

## Original Research

# Hepatitis B virus seroprevalence among Malawian medical students: A cross-sectional study

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## Abstract

### Background

Hepatitis B virus (HBV) predominantly spreads through contact with infected blood or other body fluids and causes liver disease. HBV vaccination for students at the College of Medicine, University of Malawi, is done without screening for the virus. It is important to assess the prevalence of HBV antigens among foundation-year students in order to consolidate evidence in support of HBV screening before vaccination.

The aim of this study was to determine the seroprevalence of HBV antigens among 2013-2014 foundation-year students at the University of Malawi College of Medicine.

### Methods

A prospective cross-sectional descriptive study was conducted among 2013-2014 foundation year students at the Malawi College of Medicine. Out of the 234 foundation-year students, written consent was obtained from 89 students. Venous blood samples were collected and tested for HBV surface antigen using SD Bioline immunochromatographic rapid assays.

### Results

Out of the 62 (69.7%) male students, none tested HBV-positive, and out of 27 (30.3%) female students, none were seropositive. This suggested the absence of HBsAg among students or presence of HBsAg levels below detectable limits.

### Conclusions

This study showed levels of HBsAg below detectable limits among healthy young adults in Malawi. HBV screening for medical students should further be assessed to ensure adequate protection before they are assigned clinical duties. These findings provide enough grounds to agitate for further surveys to support the establishment of a universal HBV immunisation programme in Malawi.

## Introduction

Hepatitis B virus (HBV) is a partially double-stranded (ds) deoxyribonucleic acid (DNA) virus, which can potentially cause liver disease that may progress to chronic hepatitis, cirrhosis, and hepatocellular carcinoma.<sup>1,2</sup> According to the World Health Organization (WHO), about a third of the global population is infected with HBV, with an estimated 240 million people living with chronic HBV and approximately 780,000 HBV-attributable deaths reported annually.<sup>3</sup> HBV is ubiquitous, but high prevalence rates are reported in sub-Saharan Africa (10 to 20%),<sup>4</sup> compared to the developed world (0.2 to 0.5%).<sup>5</sup> HBV remains an occupational health hazard; therefore, assessment of the magnitude of pre-exposure and possible infection among Malawian medical students doing clinical placements in public hospitals in Malawi is pertinent. The Malawi Ministry of Health recommends immunisation of medical students and healthcare workers before they come in contact with patients at all levels, but adherence to and enforcement of such recommendations has been inconsistent. Healthcare personnel, including medical students, are at risk of occupational exposures, such as HBV and other blood-borne viruses, through needlestick injuries and contact with infected blood or blood products.<sup>6</sup> Likewise, uninfected hospitalised patients are at risk of HBV exposure from infected healthcare workers. Therefore, HBV vaccination either pre- or post-screening is recommended among medical students and other healthcare workers.

In 1991, the WHO recommended that all countries introduce universal HBV immunisation policies. Countries such as Taiwan (1984), Italy, Spain and the United States of America (1991), and Israel (1992) were some of the early adopters of HBV universal immunisation.<sup>8</sup> Subsequently, global HBV immunisation coverage increased from < 1% in 1990 to 60% in 2006.<sup>7</sup> Malawi adopted the HBV universal vaccination programme in 2002.

HBV diagnosis is done by performing serological assays to detect different viral markers, biochemical investigations to assess the hepatic injury, molecular techniques to detect genetic markers, and liver biopsy, amongst others.<sup>9,10</sup> In Malawi, screening for hepatitis B virus surface antigen (HBsAg) in public hospitals and health centres is done by rapid immunochromatographic diagnostic test (RDT) kits that are readily available at the point of care or in laboratories. There are no contemporary published data regarding the national HBV prevalence among medical students in Malawi. However, few data for HBV screening among small targeted populations exist. Previous research revealed a 7.6% HBV prevalence among blood donors, and an estimated 9.5% HBV prevalence among hospitalised patients without observable liver disease.<sup>11</sup> The HBV prevalence rate among blood donors in Ntcheu District, Malawi, has been reported to be about 8.1%.<sup>12</sup> Estimates of HBV prevalence amongst healthy young adults in Africa vary greatly. A 15.5% HBsAg prevalence has been reported among high school and university students.<sup>13</sup> Such high HBV prevalence estimations reflect substantial risk to healthcare workers.

RDTs are accurate for HBsAg screening purposes.<sup>2,3</sup> Public referral hospitals and other health institutions perform additional supplementary or confirmatory laboratory testing for the presence or absence of HBV biomarkers.

The aim of this study was to estimate the epidemiology and seroprevalence of HBsAg among medical students at the University of Malawi.

## Methods

This quantitative descriptive cross-sectional study was conducted at the College of Medicine (COM), University of Malawi, Blantyre, in 2013. The study population comprised all foundation-year (premedical) students. The optimal sample size to detect statistical significance was estimated at 89 students, calculated using Epi-info version 3.5, with a

confidence interval of 95%, an estimated frequency of 10%, and a worst acceptance value of 5%. Out of 234 premedical students who were enrolled in all COM programmes at the time of data collection, 89 unvaccinated students were recruited into this study. The study was approved by the College of Medicine Research and Ethics Committee (COMREC). Written consent was obtained from all study participants. Anonymisation of study participants' personal information and adherence to confidentiality standards was performed in compliance with COMREC guidelines.

Samples were collected, processed, and tested following detailed standard operating procedures (SOPs), as provided by the test kit manufacturer. Results were interpreted 20 minutes after addition of samples on test strips. HBV-positive samples were provided by the serology division of the Queen Elizabeth Central Hospital Laboratory in Blantyre. Both sensitivity and specificity of the test kits was greater than 99%, with a detection limit of 2 ng/mL (meaning that a positive result indicated the presence of  $\geq$  2 ng/mL of HBsAg), as indicated on the manufacturer's instruction leaflet.

**Results**

Out of the 89 consenting participants, 62 (69.70%) were males (Table 1). All 89 study participants were HBsAg seronegative, representing 100% seronegativity among the the study participants (Table 1).

There were no negative or invalid (absence of both test and control bands in the results window of a test strip) results in this study.

**Table 1: Hepatitis B surface antigen (HBsAg) seroprevalence test results for University of Malawi foundation year students**

	Positive	Negative
<b>Controls</b>	Positive QC	Negative
	Negative QC	Negative
<b>Males</b>	None	62 (69.70%)
<b>Females</b>	None	27 (30.30%)
<b>Total</b>	None	89 (100%)

Summary of HBV HBsAg serum testing results using BIOLINE HBsAg one-step immunochromatographic rapid test kit batch number 008283. All study samples showed negative or low HBVsAg levels below the detectable limit. QC = quality control

**Discussion**

This study included University of Malawi College of Medicine premedical students from all regions of the country. The HBV screening results suggest either an absence or low (undetectable) levels of HBV surface antigen in the study population. The rapid serological diagnostic assay was chosen because it was the same one used in public health facilities in Malawi for HBV biomarker screening. The rapid test kits are highly sensitive and specific, do not require robust equipment or highly skilled labour, and they can be stored at ambient temperature.<sup>14</sup> HBV vaccination is recommended for medical students at the University of Malawi, but HBV pre-screening is not routinely performed for all students who receive the HBV vaccine prior to clinical placements in public hospitals.

There are no contemporary published data about HBV prevalence among medical students and healthcare workers in

Malawi. The available HBV prevalence rates vary depending on HBV/HIV coinfection and between risk groups, such as pregnant women and hospital inpatients, among others. Our recommendations for HBV pre-screening concur with conclusions drawn from other studies carried out in Africa. Fritzsche et al. recommended that HBV screening should always be done among healthcare workers in Cameroon prior to vaccination.<sup>15</sup> A similar study conducted on medical students at Makerere University in Uganda concluded that medical students should be offered more HBV sensitisation and prevention information, as well as public health interventions, including universal precautions for infection control.<sup>16</sup>

Utilisation of different testing methods to detect multiple biomarkers improves the power estimation for HBV infection. Demographic and geographic differences that could determine the risks of exposure among different populations also influence the varying prevalence rates determined in different regions of Africa and the rest of the world. Our findings suggest that there was a low prevalence of hepatitis B virus in the study population. These results are different from previous studies conducted on medical inpatients in Malawi, where HBsAg prevalence was estimated at 38% using point-of-care testing, and 17.5% after confirmatory assays were performed at reference laboratories outside Malawi. Our prevalence findings also differ from those of the study conducted at Makerere University, where an overall HBsAg prevalence of 11.0% and anti-HBc prevalence of 65.9% were reported.<sup>16</sup> Similar research carried out at Lagos State University College of Medicine, in Nigeria, reported a 3.2% HBsAg prevalence and a prevalence of 17.9% for anti-HBs antibodies among medical students at that institution.<sup>17</sup> An HBV prevalence of 48% was reported among preclinical and clinical medical students in the United Arab Emirates; half of the students tested had prior immunisation at childhood but were reported to be susceptible to HBV infection.<sup>19</sup> A study carried out at the University of Malaya, in Malaysia, found a 0.62% HBV infection prevalence among medical students; that study used automated diagnostic assays to detect HBsAg, anti-HBs, and anti-HBc biomarkers.<sup>20</sup>

There continues to be vigorous campaigns by government, nongovernmental organisations (NGOs), and private institutions to sensitise the public against HIV infection in Malawi. Such awareness campaigns could also have a bearing on the reduction of HBV exposure and subsequent infection among medical students.

Over the years, blood transfusion in Malawi has presumably been safe, after the establishment of the Malawi Blood Transfusion Service (MBTS), whose overall objective is to supply safe blood and blood products in order to reduce the incidence of HIV and other blood-borne infections. The absence of HBV antigens reported in this study could either reflect a true low prevalence or low HBV viral load below detectable limits. HBsAg is the early marker detected in acute HBV infection. A combination of HBV testing assays targeting different biomarkers would be ideal for conclusive HBV prevalence results. Anti-hepatitis B core (Anti-HBc) IgM antibodies are early biomarkers in acute HBV infection, produced in response to the core HBV antigen and persist for life, suggesting a past horizontal transmission in childhood and adulthood.<sup>21</sup> Detection of HBV DNA could be useful in establishing HBV infection, but the technique is obviously expensive and less appropriate in resource-limited settings. Therefore, confounding factors contributing to a low HBV prevalence cannot be ruled out in our findings. The use of external control samples (both positive and negative) offered an in-house validation of the results.

On the whole, our findings require further investigations to establish if the low undetectable levels of HBVsAg



among medical students reported in this study attest to the utility of the universal HBV immunisation policy against HBV infection introduced in 2002 by the government of Malawi. HBV prevalence is high in sub-Saharan Africa,<sup>22</sup> therefore healthcare workers, including clinical medical students, are at particular risk of exposure, particularly in areas of high endemicity.<sup>23–26</sup> The implementation of appropriate vaccination programmes would reduce the risk of HBV infection among risk groups and those not suffering underlying chronic HBV infection.<sup>27</sup> Vaccination programmes for undergraduate students enrolled at the University of Malawi, as well as the vigorous implementation of a universal immunisation programme, focusing on adolescents and the provision of maternal prophylaxis to limit infant transmission, would help reduce HBV infection rates. Despite the small sample size investigated, these findings will provide part of the baseline for future research work that could describe the epidemiology and seroprevalence of HBV among future healthcare workers and clinicians. The findings are not concordant with the available published data in Malawi and other parts of Africa. Therefore, this calls for further studies and comprehensive systematic reviews.

## Conclusions

This study, the first performed in a sub-population of medical students in Malawi, suggests low levels of HBV exposure. The study findings suggest that there is little evidence to encourage preclinical HBV screening of medical students at the Malawi College of Medicine before vaccination. Thus, despite study limitations that included time, small sample size, lack of confirmatory tests, and financial constraints, the study provides important baseline information, which forms part of the nationwide assessment of HBV prevalence, and informs the universal immunisation policy. Other reports indicated high HBV prevalence rates in the country, which suggests that a significant proportion of the population are susceptible to HBV infection. Therefore, HBV screening for medical students should further be assessed to ensure adequate protection before they are assigned clinical duties.

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## Competing interests

The authors declare that they have no conflicts of interest.

## References

1. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J Viral Hepat* 2004;11:97–107.
2. Gerlich WH. Medical virology of hepatitis B: how it began and where we are now. *Virol J* 2013;10:239.
3. WHO. WHO | Hepatitis B [Internet]. World Heal. Organ.2015 [cited 2015 Nov 26]; Available from: <http://www.who.int/mediacentre/factsheets/fs204/en/>
4. Howell J, Lemoine M, Thursz M. Prevention of materno-foetal transmission of hepatitis B in sub-Saharan Africa: The evidence, current practice and future challenges. *J. Viral Hepat.*2014;21:381–96.
5. Lai CL, Ratziu V, Yuen M-F, Poynard T. Viral hepatitis B. *Lancet* 2003;362:2089–94.
6. Okeke EN, Ladep NG, Agaba EI, Malu AO. Hepatitis B vaccination status and needle stick injuries among medical students in a Nigerian university. *Niger J Med* 2015;17:330–2.

7. Zanetti AR, Van Damme P, Shouval D. The global impact of vaccination against hepatitis B: A historical overview. *Vaccine* 2008;26:6266–73.
8. Shepard CW, Simard EP, Finelli L, Fiore AE, Bell BP. Hepatitis B virus infection: Epidemiology and vaccination. *Epidemiol. Rev.*2006;28:112–25.
9. Dufour DR, Lott J a., Nolte FS, Gretch DR, Koff RS, Seeff LB. Diagnosis and monitoring of hepatic injury. I. Performance characteristics of laboratory tests. *Clin Chem* 2000;46:2027–49.
10. Tanaka E, Ohue C, Aoyagi K, Yamaguchi K, Yagi S, Kiyosawa K, Alter HJ. Evaluation of a new enzyme immunoassay for hepatitis C virus (HCV) core antigen with clinical sensitivity approximating that of genomic amplification of HCV RNA. *Hepatology* 2000;32:388–93.
11. Molyneux ME, Supran EM, Islam MN, Banatvala JE, Hutt MSR. Hepatitis-B virus determinants in patients with liver disease in Malawi. *Trans R Soc Trop Med Hyg* 1980;74:383–8.
12. Candotti D, Mundy C, Kadeweze G, Nkhoma W, Bates I, Allain J-P. Serological and molecular screening for viruses in blood donors from Ntcheu, Malawi: High prevalence of HIV-1 subtype C and of markers of hepatitis B and C viruses. *J Med Virol* 2001;65:1–5.
13. Komas NP, Baï-Sepou S, Manirakiza A, Léal J, Béré A, Le Faou A. The prevalence of hepatitis B virus markers in a cohort of students in Bangui, Central African Republic. *BMC Infect Dis* 2010;10:226.
14. Maity S, Nandi S, Biswas S, Sadhukhan S, Saha M. Performance and diagnostic usefulness of commercially available enzyme linked immunosorbent assay and rapid kits for detection of HIV, HBV and HCV in India. *Virol J* 2012;9:290.
15. Fritzsche C, Becker F, Hemmer CJ, Riebold D, Klammt S, Hufert F, Akam W, Kinge TN, Reisinger EC. Hepatitis b and c: Neglected diseases among health care workers in cameroon. *Trans R Soc Trop Med Hyg* 2013;107:158–64.
16. Pido B, Kagimu M. Prevalence of hepatitis B virus (HBV) infection among Makerere University medical students. *Afr Health Sci* 2005;5:93–8.
17. Odusanya OO, Meurice FP, Hoet B. Nigerian medical students are at risk for hepatitis B infection. *Trans R Soc Trop Med Hyg* 2007;101:465–8.
18. Nyirenda M, Beadsworth MJB, Stephany P, Hart C a, Hart IJ, Munthali C, Beeching NJ, Zijlstra EE. Prevalence of infection with hepatitis B and C virus and coinfection with HIV in medical inpatients in Malawi. *J Infect* 2008;57:72–7.
19. Sheek-Hussein M, Hashmey R, Alsuwaidi AR, Al Maskari F, Amiri I, Souid A-K. Seroprevalence of measles, mumps, rubella, varicella-zoster and hepatitis A–C in Emirati medical students. *BMC Public Health* 2012;12:1047.
20. Ng KP, Ngeow YF, K R, M R. Hepatitis B seroprevalence among University of Malaya Students in the Post-universal Infant Vaccination Era. *Med J Malaysia* 2013;68:144–7.
21. Zampino R, Boemio A, Sagnelli C, Alessio L, Adinolfi LE, Sagnelli E, Coppola N. Hepatitis B virus burden in developing countries. *World J Gastroenterol* 2015;21:11941–53.
22. Hosegood V, Floyd S, Marston M, Hill C, McGrath N, Isingo R, Crampin A, Zaba B. The effects of high HIV prevalence on orphanhood and living arrangements of children in Malawi, Tanzania, and South Africa. *Popul Stud (NY)* 2007;61:327–36.
23. Koenig S, Chu J. Medical student exposure to blood and infectious body fluids. *Am J Infect Control* 1995;23:40–3.
24. Norsayani MY, Hassim IN. Study on incidence of needle stick injury and factors associated with this problem among medical students. *J Occup Health* 2003;45:172–8.
25. Sharma GK, Gilson MM, Nathan H, Makary M a. Needlestick injuries among medical students: incidence and implications. *Acad Med* 2009;84:1815–21.
26. DeVries B, Cossart YE. Needlestick injury in medical students. *Med J Aust* 1994;160:398–400.
27. Kane A, Lloyd J, Zaffran M, Simonsen L, Kane M. Transmission of hepatitis B, hepatitis C and human immunodeficiency viruses through unsafe injections in the developing world: Model-based regional estimates. *Bull. World Health Organ.*1999;77:801–7.