlighting the diversity of outcomes in inactive carriers. Therefore, additional preventive measures are crucial, including targeted screening of at-risk age groups and the development of strategies to prevent mother-to-child transmission. These interventions are essential for improving disease management outcomes and reducing the overall disease burden associated with HBV infection in Oman.

## Conflict of Interest

The authors declare no conflicts of interest.

## Funding

No funding was received for this study.

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