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Seroprevalence of hepatitis B virus surface antigens and antibodies among healthcare workers in selected hospitals in Rivers State, Nigeria

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ABSTRACT

Background: Hepatitis B virus (HBV) infection is a major cause of liver-associated death and disability affecting over 350 million people globally. Individuals with chronic hepatitis B may progress to a more severe and deadly form of disease, mainly cirrhosis, end-stage liver disease and hepatocellular carcinoma (HCC). Healthcare workers (HCWs) are at a high risk of occupational exposure to HBV infection.

Objectives: The objectives of the study were to determine the risk factors and seroprevalence of HBV infection and protective antibodies in HCWs at selected hospitals in Port Harcourt.

Methods: Socio-demographic data and venous blood specimens were collected from consenting HCWs in the selected hospitals and tested for the presence of HBV immunological markers using immuno-chromogenic and enzyme-linked immunosorbent assay methods. Data generated was analyzed using descriptive statistics and chi square.

Results: This study revealed low levels of HBV infection (2%), high HB vaccination coverage (98%) and HBsAg - anti-HBs double seropositivity in chronic carriers that increases the risk of HCC and liver failure. Having a family member with liver disease, history of blood transfusion, blood donation and needle stick injury were significant risk factors ($p< 0.05$) for HBV infection. However, a history of blood splash was the only significant risk factor for anti-HBs seronegative HCWs.

Conclusion: HBV infection is present among HCW in Rivers state. From the findings, the infection and its attendant protective antibodies could be attributed to some invasive risk factors. Following from these, there is an important need for more awareness and public health education on prevention of HBV infection in order to achieve WHO Global health Sector Strategic plan by year 2030.

Keywords: HBV vaccination, HBV infection, healthcare workers

Séroprévalence des antigènes et des anticorps de surface du virus de l'hépatite B chez les travailleurs de la santé de certains hôpitaux de l'État de Rivers, Nigéria

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RÉSUMÉ

Contexte: L'infection par le virus de l'hépatite B (VHB) est une cause majeure de décès et d'invalidités d'origine hépatique, touchant plus de 350 millions de personnes dans le monde. Les personnes atteintes d'hépatite B chronique peuvent évoluer vers une forme plus grave et mortelle de la maladie, principalement la cirrhose, la maladie hépatique terminale et le carcinome hépatocellulaire (CHC). Les travailleurs de la santé (TS) courent un risque élevé d'exposition professionnelle à l'infection par le VHB.

Objectifs: Les objectifs de l'étude étaient de déterminer les facteurs de risque et la séroprévalence de l'infection par le VHB et des anticorps protecteurs chez les travailleurs de la santé des hôpitaux sélectionnés de Port Harcourt.

Méthodes: Des données sociodémographiques et des échantillons de sang veineux ont été prélevés auprès de travailleurs de la santé consentants dans les hôpitaux sélectionnés et testés pour la présence de marqueurs immunologiques du VHB à l'aide de méthodes de dosage immuno-chromogénique et immuno-enzymatique. Les données générées ont été analysées à l'aide de statistiques descriptives et du chi carré.

Résultats: Cette étude a révélé de faibles niveaux d'infection par le VHB (2%), une couverture vaccinale élevée contre l'HB (98 %) et une double séropositivité AgHBs - anti-HBs chez les porteurs chroniques, ce qui augmente le risque de CHC et d'insuffisance hépatique. Le fait d'avoir un membre de la famille atteint d'une maladie du foie, des antécédents de transfusion sanguine, un don de sang et une blessure par piqûre d'aiguille étaient des facteurs de risque significatifs ($p< 0,05$) d'infection par le VHB. Cependant, les antécédents d'éclaboussures de sang constituaient le seul facteur de risque significatif pour les travailleurs de la santé séronégatifs aux anti-HBs.

Conclusions: L'infection par le VHB est présente parmi les travailleurs de la santé de l'État de Rivers. D'après les résultats, l'infection et les anticorps protecteurs qui l'accompagnent pourraient être attribués à certains facteurs de risque invasifs. Par conséquent, il est nécessaire de sensibiliser et d'éduquer davantage la population à la prévention de l'infection par le VHB afin d'atteindre le plan stratégique mondial du secteur de la santé de l'OMS d'ici à 2030.

Mots-clés: vaccination contre le VHB, infection par le VHB, travailleurs de la santé

INTRODUCTION

Hepatitis B virus (HBV) infection is a major cause of liver-associated death and disability affecting over 350 million people globally. Unvaccinated children exposed to HBV have >95% risk of developing a chronic infection while infection in unvaccinated adults have <2% risk of developing a chronic disease.[1] Liver cancer is the third leading cause of death by cancer and the seventh in global incidence.[2] HBV infection is the third leading cause of carcinogenic infections globally.[3] Most people acquire infection at birth or early in life. Individuals with chronic hepatitis B (CHB) will progress to a more severe form of disease mainly cirrhosis, end-stage liver disease and hepatocellular carcinoma (HCC).[4,5] HCC is the most common primary liver cancer and occurs after a patient develops protracted chronic hepatitis associated with cirrhosis due to HBV or HCV infection. HCC is more common in HBV/HCV co-infection than HBV or HCV mono-infection probably due to chronic infection, high degree of fibrosis and carbohydrate intolerance.[6] Other risk factors for HCC include alcohol consumption, fatty liver (hepatic steatosis), genetic factors, male gender, exposure to aflatoxins and >50 years of age.[7]

The hepatitis B virus is a highly infectious and resistant virus that can infect humans of any age group. Although everyone is at risk of HBV infection during their lifetime, some people are more at risk of infection more than others. Due to the fact that the major means of transmission is through contact with contaminated blood or body fluids, people who come in contact with such samples are more at risk. Healthcare providers and emergency responders who are exposed to the blood or body fluids of infected person may be at risk of accidental exposure such as with needle prick accidents.[8,9] Also, sexually active persons with more than one sexual partner, sexual partners of infected persons, illegal drug users who usually share needles and other sharp objects,[10] men who have sex with men[11] and blood transfusion recipients.[12,13] In addition, inmates in a correctional facility,[14] haemodialysis patients[15] and pregnant women[16] are also at risk. People living with HIV or HCV are also at higher risk of getting HBV infection.[17]

Diagnosis of HBV infection involves the detection of the presence of the HBV DNA, HBV antigens (HBsAg, HBeAg) or antibodies to viral antigens (anti-HBs, anti-HBc).[18] Antibodies to HBV antigens begin to appear as early as 1 week after exposure and can be used to detect infection, assess disease prognosis or monitor treatment. Molecular techniques used in diagnosis of HBV infection include polymerase chain reaction (PCR) for amplification of HBV specific genes and immunological assays involving viral antigen - antibody reactions. In screening for HBV, presence of HBsAg is determined. If positive, antibodies to surface and core antigens (anti-HBs and anti-HBc) are tested to differentiate between infection and immunity.[19-22]

Immunity to HBV is acquired through vaccination or a resolved infection. There is no cure for HBV infection most importantly in chronic HBV/HDV carriers. Even in patient who have recovered from HBV infection, there is still a risk of reactivation because of the integration of the viral genome into the host's genome. Reactivation of HBV replication has been observed in patients who become immunosuppressed later in life.[23] Hence, prevention of HBV and HDV infection is best achieved through vaccination. Vaccination against HBV also protects against HDV as HDV infection cannot occur in the absence of HBV. Unfortunately, there is still no vaccine for HCV infection.

Considering that HBV is an important etiological agent of chronic hepatopathy, and that patients with this acute infection may not develop symptoms in most cases. Knowledge of aspects of this infection, such as prevalence, effectiveness of vaccination and relations to occupational exposure are fundamental for the improvement of preventive measures for health professionals. In addition, early detection of infection will help with better management and slow the disease progression or complications that may arise. The aim of this study is to determine the seroprevalence of HBV infection and protective antibodies in healthcare workers at three selected private and government-owned hospitals in Port Harcourt, Rivers State, Nigeria. Also, identifying the associated risk factors among this group will provide insights on making and implementing healthcare policies within the state.

MATERIALS AND METHODS

Study setting and design

The study was conducted in three hospitals located within the Port Harcourt metropolis of Rivers State, Nigeria. Obio Cottage Hospital is a Rivers State secondary healthcare facility; Ozuoba Model Primary Health Centre is a State Government-owned healthcare facility; and Rivon Clinic is a private specialist hospital for management of kidney-related diseases. A descriptive hospital-based, cross-sectional study was conducted between May - June 2022 using random sampling technique. One hundred and

twelve consenting healthcare workers at the selected healthcare facilities, mainly physicians, dentists, pharmacists, nurses, laboratory scientists, administrative staff and cleaning staff were recruited in the study.

Ethical consideration

The Research and Ethics committee of the University of Port Harcourt Teaching Hospital approved this study (reference number: UPTH/ADM/90/S.II/VOL.XI/1360). All participants signed a written consent prior to commencement of the study.

Sample size determination

The minimum sample size was determined using the formula for cross-sectional surveys[24]:

$$\frac{n = 1.96^2 \times p\ (1 - p)}{d^2}$$

where n is the minimum sample size; p is the estimated prevalence obtained from a previous study and d is the precision or acceptable error margin, usually 5%. The most recent study by[25] revealed a 5% prevalence of HBV infection among HCWs in Nigeria following a HBsAg rapid diagnostic test kit. Hence, the calculated minimum sample size for this study was 72 respondents [1.96^2 x 0.05 (1 - 0.05) / 0.05^2]. However, 10% was added in anticipation of non-response or attrition rates to give 80 as the sample size. However, 112 participants were randomly recruited for this study.

Data collection

A self-administered semi-structured questionnaire was used to collect information from participants such as socio-demographic characteristics, risk factors associated with liver disease, knowledge of HBV infection and their practices adopted towards prevention of HBV infection. The questionnaires were validated and pre-tested to determine the effectiveness of the questionnaire prior to distribution to the target population. Five millimetres of blood were collected from each participant by venous puncture and transferred into labelled, sterile containers containing EDTA. Thereafter, the blood samples were separated by low-speed centrifugation at 500 g for 5 minutes. The supernatant fraction (serum) was collected into a labelled cryovial and stored at -$2^{o}0$ C until needed.

Immunological assays

Three immunological markers for HBV infection namely HBsAg, anti-HBs and anti-HBc IgM were tested. The qualitative detection of HBsAg in serum samples was determined using a rapid diagnostic test (RDT) kit (Atlas Medical, Cambridge, UK) following manufacturer's protocols. In brief, the sealed pouches containing the test strips were brought down to room temperature before they were opened. The test strips were placed on a clean flat surface and two drops (80 µl) of serum sample were applied to specimen application site on the strip. The result was read after 15 minutes of sample application.

The presence of anti-HBs and anti-HBc IgM antibodies in the serum samples were determined qualitatively and quantitatively using a commercial Enzyme-linked immunosorbent assay (ELISA) kit (Diapro Diagnostic Bioprobes, Milano-Italy) following manufacturer's protocols. The anti-HBs and anti-HBc IgM ELISA kits contains highly purified HBsAg and HBcAg adsorbed onto the solid phase of a 96-well plate respectively. The kit and reagents were removed from their pack and brought to room temperature before the test started. A plate layout plan was used to assign test and control samples to specific wells of the microwell plate. One hundred microlitres of negative control, positive control and test samples were pipetted into the appropriated well and allowed to incubate at 37^{o}C for 1 hour. After incubation, wells were washed three times with wash buffer. The enzyme-linked secondary antibody conjugate was applied into each well and incubated at 37^{o}C for 1 hour. The plates were washed as described previously. Subsequently, the 100 µl of the substrate was added and allowed to incubate at room temperature for 20 mins. The reaction was stopped by the addition of 100 µl of stop solution. The absorbance readings were read at 450 nm using a microplate reader.

Data analysis

The questionnaires were checked for completeness and consistency. Data were entered into a Microsoft Excel workbook and analysed using Jeffrey's Amazing Statistics Program (JASP$^{(R)}$) version 0.16.3 for mac (University of Amsterdam, Netherlands). The main outcome variable was HBV serostatus while the independent variables were socio-demographic characteristics, risk factors and knowledge for HBV infection and prevention practices. Descriptive statistics was generated for variables including frequencies and percentages for categorical variables. Bivariate analyses were carried out and the Chi-square (x^2) was used to test associations between variables. A p-value less than 0.05 was used as the cut off level for statistical significance.

RESULTS

A total of one hundred and twelve (112) healthcare workers (HCWs) participated in the study. Fifty participants were from Obio Cottage Hospital, eleven from Rivon Clinic and fifty-one from Ozuoba Health Centre. As shown in Figure 1, distribution of the HCWs that participated in this study include Medical doctors (10, 8.93%), Dentists (1, 0.89%), Pharmacists (11, 9.82%), Physiotherapists (3,2.68%), Nurses (19,16.96%), Laboratory scientists (14,12.5%), Administrative staff (17, 15.18%), House-keeping staff (16, 14.29%), Students (9,8.04%) and Others that represent non-paid staff or volunteers (12,10.71%).

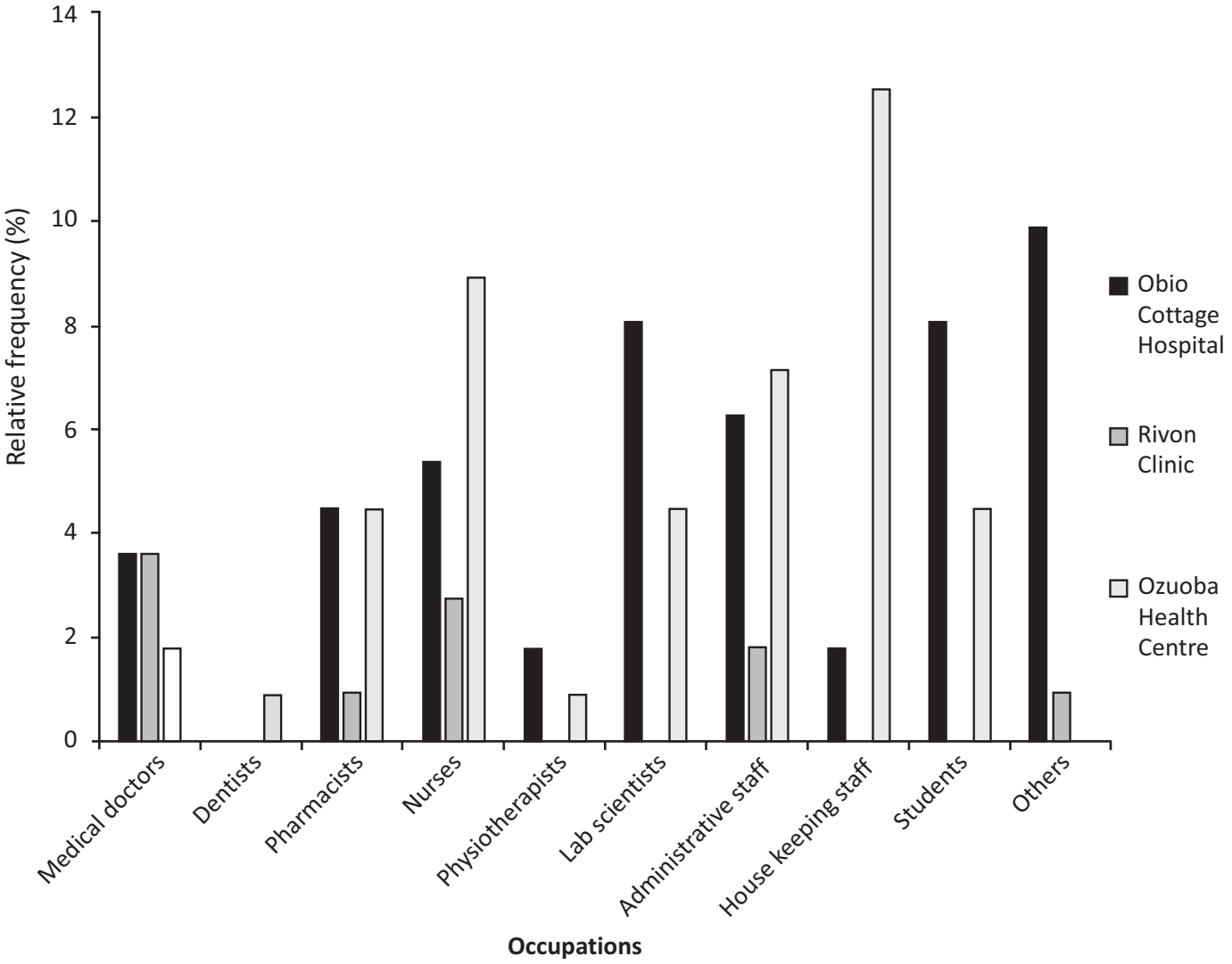

Figure 1: Distribution of study participants

Socio-demographic Characteristics of Study Participants and Infection and vaccination status of healthcare workers against Hepatitis B virus

The socio-demographic characteristics of the study participants is represented in Table 1. It showed that most respondents were within 30 - 39 years old (50.9%), female (74.1%), Christians (92%), were married (63.4%), were graduates of a tertiary institution (62.5%), have worked in the hospital for less than 5 years (52.7%), had no known medical condition (67.9%) and rarely consumed alcohol (41.1%). The HCWs positive for HBsAg were less than 30 years old, female Christian, one of which was married and the other single. Both had worked for less than 5 years. One had no known medical condition while the other had ulcer. One rarely consumed alcohol while the other did often. On the other hand, the two HCWs without detectable HBs antibodies were within 30 - 49 years of age, female Christians with tertiary education, no known medical

condition and never or rarely consumed alcohol. One was single and the other married. One had worked for less than 10 years while the other has worked for over 20 years. Based on the level of significance ($p<0.05$), length of years in service and presence of a known medical condition were they only demographic characteristics that had a link with anti-HBs or HBsAg status respectively.

Table 2 shows the state of health of participants with respect to different HBV immunological markers that reflect their infection and vaccination statuses. Negative or positive test results implied absence or presence of the immunological markers tested on the blood samples. Unused samples represented participants who did not provide any blood sample. Of the ninety-nine (99) samples tested for the presence of HBsAg, ninety-seven (98%) were negative while two (2%) samples tested positive. On the other hand, ninety (90) samples tested positive to the presence of anti-HBs while two (2) samples (2.2%) did not detect any HBs antibodies. Interestingly, the two samples that tested positive for the presence of HBsAg were also positive for HBs antibodies. However, none of the samples were positive for anti-HBc IgM as all ninety-two (92) samples were negative.

The two samples that tested positive for the presence of HBsAg were obtained from nurses. While the two samples that were absent for HBs antibodies were obtained from a medical doctor and a laboratory scientist. This is shown in Table 2.

Table 1: Socio-demographic characteristics of study participants

Socio-demographics	n* (%)	HBsAg +	p-value	Anti-HBs –	Anti-HBs +	p-value
Age (years)			0.24			0.626
18 - 29	28 (25.00%)	2		0	20	
30 - 39	57 (50.89%)	0		1	47	
40 - 49	24 (21.43%)	0		1	20	
> 50	2 (1.79%)	0		0	2	
Gender			0.12			0.051
Female	83 (74.11%)	2		2	70	
Male	27 (24.11%)	0		0	18	
Religion			0.307			0.718
Christian	103 (91.96%)	2		2	84	
Islam	3 (2.68%)	0		0	2	
Traditional	2 (1.79%)	0		0	1	
Marital Status			0.998			0.993
Single	34 (30.36%)	1		1	26	
Live-in partner	1 (0.89%)	0		0	1	
Married	71 (63.39%)	1		1	57	
Separated	2 (1.79%)	0		0	2	
Widowed	1 (0.89%)	0		0	1	
Highest level of education			0.918			0.935
Primary	3 (2.68%)	0		0	3	
Secondary	18 (16.07%)	0		0	15	
Tertiary	70 (62.50%)	1		2	55	
Postgraduate	15 (13.39%)	0		0	12	
Length of years in service			0.972			<0.001
0 – 5	59 (52.68%)	2		0	47	
6 – 10	24 (21.43%)	0		1	19	
11 – 15	11 (9.82%)	0		0	8	
16 – 20	3 (2.68%)	0		0	3	
> 20	1 (0.89%)	0		1	0	
Known medical condition			0.05			0.705
None	76 (67.86%)	1		2	59	
Diabetes	9 (8.04%)	0		0	8	
Hypertension	6 (5.36%)	0		0	3	
HIV	5 (4.46%)	0		0	4	
Ulcer	4 (3.57%)	1		0	4	
Frequency of alcohol consumption			0.704			0.996
Never	41 (36.61%)	0		1	32	
Rarely	46 (41.07%)	1		1	37	
Often	16 (14.29%)	1		0	13	
Daily	4 (3.57%)	0		0	3	

*n<112 due to missing data not captured in the questionnaire; HBsAg: Hepatitis B surface antigen; Anti-HBs: Antibodies to Hepatitis B surface protein; Anti-HBc: Antibodies to Hepatitis B core protein; -: negative; +: positive; A p-value less than 0.05 was used as the cut off level for statistical significance obtained from Chi-square (x^2) analysis between 2 variables.

Table 2: Infection and vaccination status of HCWs

Study Site	Occupations	HBsAg				Anti-HBs Ab				Anti-HBc IgM			
		–	NT	+	Total	–	NT	+	Total	–	NT	+	Total
Obio Cottage Hospital	Medical doctors	4	0	0	4	1	1	2	4	3	1	0	4
	Dentists	0	0	0	0	0	0	0	0	0	0	0	0
	Pharmacists	2	3	0	5	0	3	2	5	2	3	0	5
	Physiotherapists	2	0	0	2	0	0	2	2	2	0	0	2
	Nurses	3	3	0	6	0	3	3	6	3	3	0	6
	Lab scientists	9	0	0	9	1	2	6	9	6	3	0	9
	Admin	5	2	0	7	0	2	5	7	4	3	0	7
	House-keeping	2	0	0	2	0	0	2	2	2	0	0	2
	Students	2	2	0	4	0	2	2	4	2	2	0	4
	Others	8	3	0	11	0	3	8	11	8	3	0	11
	Total	**37**	**13**	**0**	**50**	**2**	**16**	**32**	**50**	**32**	**18**	**0**	**50**
Ozuoba Health Centre	Medical doctors	2	0	0	2	0	0	2	2	2	0	0	2
	Dentists	1	0	0	1	0	0	1	1	1	0	0	1
	Pharmacists	5	0	0	5	0	0	5	5	5	0	0	5
	Physiotherapists	1	0	0	1	0	0	1	1	1	0	0	1
	Nurses	8	0	2	10	0	0	10	10	10	0	0	10
	Lab scientists	5	0	0	5	0	0	5	5	5	0	0	5
	Admin	8	0	0	8	0	0	8	8	8	0	0	8
	House-keeping	14	0	0	14	0	1	13	14	14	0	0	14
	Students	5	0	0	5	0	3	2	5	3	2	0	5
	Others	0	0	0	0	0	0	0	0	0	0	0	0
	Total	**49**	**0**	**2**	**51**	**0**	**4**	**47**	**51**	**49**	**2**	**0**	**51**
Rivon Clinic	Medical doctors	4	0	0	4	0	0	4	4	4	0	0	4
	Dentists	0	0	0	0	0	0	0	0	0	0	0	0
	Pharmacists	1	0	0	1	0	0	1	1	1	0	0	1
	Physiotherapists	0	0	0	0	0	0	0	0	0	0	0	0
	Nurses	3	0	0	3	0	0	3	3	3	0	0	3
	Lab scientists	0	0	0	0	0	0	0	0	0	0	0	0
	Admin	2	0	0	2	0	0	2	2	2	0	0	2
	House-keeping	0	0	0	0	0	0	0	0	0	0	0	0
	Students	0	0	0	0	0	0	0	0	0	0	0	0
	Others	1	0	0	1	0	0	1	1	1	0	0	1
	Total	**11**	**0**	**0**	**11**	**0**	**0**	**11**	**11**	**11**	**0**	**0**	**11**
Total	Medical doctors	10	0	0	10	1	1	8	10	9	1	0	10
	Dentists	1	0	0	1	0	0	1	1	1	0	0	1
	Pharmacists	8	3	0	11	0	3	8	11	8	3	0	11
	Physiotherapists	3	0	0	3	0	0	3	3	3	0	0	3
	Nurses	14	3	2	19	0	3	16	19	16	3	0	19
	Lab scientists	14	0	0	14	1	2	11	14	11	3	0	14
	Admin	15	2	0	17	0	2	15	17	14	3	0	17
	House-keeping	16	0	0	16	0	1	15	16	16	0	0	16
	Students	7	2	0	9	0	5	4	9	5	4	0	9
	Others	9	3	0	12	0	3	9	12	9	3	0	12
	Total	**97**	**13**	**2**	**112**	**2**	**20**	**90**	**112**	**92**	**20**	**0**	**112**

HBsAg: Hepatitis B surface antigen; Anti-HBs: Antibodies to Hepatitis B surface protein; Anti-HBc: Antibodies to Hepatitis B core protein; Admin: Administrative staff; NT: Not tested; -: negative; +: positive

Risk perception of hepatitis B viral transmission

The occupational and non-occupational risk factors for HBV infection was determined among the HCWs as represented in Table 3. Almost half (46.4%) of the respondents had received injections in the past, 22.3% had a history of needle-prick injury, 21.4% has undergone surgery, 18.8% had donated blood or were involved in a road traffic accident, 16.1% had a dental procedure or had unprotected sexual intercourse with non-legal partner, 15.2% had a history of blood splash accident, 13.4% has a family member with liver disease and 11.6% had received blood.

The statistical analyses showed that significant risk factors (p-value <0.05) for presence of HBsAg were having a family member with liver disease, history of blood transfusion, blood donation and needle stick injury. However, a history of blood splash was the only significant risk factor for anti-HBs seronegative HCWs. It was noted that the two HCWs who were positive for HBsAg had a family member with liver disease, had received or donated blood, injections, or had had a history of needle stick injuries. One out of the two have had a road traffic accident, surgery, dental procedure, unprotected sexual intercourse with non-legal partner, or a sexually transmitted infection (STI). Healthcare workers lacking protective HBs antibodies have neither received nor donated blood, had a dental procedure, tattoos or piercings, STI or unprotected sex with non-legal partner. However, one has been involved in a road traffic accident, has a family member with liver disease, has undergone surgery, dental procedure, received injections or needle stick injury.

Table 3: Influence of risk factors to prevalence of HBV infection or HB antibodies

Risk factors	n* (%)	HBsAg +	p-value	Anti-HBs –	Anti-HBs +	p-value
Number of sexual partners			0.357			0.668
None	21 (18.75%)	1		1	15	
One	73 (65.18%)	0		1	58	
Two – five	4 (3.57%)	0		0	4	
Family history of liver disease			0.016			0.799
Don't know	23 (20.54%)	0		1	50	
None	62 (55.36%)	0		1	17	
Yes	15 (13.39%)	2		0	11	
Blood transfusion			<0.001			0.428
No	90 (80.36%)	0		2	69	
Yes	13 (11.61%)	2		0	12	
Blood donation			0.018			0.595
No	82 (73.21%)	0		2	63	
Yes	21 (18.75%)	2		0	18	
Road traffic accident			0.527			0.483
No	82 (73.21%)	1		1	64	
Yes	21 (18.75%)	1		1	17	
Surgery			0.238			0.462
No	79 (70.54%)	1		1	64	
Yes	24 (21.43%)	1		1	17	
Dental procedure			0.307			0.773
No	85 (75.89%)	1		2	67	
Yes	18 (16.07%)	1		0	14	
Receiving injections			0.256			0.999
No	51 (45.54%)	0		1	40	
Yes	52 (46.43%)	2		1	41	
Needle stick injury			0.016			0.629
No	78 (69.64%)	0		1	61	
Yes	25 (22.32%)	2		1	20	
Blood splash			0.52			0.005
No	86 (76.79%)	2		0	68	
Yes	17 (15.18%)	0		2	13	
Unprotected sex with multiple sex partners			0.468			0.475
No	85 (75.89%)	1		2	65	
Yes	18 (16.07%)	1		0	16	
Piercings or tattooing			0.72			0.428
No	90 (80.36%)	2		2	69	
Yes	13 (11.61%)	0		0	12	
Presence of STIs			0.078			0.791
No	95 (84.82%)	1		2	74	
Yes	8 (7.14%)	1		0	7	

*n<112 due to missing data not captured in the questionnaire; STI: sexually transmitted infections; -: negative; +: positive; A p-value less than 0.05 was used as the cut off level for statistical significance obtained from Chi-square (x^2) analysis between 2 variables.

Uptake of full dose of hepatitis B vaccine

The prevalence of vaccination among participants was determined via the structured questionnaire as represented in Table 4. About half (48.6%) of the HCWs that responded to the survey were vaccinated, 37.6% did not know if they were vaccinated while 13.8% said that they had not taken the vaccine. Only 15.9% of the respondents had received the full dose of the vaccine (3 doses), 3.7% had received an additional dose that is usually recommended for HCWs, 16.8% received 1 or 2 doses while 29.9% said they did not receive the vaccine. Furthermore, the barriers to HB vaccine uptake were also evaluated. Less than half (38.9%) of the HCWs knew the relevance of getting vaccinated against HBV infection, 12.9% felt it was not important for them, 11.1% were afraid of possible side effects, 8.3% were ignorant of the need to be vaccinated while the rest (6.5%) said it was expensive or unavailable. It is worthy to note that the relationship between HBsAg infection and HB vaccine received were found significant (p-value = 0.012).

Table 4: HB vaccine uptake

	Occupations										Total* n (%)	p-value
	MD	D	PH	P	N	LB	AD	HK	ST	O		
HB vaccination received												0.012
No	1	1	2	0	5	2	0	2	2	0	15 (13.76%)	
Yes	8	0	8	1	7	9	8	4	1	7	53 (48.62%)	
I don't know	1	0	1	2	6	3	7	10	6	5	41 (37.61%)	
Number of doses of HB vaccine received												
None	2	0	2	1	8	2	1	8	6	2	32 (29.91%)	
One	1	0	0	0	1	1	3	0	1	2	9 (8.41%)	
Two	1	0	2	0	3	0	1	2	0	0	9 (8.41%)	
Three	4	0	6	0	2	1	1	0	1	2	17 15.89%)	
Four	0	0	0	1	0	1	1	1	0	0	4 (3.74%)	
I don't know	2	0	1	1	4	8	8	5	1	6	36 (33.64%)	
Reasons for presence or absence of HB vaccination												
It is not important	0	0	0	0	6	1	1	3	3	0	14 (12.96%)	
It is expensive	0	0	0	0	0	0	1	2	0	0	3 (2.78%)	
Vaccine was unavailable	0	0	0	0	0	0	1	0	0	2	3 (2.78%)	
Fear of side effects	0	0	1	1	2	0	2	4	2	0	12 (11.11%)	
Pregnancy	0	0	0	0	0	0	1	0	0	0	1 (0.93%)	
I wasn't required to get vaccinated	0	0	0	0	1	2	1	1	1	3	9 (8.33%)	
I know the need for the vaccine	8	0	8	1	5	6	6	4	2	2	42 (38.89%)	
Others	2	0	2	1	4	4	3	2	1	5	24 (22.22%)	

*n<112 due to missing data not captured in the questionnaire; MD: Medical doctor; D: Dentist; PH: Pharmacist; P: Physiotherapists; N: Nurse; LB: Laboratory scientists; AD: Administrative staff; HK: House-keeping staff; ST: Students; O: Others.

Knowledge of hepatitis B infection among health care workers in Port Harcourt

The knowledge of HBV infection among HCWs were evaluated. The results of their evaluation are shown in Tables 5 and 6. With respect to symptoms of the infection, 29.7% of the respondents (mostly medical doctors and pharmacists) identified all or most of the symptoms listed in the questionnaire. Likewise, 46.4%, 55.4% and 44.6% of respondents knew the methods of transmission and prevention of HBV infection or who should receive the vaccine respectively. The knowledge of HBV infection was statistically significant for HBsAg serostatus (p-values < 0.05). A fair general knowledge of HBV infection is reported as shown by correct answers more than 40%.

Table 5: Knowledge of symptoms, transmission or prevention of HBV infection

	Occupation										Total	p-value
	MD	D	PH	P	N	LB	AD	HK	ST	O		
Symptoms of HBV infection												0.012
Identified none	2	1	2	2	8	2	5	8	3	6	39 (35.14%)	
Identified <50%	1	0	1	0	7	7	9	7	4	3	39 (35.14%)	
Identified >50%	7	0	8	1	4	4	3	1	1	3	32 (28.83%)	
Identified all	0	0	0	0	0	0	0	0	1	0	1 (0.9%)	
Modes of transmission												<0.001
Identified none	1	1	1	2	8	4	4	9	1	4	35 (31.25%)	
Identified <50%	0	0	1	0	6	3	7	4	4	0	25 (22.32%)	
Identified >50%	0	0	4	0	1	3	3	2	2	6	21 (18.75%)	
Identified all	9	0	5	1	4	4	3	1	2	2	31 (27.68%)	
Methods of prevention												0.005
Identified none	0	1	0	1	4	1	2	0	0	0	9 (8.04%)	
Identified <50%	2	0	3	1	3	5	7	12	6	2	41 (36.61%)	
Identified >50%	2	0	3	0	6	5	4	3	2	6	31 (27.68%)	
Identified all	6	0	5	1	6	3	4	1	1	4	31 (27.68%)	
Who is HB vaccine for?												<0.001
Identified none	0	1	0	0	5	0	3	0	0	2	11 (9.82%)	
Identified <50%	0	0	1	2	7	10	9	10	7	5	51 (45.54%)	
Identified >50%	5	0	3	1	3	1	2	5	2	3	25 (22.32%)	
Identified all	5	0	7	0	4	3	3	1	0	2	25 (22.32%)	
Total	**10**	**1**	**11**	**3**	**19**	**14**	**17**	**16**	**9**	**12**	**112**	

*n<112 due to missing data not captured in the questionnaire; MD: Medical doctor; D: Dentist; PH: Pharmacist; P: Physiotherapists; N: Nurse; LB: Laboratory scientists; AD: Administrative staff; HK: House-keeping staff; ST: Students; O: Others. A p-value less than 0.05 was used as the cut off level for statistical significance obtained from Chi-square (x^2) analysis between 2 variables.

Table 6: General knowledge of hepatitis B virus

Knowledge of HBV	Correct answer		Wrong answer	
	n	%	n	%
Hepatitis B is caused by a virus* (Yes)	81	72.32	28	25.00
A person infected with hepatitis B may not show any symptoms (Yes)	60	53.57	52	46.43
Hepatitis B infection may lead to liver cancer (Yes)	71	63.39	41	36.61
A person infected with hepatitis B may also be affected with HIV (Yes)	52	46.43	60	53.57
A person infected with hepatitis B may also be infected with Hepatitis D (Yes)	50	44.64	62	55.36
There is no cure for Hepatitis B infection (Yes)	51	45.54	61	54.47
Hepatitis B infection can cause liver cirrhosis (Yes)	58	51.79	54	48.21
Hepatitis B infection increases the risk of Hepatitis D infection (Yes)	45	40.18	67	59.82
HBV can survive outside the body for at least a week and remain infectious (Yes)	49	43.75	63	56.25
Healthcare workers require a 4th or booster dose of HBV vaccine (Yes)	56	50.00	56	50.00
Hepatitis B vaccine can be given as post exposure prophylaxis (Yes)	45	40.18	67	59.83
Hepatitis B vaccine can be used to treat acute hepatitis B infection (No)	40	35.71	72	64.29
HBV vaccine is recommended for some but not all healthcare professionals (No)	68	60.71	44	39.29

*Three missing data

The health care workers' practice of hepatitis B preventive measure

The practice of HCWs towards preventing and transmitting HBV infection is captured in Table 7. Most (> 80%) HCWs put on hand gloves while handling blood, blood-containing clinical specimens or cleaning spilled blood. Less than a half (37%) of the surveyed population thought it was important to confirm immunity after taking the full does of the vaccine. More than 50% know the need for HBV screening before employment, surgery or blood donation. Likewise, more than 75% of respondents sterilise equipment before use and wash hands thoroughly with soap, water and alcohol as a first aid after a needle-prick injury. Practices such as HBV screening, sterilization of instruments and proper hand washing were statistically significant (p-value < 0.05) for HBsAg serostatus.

Table 7: Practice to prevent HBV infection

	Occupations										Total*	p-value
	MD	**D**	**PH**	**P**	**N**	**LB**	**AD**	**HK**	**ST**	**O**		
I wear gloves when handling blood or blood-containing specimens												0.159
Never	0	0	0	0	0	0	0	0	0	0	0	
Sometimes	0	0	0	0	1	0	3	3	0	0	7 (7.29%)	
Always	10	1	8	3	16	12	10	11	7	11	89 (92.71%)	
I clean spilled blood with bleach solution												0.211
Never	0	0	0	0	0	0	0	0	1	0	1 (1.05%)	
Sometimes	1	0	0	0	4	1	3	4	0	0	13 (13.68%)	
Always	9	1	8	3	13	10	10	10	6	11	81 (85.26%)	
After taking full dose of HBV vaccine, there is no need to confirm immunity												0.163
Never	4	1	6	0	4	5	6	6	4	1	37 (40.22%)	
Sometimes	3	0	1	3	6	3	5	4	0	8	33 (35.37%)	
Always	1	0	1	0	5	3	3	3	3	3	22 (23.91%)	
HBV screening is required for employment in a hospital												0.025
Never	0	0	0	1	3	3	3	4	3	0	17 (17.53%)	
Sometimes	0	0	2	1	9	3	3	6	1	2	27 (27.84%)	
Always	9	1	7	1	4	5	9	4	3	10	53 (54.64%)	
HBV screening is required for patients for surgery, blood donation etc.												0.007
Never	0	0	0	1	1	2	1	2	1	0	8 (8%)	
Sometimes	0	0	0	1	3	0	2	7	3	0	16 (16%)	
Always	10	1	10	1	13	9	12	5	3	12	76 (76%)	
I always sterilize instruments before use												0.017
Never	0	0	0	0	0	0	0	0	0	0	0 (0%)	
Sometimes	0	0	0	1	2	2	4	6	4	0	19 (20%)	
Always	10	1	8	2	15	9	9	8	3	11	76 (80%)	
I wash with water, soap and alcoho l after a needle stick injury												0.047
Never	0	0	0	0	1	1	1	2	1	0	6 (6%)	
Sometimes	0	0	1	1	0	1	2	6	3	0	14 (14%)	
Always	9	1	9	2	16	10	12	6	3	12	80 (80%)	
Total	**9**	**1**	**10**	**3**	**17**	**12**	**15**	**14**	**7**	**12**	**100**	

*n<112 due to missing data not captured in the questionnaire; MD: Medical doctor; D: Dentist; PH: Pharmacist; P: Physiotherapists; N: Nurse; LB: Laboratory scientists; AD: Administrative staff; HK: House-keeping staff; ST: Students; O: Others. A p-value less than 0.05 was used as the cut off level for statistical significance obtained from Chi-square (x^2) analysis between 2 variables

DISCUSSION

The prevalence of HBV infection has a worldwide distribution. Like many other West African Countries, the endemicity of HBV infection is high in Nigeria especially among HCWs who are at a higher risk of infection due to their occupation. This study was performed to determine the prevalence of HBV infection among HCWs working in private, primary and secondary healthcare facilities in Port Harcourt metropolis. It also assessed the vaccination status, risk and knowledge of infection as well as practices adopted to minimize occupational hazards of infection.

The prevalence of HBV infection was measured by detecting the presence of HBsAg and anti-HBc IgM in blood samples collected from HCWs. The reported prevalence for this study was 2% which is low compared to 14.5% that was obtained from a previous study conducted in a tertiary healthcare facility in Port Harcourt.[26] However, the study was restricted only to staff of the chemical pathology department. Similar studies that were carried out in Nigeria using serological-based methods have shown various HBV prevalence among HCWs.[27,28] Although this study detected the presence of HBsAg in two samples, those samples were negative for IgM antibodies to hepatitis B core protein. Anti-HBc are found only in patients with a natural history of HBV infection. Immunoglobulin M antibody was the first antibody to be secreted in response to an infection and signifies an early or acute infection.[29] The absence of anti-HBc IgM in the serum samples of the HBsAg positive patients implies that the HB infection is not acute and may be chronic.

HBV infection has been documented as an occupational hazard for HCWs. The frequent exposure to blood and blood products that may be contaminated with HBV increases their risk of infection. Also, they are at a higher risk of occupational accidents such as needle prick injuries, blood splash, or even percutaneous and per-mucosal exposure to blood and body fluids. Due to the high occupational exposure and risk of infection, it is recommended that HCWs are vaccinated with HB vaccine for protection against the harmful effect of the virus. The HB vaccination was introduced into the Nigerian immunization schedule in 1995, however, it was implemented in 2004 when it was included in the National Programme on Immunization, supported by the World Health Organization (WHO).[30] Till date, the advent of vaccination is one of the great accomplishments ever recorded in medicine whereby the risk of exposure to many infectious agents is highly minimized by the timely receipt of protective vaccines. According to WHO, HB vaccine has been introduced in 184 countries in the world where the average global uptake is about 84%.[31]

In this study, the vaccination status of the HCWs was obtained from the questionnaires as well as testing for the presence of anti-HBs biomarkers. Although only 48.62% claimed to have received at least one dose of HB vaccine, only 36.45% knew the number of doses they had taken. One-third of the sampled population did not know if they had taken the vaccine or the number of doses taken. However, the presence of anti-HBs in 97.8% of the tested samples shows a very high level of vaccine coverage or protection to HBV infection among HCWs. The high HB vaccine uptake among HCWs could be linked to availability and affordability of the vaccine which has been provided by the government or the institutions. This is deduced from the responses obtained following reasons for presence or absence of vaccination. There is an increasing awareness of HB vaccination created by many medical outreach programmes carried out in churches and in the communities at different times of the year and to mark the world hepatitis day. It is one of the strategies adopted in the WHO Global health Sector Strategy on eradication of chronic viral hepatitis by 2030. Also, many hospitals perform a pre-employment health screening for all newly recruited staff to determine their fitness for work as well as yearly routine medical check-ups to detect early signs of health changes that may arise in the course of work.

It is interesting to note that the two HBsAg positive HCWs were also seropositive for anti-HBs. The resolution of chronic HB infection occurs when HBsAg is cleared and anti-HBs can be detected. In rare cases, chronic carriers can show detectable levels of both HBsAg and anti-HBs.[32] Studies have shown that HBsAg and anti-HBs can co-exist during seroconversion to form immunocomplexes that are rarely detected in clinical studies. However, the co-existence of HBsAg and anti-HBs is becoming more prevalent due to the promotion of HB vaccination as well as anti-viral treatment. The simultaneous HBsAg / anti-HBs double positivity have been reported in 2.45 - 5.8% of chronic HBV infected patients in China, 2.8% - 5% in France, 1.2% in North America and as high as 21% in Japan and Singapore.[33] Mutations in the HB viral genome, immune function, as well as host's genetic factors may contribute to the co-existence of HBsAg and anti-HBs biomarkers.[33] Due to the presence of HBsAg, such patients are still known to be infectious. Furthermore, co-existence of HBsAg and anti-HBs signifies an increased risk of complications as it is strongly associated with

progressive liver diseases especially in HCC.[34] There is a 3-fold increase in risk of HCC in HBsAg / anti-HBs double positivity than in HBsAg single positive patients.[35]

The selected hospitals provide many services such as pharmaceutical care, maternal care, immunization, paediatrics, minor surgeries, community health, family planning, emergency services, renal management, nutritional and weight management, and eye and dental services. Such services can expose the HCWs to infected specimens if adequate infection prevention and control managements are not put in place by the hospital management. The regulation and implementation of health policies may vary between institutions and this may influence the quality of care within the hospitals. A recent study also showed good knowledge (>80%) of the risks and modes of transmission of HBV infection among HCWs in University of Nigeria Teaching Hospital, Enugu.[9] Based on the level of significance (p-value <0.05), the risk factors identified in this study that contributes to the prevalence of HBV infection among the study participants include family history of liver disease, history of blood transfusion, history of blood donation and a previous needle-stick injury. Although the levels of knowledge of symptoms, transmission and prevention of HBV infection were less than 50%, the clinical HCWs were more knowledgeable of the disease compared to the non-clinical staff. This may be attributed to their level of education and training. This highlights the need to intensify health education not just in the communities but in hospitals as well where the risk of exposure is higher. Public health education helps to correct misconceptions in causes and treatment of many infectious diseases including HBV infection.

The general knowledge of HBV infection among the HCWs studied can be seen to reflect in their daily work practices of infection prevention and control. Practices such as pre-employment screening, screening of patients for surgery, blood donation or childbirth, sterilization of instruments before use and proper hand washing following a needle-stick injury were significant in the prevention of HBV infection among the HCWs. Waste disposal management, such as management of sharps and needles, is an important aspect of infection control. Used needles are not recapped after use and are disposed of in a separated box so as to prevent the risk of accidental puncture. New patients that will require invasive treatment such as surgeries, child birth, insertion of birth control devices etc, HBV and HIV pre-screening is performed in these hospitals as a way of mitigating the risk of exposure of HBV infection. In a resource-limited country such as Nigeria, where prophylactic anti-HBV human immunoglobulin is unavailable, vaccination remains the cheaper and safer alternative to HBV infection prevention.

CONCLUSION

Public health is the science and art of preventing disease, prolonging life and promoting health through the organised efforts and informed choices of the society, organizations, public and private, communities and individuals. This study has revealed HBV among HCWs in Rivers state as an infection associated with variously identified occupational risks. However, the seroprevalence of infection and protective antibodies reflected adequate knowledge and prevention practices among the study population. Nonetheless, more needs to be done in the area of increase in awareness and public health education for both the clinical and non-clinical staff in order to achieve total elimination of the infection intended by WHO Global health Sector Strategic plan.

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REFERENCES

1. Hyams KC. (1995). Risks of chronicity following acute hepatitis B virus infection: A review. *Clinical Infectious Diseases.* 20(4):992-1000.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. (2018). Global cancer statistics 2018: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: *Cancer Journal for Clinicians*. 68(6):394-424.
3. Plummer M, de Martel C, Vignat J, Ferlay J, Bray F, Franceschi S. (2016). Global burden of cancers attributable to infections in 2012: A synthetic analysis. *Lancet Global Health.* 4(9):e609-616.
4. Beasley RP. (1988). Hepatitis B virus. The major etiology of hepatocellular carcinoma. *Cancer.* 61(10):1942-1956.
5. Yang HI, Lu SN, Liaw YF, You SL, Sun CA, Wang LY, Hsiao CK, Chen PJ, Chen DS, Chen CJ, Taiwan Community-Based Cancer Screening Project Group. (2002). Hepatitis B e antigen and the risk of hepatocellular carcinoma. *New England Journal of*

Medicine. 347(3):168-174.

6. Zampino R, Pisaturo MA, Cirillo G, Marrone A, Macera M, Rinaldi L, Stanzione M, Durante-Mangoni E, Gentile I, Sagnelli E, Signoriello G, Del Giudice EM, Adinolfi LE, Coppola N. (2015). Hepatocellular carcinoma in chronic HBV-HCV co-infection is correlated to fibrosis and disease duration. *Annals of Hepatology.* 14(1):75-82.
7. Yang JD, Hainaut P, Gores GJ, Amadou A, Plymoth A, Roberts LR. (2019). A global view of hepatocellular carcinoma: Trends, risk, prevention and management. Nature Reviews *Gastroenterology Hepatology.* 16(10):589-604.
8. Alese OO, Alese MO, Ohunakin A, Oluyide PO. (2016). Seroprevalence of hepatitis B surface antigen and occupational risk factors among health care workers in Ekiti State, Nigeria. *Journal of Clinical Diagnostic Research.* 10(2):LC16-18.
9. Ijoma UN, Meka IA, Omotowo B, Nwagha TU, Obienu O, Onodugo OD, Onyekonwu CL, Okoli EV, Ndu AC, Ugwu EO. (2021). Sero-prevalence of hepatitis B virus infection: A cross-sectional study of a large population of health care workers in Nigeria. *Nigerian Journal of Clinical Practice.* 24(1):38-44.
10. Fadil RA, Abdelmutalab NA, Abdelhafeez SA, Mazi W, Algamdi S, Shelwy MM, Bouafia N, Alzahrani SE. (2021). Pattern and risk factors of sharp object injuries among health care workers in two tertiary hospitals, Al Taif-Kingdom of Saudi Arabia 2016-2018. *Saudi Journal of Biological Sciences.* 28(11):6582-6585.
11. Mmbaga EJ, Moen K, Leyna GH, Mpembeni R, Leshabari MT. (2018). HIV prevalence and associated risk factors among men who have sex with men in Dar es Salaam, Tanzania. *Journal of Acquired Immune Deficiency Syndrome.* 77(3):243-249.
12. Jary A, Dienta S, Leducq V, Le Hingrat Q, Cisse M, Diarra AB, Fofana DB, Ba A, Baby M, Achenbach CJ, Murphy R, Calvez V, Marcelin AG, Maiga AI. (2019). Seroprevalence and risk factors for HIV, HCV, HBV and syphilis among blood donors in Mali. *BMC Infectious Diseases.* 19(1):1064.
13. Otegbayo JA, Fasola FA, Abja A. (2003). Prevalence of hepatitis B surface and E antigens, risk factors for viral acquisition and serum transaminase among blood donors in Ibadan, Nigeria. *Tropical Gastroenterology.* 24(4):196-197.
14. Moradi G, Mohamadi P, Zareie B, Rasouli MA, Gouya MM, Jafari S. (2020). Prevalence of and risk factors for HBV and HCV among incarcerated people who inject drugs in Iran: A cross sectional study. *BMC Infectious Diseases*. 20(1):806.
15. Mhalla S, Hammoud R, Frih A, Kadri Y, El Argoubi A, Elmay M, Mastouri M. (2018). Prevalence and risk factors of hepatitis B and C among hemodialysis patients in Tunisia. *Medical Malpractice and Infection.* 48(3):175-179.
16. Guo Z, Shi XH, Feng YL, Wang B, Feng LP, Wang SP, Zhang YW. (2013). Risk factors of HBV intrauterine transmission among HBsAg-positive pregnant women. *Journal of Viral Hepatitis.* 20(5):317-321.
17. Lyu X, Liu K, Chen Y, Wang Z, Yao J, Cai G, Jiang Z, Jiang J, Gu H. (2016). Analysis of risk factors associated with the development of hepatocellular carcinoma in chronic HBV-infected Chinese: A meta-analysis. *International Journal of Environmental Research and Public Health.* 13(6):604.
18. Terrault NA, Bzowej NH, Chang KM, Hwang JP, Jonas MM, Murad MH, American Association for the Study of Liver Diseases. (2016). AASLD guidelines for treatment of chronic hepatitis B. *Hepatology.* 63(1):261-283.
19. LeFevre ML, Force USPST. (2014). Screening for hepatitis B virus infection in nonpregnant adolescents and adults: U.S. Preventive services task force recommendation statement. *Annals of Internal Medicine.* 161(1):58-66.
20. Mast EE, Weinbaum CM, Fiore AE, Alter MJ, Bell BP, Finelli L, Rodewald LE, Douglas JM, Janssen RS, Ward JW, Advisory Committee on Immunization Practices (ACIP), Centers for Disease Control and Prevention (CDC). (2006). A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: Immunization of adults. *Mortality and Morbidity Weekly Report: Recommendation Reports.* 55(RR-16):1-33; quiz CE1-4.
21. Weinbaum CM, Williams I, Mast EE, Wang SA, Finelli L, Wasley A, Neitzel SM, Ward JW, Centers for Disease Control and Prevention (CDC). (2008). Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *Mortality and Morbidity Weekly Report: Recommendation Reports.* 57(RR-8):1-20.
22. Abara WE, Qaseem A, Schillie S, McMahon BJ, Harris AM, Abraham GM, Centor R, DeLong DM, Gantzer HE, Horwitch CA, Humphrey LL, Jokela JA, Li JMW, Lohr LH, Lopez AM, McLean RM (2017). Hepatitis B vaccination, screening, and linkage to care: Best practice advice from the American College of Physicians and the Centers for Disease Control and

Prevention. *Annal of Internal Medicine.* 167(11):794-804.
23. Lok AS, Zoulim F, Dusheiko G, Ghany MG. (2017). Hepatitis B cure: From discovery to regulatory approval. *Hepatology.* 66(4):1296-1313.
24. Whitley E, Ball J. (2002). Statistics review 4: Sample size calculations. *Critical Care.* 6(4):335-341.
25. Ogundele OA, Olorunsola A, Bakare B, Adegoke IA, Ogundele T, Fehintola FO, Okotie S. (2021). Seroprevalence and knowledge of hepatitis B and C among health care workers in a specialist hospital in Nigeria. *European Journal of Preventive Medicine.* 5(1):7-12.
26. Ejele OA, Ojule AC. (2003). Hepatitis B antigenemia (HBsAg): Risk of occupational exposure in a chemical pathology laboratory in Nigeria. *Nigeria Journal of Clinical Practice.* 6(2):99-101.
27. Ola SO, Odaibo GN, Olaleye OD, Ayoola EA. (2012). Hepatitis B and E viral infections among Nigerian healthcare workers. *African Journal of Medicine and Medical Sciences.* 41(4):387-391.
28. Musa BM, Bussell S, Borodo MM, Samaila AA, Femi OL. (2015). Prevalence of hepatitis B virus infection in Nigeria, 2000-2013: A systematic review and meta-analysis. *Nigeria Journal of Clinical Practice*. 18(2):163-172.
29. Pondé RA. (2013). Atypical serological profiles in hepatitis B virus infection. *European Journal of Clinical Microbiology and Infectious Diseases.* 32(4):461-476.
30. Ikobah J, Okpara H, Elemi I, Ogarepe Y, Udoh E, Ekanem E. (2016). The prevalence of hepatitis B virus infection in Nigerian children prior to vaccine introduction into the national programme on immunization schedule. *Pan African Medical Journal.* 23:128.
31. Simidele OM, Oladimeji A, Joseph AA, Aduayi V, Samuel NI. (2018). Burden of hepatitis B viral infection among workers in a tertiary health institution in southwestern Nigeria. *Open Journal of Medical Microbiology.* 8:85-97.
32. Krajden M, McNabb G, Petric M. (2005). The laboratory diagnosis of hepatitis B virus. *Canadian Journal of Infectious Diseases and Medical Microbiology.* 16(2):65-72.
33. Jiang X, Chang L, Yan Y, Wang L. (2021). Paradoxical HBsAg and anti-HBs coexistence among chronic HBV infections: Causes and consequences. *International Journal of Biological Sciences.* 17(4):1125-1137.
34. Jin ZZ, Jin FF, Liu X, Liu N, Wen F, Lou JL. (2019). Coexistence of low levels of HBsAg and high levels of anti-HBs may increase risk of hepatocellular carcinoma in chronic hepatitis B patients with high HBV load. *Brazilian Journal of Infectious Diseases.* 23(5):343-351.
35. Kwak MS, Chung GE, Yang JI, Yim JY. (2019). Long-term outcomes of HBsAg/anti-HBs double-positive versus HBsAg single-positive patients with chronic hepatitis B. *Scientific Reports.* 9(1):19417.