Journal of Virus Eradication 10 (2024) 100369

Contents lists available at ScienceDirect

Journal of Virus Eradication

journal homepage: www.sciencedirect.com/journal/journal-of-virus-eradication

Original research

Opportunistic screening using point-of-care testing leads to successful linkage to care of HBV-infected migrant populations in a low endemic country

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ARTICLE INFO

Keywords:
Hepatitis B virus (HBV)
Public health
Screening

ABSTRACT

Background and aims: In low endemic countries, screening for hepatitis B surface antigen (HBsAg) in migrants is cost-effective in reducing the disease burden of hepatitis B virus (HBV) infections, but linkage to care (LTC) remains a challenge. This study aims to guide future screening initiatives, with 3 objectives: 1. to compare LTC between different ethnic groups screened for HBsAg with point-of-care testing (POCT) in an outreach setting; 2. to estimate the proportion of HBsAg seropositivity for ethnic minorities; and 3. to investigate the association between seropositivity and HBV risk factors.

Methods: Opportunistic outreach screenings using finger prick HBsAg tests were performed at civic integration programmes between 11/2017 and 09/2022. If an individual tested positive, an appointment was given immediately at the outpatient hepatology clinic for follow-up and confirmation of HBsAg positivity in blood. Dedicated personnel contacted these individuals to motivate them for further LTC, which was defined as being assessed by a hepatologist, a blood test and an abdominal ultrasound.

Results: A total of 677 people from different ethnicities (Asian, Middle Eastern and African) were serologically screened using POCT. The observed positivity for HBsAg was 3.4 % (95% CI 2.17-5.05, 23/677). Apart from ethnicity and male sex, none of the surveyed HBV risk factors were associated with HBsAg seropositivity. All HBsAg positive individuals were linked to care and assessed by a hepatologist, despite the COVID-19 pandemic increase in time to follow-up of 82 days (95% CI 51–112 days) vs. 24 days (95% CI 5–43 days, p = 0.008)). Among HBV-infected patients, 31.8% (7/22), 100 % (22/22) and 26.1% (6/23) met the criteria for treatment indication, intrafamilial transmission risk and need for hepatocellular carcinoma surveillance, respectively.

Conclusion: The proportion of HBsAg seropositivity in ethnic minorities was 3.4%. POCT and commitment of dedicated personnel can overcome previously identified barriers resulting in a 100% LTC.

1. Introduction and aims

Hepatitis B virus is a major global health issue, with approximately 296 million people living with chronic hepatitis B infection worldwide.[1] The virus affects the liver and can lead to chronic liver disease and hepatocellular carcinoma (HCC), resulting in an annual mortality of 820,000.[1] Hepatitis B prevalence in migrants can be much higher than that of the native population of the host country. The World Health Organization (WHO) recommends targeted HBV testing for migrants from regions where hepatitis B is intermediate and high endemic.[2] In low endemic countries, hepatitis B surface antigen (HBsAg) screening in migrants is cost-effective to reduce the burden of HBV infection.[3] Belgium is a low endemic country with an estimated HBsAg prevalence of 0.66% (95% CI 0.51–0.84) for Flanders in 2003.[4] Our previous study showed a high HBsAg positive proportion of 6.8% using point-of-care testing (POCT) during outreach screenings in a Chinese migrant population in Antwerp, Belgium.[5] To estimate the HBsAg proportion in other migrant populations in Belgium, we expanded the use of POCT during opportunistic

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https://doi.org/10.1016/j.jve.2024.100369
Received 12 February 2024; Received in revised form 22 March 2024; Accepted 25 March 2024
Available online 27 March 2024

screenings to Sub-Saharan, Asian and Middle Eastern migrants and added dedicated screening personnel to improve communication and maximize participation.

Following the initial call and "Global Health Sector Strategy" of the WHO to eliminate hepatitis B infection worldwide by 2030, updated interim country guidance to achieve this goal was published recently.[6] A key objective is to "establish key linkages between testing and other services to improve referral and access to quality-assured treatment and other support services." Linkage to care is essential for the management of hepatitis B in migrants. The diagnosed individuals should receive medical care and treatment, and their close contacts should be vaccinated. Barriers to healthcare access, such as issues with language, lack of knowledge, stigmatisation and discrimination, may make it difficult for immigrants to use these medical services. By increasing access to care, we can improve health outcomes in migrants and reduce the burden of hepatitis B. Previously, we showed that outreach screenings for HBV using POCT compared to venepunctures resulted in a 2.5 times higher linkage to care in a Chinese population in Belgium.[5] In this study, we compared the linkage to care between different ethnic groups screened for HBsAg with POCT during opportunistic screenings.[7] As defined by the European Centre for Disease Prevention and Control (ECDC), this "refers to when a healthcare provider takes the opportunity to offer a test to a patient who is presenting with another indication or healthcare need." The association between seropositivity and HBV risk factors such as demographics and high-risk behaviours was examined.

Finally, the effect of the COVID-19 pandemic on patient follow-up was investigated. The duration between diagnosis by POCT and the outpatient clinic visit was compared before (prior to 1/2020) and during the global COVID-19 pandemic (declared a Public Health Emergency of Global Concern by the WHO on January 30, 2020).

2. Methods

2.1. Definitions for categorizing: Sub-Saharan Africa, the Middle East and Asia

In this study, the following countries were defined as being Middle Eastern: Afghanistan, Armenia, Egypt, Iran, Iraq, Lebanon, Libya, Morocco, Pakistan, Palestine, and Syria. The following countries from Sub-Saharan Africa were included in this study: Benin, Burundi, Cameroon, DRC, Eritrea, Ethiopia, The Gambia, Ghana, Kenya, Nigeria, Rwanda, Senegal, Sierra Leone, Somalia, and Sudan. For Asia, the following countries were included: Bangladesh, China, India, Indonesia, Malaysia, Myanmar, Nepal, The Philippines, Sri Lanka and Thailand.

2.2. HBsAg proportions: assumptions for sampling

An analysis to evaluate the number needed to screen for HBsAg in the Asian, Sub-Saharan African and Middle Eastern migrants arriving in Belgium was performed using published data, inferring precision from seroprevalence confidence intervals and the approximate population size in Belgium. We also assumed that the seroprevalence of migrants from said populations, is the same as their corresponding general populations and inferred the required number needed to screen based on the seroprevalence of their region or country of origin.

Approximating the Asian population as 20,000 individuals with an HBsAg prevalence of 8.5% and precision of 5.0%, the required number to screen is 119.[8–10]

Officially, approximately 17,000 people from Sub-Saharan African origin are living in the City of Antwerp. Almost half originate from three countries: the Democratic Republic of Congo, Ghana and Nigeria.[11] Estimation of chronic hepatitis B in the Congolese population in Belgium indicates an approximate prevalence of 11.4%.[12] Assuming precision of 5.0% and an estimated HBV prevalence of 11%, the required sample size to determine the proportion of HBsAg seropositive migrants originating from Sub-Saharan countries to be 120, considering the Congolese population is the largest Sub-Saharan African population in Belgium.

To estimate the HBsAg seroprevalence of a Middle Eastern population, a population size of 2890 was assumed (number of Syrians in Belgium). For HBsAg, a seroprevalence of 2.2% with a precision of 1.7% (95% CI 0.5%–3.9%) was assumed.[13] This resulted in a required sample of 261 screened individuals.

During outreach screenings, we also screened for the hepatitis C virus using POCT. In Asian and Middle-Eastern populations, we found a positive seropositivity proportion of 1/589 and 0/97, respectively. Due to these low levels, we subsequently focused on screening for the hepatitis B virus.

2.3. Opportunistic screening at civic integration programmes

Opportunistic screenings were performed using finger prick HBsAg POCT *(VIKIA© HBsAg (bioMérieux SA, Marcy-l'Etoile, France* and *Determine™ HBsAg2 (Abbott Diagnostics Medical Co, Chiba, Japan))* at the civic integration programme in Antwerp, Belgium *("Atlas, integratie & inburgering Antwerpen")*. These two tests have been evaluated and found to have high sensitivity and specificity to diagnose HBsAg.[14;15] All migrants from outside the European Union are required to enrol into integration classes organized by "Atlas," which is also a prerequisite to obtain Belgian citizenship. Screening of HBsAg was offered during the integration classes and performed from 11/2017 until 09/2022 by dedicated screening personnel, a study nurse or a researcher. A non-obligatory questionnaire was used to investigate demographic data and risk factors associated with HBsAg positivity. Quality control of the HBsAg POCT tests was performed batchwise, with samples determined to be HBsAg positive or negative by routine clinical laboratory analysers (DiaSorin Liaison XL HBsAg Murex and Roche Cobas 8000).

The results of POCT were available on-site, photographed and archived for quality control and if returned positive, an appointment at the outpatient hepatology clinic of the Antwerp University Hospital was immediately offered for confirmation of the HBsAg result. Confirmation was obtained through venepuncture with subsequent laboratory analysis on the aforementioned routine automated clinical analysers. No false positives from the POCT tests were found during confirmatory testing. If confirmed, subsequent HBV infection follow-up was offered. Further follow-up care was managed by dedicated screening personnel, who contacted patients through phone calls or messages or by making home visits prior to scheduled follow-up appointments.

Ethnicity is determined by country of birth, and migrants are defined as those who do not have a Belgian nationality as their first nationality. Being linked to care was defined as having had a hepatologist consultation, an abdominal ultrasound, and a laboratory evaluation at the outpatient clinic. Need for HCC surveillance was defined and based on the American Association for the Study of Liver Diseases (AASLD) guidelines.[16] Indicators for HCC surveillance are: Asian men >40 years, Asian women >50 years, African and African American ethnicity and family history of HCC. Treatment indication was defined using the European Association for the Study of the Liver (EASL) guidelines as having an ALT >40 U/L and HBV DNA >2000 IU/mL.[17] Transmission risk was defined as positive if there was counselling necessary to prevent intrafamilial or sexual transmission.

2.4. Statistical analysis

The association of HBsAg seropositivity and HBV risk factors was tested using available questionnaire data, by the Mann–Whitney *U* test for continuous variables and the chi-square test for categorical variables. To evaluate the effect of the COVID-19 pandemic, a Wilcoxon signed-rank test was performed to compare the number of days between the positive POCT (diagnosis) and the effective hospital visit. For graphical representations and for statistical data analyses, Graph Pad Prism 9.0 and SPSS version 28.0 were used. (GraphPad Prism version 9.0.0 for Windows, GraphPad Software, Boston, Massachusetts USA, www.gra

phpad.com, IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp).

3. Results

3.1. Baseline characteristics

A total of 677 people were tested for HBsAg with POCT. The mean age was 31.47 years (95% CI 31.10-31.85). The Sub-Saharan African, Middle Eastern and Asian groups contained 176, 383 and 118 individuals, respectively. The person selection flowchart is summarized in Fig. 1. The study included individuals from 15 Sub-Saharan African countries, 10 Asian countries and 11 Middle Eastern countries. The largest groups that were screened were from Afghanistan (287 people), Eritrea (65 people) and Somalia (65 people).

The characteristics of people who screened positive for HBsAg are shown in Table 1. In the three ethnic groups, all HBsAg positive individuals were less than 40 years. Among HBsAg positiveindividuals, mean ages from Africa and the Middle East were 31.33 (95% CI 28.54-34.12) and 27.38 years (95% CI 28.54-34.12), respectively. There was one HBsAg positive person from Asian descent aged 31 years. The overall mean age of all screened persons was 28.6 years. Most of them were male (78.3%).

3.2. HBsAg + proportion

Overall, we observed a HBsAg + proportion in the screened migrant population following obligatory civic integration classes in Belgium of 3.4% (95% CI 2.2-5.1, 23/677). For persons originating from Sub-Saharan Africa, the Middle East and Asia, this proportion was 3.4% (6/176), 4.2% (16/383) and 0.9% (1/118), respectively.

3.3. Clinical characteristics and linkage to care of HBsAg-positive persons

All the people who tested positive for HBsAg were linked to care (Table 1). Of all HBsAg-positive individuals, 39.1% (9/23) had ALT levels above 40 U/L, 52.2% (12/23) had HBV DNA levels higher than 2000 IU/mL, and 17.4% (4/23) had a viral load higher than 20,000 IU/mL. Only two of the 23 individuals were HBeAg positive. Liver stiffness was evaluated using a FibroScan in 22 individuals and was higher than 7 kPa in 3 of the 22. Notably, 17.4% (4/23) of the migrants were anti-HDV antibody positive but HDV RNA negative. All individuals exposed to hepatitis D were born in Afghanistan.

Among the people who tested positive for HBsAg, 26.1% (6/23), 100% (22/22) and 31.8% (7/22) met the criteria for HCC surveillance, transmission risk and treatment indication, respectively. Only 38.1% (8/21) were aware of their HBV infection.

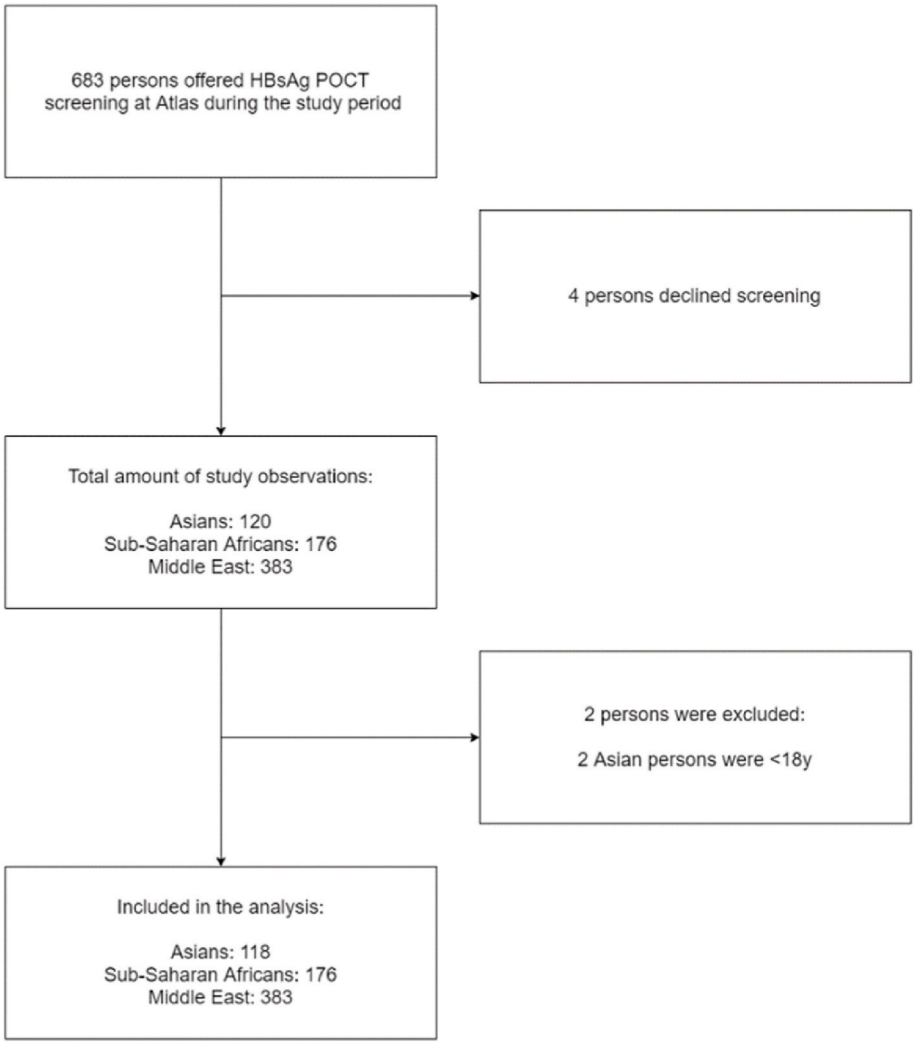

Fig. 1. Screening selection flowchart: number needed to screen, inclusion and exclusion of the study.

Table 1
Baseline and clinical characteristics of people who tested positive for HBsAg, per geographical population.

	All (n=23)	Africa (n=6)	Middle-East (n=16)	Asia (n=1)
Demographics				
Age (mean, years)	28.6	31.3	27.4	31
Gender (female, %)	5 (21.7)	0 (0)	5 (31.3)	0 (0)
Country of birth		Somalia: 3 (50%), Eritrea: 3 (50%)	Afghanistan: 16 (100%)	China: 1 (100%)
Lab parameters + fibroscan				
ALT > 40(%)	9 (39.1)	3 (50)	6 (37.5)	0 (0)
HBV DNA > 2000 IU/mL (%)	12 (52.2)	4 (66.7)	8 (50)	0 (0)
HBV DNA > 20 000 IU/mL (%)	4 (17.4)	1 (16.7)	3 (18.8)	0 (0)
HBeAg+ (%)	2 (8.7)	0 (0)	2 (12.5)	0 (0)
HDV IgG+ (yes, %)	4 (17.4)	0 (0)	4 (25)	0 (0)
Fibroscan > 7kPa	3 (13.6) 1 UNK	1 (16.7)	2 (13.3) 1 UNK	0 (0)
Criteria				
Linkage to care (yes, %)	23 (100)	6 (100)	16 (100)	1 (100)
HCC surveillance (yes, %)	6 (26.1)	6 (100)	0 (0)	0 (0)
Transmission risk (yes, %)	22 (100)	6 (100)	15 (100) 1 UNK	1 (100)
Treatment indication (yes, %)	7 (31.8) 1 UNK	2 (33.3)	5 (33.3) 1 UNK	0 (0)
Awareness HBV infection (yes, %)	8 (38.1) 2 UNK	2 (33.3)	6 (40) 1 UNK	1 UNK

ALT = alanine transferase/HBV = Hepatitis B Virus/HBeAg = Hepatitis B e Antigen/HDV IgG = Hepatitis Delta Virus IgG/HCC = hepatocellular carcinoma/UNK = unknown.

3.4. Analysis of risk factors

Overall, males were more likely to be HBsAg+ (18/293 or 6.1% males vs. 5/294 or 1.7% females, p = 0.006). In 586/677 (86.6%) returned questionnaires, associations were investigated between HBsAg positivity and correctional residence, IV drug use, tattoos or piercings, extramarital unprotected sexual contact, MSM, previous hospitalization, previous dental care, previous blood transfusion and employment in the healthcare profession. None of these were statistically significant (Table 2).

3.5. Influence of the COVID-19 pandemic on HBV follow-up

During the COVID-19 pandemic, linkage to care of POCT-diagnosed individuals was unchanged through the commitment of a dedicated nurse or researcher who regularly followed up patients. However, the time frame between screening and the first hospital visit increased significantly (82 days (95% CI 49–116 days) during the COVID-19 pandemic compared to the prepandemic period (24 days (95% CI 5–43 days) p = 0.008. The latter substantiates the reduction in outpatient visits for non-life-threatening ailments during the COVID-19 pandemic as required by hospital management staff.

4. Discussion

In this study, we have screened 677 people from different ethnic origins (Sub-Saharan Africa, Asia and the Middle East) for HBsAg using POCT. The mean age of migrants outside the EU coming to Belgium, is lower than that of EU migrants or those whose first nationality is Belgian: 37 years versus 42 years.[18] The mean age of the screened persons in our study was 31.5 years. The HBV prevalence measured in 2016 by the CDA Foundation for Africa, the EMRO and Asia was 6.0%, 2.0%, and 4.0%, respectively.[19] We found proportions of HBsAg seropositivity to be somewhat different from this modelled study with 3.4% (6/176), 4.2% (16/383) and 0.9% (1/118) for migrants from Sub-Saharan, Middle-Eastern and Asian origin, respectively. Several factors may contribute to these observed differences. On the one hand, our sample size was not powered to compare national seroprevalences from the region of birth, but merely to determine a convenience sample to obtain a reliable proportion of HBsAg seropositivity of first generation migrants arriving in Belgium and participating to obligatory civic integration classes. Secondly, recent data suggests that seroprevalence of migrants is higher than that of the country of origin. This may be due to migrants constituting a higher proportion of risk groups and also conditions during migration itself that contribute to a higher HBV and HCV seroprevalence.[20]

Table 2
Risk factors in people who are HBsAg+ and linked to care.

	HBsAg+	%	HBsAg-	%	Total	%	p value
Correctional residence	3/21	14.3	53/565	9.4	56/586	9.6	0.7
IV drug use	0/21	0	5/565	0.9	5/586	0.9	1.0
Tattoos/piercings	4/21	19.1	175/565	31.0	179/586	30.6	0.3
Extramarital unprotected sex	5/21	23.8	94/565	16.6	99/586	16.9	0.6
MSM	0/21	0	9/553	1.6	9/574	1.6	1.0
Previous hospitalization	5/21	23.8	180/565	31.9	185/586	31.6	0.5
Previous dental care	5/21	23.8	208/565	36.8	213/586	36.4	0.3
Previous blood transfusion	0/21	0	41/565	7.3	41/586	7.0	0.4
Healthcare profession	0/21	0	19/565	3.4	19/586	3.2	0.6

IV = intravenous/MSM = men having sex with men/HbsAg+: hepatitis B surface antigenpositive.

Our study also shows that half of the African individuals originated from Somalia, and the other half from Eritrea. Migration data is dynamic, and influenced by current events. In 2021 eg, 1500 asylum seekers from Eritrea arrived in Belgium.[21]

This study has investigated risk factors associated with HBsAg positivity in migrant populations. No risk factors were found, except for male sex. With 86.6% completed questionnaires, a bias may have arisen on risk behaviour given that certain acts are forbidden by religion and culture, or by fear of stigmatisation. Additionally, only 38.1% of the people who tested positive for HBsAg were aware of their hepatitis B infection. Being unaware of one's HBV infection is frequently linked with an increased risk of developing liver damage, transmittion of the virus and missing linkage to care and treatment.[2] This finding, as well as the aforementioned lack of other associated risk factors for HBsAg positivity, underlines the need to screen, Middle Eastern and Sub-Saharan African migrants for HBsAg to meet the WHO's goals of eliminating hepatitis B by 2030. For Asians we found a lower seropositivity rate than anticipated, however currently not enough data is available to omit HBV screening in Asian migrants, given the persistent high HBsAg seroprevalences in their countries/region of origin.[19]

A recent study in the Netherlands features a similar opportunistic screening approach as our study. Migrants who consulted a low-threshold primary care facility were offered HBV, HCV and HIV screening. An HBV seroprevalence of 2.5% was found (n = 11/438, 95% CI 1.3%–4.5%).[22]

A recent systematic review including 175 screening studies of blood borne infections, showed an overall lower HBV seroprevalence amongst migrants compared to our study (1.19% vs. 3.4%).[23] This study also found a higher HBV seroprevalence in persons reporting previous healthcare attendance (7.21%) as well as previous drug use (9.87%). A similarly high proportion of HBsAg positive individuals reported a previous hospitalization (23.8%) or dental care (23.8%), but statistical significance was not met for this risk factor in our study.

Linkage to care was 100% in all people who tested positive for HBsAg. This corroborates and expands upon our previously published data, the methods described herein and that this method to achieve high levels of LTC is also valid in population groups outside China.[5] In a previous study, standard venepuncture for hepatitis B testing in a Chinese population led to an LTC of 34.4% (12/32).[5] A paper by Le et al. further argues for the importance of providing LTC support in all migrant populations.[24]

A crucial element is the employment of dedicated staff to ensure LTC. This is discussed in the previously cited paper by Klok et al., where providing specialty care for undocumented migrants required extensive mediation from the researchers.[22] While undocumented status should have a minimal impact in a Belgian context, other factors such as social stigma and financial disincentives continue to pose challenges towards achieving high rates of linkage to care and, ultimately, HBV elimination.[6] Dedicated staff are called "advanced practice providers (APP)" in a recent paper by Kam et al..[25] These can be nurse practitioners, physician assistants, and pharmacists. In our study, a study nurse and a researcher provided follow-up support for people who screened positive for HBsAg. Kam et al. showed that treatment-eligible HBV ndividuals were more likely to receive treatment when followed-up by advanced practice providers (APPs) (OR 1.18-1.24). In another study that evaluated sustained viral response (SVR) in hepatitis C care, employing nonphysician care personnel did not show lower SVR rates or treatment discontinuation rates.[26]

Two papers provide additional arguments for opportunistic screening and its positive impact on LTC. These studies reported LTCs of 87% and 83% in the United Kingdom and Australia, respectively, in emergency wards of large metropolitan hospitals. Both studies used automated, integrated screening protocols on all admitted patients, where laboratory tests were automatically added, based on data and risk factors found in a person's medical record. Viral hepatitis screening was initiated based on risk factors and criteria associated with HBV infection found in the electronic patient record.[27,28]

This study investigated the impact of the COVID-19 pandemic on the duration of linkage to care. We report a significant Covid-19 related increase in time before people screened for HBsAg were linked to care (24 days vs. 82 days). This finding is in line with a recent survey conducted by the European Association for the Study of the Liver.[29] A total of 45 clinical centres reported decreases in chronic HBV consultations, new referrals, HBsAg and HBV DNA testing rates and new HBV treatments.

One of the strengths of this study is that it uses opportunistic screening instead of outreach screening. The individuals are screened during their routine integration classes in Antwerp instead of actively seeking out individuals in the community or screening in an outpatient clinic or other health institution. This method aims to improve case detection by providing screening and care to individuals who are not accessing healthcare or who might be reluctant to seek medical care due to fear of stigmatisation. Duplicate data entries do not occur during screening sessions because each student is required to take the integration classes only once.

A limitation of the study is the lack of a comparison of HBsAg prevalence in migrants versus that of a general Belgian population. A recent seroprevalence study in the general population in Belgium is lacking. The study by Quoilin et al. investigated HBV in saliva in Flanders (the northern, Dutch speaking part of Belgium, representing approximately 60% of Belgium's population) and found an HBV seroprevalence of 0.66%. Our group is currently performing a Belgian HBV seroprevalence study. Preliminary data on persons aged 18 or above, shows an HBV positivity rate of 0.31% (95% CI 0.14%–0.49%), which is numerically lower than the HBV seroprevalence reported here for first generation migrants. Another recent study in Turkish migrants residing in the north-eastern province of Belgium, showed a similarly higher regional HBV seroprevalence (2.55%).[30] During the COVID-19 period, there were no classes for Chinese migrants due to the strict travel measures in China. This resulted in fewer Asian individuals being screened than the initial target sample size. Finally, within the group who screened positive for HBsAg, the statistical power to detect differences in seroprevalence between sub-groups was limited. A more thorough evaluation is ongoing as well within our research group.

5. Conclusion

We found an HBsAg seroprevalence of 3.4% among 677 migrants in Belgium from Sub-Saharan Africa, the Middle East and Asia. A 100% linkage to care was achieved using POCT during opportunistic screenings and with the help of dedicated personnel. As no specific risk factors waereassociated with HBsAg positivity, except for male sex, we propose to perform HBV screening for migrants from these geographic regions.

Ethics approval and consent to participate

The study is performed in accordance with the Declaration of Helsinki. The Antwerp University Hospital/University of Antwerp Ethics Committee approved the study, (reference number B300201629236/ August 01, 2016). All screening participants signed an informed consent form.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Funding

Thomas Vanwolleghem is supported by a senior clinical investigator grant from the Research Foundation Flanders (grant number 18B2821 N). Part of these studies have been supported by grants from the Flemish Government (Centrum Medische Innovatie Vlaanderen-Hepatotrope Organismen, 2015), Gilead Sciences (Gilead BELUX Fellowship 2017) and AbbVie.

CRediT authorship contribution statement

Erwin Ho: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Axelle Vanderlinden:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Liesbeth Govaerts:** Writing – review & editing, Project administration, Investigation. **Bo De Fooz:** Writing – review & editing, Project administration, Investigation. **Pierre Van Damme:** Writing – review & editing, Validation, Supervision, Conceptualization. **Peter Michielsen:** Writing – review & editing, Validation, Supervision, Investigation, Conceptualization. **Thomas Vanwolleghem:** Writing – review & editing, Validation, Supervision, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Thomas Vanwolleghem is supported by a senior clinical investigator grant from the Research Foundation Flanders (grant number 18B2821 N). Part of these studies have been supported by grants from the Flemish Government (Centrum Medische Innovatie Vlaanderen-Hepatotrope Organismen, 2015), Gilead Sciences (Gilead BELUX Fellowship 2017) and Abbvie.

Data availability

Data will be made available on request.

Acknowledgements

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