

## Original Research Article

# SEROPREVALENCE AND ASSOCIATED RISK FACTORS OF HEPATITIS B VIRUS INFECTION IN BOUAKÉ, CÔTE D'IVOIRE.

### ABSTRACT

#### Abstract

**Aim:** Determine the prevalence of serological markers and identify risk factors associated with hepatitis B virus (HBV) infection in patients screened at the Bouake teaching hospital.

**Study design:** Retrospective cross sectional study was conducted

**Study kSite and period:** Bacteriology-Virology Laboratory/Bouake teaching hospital, Côte d'Ivoire, from April 2016 to January 2018.

**Methodology:** In all study participants, venous blood sample was collected and screened for HBV surface antigen (HBsAg) and antibody against HBV core antigen (anti-HBc), by electrochemical-luminescence following the manufacturer protocols. Additionally, questionnaires were used to collect information regarding sociodemographic variables and possible risk factors for hepatitis B infection. Data were processed and analyzed using EPI INFO 7 software.

**Results:** A total of 1076 participants were included in this study with a median age of 30.0 years (range: 3 months; 82 years). Of which, 514 (48%) were female and 562 (52%) were male with female / male ratio 1.09. HBsAg was detected in 24,3% of participants and 82 1 (76,3%) were exposed to the risk of HBV infection (anti-HBc positive). High rate of HBV infection was detected in male (27.93%) ( $p<0.0001$ ). The age group of 15–45 years were more infected (27.18%) ( $p<0.0001$ ). The detection rate of HBe antigen (HBeAg), anti-HBe and anti-HBc (total antibodies) were respectively 12%; 86% and 7%. Of 938 participants who were not vaccinated against HBV, 240 (25.58%) were HBsAg-positive. HBV vaccine uptake was protective against HBV infection (AOR =0.580; 95% CI 0.359-0.938;  $p=0.024$ ).

**Conclusion:** The prevalence of HBV infection was 24.25% among patients screened at the Bouake teaching hospital, which is higher than to national prevalence 10%. People not vaccinated against HBV were more exposed to infection. This study reaffirms the need of awareness campaigns of general population about preventive measures and the strengthening of vaccination programs against HBV.

**Keywords:** Hepatitis B, HBsAg, anti-HBc, Bouake, Côte d'Ivoire

### 1. INTRODUCTION

Hepatitis B virus (HBV) infection is a global pandemic with 2 billion people infected [1, 2]. Of this, 300–400 million people are chronically infected [3]. About 500,000 to 1.2 million HBV-infected people die yearly from cirrhosis of the liver and hepatocellular carcinoma (HCC) worldwide [3, 4]. HBV is the most common and contagious worldwide. In 2015, more than 1.34 million people died from HBV infection. This figure is higher than death from tuberculosis and the human immunodeficiency virus (HIV). However, mortality attributable to TB and HIV is decreasing, while that due to hepatitis is constantly increasing [5, 6]. The HBV reservoir is represented by the large number of chronic carriers worldwide [7]. Studies reported that factors such as unprotected sexual intercourse, needle stick injuries, splash, intravenous and/or intramuscular injections, blood transfusion, and unvaccinated population has been associated with increased risks toward hepatitis B infections [8, 9]. vertical transmission is the main route of disease transmission to children from mothers, whereas principal means of transmission for sexually active partners is sexual intercourse [9, 10]. Côte d'Ivoire is a highly endemic area for HBV with a prevalence of more than 10% [2]. A study conducted in Abidjan detected a prevalence of HBsAg of 18.2% among pregnant women [11]. Another study conducted in 2001 allowed to detect a 12.5% prevalence of HBsAg among blood donors in Bouaké [12]. The increasing prevalence of HBV in Côte d'Ivoire requires adequate management and the implementation of effective preventive measures to limit the spread of the virus. One of the main routes of HBV-transmission might be blood transfusion, especially when donated blood is not tested for HBs antigen (HBsAg) [3, 13]. Systematic screening for hepatitis B surface antigen in blood donors and in pregnant women is necessary to identify and promptly treat those infected [9].

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Despite the scientific advances and opportunities for management and patient treatment, most people infected with HBV remain unaware of their statute and therefore frequently present with advanced disease and may transmit infection to others [6]. A qualitative study conducted in Abidjan in 2013 by Enel et al to assess the screening and management of these infections revealed a lack of knowledge about hepatitis among both the general population and non-specialist caregivers [14]. The updated World Health Organization (WHO) recommendations indicate that all suspected cases of hepatitis B must be confirmed with a laboratory diagnostic test before treatment. Implementation of the Global Health Sector Strategy would prevent 7.1 million deaths between 2015 and 2030 [15, 6].

There is growing body of literature in Côte d'Ivoire on HBV infection. But Thus far, there are limited information on the prevalence of HBsAg and associated risk factors in Bouaké.

This study was conducted to determine the prevalence of serological markers and identify risk factors associated with HBV infection in patients screened at the Bouaké teaching hospital (CHU of Bouaké).

## 2. METHODOLOGY

### 2.1 Study design and period:

This was a retrospective cross sectional study conducted from April 2016 to January 2018, to determine the prevalence of serological markers of HBV infection in people screened at the teaching hospital of Bouake (CHU).

### 2.2 Study Site:

The study was conducted at the Laboratory of CHU of Bouake, at the Microbial Serology Unit. Bouake is the second city of Côte d'Ivoire, located in the center 20 km from Abidjan. The city of Bouake covers an area of about 72km<sup>2</sup> with an estimated population of 1,542,000 inhabitants. This population is mainly made up of indigenous "Baoulé ethnic group" and of Malinké and Burkinabé allogeneic people. The CHU of Bouake is built on an area of 23 hectares. It currently has a wide range of medical, surgical and biological specialties. The laboratory of CHU is made up of a microbiology unit (bacteriology-virology/parasitology-mycology), serology, biochemistry, immunology-hematology and two molecular biology platforms: one for the diagnosis of viral hepatitis and HIV and the other for the diagnosis of viral hemorrhagic fevers.

### 2.3 Study population

The study population consisted of patients of all ages and **sexes** who came voluntarily or on medical advice for hepatitis B screening at the Laboratory of CHU of Bouake. A comprehensive sampling that took into account all patient results correctly recorded in the laboratory records during the study period.

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### 2.4 Sample collection

In all of the study participants, about 3 milliliter (ml) of venous blood sample was collected by dry tube aseptically. After coagulation, the blood was centrifuged at 3000 rpm for 10 minutes. Serum was separated from each sample and The collected sera were immediately tested or stored in the refrigerator at -20°C for a maximum of 03 days. samples were labeled with unique identification numbers which are similar to the code given in the questionnaire. All participants were screened according to the algorithm in **Fig. 1**. The sera of participants were analyzed for HBV surface antigen (HBsAg) and antibody to HBV core antigen (anti-HBc) by electrochemical-luminescence method, according to the manufacturer protocols. Samples reported to be positive for HBsAg were double checked for other markers of HBV infection (HBeAg, anti-HBe, anti-HBc type M).

### 2.5 Data Collection

Structured and pretested self-administered questionnaire was used to collect information regarding sociodemographic variables (age, sex, occupation, level of education) and possible risk factors for hepatitis B infection acquisition such as tattooing, blood transfusion history, vaccination status. The questionnaire was previously validated by the coordinating committee for viral hepatitis studies at Bouake teaching hospital.

### 2.6 Data analysis:

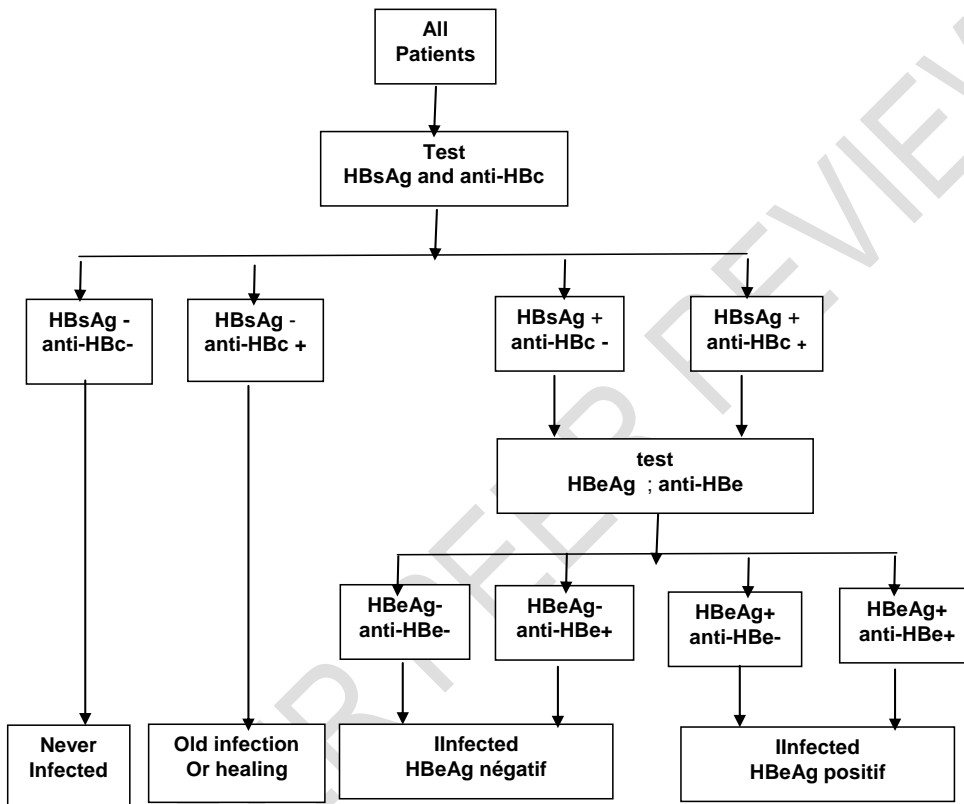
Data from the questionnaires and laboratory test results were entered into a database and analysed using EPI INFO 7 software. Descriptive statistics were used to describe the socio-demographic characteristics of the study participants. Exact Fisher's test was used to compare the prevalence of HBV infection. **Multivariate logistic regression** was used to determine the factors associated with HBV infection among study participants. The significance threshold was set at 5%.

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## 2.7 Ethical Consideration

The study was carried out with the approval of the Medical and Scientific Department (DMS) of CHU of Bouaké, which acts as the institutional ethics committee. Data confidentiality was preserved by assigning an anonymity number to each survey form. All questionnaires were stored in a secure room the information's of study participants were was secured in a password protected laptop.



**Fig.1. Algorithm for hepatitis B serology testing.** anti-HBc, antibody to hepatitis B core antigen; anti-HBe, antibody to hepatitis B 'e' antigen; HBeAg, hepatitis B 'e' antigen; HBsAg, hepatitis B surface antigen.

### 3. RESULTS

#### 3.1 Socio-demographic characteristics

A total of 1076 people were included in this study. the mean age of participants was 30 years (range: 3 months; 82 years). About 802 (74%) study participants were between 15 and 45 years while 175 (16%) were between 45 and 60 years. Over 562 (52.23%) of all participants were males. Above 499 (46%) of the study participants had a university education level and 149 (13%) of the participants had no level. regarding study participant's occupations, pupils and students accounted for 30% of the participants, salaried civil servants accounted for 27% of the participants (**Table 1**).

**Table 1:** Distribution of socio-demographic data of the study population according to the variables studied

variables		participants (N=1076)	Frequencies (%)
Sex	Female	514	47,77
	Male	562	52,23
Age (years)	0-15	52	4,83
	15-45	802	74,53
	45-60	175	16,26
	> 60 ans	46	4,27
	Pupils / students	331	30,76
Occupations	public servants	294	27,32
	Cultivators	72	6,69

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15-45  
46-60  
More than 60

	Housewives	99	9,2
	Informal sector	258	23,98
	Unemployed	22	2,05
Education level	Primary	138	12,83
	Secondary	290	26,95
	university	499	46,38
	Others	149	13,85

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### 3.2 Prevalence of HBV serological markers

Of the 1076 participants in this study, the prevalence of HBV infection (HBsAg) was 24.25% (261/1076) (Table 2). There was a significant difference in the prevalence of HBsAg between male (27.93%) and female (20.23%) ( $p=0.003$ ) in participants. The HBV infection rate gradually increased from 9.61% in those <15 years old to a peak of 27.18% in those 15–45 years old, but then it declined to 13.04% in the group older than 60 years old. The differences observed were significant between age groups ( $p=0.001$ ).

The infection rate was highest among farmers (36.11%), followed by salaried civil servants (25.51%). The detection rate of HBsAg was even lower among unemployed participants ( $p=0.081$ ). Also among patients with no education level, the infection rate was higher followed by patients with primary, secondary and university education level ( $p=0.893$ ).

Regarding total anti-HBc, a marker of HBV exposure, the positivity rate was 76.30% in participants and a significant variation was noted between genders ( $p < 0.0001$ ).

HBV exposure increased with age in both sexes, and it reached a peak in the group older than 60 years old (91.30%), indicating that exposure to HBV had occurred in every age group. The detection rate of anti-HBc was higher among farmers (90.27%), followed by salaried civil servants (81.97%), workers in the informal sector (77.90%) and housewives (76.76%) ( $p < 0.0001$ ). The positivity of anti-HBc was higher among study participants with no education level ( $p < 0.0003$ ) (Table II).

Table II: Serological markers to detect HBV infection

variables		participants	Ag HBs + Nbre (%)	P. Value	anti-HBcT Nbre (%)	P. Value
Sex	Female	514	104 (20,23)	0,003	460 (70,23)	< 0,0001
	Male	562	157 (27,93)		361 (81,85)	
	Total	1076	261		821	
Age (years)	0-15	52	5 (9,61)	0,001	13 (0,25)	< 0,0001
	15-45	802	218 (27,18)		615 (76,68)	
	45-60	175	32 (18,28)		151 (86,28)	
	> 60 ans	46	6 (13,04)		42 (91,30)	

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Occupations	Pupils / students	331	68 (20,54)	0,081	224 (67,67)	< 0,0001
	public servants	294	75 (25,51)		241 (81,97)	
	Cultivators	72	26 (36,11)		65 (90,27)	
	Housewives	99	23 (23,23)		76 (76,76)	
	Informal sector	258	64 (24,80)		201 (77,90)	
	Unemployed	22	5 (22,72)		14 (63,63)	
Education level	Primary	138	35 (25,36)	0,893	98 (71,01)	0,0003
	Secondary	290	67 (23,10)		216 (74,48)	
	university	499	120 (24,04)		373 (74,74)	
	Others	149	39 (26,17)		134 (89,93)	

A total of 107 (40.99%) patients who were HBsAg-positive had sufficient sample to allow further testing for HBeAg, anti-HBe and anti-HBc IgM-type. A total of 103 (37%) were HBeAg-positive and 127 (45%) were anti-HBe-positive. The positivity rates were respectively 3.73% for patients in the acute phase of infection (anti-HBc IgM-type); 12.14% for patients in the active replication phase of the virus (HBeAg); and 94.39.6% for those in the healing phase (anti-HBe Antibodies).

### 3.3 Factors associated with HBV infection

The following associated factors were assessed for hepatitis B virus infection: history of blood transfusion, history of vaccination status, tattooing, and blood exposure. Of the total study participants only 138 (12.82%) were vaccinated for HBV. Among those who were not vaccinated, 240 (25,58) were positive for HBsAg and this was statistically significant (AOR = 0.58, 95% CI = 0.35–0.93, P = 0.0024). Of 66 (6.13%) participants who had history of blood transfusion, 15 (22,72) were positive for HBsAg (AOR = 1.07, 95% CI, 0.60–1.91, P = 0.81). Other factors such as tattooing, and blood exposure were not significantly associated with HBV infection (**Table III**).

**Table III:** Factors Associated with HBV Infection

variables	participants	AgHBS+ (%)	AOR	IC (95%)	P-value
Blood transfusion					
Yes	66	15 (22,72)	1,07	0,60-1,91	0,81
No	1010	246 (24,35)			
Vaccination			0,58	0,359-0,938	<b>0,024</b>
Yes	138	21 (15,21)			
No	938	240 (25,58)			
tattoo					
Yes	6	0 (0,0)	-----	-----	0,6
No	1070	261 (100,00)			
Blood Exposure Accident			0,804	0,320-2,024	0,64
Yes	20	6 (0,30)			
No	1056	255 (24,14)			

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#### 4. Discussion

This study was carried out to determine seroprevalence of serological markers of HBV infection and risk factors associated with seropositivity among people tested in CHU of Bouaké. Though HBV infection is preventable and there is a protective vaccine, it remains a public health problem in Africa especially in Côte d'Ivoire.

Serological testing revealed a global prevalence of HBsAg positivity of 24.25%. These results show that Bouaké is a highly endemic area, with HBsAg carriage rate higher than the national prevalence of 10% [16, 17]. The positivity rate of AgHBs was higher among males (27.93%) than females (20.23%) ( $p=0.003$ ). The study also showed that the detection rate of marker of HBV exposure (total anti-HBc) was 76.30% and HBeAg positivity rate was 12.14%. These results, especially the high prevalence of HBsAg and current HBV infection, suggest that hepatitis B is a very serious health concern in Bouaké (Côte d'Ivoire).

In this study, HBV vaccine uptake were the only factors associated with HBV infection.

This high HBsAg positivity could be explained by the lack of implementation of the guidelines, screening and care algorithms proposed by the National Program for the Fight against Viral Hepatitis (PNLHV) and the Ivorian Network for the Fight against Viral Hepatitis (RILHVi) created in 2004 [14].

Indeed, the PNLHV is encountering structural difficulties due to the low budget allocated by the State and the lack of commitment from national and international donors. Because this pathology is not financially covered, the PNLHV does not have the resources needed to organize screening and awareness campaigns of the population [14]. This prevalence of HBsAg positivity obtained in our study is higher than that reported by Kra *et al.*, 12.5% among blood donors in Bouaké [12] and that obtained by Kouacou MJ *et al.* among pregnant women in Abidjan, which was 18.2% [11]. These differences in reported prevalence might be explained by a difference in study methodology (study population and sample size). Other studies of HBsAg reported a similar prevalence of 28.4% obtained by Balogun *et al.* in Nigeria among subjects infected with human immunodeficiency virus (HIV) [18]. Alao *et al.* also reported a prevalence of 20% among potential blood donors in Otukpo, Nigeria [19] and in Cameroon, Noubiap *and coll.* reported a prevalence of 23.7% among HIV-infected individuals [20]. Furthermore, in the study which was done by Kabinda *et al.* in Congo, lower prevalence of 4.2% were reported among 1079 volunteer blood donors tested [21], and 10.87% among 230 people voluntarily screened in Togo [22]. The study of the prevalence of HBsAg according to sex and age showed a predominance of infection in men with 27.98% versus 20.23% in women ( $p<0.05$ ). This could be related on the one hand to the direct effect of the predominance of the male sex in the sample, and on the other hand to the fact that multi-sexual partnership is more frequent in men than in women. These results are similar to those reported by Kabinda *et al.* in DRC among voluntary blood donors [23] and by Bivigou-Mboumba B *et al.* in Gabon on viral hepatitis carriage [24].

The age of HBV infection is one of the determining factors in incidence and prevalence rates. In resource limited settings like Côte d'Ivoire, most HBV infection take place during childhood due to high endemicity nature of hepatitis B virus infection [8]. However, this has not been supported by our study which showed a significant association between age and HBsAg positivity ( $p<0.05$ ). More than 27.18% of HBsAg positive patients were between 15 and 45 years of age. HBsAg carriage was more common in adults than children, which means many study participants, has been infected during adulthood. In a similar study of HBsAg carriage which was done in Mali by Dao *et al.*, adults were more infected [25].

The majority of patients in this age group is made up of public servants and students, who constitute a very sexually active population, which would represent a high risk due to the sexual transmission of the virus [23].

One of the main routes of HBV transmission in our case would probably be the sexual route, hence the need to strengthen information, education and communication campaigns to combat HBV and other sexually transmitted diseases. Other factors such as homosexuality and intravenous drug use have been documented in previous studies as factors associated with HBV infection [8]. In this study, only 5 (9.61%) HBsAg-positive patients were between the ages of 0 and 5 years, which indicates that the majority of patients were infected in adulthood. This low prevalence of HBV in children is good news, as children are easily exposed to the disease, particularly through vertical transmission by their mothers. The low HBsAg carriage in children could also be explained by the introduction of hepatitis B vaccine in the expanded program of vaccination (PEV) in Côte d'Ivoire since 2001 [26].

The positive impact on the reduction of HBsAg carriage in children shows the effectiveness of the HBV vaccine within the PEV in Côte d'Ivoire. Moreover, this low rate might also be the consequence of the low representation of children in our sample. Previous reports showed that more than 90% of exposed newborns and about 30% of children under 5 years of age fail to clear HBV from the body, which later progresses to a chronic infection, while 95% of infections acquired in adulthood result in spontaneous recovery [9]. In a Tanzania study conducted by Elichilla *et al.*, HBV infection among health care workers was not associated with gender, and patients were infected mostly during childhood [8].

The results of our study showed a detection rate of HBsAg of 26.17% in people with no education. However, HBsAg positivity was not associated with education level. Other authors have reported that the prevalence of HBV was significantly higher among illiterate women than among those with high education level [27].

Regarding total anti-HBc, 76.30% of the study participants had already been in contact with HBV. The positivity of total anti-HBc was significantly associated with gender and age ( $p<0.05$ ). Positivity was also associated with occupation and education level ( $p<0.05$ ). In similar study conducted in Ethiopia, authors obtained a prevalence of total anti-HBc of 25.8%

among 5009 pregnant women tested [27], while Yu-Ling *and coll.* reported a positivity of 13.3% in Sierre Leonne study [15].

Out of 107 patients tested for follow-up markers of HBV infection, the positivity rate of HBeAg was 12.14%, and the positivity rate was 94% for anti-HBe. These rates are higher than those of Nahom *and coll.*, who reported a prevalence of 3.9% for HBeAg and 17.4% for anti-HBe [27]. In another study Lohouès-Kouacou et al. reported a prevalence of 15.3% of HBeAg [11].

Our results revealed that only 12.82% of the study population had a history of HBV vaccination. This low vaccination rate could be explained by a lack of information and a lack of knowledge of the disease in the general population

Indeed, the proportion of students aware of the existence of HBV is low, as demonstrated in a study conducted in Abidjan among students at the University of Cocody [11]. Good level of knowledge was protective towards hepatitis B infection, therefore those with poor knowledge has more chances of been infected.

Risk factor analysis showed that vaccination status was significantly associated with HBV infection as a protective factor (OR= 0.594; CI 0.395 - 0.895; p= 0.0076).

In this study more than two thirds of the participants were not vaccinated against HBV and of these 25.58% were HBsAg carriers.

Other factors such as ethnicity, region of origin and religion might influence the chance of participants to be infected or not. However, in the current study these data could not be collected. Given the inaccessibility of treatment due to the high cost, vaccination remains the most effective means of prevention against this infection.

However, among patients vaccinated against HBV, 21 (8.04%) were HBsAg positive. This could be explained by the fact that these patients were already exposed to HBV infection before vaccination or that they did not receive the three protective doses of the vaccine. In another study, authors showed that the percentage of good knowledge HBV was very low and about half of the participants didn't know that antibody titer should be done after finishing the third dose [8]. Other factors studied such as blood transfusion, tattooing, blood exposure accidents were not statistically associated with HBV infection. However, the results showed that 15 (22, b72%) HBsAg-positive patients had a history of transfusion.

In a similar Tanzania study, the authors showed that people with a history of blood transfusion were 21 times more likely to be infected with HBV than those who did not receive a blood transfusion (OR=21.44; 95% CI; 6.05-76.01) [8].

To ensure transfusion safety in Côte d'Ivoire, the National Blood Transfusion Centre (CNTS) has been practicing systematic HIV screening since 1992, HBsAg (HBsAg) testing since 1993 and anti-HCV antibody testing since 1997.

However, it has been reported that HBsAg-negative donors who are newly infected with HBV are capable of transmitting the virus. This risk is associated with donations collected during the virological and serological windows that precede the appearance of biological markers of infection, or during the pre-conversion phase of recent infection, which is characterized by HBsAg levels in the circulation below detectable limits. The use of molecular tests or more sensitive serological tests to detect HBsAg might further reduce the risk of HBV transmission through blood transfusion [28].

#### 4. CONCLUSION

This study allowed to determine a prevalence of HBV infection of 24.25% among patients screened at the CHU of Bouaké from April 2016 to January 2018. More than 76% of the study participants were exposed to potential risks of infection. HBsAg positivity was significantly associated with gender and age groups. Majority of infected patients were between 15 and 45 years of age and the rate of vaccinated persons was 12.82%. Vaccination against HBV is the best way to prevent and control this infection. It is therefore important to encourage screening and vaccination program in the general population.

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#### ETHICAL APPROVAL

The study was carried out with the approval of the Medical and Scientific Department (DMS) of CHU of Bouaké, which acts as the institutional ethics committee. Data confidentiality was preserved by assigning an anonymity number to each survey form. All questionnaires were stored in a secure room the information's of study participants were secured in a password protected laptop.

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