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ORIGINAL PAPER

Sero-epidemiology of Hepatitis B Among New Refugees to Minnesota

Chris Ugwu · Prathibha Varkey · Stephanie Bagniewski · Timothy Lesnick

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Abstract Hepatitis B virus (HBV) infection is endemic in many parts of the world, and prevailing conditions in refugee situations result in greater risk of infection. The objectives of this study were to determine the period prevalence of HBV infection among primary refugees in Minnesota during 1998–2001; describe trends in prevalence over time and identify patterns of infection and immunity in various refugee populations. A retrospective analysis of health examination data from the Minnesota Department of Health was conducted to examine serologic markers for hepatitis B: HBcAb, HbsAg, and HBsAb among 12,505 refugees who participated in the voluntary domestic health examination from 1998 to 2001. One hundred and eleven refugees had at least one immunization before arrival and were excluded. There was documented HBV test results in 8,754 (70.6%) of refugees; period prevalence of hepatitis B infection was 7.1%. Africans were three times more likely and Asians 2.4 times more likely to be infected than Europeans ($P < 0.001$). Older African refugees and African males were more likely to be infected than younger African refugees and women African refugees ($P < 0.001$). Younger persons below 30 years of age accounted for over 70% of all infected refugees in this study. Reducing the burden of infection among refugees requires enhanced provider awareness as well as intensified efforts aimed at identifying new at-risk populations, modifying risk factors, and implementing preventive and treatment strategies at various levels in the refugee resettlement process.

Keywords Refugee · Hepatitis B · Epidemiology · Minnesota

Introduction

Hepatitis B virus (HBV) infection poses a serious global public health problem. Approximately 2 billion people are infected worldwide and chronic infection exists in more than 350 million individuals who become carriers of the virus [1]. Refugees form a small albeit important fraction of immigrants to the United States but HBV infection is endemic in most areas of the world from where refugees originate [2]. The prevalence of HBV markers is 20–60% and greater than 60% in intermediate and high endemicity countries, respectively [3]. Most countries with high endemicity do not have comprehensive HBV immunization programs for populations at risk [4–6]. In addition, conflict, transit, and camping conditions inherent in refugee situations hinder the delivery of adequate healthcare. It is also likely that living conditions in refugee camps directly enhance transmission beyond the usual rates in original countries. The current immunization recommendations for refugee healthcare in the acute phase do not include vaccination against HBV infection.

Dr Ugwu was a Fellow in Preventive Medicine, Mayo Clinic, Minnesota and a student in the School of Public Health, University of Minnesota at the time of this study.

C. Ugwu
Department of Medicine, Buffalo Clinic, University of Minnesota, Buffalo, MN, USA

P. Varkey (✉)
Division of Preventive Medicine, Mayo Clinic College of Medicine, 200 1st Street SW, Rochester, MN 55905, USA
e-mail: Varkey.prathibha@mayo.edu

S. Bagniewski · T. Lesnick
Division of Biostatistics, Mayo Clinic, Rochester, MN, USA

This study aims to determine the period prevalence of HBV infection in a large population of new refugees resettling in Minnesota, identify patterns of infection and immunity among different refugee populations, and describe trends in prevalence over time.

Methods

Refugees are individuals who are outside their country and cannot return because of a well-founded fear of persecution related to their race, religion, and political or social affiliations. Following designation, refugees are screened in their departure locations to detect serious medical conditions and treat infectious diseases of public health concern. Diseases requiring treatment or active intervention prior to arrival to the United States include active tuberculosis, HIV infection, syphilis, gonorrhea, lymphogranuloma venereum, chancroid, leprosy, and severe physical or mental disability. On arrival in Minnesota, refugees are scheduled for a voluntary domestic health assessment usually within 90 days of arrival. The purpose of this assessment is to identify missed or new health problems that may hinder successful resettlement, provide required vaccinations and familiarize refugees to the local health care system. The Minnesota Department of Health (MDH) provides a guide to health departments and local providers for screening newly arrived refugees. Assessment includes a health history, physical examination, immunization review, screening for tuberculosis, hepatitis B infection, sexually transmitted diseases, helminthic infestation, and malaria. Screening for hepatitis B involves serologic tests for HBsAg and HBsAb usually done at the time of first screening. According to current state refugee screening guidelines, serologic testing for core antibody (HBcAb) is optional. Follow-up testing and management of chronic disease is performed as pertinent by the refugee's primary care provider, usually outside of the public health setting. Providers complete the MDH initial refugee health assessment form following medical examination. Information contained in the assessment form include name, date of birth, gender, country of origin, alien number, arrival date, status, results of medical evaluation, and screening tests. Screening records are stored in refugee health databases at the MDH.

For this study, medical records of 12,505 refugees who participated in the domestic health assessment program were examined for presence of serologic markers of hepatitis B. One hundred and eleven were found to have had at least one immunization before arriving and were excluded. Serologic results indicating prevalence of past hepatitis B virus exposure (HBcAb+), infection (HBsAg+) or immunity(HBsAb+) were compared across demographic variables such as geographic area of origin represented as countries or continents of origin, age groups (10-year categories) and gender. This information was fairly complete on the refugees, with only 13 missing gender and three missing age variables. Countries were classified into continents based on geopolitical subdivisions. Health assessment records with pending or missing data were excluded for the respective categories and analyzed separately.

Logistic regression was used to obtain general odds ratios, 95% confidence limits, and *P*-values, and to test for linear trend of HBV infection prevalence across year of arrival. For demonstrative purposes, age was classified into 10-year categories. However, for analysis it was used as a continuous variable. For comparison of prevalence across continental subgroups, differences in age (1 year age increments) and gender composition were accounted for by adjusting for these variables in logistic regression models. A P-value > 0.05 was considered statistically significant for differences between proportions. Statistical analysis was performed using SAS statistical software, version 8.0 (SAS Institute Inc., Cary, NC). The study was approved by the Institutional Review Board of the University of Minnesota and deemed exempt by the Mayo Clinic IRB as information was obtained from a public database.

Results

A total of 12,596 primary refugees arrived in Minnesota during 1998–2001 based on notifications received by MDH. Of these, 12,505 (99.3%) participated in the domestic health assessment program. The median age of refugees on arrival was 19 years (interquartile range: 13–31 years) and the median time from arrival to screening was 49 days (interquartile range: 27–84 days). One hundred and eleven refugees were immunized before their arrival and were removed from the remainder of the analysis. Refugees from Africa made up the largest group of participants at 8,889 (71.7%), followed by refugees from Europe 2,874 (23.2%), Asia 626 (5.1%), and South/Central America 5(<1%) (Table 1). A total of 8,754 (70.6%) refugees were tested for HBsAg, 8,484(68.5%) for HBsAb, and 1,842 (14.9%) for HBcAb.

The period prevalence of HBV infection was 7.1% (623/8,754). As a subgroup, infection (positive HBsAg) was most prevalent (8.4%) among refugees from Africa (Table 2). This constituted 85.4% of infected refugees. About 7.1% of refugees from Asia and 3.1% (61/1,962) of refugees from Europe were infected. Refugees from Africa were 3 times more likely and refugees from Asia 2.4 times more likely to be infected compared to refugees from Europe ($P < 0.001$). There was no significant difference in

Table 1 Prevalence of HBV markers by continent of origin

Continent	Total refugees (%)	HbsAg+	*OR* (95%CI), *P*-value	HbsAb+	*OR* (95% CI) *P*-value
Africa	8,889 (71.72)	8.36% (532/6,366)	3.0 (2.3–3.9), $P < 0.001$	36.3% (2,246/6,184)	4.0 (3.5–4.6), $P < 0.001$
Asia	626 (5.05%)	7.08% (30/424)	2.4 (1.5–3.8), $P < 0.001$	31.7% (126/398)	3.0 (2.3–3.9), $P < 0.001$
Europe	2,874 (23.19%)	3.11% (61/1,962)	Reference	14.2% (270/1,900)	Reference
S/C America	5 (0.04%)	0% (0/2)	n/a	0% (0/2)	n/a

HbsAg+, Hepatitis B surface antigen positive; HbsAb+, Hepatitis B surface antibody positive; HbcAb+, Hepatitis B core antibody positive; S/C, South/Central

the proportion of HBV infection between refugees from Africa and Asia ($P = 0.28$). Countries with the highest numbers of infected refugees were Somalia, countries of the former Soviet Union, Ethiopia, Bosnia, and Liberia.

About 31.1% (2,642/8,484) of refugees screened for HBsAb had serologic proof of immunity. HBsAb was most prevalent among refugees from Africa (36.3%), Asia (31.7%), and Europe (14.2%) (Table 1). Refugees from Africa were 1.3 times more likely than those from Asia to have positive HBsAb serology ($P < 0.001$). Country-specific analysis showed that refugees from Ethiopia (41.5%, 453/1,091) had the highest proportions of immunity.

Core antibody testing was performed less frequently. Of those tested, more refugees from Africa had HBcAb (44.9%) testing, followed by those from Asia (42.9%), and Europe (14.8%). Refugees from Africa were six times more likely and those from Asia five times more likely to have positive core antibody serology when compared to refugees from Europe ($P < 0.001$). There was no significant difference in the prevalence of positive HBV core antibody serology between refugees from Africa and Asia ($P = 0.36$).

The gender distribution of serologic markers (see Table 3) indicate higher prevalence of infection among male refugees (age adjusted, male versus female: $OR = 1.6$, $P < 0.001$), as well as higher prevalence of core-antibody serology ($OR = 1.5$, $P < 0.001$), but no gender difference in surface antibody prevalence ($P = 0.08$). Continent-specific gender sub-group analysis showed that all positive markers were significantly more prevalent among male refugees from Africa than female refugees from Africa (Table 2). Though fewer refugees were screened for HBV core antibody marker, a greater proportion of male refugees from Africa expressed positive core antibody presence than their female counterpart (Table 2). Refugees from Africa and Europe had significant increases in all three markers with age. Overall, younger persons below 30 years of age accounted for over 70% of all infected refugees in this study. The prevalence of surface antibody increased with age among refugees from Asia, but this was not the case with the other two markers (Table 3).

The annual prevalence of HBV generally remained stable among primary refugee populations screened for HBV infection through the years of study. Annual immunity levels (HBsAb+) were highest in 1999 (33.8%) and 2000 (33.4%). Only three refugees were checked for HBcAb in 1998; testing increased significantly over the next 3 years of the study. Core antibody testing was highest in 1999 (40.1%) and 2000 (40.9%).

Table 2 Gender distribution of HBV markers

Continent	Male	Number (%)	HbsAg+	HbsAb+	HBcAb+
Africa	Female	4,163 (33.62%)	6.47% (193/2,982)	35.4% (1,022/2,889)	40.5% (229/566)
	Male	4,719 (38.11%)	10.02% (339/3,382)	37.1% (1,222/3,293)	48.4% (338/698)
OR (95% CI) and *P*-value[a,]*			1.6 (1.4–2.0), $P < 0.001$	1.1 (1.0, 1.3), $P = 0.03$	1.5 (1.2–1.9), $P < 0.001$
Asia	Female	294 (2.37%)	5.91% (12/203)	32.1% (62/193)	40% (28/70)
	Male	329 (2.66%)	8.26% (18/218)	31% (63/203)	46.4% (32/69)
OR (95% CI) and *P*-value[a,]*			1.4 (0.7–3.1), $P = 0.35$	1.0 (0.6–1.5), $P = 0.83$	1.2 (0.6–2.5), $P = 0.53$
Europe	Female	1,436 (11.6%)	2.65% (26/980)	15.1% (142/941)	11.9% (27/227)
	Male	1,435 (11.59%)	3.47% (34/980)	13.3% (127/957)	18% (38/211)
OR (95% CI) and *P*-value[a,]*			1.3 (0.8–2.2), $P = 0.28$	.9 (0.7–1.1), $P = 0.26$	1.7 (1.0–2.9), $P = 0.08$

M, Male; F, Female; HbsAg+, Hepatitis B surface antigen positive; HbsAb+, Hepatitis B surface antibody positive; HbcAb+, Hepatitis B core antibody positive

[a] Reference group was females

**ORs* and *P*-values were derived from age-adjusted logistic regression

Table 3 HBV seroprevalence by age distribution

Continent	Age (years)	Number (%)	HbsAg+	HbsAb+	HBcAb+
Africa	0–10	1,512 (12.2%)	3.96% (41/1,036)	20.5% (203/990)	17.7% (37/209)
	11–20	4,261 (34.39%)	8.45% (254/3,005)	32.5% (945/2,906)	41% (243/592)
	21–30	1,270 (10.25%)	10.45% (100/957)	41.1% (388/943)	57.2% (107/187)
	31–40	502 (4.05%)	11.2% (43/384)	46% (173/376)	63.8% (44/69)
	41–50	453 (3.66%)	6.99% (23/329)	55.6% (180/324)	58.3% (35/60)
	51+	889 (7.17%)	10.86% (71/654)	55.4% (357/644)	68.7% (101/147)
OR (95% CI)[a] and *P*-value			1.13 (1.06–1.18), $P < 0.001$	1.31 (1.28–1.37), $P < 0.001$	1.48 (1.34–1.63), $P < 0.001$
Asia	0–10	110 (0.89%)	1.45% (1/69)	20.9% (14/67)	24% (6/25)
	11–20	140 (1.13%)	5.77% (6/104)	27.5% (28/102)	40% (12/30)
	21–30	146 (1.18%)	11.83% (11/93)	35.6% (32/90)	43.8% (14/32)
	31–40	116 (0.94%)	7.89% (6/76)	30% (21/70)	55.2% (16/29)
	41–50	74 (0.6%)	8.62% (5/58)	40% (18/45)	47.1% (8/17)
	51+	40 (0.32%)	4.17% (1/24)	54.2% (13/24)	57.1% (4/7)
OR (95% CI)[a] and *P*-value			1.21 (0.99–1.48), $P = 0.15$	1.22 (1.01–1.48), $P = 0.002$	1.22 (0.99–1.62), $P = 0.06$
Europe	0–10	707 (5.71%)	1.12% (5/448)	7.8% (34/436)	2.4% (2/85)
	11–20	557 (4.5%)	2.84% (11/388)	11.6% (43/370)	8.3% (9/109)
	21–30	459 (3.7%)	4.55% (15/330)	11.7% (38/326)	16.2% (11/68)
	31–40	555 (4.48%)	3.73% (15/402)	17.5% (69/394)	18.4% (16/87)
	41–50	288 (2.32%)	3.72% (8/215)	24.3% (49/202)	30.2% (16/53)
	51+	307 (2.48%)	3.91% (7/179)	21.5% (37/172)	30.6% (11/36)
OR (95% CI)[a] and *P*-value			1.22 (1.00–1.34), $P = 0.03$	1.24 (1.16–1.33), $P < 0.001$	1.48 (1.22–1.63), $P < 0.001$

[a] *OR* and CI's represent every 10-year increment in age

Discussion

This study reports findings on hepatitis B prevalence in a large population of refugees who were screened following their resettlement in Minnesota. The data used for this study was limited to refugees who participated in the domestic health assessment during the specified time period and might not necessarily represent the reality of hepatitis B infection in the general refugee population in Minnesota or reflect national prevalence of infection or immunity in this population. Nonetheless, the results of this study present important findings of epidemiological and public health interest.

Periodically identifying the prevalence of hepatitis B infection in a large population of refugees is important for assessing the burden of disease and for planning or adjusting prevention and treatment programs. Due to changes in the patterns of refugee admissions closely linked with changing world events, period prevalence estimates from large aggregate populations of refugees reflect a better picture of the burden of disease in this population. The seroprevalence of 7.1% hepatitis B infection reported in this study is similar to the prevalence data reports for individual countries of origin. The annual infection rate among refugees in this study remained stable across the years of the study. In this study, 42% and 32% of refugees were from Africa and Asia, respectively, both of which constitute areas with high HBV endemicity and from where most refugees are admitted to Minnesota. Higher HBV carrier rates of 19% have been reported in other refugee and ethnic populations such as among Albanian refugees in Southern Italy and 20% carrier rates in some populations in sub-Saharan Africa [6, 7].

Overall, more male refugees were infected than females in this study. Further analysis of continent-specific data revealed significant gender differences in infection rates among refugees from Africa. However, epidemiologic studies of indigenous African populations or ethnic refugee populations have shown inconsistent gender differences among chronic hepatitis B carriers [8, 9]. Gender differences are not likely to be prominent in hyperendemic areas where significant transmission occurs during childhood, though males may be at slightly higher risk for horizontal transmission of infection due to participation in contact sports or fights. Furthermore, additional risk may be posed by increased transmission via casual sex in societies where men predominantly work far away from home or where rape is rampant during conflicts or wars.

Age-specific prevalence of hepatitis B infection indicates that younger persons below 30 years of age account for over 70% of all infected refugees in this study. Transmission of infection in hyperendemic countries occurs

heavily at younger ages during childbirth and among siblings as they share personal items while living in close quarters [10–14]. In addition, lack of safe health care delivery largely contributes to viral transmission particularly in the perinatal period and in pediatric populations. Estimates suggest that contaminated needles account for 8–16 million HBV infections each year in developing countries [15]. Transmission of infection through traditional practices such as scarifications and ear-piercing in hyperendemic areas has also been described [16, 17]. The burden of disease in children is huge as they are less likely to clear initial viremia thereby progressing to chronic infection with development of long-term sequelae [18–20]. Increasing infection rates among most refugee populations with age implies ongoing transmission in adults. Transmission through sexual intercourse and parenteral drug use remain important contributors to hepatitis B infection in adults.

Refugees from Africa exhibited higher levels of immunity compared with other continental sub-groups. Among those tested, refugees from Africa were also noted to have higher levels of seropositivity for the core antibody marker. This reflects the impact of transmission in adults who are more likely to recover from acute HBV infection followed by the development of post-exposure immunity.

The fact that only 70% of the study population received testing for hepatitis B infection is of concern, especially in light of the high prevalence of infection among refugee populations and the need for active intervention to reduce the overall burden of disease. On an individual level, refugees who have active or chronic hepatitis need close medical follow-up for immediate chemotherapy or close surveillance to monitor for progression to cirrhosis or hepatocellular carcinoma, and to treat these and other complications as they arise. From a public health perspective, prevention of viral transmission by those infected is essential. The high infectivity of HBV means that the virus can spread relatively easily to non-immune household members, coworkers, and individuals exposed to the infected person. Identifying carriers of the virus will allow for targeted education to reduce transmission as well as active screening and vaccination of close contacts.

This study has several limitations. Participation in the domestic health examination is voluntary. Though the majority of refugees (99.3%) presented for health examination during the study period, some were not screened or had incomplete screening and documentation. Although it is recommended as standard screening policy for refugees on arrival, only about 70% of refugees in the study were screened for HBsAg and HBsAb. Given the prevalence of HBV infection in this population, the likelihood of complications with chronic disease, and the ease of viral transmission, a concerted effort to enhance screening on arrival, referral for treatment and vaccination remains necessary for new refugees. Currently, screening on arrival to the United States, remains voluntary, although highly encouraged by the State. Future research should focus on evaluating the efficacy and effectiveness of various approaches for the prevention and treatment of Hepatitis B in newly arrived refugees.

Missing or incomplete data may bias results and affect conclusions. Refugees who were not tested for HBV infection differed from refugees with documented results by geographic area of origin ($P < 0.001$), arrival year ($P < 0.001$), and age ($P < 0.001$). Also, serologic testing was performed in different laboratories across the state, though there are no known reports of quality assurance problems which may differentially influence the reporting of serologic tests. Further research that focuses on evaluating the implementation, benefits and cost-effectiveness of existing primary and secondary prevention strategies is needed to assess the current hepatitis B screening practices in refugee populations. Periodic surveillance studies are necessary to monitor changes in prevalence and disease burden in high-risk refugee populations.

In conclusion, this study suggests a higher prevalence of hepatitis B infection among primary refugees to Minnesota than that among the general United States population. In light of this information, it is imperative to actively screen refugee populations for hepatitis B infection and immunity on arrival to the state, as well as to include them in universal screening and immunization programs. Although these numbers were specific to refugees arriving in Minnesota, they would likely be similar for other states, particularly those whose refugee populations are similar to those settling in Minnesota. Prevention efforts aimed at vaccinating unexposed persons and providing health education tailored to the needs of specific refugee populations will reduce the disease burden in the general population.

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