

## Viral Activity Among Incidentally Detected Asymptomatic HBSAG Positive Patients in Khartoum State

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### Abstract

One of the commonest modes of detection of hepatitis-B virus (HBV) infection is incidental detection. Incidentally detected asymptomatic HBsAg (IDAHS) positive patients represent a heterogeneous group with variable serological and clinical profile. The aim is to study the viral activity of IDAHS positive patients.

**Keywords:** Asymptomatic HBSAG; Positive Patients; Viral Activity

### Introduction

Hepatitis B virus (HBV) is the leading cause of chronic viral hepatitis across the world and a major health problem in Sudan. Sudan is classified among countries with a high hepatitis B surface antigen (HBsAg) with an endemicity of more than 8%. Approximately 400 million infected individuals worldwide run a high risk of developing liver cirrhosis and hepatocellular carcinoma (HCC) [1-3]. Moreover, annually up to 1 million persons die secondary to HBV-related consequences such as cirrhosis and hepatocellular carcinoma [4].

Incidentally detected asymptomatic hepatitis B surface antigen (HBsAg)-positive subjects (IDAHS) are defined as subjects who have no present/past symptoms or signs of liver disease and have HBsAg positivity on two occasions more than six months apart. IDAHS is usually detected during a routine checkup, blood donation, family screening of contacts of patients with HBV related chronic liver disease or a routine test following abnormal ALT or AST values [5].

A large proportion of IDAHS patients acquire the infection through perinatal exposure or horizontal transmission by sexual intercourse, surgeries or blood transfusion. Although on presentation these patients are symptom free; a proportion of them show biochemical (bilirubin, ALT and AST) or histological abnormalities and have been shown to progress to symptomatic chronic liver disease, cirrhosis, or ultimately HCC upon long-term follow up [6,7].

The course and outcome of IDAHS is quite variable from asymptomatic to complications related to cirrhosis and HCC. Milder forms are non- or slowly-progressive and are usually accompanied by the loss of serum HBV DNA and seroconversion from hepatitis B e antigen positive serology to e antibody positive serology (anti-HBeAg) [8].

The prevalence of HBeAg-negative variant among HBV patients is geographically variable, being high in Sub-Saharan Africa and Middle East countries; there are many reports that this mutant vi-

rus causes a more severe disease and is less responsive to treatment [9]. El-Zayadi, *et al.* reported that HBeAg - negative hepatitis B represents more than 80% of chronic hepatitis B in Egypt [10]. In one Sudanese study, 16% of HBV patients tested for HBeAg were found reactive [11]. The aim of this study is to study the viral activity of IDAHS positive patients in Khartoum State.

## Objectives

### General objective

To study the viral activity of incidentally detected asymptomatic HBsAg positive (IDAHS) patients in Khartoum state.

### Specific objectives

- To assess the frequency of active HBV infection among IDAHS patients.
- To study the risk factors of HBV transmission in IDAHS patients.
- To evaluate the infectivity status among IDAHS patients.
- To determine the results of Fibroscan among IDAHS patients.

## Methods

### Study design

This is a descriptive, hospital-based, cross-sectional study.

### Study area

The study was conducted in Omdurman Military Hospital, Omdurman Teaching Hospitals and Ibn-Sina Specialized Hospital.

### Study duration

The study was carried out during the period of September 2021 to March 2022.

### Study population:

All incidentally detected asymptomatic HBsAg positive patients during study period

### Inclusion criteria

- Being an IDAHS patient.

### Exclusion criteria

- Chronic hepatitis B virus patient.
- Patients with coexistent liver disease.
- Refusal of participation in the study.

## Sample size

Given the rarity of IDAHS, total coverage sampling was used in this study, where we involved all IDAHS patients encountered during the study period. A total of 100 participants were involved.

## Data collection tools and methods

Data collection carried out by the principal investigator. Data was collected through structured questionnaires consisting of demographics, risk factors of HBV, ultrasound findings, laboratory investigations, and HBV DNA load. FibroScan (Echosens machine) was conducted by an expert gastroenterologist and patients were fasted to detect the FibroScan liver stiffness scores (LMS).

The results of FibroScan were interpreted as follow:

- F0 - F1(KPa 2-7) indicate no liver fibrosis to mild.
- F2 (KPa 7-9.5) indicating moderate fibrosis.
- F3 (KPa 9.5-12.5) indicating severe liver fibrosis.
- F4 (KPa > 12.5) indicating advance liver fibrosis, where the scarring is permanent and the damage is irreversible

## Study variables

- Socio-demographic variables: Age, Gender, occupation, marital status
- HBV risk factors
- Abdominal US
- Liver profile: bilirubin, ALT and AST
- HBeAg
- HBV DNA load
- FibroScan measurements

## Data analysis

Data was analyzed using the statistical package for social sciences (SPSS) version 21. Descriptive statistics were applied to all the study variables; in the form of frequencies and percentages for categorical data; means, medians, and standard deviations for numerical data.

## Ethical consideration

An ethical approval was obtained from Sudan medical specialization board (SMSB). An additional approval was obtained from the administration of hospitals where the data was collected from. An informed consent was obtained from the study participants prior to their enrollment in the study, and personal identifying data were not collected.

## Results

### Socio-demographic data

A total of 100 IDAHS patients were involved in this study, 76(76%) were males and 24 (24%) were females (Figure 1). The mean age of participants was  $36 \pm 14$  years and most of them 40(40%) aged from 20-29 years (Figure 2). Most of the participants were soldiers (n = 40, 40%) and free workers (n = 30, 30%). Nearly half of the cases (n = 52;52%) were singles and 48(48%) were married.

### Risk factors for HBV transmission

Illegal sexual activities (n = 44; 44%) were the commonest HBV risk factors followed by history of surgical procedures (n = 17; 17%) and intra-family transmission (n = 12;12%) (Figure 3).

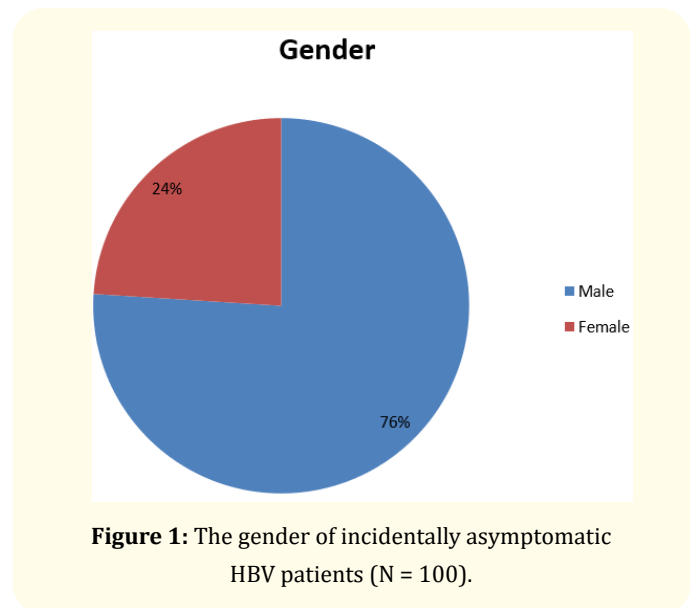
### Investigation findings

Ultrasonography (US) showed abnormal findings in 16(16%) patients and normal findings in remaining 84(84%) patients (Figure 4). Detected abnormalities were in the form of: ascities (n = 5, 5%), splenomegaly (n = 3, 3%), hepatomegaly (n = 3, 3%) and coarse texture (n = 2, 2%). The average of SBP was 121 mmHg and DBP was 77 mmHg, elevated SBP and DBP were found in 5(5%) patients.

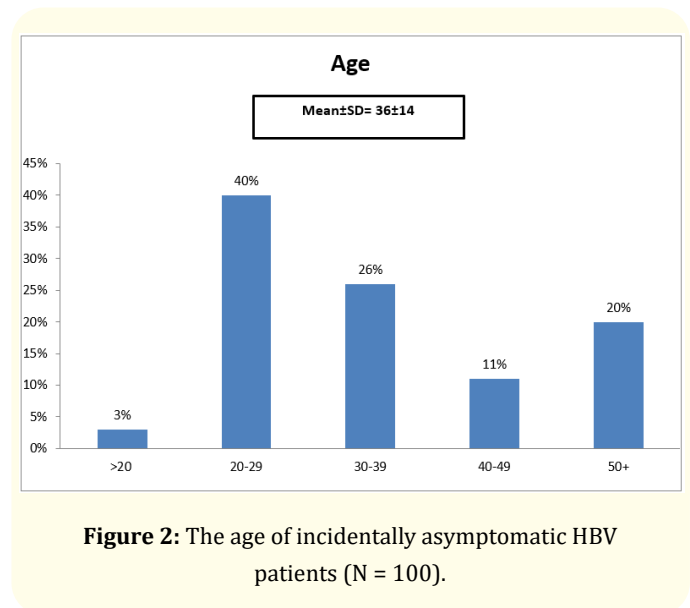
Median bilirubin level was 7 mg/dl, and 17 (17%) patients were jaundiced (Figure 5). The median of HBV DNA viral load was 800 IU/ml. The majority of the patients 79 (79%) had DNA levels below 2,000 IU/ml and 6 (6%) patients had DNA levels above 2,000 IU/ml (Figure 6). HBeAg was found to be positive in 46(46%) patients and negative in remaining 54 (54%) patients.

The median of ALT enzyme was 22 U/L, elevated levels were found in 20% of the cases and 80 (80%) patients had ALT levels below or equal to the upper limits of normal (ULN). In addition, the median of AST enzyme was 19 U/L. Elevated level were encountered in 15% of the patients and 85 (85%) patients had AST levels  $\leq$  ULN and 15% of the cases had elevated levels.

The FibroScan results showed normal to mild (non-significant) fibrosis in 59(59%) patients, moderate fibrosis (F2) in 19 (19%) patients, severe fibrosis (F3) in 4(4%) and advanced fibrosis (F4) in 18(18%) patients. Liver cirrhosis was found in one patient.

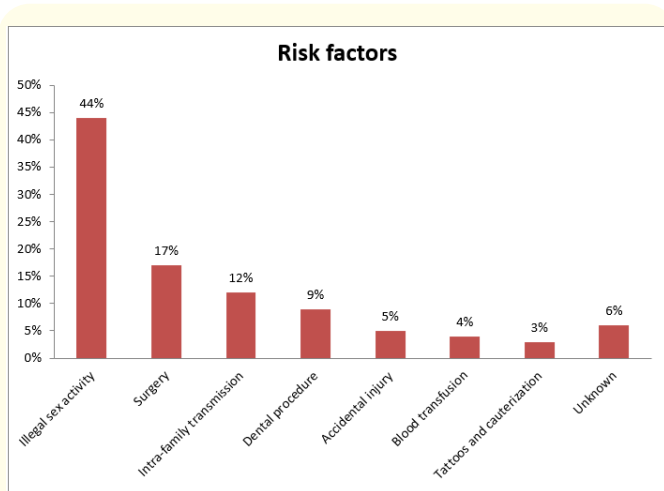


**Figure 1:** The gender of incidentally asymptomatic HBV patients (N = 100).

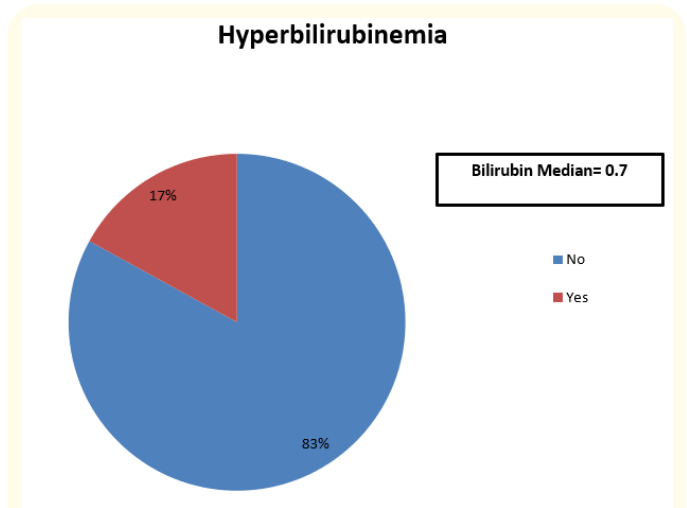


**Figure 2:** The age of incidentally asymptomatic HBV patients (N = 100).

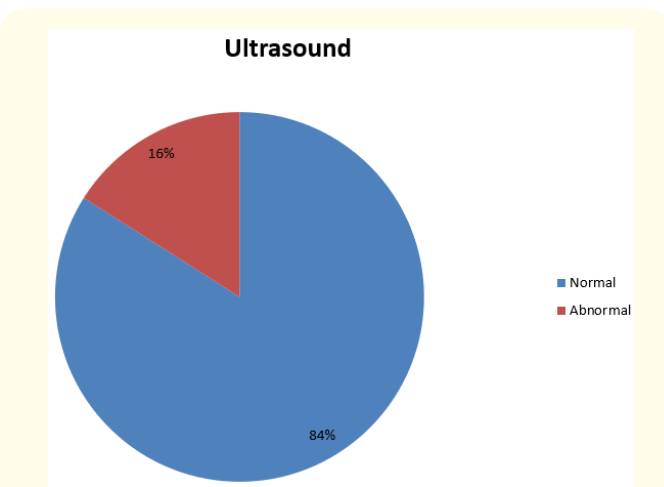
subject with no clinical evidence of liver disease, the other extreme being end stage cirrhosis and Hepatocellular Carcinoma (HCC). For many decades these incidentally detected HBsAg individuals were considered to have a benign non-progressive infection and referred to as “inactive HBsAg carrier”. In this study we aimed to assess demographical and clinical characterization in addition to viral activity in 100 patients with IDAHS.



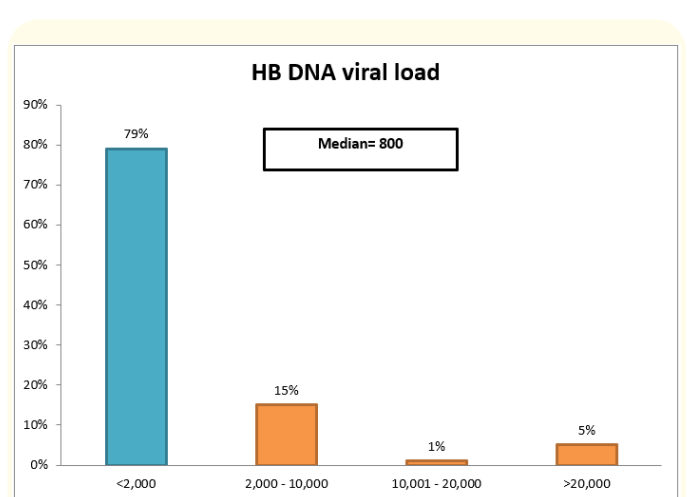
**Figure 3:** The risk factors among incidentally asymptomatic HBV patients (N = 100).



**Figure 5:** The hyperbilirubinemia and bilirubin levels among incidentally asymptomatic HBV patients (N = 100).



**Figure 4:** Ultrasonography (US) findings among incidentally asymptomatic HBV patients (N = 100).



**Figure 6:** The HBV DNA viral load of incidentally asymptomatic HBV patients (N = 100).

With respect to sex related prevalence, this study showed the rate of IDAHS was higher in males more than females (76% vs 24%). This could be explained by males are exposed to HBV risk factors more than females. This finding is in agreement with previous studies, which demonstrated higher rates of HBsAg among the male population like Shiha G., *et al.* in Egypt [4], Badawi M., *et al.* in Sudan [11], Choudhuri G., *et al.* [12], Arora D., *et al.* [13] and Unnikrishnan B., *et al.* in India [14], and Cheng-Jen C., *et al.* in Taiwan [15].

In this study IDAHS was more common among those in the age group of 20-29 years (40%) with mean age  $36 \pm 14$  years. This result was in accordance with several studies such as; Nasir K., *et al.* in Pakistan (mean age =  $32.45 \pm 11.85$  years) [16], Kashif M., *et al.* in Egypt (mean age = 30 years) [17], and Chia-Ming C., *et al.* in China (mean age =  $35.6 \pm 9.2$  years) [18].

Among the study participants, IDAHS was prevalent in soldiers (40%) more than other occupations. A similar finding was estab-

lished by Mudawi HM., *et al.* in a previous study assessing the epidemiological pattern of HBV in Sudan [3].

HBV is transmitted by blood or body fluids of infected patients. Globally, most infections happen from infected mother to child, child-to-child contact in household settings, unprotected sexual activity, blood transfusion, and reuse of unsterilized needles and syringes. In the current study, unprotected sexual activity (44%) was the commonest HBV risk factors followed by history of surgical procedures (17%) and intra-family transmission (12%). The risk factors of IDAHS geographically differ, in an Egyptian study, the main risk factor was dentist consultation [4], while in Pakistani study, history of intramuscular injections and surgery were the common factors [16].

Hepatomegaly and splenomegaly are rarely present among IDAHS patients [5]. Similarly, in this study, hepatomegaly and splenomegaly were presented in only 3% of the patients (for each).

DNA levels is corner stone in the assessment of HBV infection, and though HBV DNA > 20,000 IU/ml was chosen as a cutoff for initiating therapy based on non-histology-based natural history, that revealed a high rate of cirrhosis development; later histology-based studies showed that HBV DNA > 2,000 IU/ml is associated with high rates of fibrosis [19]. The current study showed that, the median of HBV DNA viral load was 800 IU/ml, all patients (100%) had detectable DNA viral load, among them 79 (79%) had low viral load (< 2,000 IU/ml) and 6 (6%) patients had DNA levels above 2,000 IU/ml. Comparable results were reported by Shiha G., *et al.*, who found that 97% of IDAHS patients had detectable DNA load [4]. Nasir K., *et al.* found 88.8% of the cases had positive HBV DNA levels [16]. While in the studies of Choudhuri G., *et al.* [12] and Kashif M., *et al.* [17], detectable HBV DNA levels were found in 61% and 11.6% of cases, respectively.

The presence of HBeAg in serum correlates with the presence of viral replication in the liver. HBeAg is generally considered as surrogated marker of hepatitis B infectivity [12]. In the present study, 46% of HBV patients were having positive HBeAg. Our findings are similar to that of a cross sectional study done from India on 157 patients, where they reported HBeAg positivity in 45% of cases

[20]. However, the Sudanese study conducted by Mukhlid Y., *et al.* in Khartoum, showed the rate of HBeAg positivity was 12.1% [21]. In numerous pervious studies, HBeAg positivity ranged from 20% to 30% of cases [5].

Regarding hepatic enzymes, this study illustrated that, elevated levels of ALT and AST were found in 20% and 15%, respectively. These observations were in accordance with the study of Mohit G., *et al.* who reported 29.2% of the patients had increased ALT [22], while Shiha G., *et al.* noticed elevated ASLT and ALT in only 3% of the patients [4]. On the other hand, higher rates were found by Choudhuri G., *et al.*, who reported elevated ALT in 65% of cases [12].

HBV fibrogenic activity may be described as a chronic inflammation with a clinical progression to liver fibrosis in most of the patients. Viral activity produces constant liver damage made by the immune system, as a result, continuous tissue repairing occurs but in a disorganized matter, consequently resulting in fibrosis [23]. Based upon FibroScan technique, the present study showed that early stages of fibrosis (F2) were found 19% and significant fibrosis (F3 and 4) in 22% of cases. In an Egyptian study, 47.7% of the cases revealed mild to moderate fibrosis and 15.9% of them showed significant fibrosis [4].

Finally, this study presented that liver cirrhosis was reported in 1% of the subjects. This finding was comparable to Cheng-Jen C study in Taiwan who found liver cirrhosis in 2.8% of IDAHS subjects [15]. However, Shiha G., *et al.* in Egypt did not report cirrhosis among IDAHS patients [4].

## Conclusion and Recommendations

In conclusion, incidentally detected asymptomatic HBsAg is more common in males, in the second decade of life, and among soldiers. Illegal sexual activities were the commonest HBV risk factors. Positive HBeAg rate were present in a significant proportion of the cases. Most of the subjects had normal hepatic enzymes levels and low viral load. Liver fibrosis among IDAHS patients was not uncommon. We recommend that conductance of community-based surveys to detect IDAHS in disease endemic countries such as Sudan. Furthermore, we recommend regular follow up for

IDAHS subjects to detect HBV-related complications such as liver fibrosis, cirrhosis, and HCC as early as possible. Lastly, prospective studies are needed to assess the final outcome of IDAHS.

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