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Original research

Hepatitis B prevalence and associated factors in adults presenting for infection screening in northern Thailand

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ABSTRACT

Background and aims: Hepatitis B is a leading cause of morbidity and mortality worldwide. In view of the World Health Organization 2030 targets, effective screening of chronic infection is crucial. We have assessed the prevalence and risk factors of hepatitis B surface antigen in adults presenting for screening.
Methods: Free-of-charge and anonymous services for simultaneous hepatitis B, hepatitis C, human immunodeficiency virus and syphilis screening and counseling were provided in four facilities in northern Thailand. Analyses were performed separately in clients born before integration into the 1992 hepatitis B vaccine Thailand's Expanded Program on Immunization and in clients born afterwards.
Results: Between October 2015 and August 2020, hepatitis B surface antigen prevalence was 7.2 % (185/2578) in clients born before 1992 (95 % confidence interval [CI] = 6.2%–8.2 %). In the multivariable analysis, characteristics independently associated with a higher risk of infection were being born male (adjusted odds ratio [aOR] = 1.49, 95 % CI = 1.10–2.01) and being part of a hill tribe (aOR = 1.65, 95 % CI = 1.01–2.70). Forty-two percent were unaware of their infection. In clients born in 1992 or afterwards, prevalence was 1.5 % (43/2933) (95 % CI = 1.1%–2.0 %) and characteristics independently associated with a higher risk were being born between 1992 and 1995 (aOR = 1.90, 95 % CI = 1.00–3.61), being born male (aOR = 2.60, 95 % CI = 1.34–5.07), being part of a hill tribe (aOR = 5.09, 95 % CI = 2.52–10.26) and having ever injected drugs (aOR = 4.33, 95 % CI = 1.23–15.24).
Conclusions: Risk factor-based screening would miss many chronic hepatitis cases. Screening all adults once in their lifetime may be beneficial until the second generation of immunized infants have reached adult age.

1. Introduction

Hepatitis B (HB) is a major public health burden worldwide: in 2019, an estimated 296 million people were living with chronic HB and 820,000 people died from related causes.[1] Available treatments are effective in slowing disease progression and recommended for all adults

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with chronic HB who either have cirrhosis or are over 30 years of age and have abnormal alanine transaminase (ALT) levels and high-level HB virus (HBV) replication.[2] Although 12 %–25 % of people living with chronic HB worldwide would be eligible for treatment based on these criteria,[3] only 2 % were receiving treatment in 2019.[1] HB treatment uptake remains low as well in Thailand, where an estimated 83 % of the 3 million people living with chronic hepatitis in 2015 were at least 35 years old.[4] A major reason for the low treatment uptake is that only 10 % of people with chronic HB infection are diagnosed.[1] Screening is the gateway for treatment; therefore, increasing uptake of HB screening by individuals most likely to be infected is a priority. In Thailand, a country with a traditionally high prevalence of HB, twelve population groups have been identified as at risk of chronic HB infection and are recommended for HB screening.[5] For example, serologic studies suggest that people from hill tribes, ethnic groups predominantly residing in or originating from the northern and western mountainous regions of Thailand, may have a higher prevalence of HB chronic infection.[6–8] A simple HB surface antigen (HBsAg) test is the entry point for interventions that could prevent HB-related morbidity and mortality.

We have assessed HBsAg prevalence and risk factors in adults presenting for screening for HB, hepatitis C, human immunodeficiency virus (HIV) and syphilis in northern Thailand.

2. Methods

2.1. Settings

Anonymous screening and counseling services were provided free of charge in four facilities in northern Thailand – three in Chiang Mai and one in Chiang Rai – as part of the "Napneung" project (ClinicalTrials.gov: NCT02752152).[9,10] The services were open to any consenting individual aged at least 18 years. Promotion was made primarily through distribution of vouchers in public areas and social media, with a focus on reaching young people. Blood was collected by venipuncture and screened using rapid tests for HBsAg (Alere Determine HBsAg, Alere Medical Co., Ltd., Chiba, Japan), hepatitis C antibodies, HIV antibodies and syphilis antibodies. Clients were invited to answer electronic questionnaires on their socio-demographic characteristics and risk factors through a tablet computer.

2.2. Statistical considerations

This analysis included all individuals who presented at one of the project screening facilities for the first time. Individuals not born in Thailand were excluded from the analysis because the HB immunization programs in other countries started at other dates.

HB infection was defined as a positive HBsAg test. HBsAg prevalence and its 95 % Clopper-Pearson confidence interval (CI) were estimated by biennial birth period. Because universal HB immunization – including a birth dose – was officially integrated into Thailand's Expanded Program on Immunization (EPI) in 1992,[11] they were also estimated in clients born before and in those born on or after 1 January 1992. In each period, we assessed the association between HBsAg positivity and each of 15 potential risk factors – listed in Supplementary Material 1 – self-reported by clients in the electronic questionnaires using logistic regression models. Missing values were imputed using multiple imputation (10 imputations) by chained equations with logistic regression.[12] HBsAg test results and all 15 covariates were included in the imputation process. Variables with more than two categories (year of birth, income in last month and number of persons in household) were dichotomized at the median. Variables with $p < 0.25$ in the univariable analysis were included in the multivariable analysis. The final model was composed of all variables with $p < 0.05$ after applying the backward elimination procedure. If variables remained in the two final models, the interaction between each of these variables and the period of birth was tested in a third multivariable model composed of all variables present in at least one of the two final models in the overall population. Statistical analyses were performed using Stata version 16.1 (Stata Corp., College Station, TX, USA).

2.3. Ethical considerations

All procedures performed in this study were in accordance with the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study. The study protocol was reviewed and approved by the ethics committees of the Faculty of Associated Medical Sciences, Chiang Mai University, and of Chiangrai Prachanukroh Hospital.

3. Results

3.1. Study population

Between 19 October 2015 and 6 August 2020, 5943 clients presented for screening, of whom 5511 were born in Thailand and included into this analysis: 2644 (48.0 %) were males, median age was 25 years (interquartile range [IQR]: 22 to 34), and 2578 (46.8 %) were born before 1992. Self-reported characteristics are described by period of birth and overall in Table 1.

Prevalence and risk factors of hepatitis B.

HBsAg positivity rate by biennial birth period is provided in Fig. 1.

Of the 2578 clients born before the integration of HB vaccine into

Table 1
Client self-reported characteristics by period of birth and overall.

Client self-reported characteristics	Born before integration of hepatitis B vaccine into Thailand's EPI N = 2578[a] n (%) or median (IQR)	Born after integration of hepatitis B vaccine into Thailand's EPI N = 2933[a] n (%) or median (IQR)
Male sex at birth	1216 (47.2 %)	1428 (48.7 %)
Birth year category		
Before 1982	1232 (47.8 %)	–
1982–1991	1346 (52.2 %)	–
1992–1995	–	1554 (53.0 %)
1996 or after	–	1379 (47.0 %)
Age (years)	35 (30–46)	22 (21–23)
Born in the capital district of a province	1095/2390 (45.8 %)	1343/2907 (46.2 %)
Received higher education	1300/2419 (53.7 %)	1824/2912 (62.6 %)
Earned <10,000 Thai Baht last month	644/2358 (27.3 %)	1928/2883 (66.9 %)
Has ever been incarcerated	127/2391 (5.3 %)	24/2902 (0.8 %)
Part of a hill tribe	182/2399 (7.6 %)	265/2907 (9.1 %)
≥3 persons in household	1491/2417 (61.7 %)	1357/2915 (46.6 %)
Man who has ever had sex with a man	323 (12.5 %)	594 (20.3 %)
≥2 sexual partners in last 3 months	598/2359 (25.3 %)	838/2892 (29.0 %)
Ever received benefits in exchange of sex	96/2334 (4.1 %)	73/2868 (2.5 %)
Ever used drugs by injection	100/2428 (4.1 %)	43/2921 (1.5 %)
Ever had a tattoo or piercing	911/2393 (38.1 %)	1123/2909 (38.6 %)
Ever shared a razor or toothbrush with someone else	641/2363 (27.1 %)	1137/2890 (39.3 %)
Ever received blood transfusion, blood products or organ transplantation	155/2362 (6.6 %)	78/2898 (2.7 %)

Abbreviations: EPI, Expanded Program on Immunization; IQR, interquartile range.

[a] Unless otherwise specified.

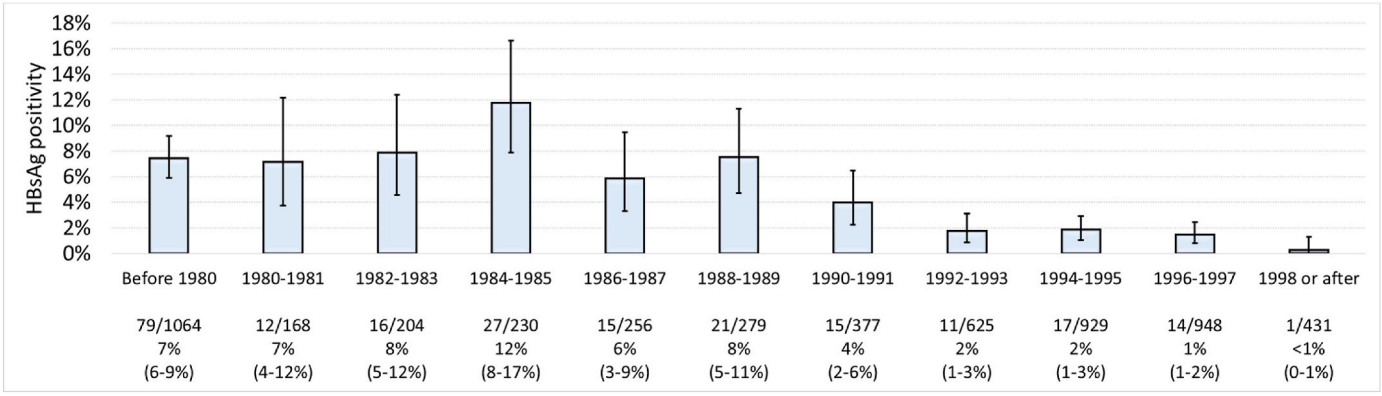

Fig. 1. HBsAg positivity rate by biennial birth period. Error bars represent 95 % Clopper-Pearson confidence intervals.

Thailand's EPI, 185 (7.2 %; 95 % CI: 6.2 %–8.2 %) had a positive HBsAg test. In the multivariable analysis, characteristics independently associated with a higher risk of HBsAg positivity were: being born male (adjusted odds ratio [aOR]: 1.49; 95 % CI: 1.10 to 2.01; p = 0.01) and being part of a hill tribe (aOR: 1.65; 95 % CI: 1.01 to 2.70; p = 0.05) (Fig. 2; full results in Supplementary Material 1).

Of the 2933 clients born after integration of HB vaccine into Thailand's EPI, 43 (1.5 %; 95 % CI: 1.1 %–2.0 %) had a positive HBsAg test. In the multivariable analysis, characteristics independently associated with a higher risk of HBsAg positivity were: being born between 1992 and 1995 (aOR: 1.90; 95 % CI: 1.00 to 3.61; p = 0.05), being born male (aOR: 2.60; 95 % CI: 1.34 to 5.07; p = 0.005), being part of a hill tribe (aOR: 5.09; 95 % CI: 2.52 to 10.26; p < 0.001) and having ever injected drugs (aOR: 4.33; 95 % CI: 1.23 to 15.24; p = 0.02) (Fig. 2; full results in Supplementary Material 1).

In a model including all variables significantly associated with HBsAg positivity in at least one of the two multivariable analyses (Supplementary Material 2), there was no significant statistical interaction between sex and period of birth (p = 0.20) but the association between being part of a hill tribe and having a positive HBsAg test was significantly stronger in clients born after integration of the HB vaccine into Thailand's EPI than in clients born before (aOR: 2.79; 95 % CI: 1.20 to 6.48; p = 0.02).

Of the 228 HBsAg-positive clients, 93 (41 %) did not report any of the characteristics that would identify them as being part of the population groups considered at risk of chronic HB infection in the Thai national guidelines, besides being born before the integration of HB vaccine into Thailand's EPI (note: of the twelve groups considered at risk, five – all of low numerical importance – could not be assessed as data were not collected). The proportion of HBsAg-positive clients who reported being previously unaware of their HB status was 42 % (78/185) among those born before the integration of the HB vaccine into Thailand's EPI and 49 % (21/43) among those born afterwards Of the 228 HBsAg-positive clients, 10 (4 %) were found co-infected with syphilis, 7 (3 %) with HIV and 2 (1 %) with hepatitis C.

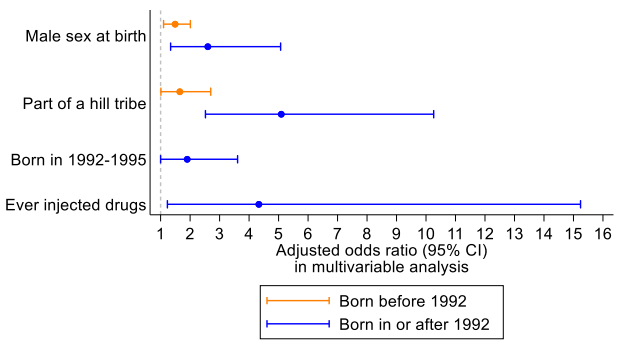

Fig. 2. Client self-reported characteristics independently associated with a higher risk of HBsAg positivity, by period of birth.

4. Discussion

Among nearly 6000 young adults (median age: 25 years) presenting for screening for HB, hepatitis C, HIV and syphilis in northern Thailand, HBsAg prevalence was 7.2 % in clients born before the integration of the HB vaccine into Thailand's EPI in 1992 and 1.5 % in clients born afterwards. Despite the successful implementation of the universal immunization program, these estimates, consistent with previous reports,[4,13–15] suggest that its coverage, possibly in terms of birth dose, was still insufficient by the end of the 1990s.[16–18]

As previously reported,[19–21] HBsAg prevalence was found higher in males, regardless of the period of birth. This could be due to a higher risk of infection as a result of lower vaccine-induced cellular immune responses, or a higher risk of developing a chronic infection as male hormones have suppressive effects on the immune response to infection.[22]

HBsAg prevalence was higher in clients being part of a hill tribe, regardless of the period of birth. The association was even stronger in clients born after the integration of the HB vaccine into Thailand's EPI. Several studies have shown a low prevalence of anti-HBs antibodies detection in children from hill tribes in Thailand such as 10 %,[6] 19 %[7] and 20 %.[8] People from hill tribes in Thailand commonly face difficulties in accessing health services, including HB vaccination, due to distance and other barriers.[23,24]

In Southeast Asia, HBsAg positivity is most often the marker of chronic HB infection due to the historical epidemiologic context. However, we cannot exclude that some clients were experiencing asymptomatic acute HBV infection at time of screening. In our study, men who have sex with men did not have a higher HBsAg prevalence than other groups. Because HB acute infection rarely evolves into a chronic infection in adults, in the absence of anti-HBc antibody testing it was not possible to estimate the prevalence of previous HB acute infection in this population and compare it with other groups.

HBsAg prevalence in participants who had ever injected drugs was higher among those born in 1992 or afterwards, but not among those born before. This may be due to sampling variations in this small subgroup (3 infected among 43) predominantly made of males.

Other factors traditionally associated with higher prevalence of chronic HB in historically low prevalence countries – including household contact, at-risk sexual behaviors, sharing of hygiene equipment or having tattoos or piercings – were not found in this study. Consistent with this finding, 41 % of HBsAg-positive clients did not report any of the characteristics that would identify them as being part of the population groups considered at risk of chronic HB infection in the Thai

national guidelines. These results suggest that, in Thailand, chronic HB was and remained predominantly acquired at birth or during infancy or childhood two decades ago (when the participants were born) in relation with its very high prevalence in the adult population at that time. Therefore, a general population screening strategy may be more effective than a risk-based screening strategy to identify individuals with chronic HB infection.

The strengths of our study include the disaggregation of prevalence estimation and risk factors assessment by birth cohort, the systematic collection of data on numerous risk factors and the large sample size. However, our study has several limitations. First, the study population's age distribution was not representative of the adult population in Thailand, as individuals aged 40–64 years were underrepresented.[25] However, the study included a large number of participants born before 1982 (1232), and the estimated HBsAg prevalence was similar between those born before 1982 and those born between 1982 and 1991. Second, the small sample size in some populations with traditionally high prevalence in historically low prevalence countries – e.g. previous incarceration or receipt of blood transfusion, blood products or organ transplantation – may have resulted in insufficient statistical power to detect significant associations. Finally, a more comprehensive laboratory investigation of participants' serologic status, including anti-HBs and anti-HBc antibody testing, would have provided more insights on the needs for prevention according to self-reported behaviors.

5. Conclusions

Using the risk factors found in this study to screen for HBsAg would have missed significant numbers of people living with chronic hepatitis B. Since chronic hepatitis B is rarely acquired at adult age, it may be worthwhile to screen all adults once in their lifetime, regardless of age, until at least the second generation of infants immunized at birth has reached adult age. Furthermore, as some young people were not immunized during infancy, screening provides an opportunity for catch-up immunization, which would prevent the occurrence of the rare but devastating fulminant hepatitis.

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CRediT authorship contribution statement

Nicolas Salvadori: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing – original draft. **Ludovic Gauthier:** Conceptualization, Data curation, Formal analysis, Mehodology, Software, Visualization, Writing – review & editing. **Marine Guy:** Conceptualization, Writing – review & editing. **Nicole Ngo-Giang-Huong:** Investigation, Resources, Writing – review & editing. **Woottichai Khamduang:** Investigation, Writing – review & editing. **Luc Decker:** Data curation, Resources, Software, Writing – review & editing. **Jullapong Achalapong:** Investigation, Writing – review & editing. **Jean Yves Mary:** Methodology, Validation, Writing – review & editing. **Wasna Sirirungsi:** Investigation, Project administration, Writing – review & editing. **Sakorn Pornprasert:** Investigation, Project administration, Writing – review & editing. **Surachet Arunothong:** Writing – review & editing. **Sumet Ongwandee:** Investigation, Project administration, Writing – review & editing. **Gonzague Jourdain:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jve.2023.100356.

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