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Laboratory-Based Monitoring of Hepatitis-B Virus Vaccination Status in North-Central Nigeria

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ABSTRACT

Background: *The World Health Assembly through the Global Health Sector Strategy on viral hepatitis calls for the elimination of viral hepatitis as a public health threat by 2030. All hands are on deck to actualize this goal through an effective and active vaccination and monitoring tool.*

Aim: *To combine the Epidemiologic with Laboratory tools in monitoring Hepatitis B Virus vaccination.*

Method: *Laboratory results analysis of subjects recruited during the World Hepatitis week from July 2020 to July 2021 was done after obtaining their epidemiologic data on Hepatitis B virus risk factors, in the Medical Microbiology Laboratory of Benue State University Teaching Hospital, Nigeria.*

Results: *A total of 500 subjects comprising males 60.0% (n=300/500) and females 40.0% (n=200/500) were recruited. A fifty-three percent majority was of the age range of 26 to 36 years. Serologic profiles were as follows, 15.0% (n=75/500) HBsAg; 7.0% (n=35/500) HBeAg; 8.0% (n=40/500) Anti-Hbe; 20.0% (n=100/500) Anti-HBc and 38.0% (n=190/500) Anti-HBs. Immune responses to vaccination were as follows, 47.0% (n=235/500) Immune naïve {no serologic marker + normal ALT}; 33%(n=165/500) Immunity by vaccination {Anti-HBs + normal ALT}; 5%(n=25/500) Immunity to previous infection {Anti-HBs, Anti-HBc, +/- Anti-HBe + normal ALT}; 8%(n=40/500) Carriers {HBsAg, Anti-HBc, Anti-HBe +normal ALT} and 7% (35/500) Anti-HBe serum- negative infections {HBsAg, HBeAg, Anti-HBc +elevated ALT}.*

Conclusion: *The present 33.0% immunity by vaccination coverage in Central Nigeria was much lower than the 41.0% national peak in 2013, and very different from the global expectation of attainment of a Global Health Sector Strategy on the elimination of viral hepatitis as a public health threat by 2030. Therefore, more creative ideas and collective effort are needed to attain this goal of the World Health Assembly.*

Keywords

Hepatitis-B Virus, Vaccination, Healthcare.

Introduction

Viral hepatitis is diffuse liver inflammation due to viral agents. It is a clinical syndrome associated with a number of viral infections [1]. The etiologic agents, within the last two decades, have exploded with progressive lengthening from A to G alphabetic taxonomy [1,2]. Among the hepatitis viruses, the Hepatitis B virus (HBV) is the most important agent in terms of prevalence and ability to cause chronic viral diseases in Sub Sahara Africa [2,3].

In Nigeria, several studies from different parts of the country have confirmed the endemicity of the infection [3,4], with the prevalence rate of up to 23% being chronic hepatitis B carriers among some study population [4]. The most effective means of transmission is through blood and blood products and sexual contact with infected individuals. The virus can also be transmitted vertically from infected mother to child and through the use of contaminated body cutting materials for scarification and herbal marks [3,4]. HBV is about 100 times more infectious than human immunodeficiency virus (HIV) [2,3,5]. Since similar routes transmit both HIV and HBV, the likelihood of the two viruses recording a high prevalence in any locality where one is found is high.

Hepatitis B surface antigen (HBsAg), which appears first within weeks of exposure, is indicative of infection [6]. Its appearance is closely followed by that of hepatitis B e antigen (HBeAg), the conventional marker of HBV replication, as well as other indicators of replication, most notably HBV DNA [6,7]. Hepatitis B core antigen (HBcAg) does not circulate in serum but is demonstrated serologically by antibodies directed against it (anti-HBc), which appears early in the course of infection before hepatic dysfunction or clinical illness [6,7]. Initially, the anti-HBc antibody is an IgM antibody, which persists for about six months after infection. This is a non-neutralizing antibody, but its IgG fraction persists indefinitely [7]. Indeed, the latter may be the sole marker of remote, resolved HBV infection because antibody to HBsAg (anti-HBs), which is neutralizing and typically appears after clearance of HBsAg, may ultimately disappear from serum many years after the resolution of HBV infection [7,8]. Naturally, acquired immunity to HBV is characterized by the presence of both anti-HBs and anti-HBc antibodies, whereas vaccine-induced immunity does not induce anti-HBc antibody production but a positive reaction to anti-HBs antibodies plus history of vaccination [9]. Immune naïve (immune susceptible) individuals are not reactive to any of the serologic /immune/molecular markers [8,9].

A comprehensive strategy to eliminate hepatitis B virus transmission was recommended in 1991; it includes prenatal testing of pregnant women for HBsAg, to identify newborns who require immunoprophylaxis for prevention of perinatal infection, and to identify household contacts who should be vaccinated, routine vaccination of infants, vaccination of adolescents, and vaccination of adults at high risk for infection [10,11]. The Hepatitis B vaccine was included in the immunization schedule in Nigeria in 1995 but the vaccine only became widely available in 2004 [11]. Recommendations to further enhance vaccination of adults at increased risk of HBV infection were published in 2011 [12]. In May 2016, the World Health Assembly endorsed the *Global Health Sector Strategy (GHSS) on viral hepatitis 2016–2021* [13]. The GHSS calls for the elimination of viral hepatitis as a public health threat by 2030 (reducing new infections by 90% and mortality by 65%) [13]. Hence, WHO policy of including HBV vaccination in the routine immunization schedule for children and adults at risk was implemented and the monitoring of immune responses to the vaccine globally has taken off [14]. In some communities, there is a false claim of being vaccinated. Such reasons include ignorance and false fear, hence the need for monitoring immune responses to the vaccine in the population at risk.

Rapid Diagnostic Testing (RDT) is a point of care (POC) test comprising small devices that provide qualitative and/or quantitative determination of viral antibodies and/or antigens. Anti -HBs seropositivity in a seronegative Anti-HB core with seronegative HBsAg and a normal enzyme alanine aminotransferase (ALT) serum level points to effective vaccination.

Rapid diagnostic testing with a lateral flow or flow-through mechanism is a cheap and efficient laboratory tool available in primary healthcare centers of poor rural communities. Therefore, efficient and true monitoring of the vaccination status of the population at risk in our rural areas should be done by combined laboratory cum epidemiologic tools. We hereby combine the Epidemiologic with Laboratory tools in the monitoring of Hepatitis B Virus (HBV) vaccination.

Method

Study Area

Benue state is in North Central Nigeria and has a teaming population of about 5 million with its state capital, Makurdi located in the northern part of the state. The state is surrounded by neighboring states; Enugu state and Kogi state on the East, Taraba state on the West, Cross River state on the South, and Nassarawa state on the North. Benue state had a total population of 4,253,641 in the 2006 census with an average population density of 99 persons per km² with a land mass of 34,059 km². Agriculture forms the backbone of the Benue State economy, engaging more than 70 percent of the working population. Makurdi harbors two tertiary medical centers namely, Benue State University Teaching Hospital and Federal Medical Center with other secondary medical centers.

Subjects and Materials

Individuals referred to the Medical Microbiology laboratory of Benue State University Teaching Hospital, Makurdi who presented with one or more of the following namely, yellowness of eyes and urine, nausea and vomiting, weakness, loss of appetite and low-grade fever or other HBV risk factors were recruited into this study. Recruitment was from the Wards and General out-patients department (GOPD) of the teaching hospital and those referred from outside the hospital for microbiology tests, during the months of commemoration of World Hepatitis Day (WHD) from July 28th, 2020 to July 27th, 2021.-Ethical clearance from Benue State University Teaching Hospital was obtained. Age, sex, risk factors, vaccination history, and complaints of subjects were documented.

The patients that were in the infectious stage were recruited for treatment in BSUTH and those that were seronegative were encouraged on full vaccination.

Laboratory Studies

Ten (10) mls of fresh blood was aseptically collected from the

Table 1: Interpretative Data of some of the Serologic Tests conducted among the study population in Makurdi, 2020 to 2021.

Clinical State	HBsAg	Anti-HBs	HBeAg	Anti-HBe	Anti-HBc	Serum Alanine Transaminase (ALT)
Immunity by Vaccination	_	+	_	_	_	NORMAL
Acute Hepatitis B	+	_	+	_	+	ELEVATED
Acute Chronic Hepatitis B	+	_	+	_	+	ELEVATED
Inactive Chronic Hepatitis B.	+	_	_	+	+	NORMAL
Immunity by previous infection	_	+	_	+ /_	+	NORMAL
Immune- naïve	_	_	_	_	_	NORMAL

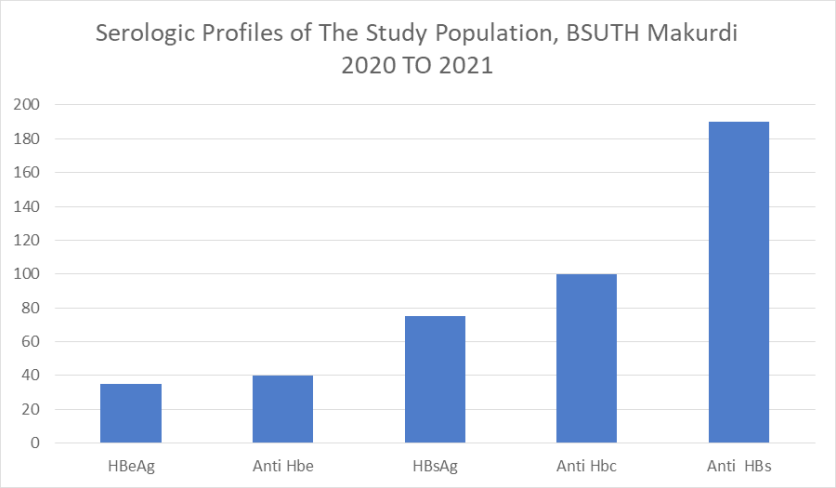

Figure 1: Serologic Profiles of the Study Population, BSUTH Makurdi 2020 to 2021.

antecubital fossa of each recruited subject and shared into 5 mls in each of the two EDTA bottles. A 5 ml of sample was used for serologic testing for the various hepatitis B viral antigens/ antibodies/profiles in the Microbiology laboratory of BSUTH. While another 5 ml was for the determination of relevant biochemical markers.

Hepatitis B virus serologic profiles By Rapid Diagnostic Testing

The serum samples were screened for HBV serologic markers namely, hepatitis B surface antigen (HB*s*Ag), hepatitis B surface antibody (anti-HB*s*), hepatitis B core antibody (anti-HB*c*), Hepatitis B envelop antigen (HB*e*Ag), HB*c*IgM and antibody to HBV envelope antigen(HBeAb). HBV combination immuno-chromatographic rapid kits manufactured by Acumen Diagnostics Incorporated (Lot SAG91108; expiry date 11/2022) were used for the analyses. The manufacturer's instructions were strictly followed.

Biochemical Markers

The liver enzyme alanine aminotransferase (ALT) was quantitatively measured using the Pars Azmoon kit (Tehran, Iran) based on the manufacturer's instructions.

Interpretation of Data

The data of the Laboratory study viz a viz the clinical pictures are expressed in table 1 below.

Statistical Analysis

Data were analyzed using SPSS version 20 statistical software; chi-square was used to compare the association between proportions and P-values <0.05 was considered significant at a 95.0% confidence level.

Ethical approval

Ethical approval to carry out this study was obtained from Benue State University Teaching Hospital. Makurdi, Nigeria.

Results

A total of five hundred subjects were tested for Hepatitis B virus serologic profiles by number, sex, and age. The HBsAg seropositive clients were fifteen percent (n=75/500), Anti-HBe 8.0% (n=40/500), HBeAg 7.0% (n=35/500), Anti-HBc 20.0% (n=100/500), and Anti-HBs (n=190/500) [Figure 1]. The mean age was 30 ± 2 years with a high-frequency age range of 26 to 36 years and male preponderance (Table 2).

Table 2: Age and Gender wise distribution of patients tested for Hepatitis B virus according to serologic positivity and negativity.

Variables	**Male N=300 (60%)**		**Female N=200 (40%)**		**Total N=500 (100%)**
Age (years)	***+ve***	***-ve***	***+ve***	***-ve***	
15 -25	5	29	4	22	60 (12.0%)
26-36	100	66	60	40	266 (53.0%)
37- 47	47	23	25	19	114 (23.0%)
48-58	10	10	7	13	40(8.0%)
>59	4	6	3	7	20 (4.0%)
Total	**166**	**134**	**99**	**101**	**500**

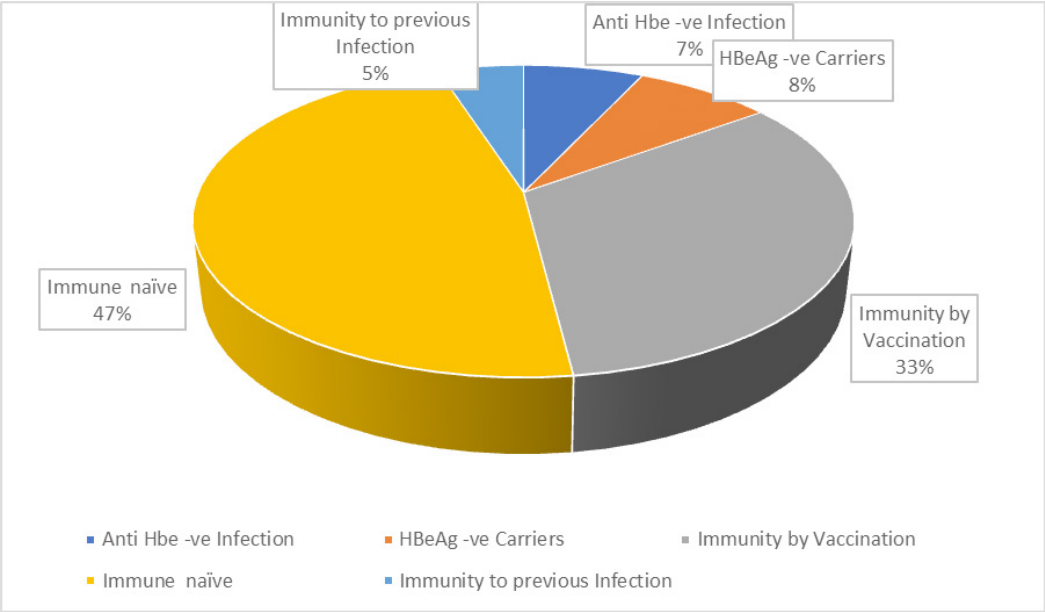

Figure 2: Hepatitis B Virus serologic Status among the study population.

In the study population, the HBV infection status of the clients was determined as follows, 7.0% (n= 35/500) Anti-HBe seronegative infection, 8.0% (n= 40/500) HBeAg seronegative infection, 33.0% (n= 165/500) immunity by vaccination, 5.0% (25/500) immunity to previous infection, and 47.0% (n= 235/500) immune naïve to HBV (susceptible) (Figure 2). Interpretative data is used as in Table 1 in the methodology.

Discussion

A finding of 33.0% immunity by vaccination and 47.0% immune naïve by serologic diagnostic tools in North Central Nigeria was done. In 2000-2005, HBV vaccination coverage in Nigeria was reported as zero by UNICEF, 18% in 2006, and peaked at 41% in 2013 [15,16]. The study observed a drop from the 41% national peak in 2013 [15], to 33% in a state in central Nigeria, in 2021. The challenge in solitary epidemiologic monitoring of vaccination status among the population at risk in some communities includes a false claim of being vaccinated. Such reasons might be based on ignorance and false belief that the Western world could depopulate Africa through vaccination, which would negatively affect the sterility or reproductivity of the young population. In order to erase this false belief, it calls for more advocacy campaigns, locally and internationally.

In May 2016, the World Health Assembly endorsed the *Global Health Sector Strategy (GHSS) on viral hepatitis 2016–2021* [13]. The strategy calls for the elimination of viral hepatitis as a public health threat by 2030 [14]. The population at risk includes as follows, all infants, beginning at birth; all children who have not been vaccinated previously; susceptible sexual partners of hepatitis B-positive persons; sexually active persons who are not in a long-term mutually monogamous relationship; persons seeking evaluation or treatment for a sexually transmitted disease; Men who have sex with men; Injection drug users; susceptible household contacts of hepatitis B-positive persons; healthcare and public safety workers at risk for exposure to blood; persons with end-stage renal disease who on dialysis; residents and staff of facilities for developmentally disabled persons; travelers to and from countries where hepatitis B is common; persons with chronic liver disease, other than hepatitis B (e.g. cirrhosis, fatty liver disease, etc.); persons with hepatitis C infection; persons with HIV infection; adults with diabetes. Mandatory vaccination is advisable for children and adults at risk [13].

While the most recently reported immunization coverage level in Nigeria is low by the worldwide average, the impact of optimum utilization of immunization can translate to a rapid reduction in HBV prevalence. However, the project might be bedeviled with Vaccine-related failures [14] such as failures in vaccination regimes, or administration, and Host-related failures as host genetics, immune status, age, health, or nutritional status, which can be associated with primary or secondary vaccine failures. In primary vaccine failure, the immune system does not produce enough antibodies when first vaccinated while in secondary vaccine failure, the antibodies levels fall over time [14]. A “non-responder" refers to a person who does not develop protective surface antibodies after completing two full series of the hepatitis B vaccine. WHO policy of HBV vaccination, therefore, included the routine immunization schedule for children and populations at risk, and the monitoring of immune responses to the vaccine [15,16].

The shortfalls or limitations in the study included the short time interval and the limited number of subjects recruited for the project. However, it may serve as a pilot study.

There are challenges in solitary epidemiologic monitoring of the true Hepatitis B vaccinees as well as non-responders in

the population at risk, especially in poor rural communities. Consequently, the *Global Health Sector Strategy* calls for the elimination of viral hepatitis as a public health threat by 2030 [2,14], hence we advocate combined epidemiologic monitoring strengthened with a laboratory tool in the vaccination status of the population at risk of Hepatitis B infection in resource-limited settings.

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