High burden of hepatitis B infection in Northern Uganda despite nine years of childhood hepatitis B vaccination: results of a population-based survey.

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Abstract

Introduction: Worldwide 2 billion people are exposed to hepatitis B infection, 350 million have chronic infection, 65 million in sub-Saharan Africa. Uganda is highly endemic with 10% national prevalence of hepatitis B infection, rates varying across the country from 4% in the southwest and 24% in the Northeast. Childhood vaccination was rolled out in 2002, the effect of which on the burden of hepatitis B has not been examined. We determined the prevalence and risk factors for hepatitis B infection in the Northern Uganda Municipality of Gulu after 9 years of HBV vaccination.

Patients and methods: We carried out a cross-sectional, population-based survey. Data on demographics, wealth index, cultural and behavioral factors, vaccination and health education on hepatitis B were collected. Hepatitis B infection (Hepatitis B surface antigen positive) and lifetime exposure (anti-hepatitis B core antibody positive) were measured. Analysis was done in 2 age groups, 1-14 years, 14 years and more. Associations between predictors and HBV infection were assessed.

Results: Information on 790 respondents were analyzed. Overall, 17.6% had hepatitis B infection and 72.4% lifetime exposure. In the younger age group 21.9% had hepatitis B infection and 48% lifetime exposure. Increasing wealth was protective for infection (OR 0.46 per quartile, 95% CI=0.26-0.82, p=0.009), while older age was protective for lifetime exposure (OR 2.70 per age group, 95% CI 1.03-7.07, p=0.043). In the older age group, overall hepatitis B infection was 17.2% while lifetime exposure was 74.9%. While male sex (OR 1.64, 95% CI=1.08-2.50, p=0.021) was a risk factor for infection, increasing age (OR 0.76 per age group, 95% CI=0.63-0.90, p=0.002) was protective. For lifetime exposure, increasing wealth was protective (OR 0.83 per quartile, 95% CI 0.70-0.98, p=0.029) and increasing number of lifetime sexual partners was a risk factor (OR 1.20 per partner category, 95% CI=1.04-1.38, p=0.012)

Conclusions: We found a high prevalence of hepatitis B infection and lifetime exposures to hepatitis B in this northern Uganda Municipality. Targeted vaccination of susceptible adults and improving existing childhood vaccinations and provision of treatment for those with infection will play roles in reducing the high prevalence rates seen in the population.

Keywords: Hepatitis B virus, prevalence, vaccination
Introduction

Hepatitis B viral infection (HBV) causes significant global burden of disease with 2 billion people exposed to the virus, more than 350 million of whom are chronic carriers. It is a cause of more than 600,000 deaths annually. Africa shares 25% of the total HBV burden, with 65 million chronic carriers. [1, 2] Infection is highly endemic in Uganda with a national prevalence estimated of 10% in a study carried out in 2004. [3] The in-country distribution of the virus however varies from region to region. The highest prevalence is found in the Northern part of the country ranging from 19% in North west to 25% in the north east. [3] The explanation for this variation in distribution is not well established.

Hepatitis B transmission occurs through blood and blood product exposures. While sexual and needle stick exposures are common modes of transmission in the low endemic areas, transmission in high endemic regions tends to occur in early childhood either perinatally or through child-to-child horizontal methods. [2] Scarifications, shown to be an important mode of HBV transmission in South Africa is also a common practice in northern Uganda but its contribution to transmission in Uganda is not studied [4] [5, 6]

Control of hepatitis B is done through immunization. Where this has been done the prevalence of infection and chronic liver diseases have been significantly reduced.[7] In Uganda the Uganda National Expanded Program on Immunizations (UNEPI) successfully helped scale-up childhood immunizations including hepatitis B. However the program strategy incorporates the hepatitis B vaccine into a combination vaccine whose first dose is administered at 6 weeks of age. This

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delay both limits the efficacy of the vaccine in the prevention of vertical transmission and allows for the potential transmission of hepatitis B through close contacts in the first weeks of life.

Over the last 25 years Northern Uganda has been affected by war and most of the population (including those in the studied Municipality) was sequestered in Internally Displaced People’s (IDP) camps. The conditions in the camps were difficult, with deterioration of health indicators in the camps as was reported in the WHO-Uganda report 2004. [8]

This war has come to an end and most of the camps have been dismantled and a number of people from various parts of the country have flocked into the region seeking for business or employments. We conducted a study to determine the prevalence and factors associated with HBV infection in Gulu Municipality after the scale up of the hepatitis B vaccination in 2002. Gulu municipality is the main town in Gulu district, Northern Uganda.

**Patients and Methods**

During the months of January and February 2010 we carried out this cross-sectional community based HBV survey in Gulu Municipality, Northern Uganda. This Municipality is made up of 16 parishes and 60 villages and the total population in the Municipality is 356,000 according to the population Census carried out in the year 2000.
During this study, we selected 8 Parishes by probability sampling proportionate to size forming clusters from which 100 households were selected by systematic random sampling. From each household, one respondent was selected by simple random sampling.

All residents in the Municipality who had been living there for six months or more, young and adult were eligible and got recruited upon provision of an informed consent (and assent for those aged 8-17 years). The study included children from 1 year and above.

For all respondents interviewer administered questionnaires collecting information on demographic factors [age, gender, marital status, occupation, religion, tribe, and wealth index was computed from ownership of household assets], cultural and behavioral factors [scarification practice, touching of the dead, sharing of towels, sharing of sweets, number of lifetime sexual partners and family history of liver disease] and preventive factors [vaccination against hepatitis B and health education about HBV] was conducted.

Research assistants, who were nurses, administered the questionnaire and collected 5-8mls of blood from respondents. Samples were stored at -2°C to -8°C in the field, and transported to Lacor hospital laboratory within 24 hours, centrifuged and sera extracted. These were used for detecting hepatitis B surface antigen (HBsAg), a marker of HBV infection, and hepatitis B core antibody (anti-HBcAb), a marker of lifetime exposure.
Ethical approval was obtained from School of Medicine research and ethics committee at Makerere University College of Health Sciences and Uganda National Council of Sciences and Technology (UNCST). The study was conducted in accordance with the Helsinki Declaration.

**Serological Assay**

Serological testing was done in Lacor hospital main laboratory using analyzers sourced from Human Diagnostics Inc®, Germany using manufacture’s operations manuals. HBsAg status was assessed using the rapid strip test, with a sensitivity of 100% and specificity of 99.7%. Total anti-HBcAb status was assessed by automated ELISA machine.

**Data management and analysis**

Laboratory results were merged with questionnaire data by unique identifiers. Data was checked for completeness and consistency, partially double entered into Epidata version 3.1 and exported to STATA version 9 for analysis.

We separated the analysis of respondents into two categories defined by age 1-14 and those above, because of the confounding effects of age on most of the variables. Prevalence of HBV infection and lifetime exposure were determined across the age strata as the proportion of tested specimens/respondents positive for HBsAg and antiHBc respectively. Associations between predictors and HBV infection and lifetime exposures were assessed using Chi square, and Odd’s ratios with their 95% confidence intervals were reported. Variables with p values ≤ 0.2 at
bivariate (and others with theoretical importance) level were entered into a multivariate logistic regression to control for confounding and interaction. A p-value of \( \leq 0.05 \) was significant. Persons who have HBV infection have both markers, while those who have eliminated the infection have only the markers of lifetime exposure.

**Results**

During the study period, a total of 804 respondents from eight parishes in four sub-counties in Gulu Municipality were interviewed, two of whom withdrew consent before blood draws. Blood samples were drawn from the remaining 802 respondents and analyzed for hepatitis B virus markers. 790 had adequate samples for analysis.

Baseline demographic characteristics of the respondents are displayed in Table 1. Of 790 respondents most, 566 (71.7\%) were of female gender, of age ranging from 1-90 years, with median 30 years. Most respondents (62.6\%) were married, mainly Catholic (77.8\%) by religion and Acholi (89\%) by tribe.

**Overall prevalence of chronic HBV infection and lifetime exposure to HBV infection**

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The overall prevalence of hepatitis B infection in the 790 participants was 17.6% (CI 14.9-20.3) while that of lifetime exposure to infection was 72.4% (CI 69.3-75.5).

Subgroup analysis for chronic HBV infection and lifetime exposures to HBV infection

Participants 1-14 years old

The overall prevalence of HBsAg in this age group was 21.9% (Table 2). On evaluation of predictive factors in this age group, only family wealth status was significant, showing protective effect of increasing wealth (OR 0.46 per quartile, 95% CI=0.26-0.82, p=0.009). Lifetime exposure within this age group was 48% and older age was associated with exposure for 11-14 year olds compared to 10 years or under, at bivariate analysis level (OR 2.70, 95% CI 1.03-7.07, p=0.043)

Participants 15 years and older

The overall prevalence of HBsAg was 17.2% (Table 3). In bivariate analysis factors that showed a significant association for chronic infection included male sex (OR 1.59, 95% CI=1.05-2.38, p=0.032) and younger age (OR 0.76 per age category, 95% CI=0.64-0.91, p=0.003). Other factors that showed border line significance were education, wealth index and occupation. In a multivariate model that included all the above factors, male sex (OR 1.64, 95% CI=01.08-2.50, p=0.021) and age (OR 0.76 per group, 95% CI=0.63-0.90, p=0.002) remained significant correlates for chronic infection.

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Analysis for life time exposure for hepatitis B showed an overall exposure of 74.9% (Table 3). In bivariate analysis, factors significantly associated with exposure were age (OR 1.18 per group, 95% CI=1.01-1.37, p=0.034), secondary education (OR 0.60, 95% CI, 0.36-0.99, p=0.049), wealth (OR 0.84 per quartile, 96% CI=0.71-0.99, p=0.035), being a child/student (OR 0.45, 95% CI=0.26-0.77, p=0.004) and number of life-time sexual partners (OR 1.19, 95% CI=1.04-1.38, p=0.014). Other borderline significant factors were tertiary level education, being widowed, and the pentecostal/other religion category. On adjusting for all the above factors in multivariate analysis, wealth status (adjusted OR 0.83 per quartile, 95% CI 0.70-0.98, p=0.029) and number of lifetime sexual partners (adjusted OR 1.20 per partner category, 95% CI=1.04-1.38, p=0.012) were significant correlates of lifetime exposures for hepatitis B infection.

Discussion

In this cross-sectional population-based study we have shown that Gulu Municipality in Northern Uganda has a high prevalence of hepatitis B virus infection of 17.6% and a lifetime exposure of 72.4% in the general population. Rates of infection and lifetime exposure in children was 21.9% and 48%, respectively, while in adults the figures are 17.2% and 74.9%, respectively. A previous national sero-survey (2004) similarly showed high rates of chronic infection and lifetime exposures of 20% and 90%, respectively, in this part of the country. [3] This study was carried out at a time when UNICEF was just scaling up vaccination against hepatitis B in the country. The high prevalence rates shown in our study predict massive potential for ongoing hepatitis B transmission, chronic liver disease and liver cancer.

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Most epidemiologic studies show transmission of hepatitis B in the areas of high endemicity occur either perinatally from mother to child exposures or horizontally from child to child in early childhood. [2, 9] The high infection rate among the children is rather surprising given this study was carried out at a time when early childhood vaccination was entering its first decade in Uganda. Table 2 already shows that by 14 years over one half of the children are already exposed to infection at a time when sexual exposure is presumably at the minimum. This, combined with the finding in Table 3 showing exposure of up 78.8% by age 45 and above means that most of the exposures seem to occur in childhood. This leaves a range of possible mechanisms for continued transmission. In the first place mother to child perinatal transmission could be taking place since mothers are not routinely screened during the antenatal period to determine infection, loosing the opportunity for intervention with post exposure prophylaxis to the babies by provision of hepatitis B immune globulin and the first dose of hepatitis B vaccine in the first 24 hours after delivery.[10] In addition, horizontal transmission is likely because of delayed administration of the initial dose of vaccine which is given at 6 weeks post delivery. Infection may also occur early through breast feeding when vaccination is not administered. A recent metanalysis confirmed breast feeding is not a significant mode of transmission of hepatitis B in vaccinated children. [9, 11] In our study setting we can speculate this transmission may occur within the period before the administration of the vaccine especially if the mother has cracked or exudative nipples. Even where vaccination is given, UNICEF estimated the prevalence of receipt of the third dose of HBV vaccination at 59% in the year 2008 although administrative coverage was reported at 79% in the same year suggesting a high level of incomplete vaccine immunity. [12] With the disruption of peace in the North there are probably a number of babies born in the Hepatitis B viral infection in Northern Uganda
villages and who are not exposed to vaccination. Another possibility would be transmission in a setting of family clustering, where a number of the persons in the family could be infected. All these factors would possibly increase chances of hepatitis B transmission to a new born baby in Northern Uganda.

Among the older group (more than 14 years) this high prevalence of chronic infection and exposures especially with the exposure increasing with number of sexual partners suggests on going transmission. Indeed increasing age and number of lifetime exposures have been shown to increase risks of hepatitis B transmission in adults.[13] Because of this high prevalence in the adults and potential for transmission, screening of the population to identify those with chronic infection and those exposed could improve decision on control. Population screening may be difficult but in a recent World Health Organization expert panel discussion it was suggested this could be done through already existing facilities as is with HIV infection. [14] Screening for HIV through voluntary counseling and testing (VCT) services and antenatal visits for prevention of mother to child transmission of HIV has been widely used and accepted in Uganda.[15, 16] Hepatitis B and HIV share similar modes of transmission and similar services could be used for hepatitis B screening. Identifying the infected and the exposed would provide information on monitoring and treatment for those who are infected, and targeted vaccination of the adults. Capitalizing on these opportunities would eventually slow down the chain of transmission and the prevalence of disease in the community.
Our study had several limitations. We were not able to measure the anti-hepatitis B surface antibody (anti-HBsAb) in those who were exposed, the hepatitis B e antigen (HBeAg) and hepatitis B viral loads (HBV DNA) in those with chronic infection. These would improve information on protective levels of the antibodies in those infected and determine requirement for treatment and transmissibility for those with chronic infection. However, the main purpose at the time was basically to determine the chronic infection and exposures in the community. This would lead to further studies that will assess effects of screening and possibilities of vaccination and treatment. Secondly, there could have been selection bias as males were not proportionately selected. In the studied population the male gender is the main income earner in the homes while most women would stay home. This could potentially lead to an underestimation of prevalence among the male population. However we used probability sampling to select available members, meaning that all available had equal opportunity of selection and our sample size was robust.

Thirdly, the study could have failed to detect persons in the window period, underestimating the prevalence rates seen. This is common in most sero-epidemiology studies on hepatitis B in Africa and may minimally affect the prevalence measure. [17-19]

In conclusion, we found a high prevalence of chronic hepatitis B and lifetime exposures to hepatitis B infection in this Northern Uganda Municipality. Maximizing on the existing childhood vaccination and identification and targeted vaccination of unexposed adults and treatment of the infected will play big roles in reducing this high prevalence rates seen in the population. Hepatitis B now has safe and effective prevention and treatment available – the time is imminent for Uganda to benefit from them.

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Competing interests

All the authors declare no conflict of interest.

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Authors’ contributions

EO and PO participated equally in conception, design and development of the proposal. EO collected the data. Both participated in statistical analysis and drafted the manuscript. CGO, JNK, ZKN and CK proofread and edited the proposal and reviewed the manuscript. WM supervised and performed the final data analysis, read, edited and approved the manuscript before submission.
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[8] Link /URL


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Additional files provided with this submission:

Additional file 1: Table2 and 3 submit.doc, 68K
http://www.biomedcentral.com/imedia/8850562327498351/supp1.doc