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Hepatitis B and C Screening and Linkage to Care in Migrants From Endemic Countries in Barcelona Through a Community Action

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Keywords: community action | dried blood spots (DBS) | hepatitis B virus (HBV) | hepatitis C virus (HCV) | migrants

ABSTRACT

Background and Aims: Migrants from endemic areas are key populations for hepatitis B virus (HBV) and hepatitis C virus (HCV) infection screening in Europe. This study assessed the feasibility and outcomes of a community action that combined education, screening, and simplified access to care for migrants in Barcelona.

Methods: Adult migrants from Pakistan, Romania, and Senegal were included from 2021 to 2023, through a community action involving education, an epidemiological questionnaire, and rapid testing for HBV surface antigen (HBsAg) and HCV antibodies. If positive, DBS samples were collected for laboratory confirmation. Viremic cases were referred to an International Health Unit (IHU).

Results: Overall, 786 participants were included (346 from Pakistan, 304 from Senegal and 136 from Romania). Previous screening for HBV and HCV was 8.0% and 7.7%, respectively. HBsAg prevalence was 0.9% for migrants from Pakistan, 8.2% for those from Senegal and 1.4% for those from Romania ($n = 30/786$, 23 new diagnoses). Among these, 69.6% attended the IHU and were HBV-DNA positive, but none met treatment criteria. Anti-HCV prevalence was 3.5%, 0.7% and 1.4% for migrants from Pakistan, Senegal and Romania, respectively ($n = 16/768$, 12 new diagnoses), and HCV-RNA prevalence was 0.9%, 0.3% and 0.7%, respectively ($N = 6$, all new diagnoses); 4 (66.6%) cases were linked to treatment and two were cured.

Abbreviations: CHW, community health workers; DBS, dried blood spots; HBeAg, hepatitis B e-antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HCV-Ab, HCV antibodies; IHU, International Health Unit; LTFU, lost to follow-up; RDT, rapid detection test; SVR12, sustained virological response at week 12 after treatment; WHO, World Health Organisation.

Conclusions: This novel community action successfully reached migrants in a situation of vulnerability and provided them access to testing and care. The high prevalence observed and the limited self-knowledge of their HBV and HCV status justify targeted screening in these groups.

1 | Introduction

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections account for a significant global disease burden [1] and together continue to cause 1.3 million deaths per year as a result of chronic liver disease and cancer [2]. Globally, 254 and 50 million people are living with chronic infection by HBV and HCV, respectively [2]. Most people living with viral hepatitis are asymptomatic and unaware of their infection [2]. In this context, the World Health Organisation (WHO) set the goal to eliminate viral hepatitis as a public health threat by 2030, with targets to increase the diagnostic rate to 90% and the treatment rate to 80% [1]. However, globally, nearly 80% of people with the hepatitis B or C virus remain undiagnosed, and affordable treatments are not being accessed [3].

The highest burden of HBV and HCV is carried by lower and middle-income countries, with a high or middle endemicity (≥ 5% or ≥ 2% seroprevalence, respectively). For this reason, migrants are a key population in Europe affected by these infections, and the WHO and European Centre for Disease Prevention and Control guidelines recommend the targeted screening of HBV and HCV in this population [4, 5]. Additionally, migrant communities often face difficulties in accessing mainstream healthcare services due to cultural and language barriers, the fragmentation existing in the continuum of these services and/or social vulnerability [6]. Bringing screening into the community increases the number of people who can be rapidly screened and linked to care, promoting a more equitable access to diagnosis [7]. The screening of HBV surface antigen (HBsAg) and antibodies to HCV (HCV-Ab) can easily be carried out in community settings using rapid detection tests (RDT) [8]. Subsequently, the presence of viremic HBV or HCV infection can be confirmed by the detection of HBV-DNA and HCV-RNA, respectively, in dried blood spots (DBS) [9]. These minimally invasive samples have been shown to facilitate screening in the community, and their use is recommended by the WHO due to (i) easy collection and high acceptability, (ii) easy transportation (room temperature) and (iii) the high sensitivity and specificity of HBV-DNA and HCV-RNA detection assays in these samples [10].

In Catalonia, prevalence estimates in 2016–18 were 0.5% for HBsAg, 1.1% for HCV-Ab and 0.5% for HCV-RNA (active HCV infection) [11]. Of note, 53% of HBsAg positive individuals were migrants from high endemicity regions (Romania, Africa, South America, China and Pakistan). It was estimated that 38% and 12% of the total cases of chronic hepatitis B and C in Spain affect the migrant population [12]. Catalonia has the second highest proportion of migrant population in Spain, accounting for 16.2% of the resident population [13]. In a previous study, we developed and piloted the Hep*Clink* model of care [14], demonstrating the feasibility of community screening for HCV and linkage to treatment in the Pakistani population in Barcelona. This community intervention was designed in a culturally and linguistically appropriate way and delivered by a community health workers (CHW), and involved HCV education with an interactive tool [15], testing and simplified access to treatment. A high degree of acceptability and satisfaction was reported by the participants, most of whom had not been screened before, despite 80.3% of them having attended primary care in the previous year. In line with this previous work we expanded the model of care based on a community action that brings together education, screening and simplified access to treatment for both HBV and HCV infections (HepBC*link* study) and included migrants from three endemic countries (Pakistan, Senegal and Romania) living in the Barcelona province, with the aim of assessing its feasibility and outcomes.

2 | Methods

2.1 | Study Design

The HepBC*link* was a community-based action, designed to promote HBV and HCV knowledge, testing and access to care for Pakistani, Senegalese and Romanian migrants (Figure 1). Migrants born in these countries, living in the Barcelona province, aged ≥ 18 years and who accepted to participate and signed an informed consent were prospectively included from March 2021 until January 2023. A convenience sample of 300 individuals for each population was initially intended, as the objective of this study was not to recruit a representative sample but to evaluate the feasibility and quality of this community screening strategy. This project was approved by the ethics committees at Germans Trias i Pujol and Vall d'Hebron Hospitals.

2.2 | HepBC*link* Community-Based Action

Recruitment, education and testing were carried out within a single event in diverse settings. The actions were coordinated by the International Health Unit (IHU) Community and Public Health Team, which consists of a doctor specialised in infectious diseases and public health, a public and community health nurse and two CHWs for each country of origin; these workers were trained in rapid HBV and HCV testing, DBS collection and pre- and post-test counselling and performed the education and testing activities in the native language of each target population (Urdu for Pakistan, Wolof and French for Senegal and Romanian for Romania).

Two community outreach actions (individual- and group-based) were initially planned based on previous experience with the Pakistani population [14]. However, due to restrictions during the COVID-19 pandemic, actions were carried out individually. Participants received information on viral hepatitis and pre-test advice using a video from the previously piloted interactive educational tool (HEPARJOC) [15] which was translated into the study languages (Urdu, Romanian, French, Wolof, Mandinka and Fulha) and administered on a

Summary

- HepBC*link* is a new intervention for hepatitis B and C carried out in a specific population and in their community. Migrants from Pakistan, Romania, and Senegal in Barcelona were provided with education, rapid testing, and easy access to care and treatment.
- It was effective at reaching a group of 786 people who had largely not been tested before, identifying 23 new HBV diagnoses and 6 new diagnoses for HCV, and linking two-thirds of individuals from these highly mobile populations into a care.

tablet. Then, participants were invited to self-complete an epidemiological questionnaire and to get tested with RDTs for HBsAg and HCV-Ab performed at the point of care (site where the community action was carried out). If positive on either test, participants were asked to provide a capillary blood sample, for which fingerstick blood was collected as DBS for HBV-DNA and HCV-RNA testing. Participants who tested negative were advised to visit primary care or the IHU for a more comprehensive health check, including HBV vaccination when necessary.

2.3 | Epidemiological Questionnaire

Participants self-completed a questionnaire with closed questions in Spanish on socio-demographic data (age, gender, education level, current job, etc.); previous access to care including HBV and HCV testing and treatment; and HBV vaccination status. Participants were assisted as required by the CHW, speaking their native language. Those migrants who refused to participate were asked to provide basic demographic data and self-reported HBV and HCV status.

2.4 | HBV and HCV Screening

Participants underwent testing from fingerstick capillary blood with CE-IVD marked RDTs for HBsAg (DETERMINE HBsAg 2, Abbott Molecular; analytical sensitivity of 0.1 IU/mL), and for HCV-Ab (Turklab Tibbi Malzemeler San. Ve TIC. A.S.). Both RDTs were visually read after 15 min. When either test was positive, DBS (four spots, 50 μL each) were collected using a 200 μL EDTA-coated Minivette (Sarstedt) and shipped to the laboratory at room temperature. For the detection of HCV-RNA, DBS samples (one spot) were eluted and analysed in the *m*2000 system with the Abbott RealTi*me* HCV assay (Abbott Molecular) according to the manufacturer's instructions. This assay has been approved for in vitro diagnostics using DBS samples (CE-IVD) and has a lower limit of detection of 462 IU/mL, compared to 12 IU/mL for the same assay in venous plasma [16]. HBV-DNA testing in DBS samples was assessed within this study, and results were not delivered to participants. For the nucleic acid extraction and detection of HBV-DNA from DBS, the Alinity m HBV Assay (Abbott Molecular) was used out of product specifications. The lower limit of detection of this assay in plasma is 10 IU/mL, and in DBS samples, it was estimated at 1115 IU/mL by Probit analysis using mock DBS samples with known decreasing HBV-DNA concentrations [17]. Additionally, HCV genotyping was performed from DBS samples as previously reported [18].

2.5 | Linkage to Care and Access to Treatment

Participants who tested positive in the community action were scheduled for a visit at the IHU for the delivery of HCV-RNA DBS results and to have blood drawn for a routine analytical exam, including biochemical (ALT, AST, GGT), serological (HBsAg, anti-HBc, HBeAg, anti-HCV, anti-hepatitis D virus (HDV) and human immunodeficiency virus (HIV)) and virological parameters (HBV-DNA). Additionally, liver fibrosis

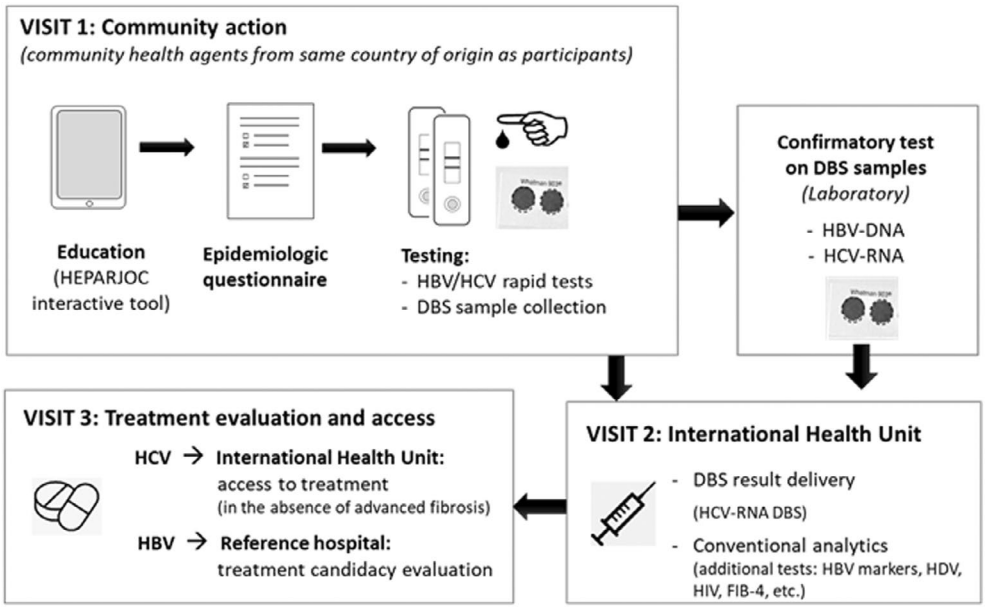

FIGURE 1 | HepBC*link* study design. HBV, hepatitis B virus; HCV, hepatitis C virus; DBS, dried blood spot; HDV, hepatitis D virus.

was evaluated in viremic HBV and HCV patients by non-invasive serum markers (FIB-4 index) [19]. For participants with hepatitis C and absence of advanced liver disease, treatment was dispensed at the IHU by a specifically trained general practitioner, once the antivirals had been prescribed by the hepatologist. Participants with hepatitis C and advanced liver disease or with HBV infection were referred to the hepatologist at the hospital.

2.6 | Participant Follow-Up

CHW contacted participants positive for HBV or HCV by telephone call to schedule the required medical visits and reinforced attendance by accompanying participants with a language barrier to medical visits. The following outcomes were recorded: (i) attendance of participants with a positive HBsAg or HCV-Ab result to the IHU to receive DBS HCV-RNA test results and undergo routine testing, and (ii) attendance of HBV-DNA positive participants to hospital visits to assess the need for antiviral treatment, and attendance of HCV-RNA positive participants to medical visits at the IHU related to antiviral treatment and assessment of sustained virological response at week 12 after treatment (SVR12). Viremic participants who did not attend the visits after repeated telephone calls were considered lost to follow-up (LTFU). Participants were followed up through electronic medical records review until 7 months after recruitment for HBV and until the assessment of cure (SVR12) for HCV.

For those patients for whom viral load, serological markers and/or liver stiffness characteristics were available, HBV infection was categorised according to current guidelines [20]. Late presentation was based on the consensus definition by Mauss et al. [21], if advanced liver disease was present at HBV or HCV diagnosis (defined as FIB-4 > 3.25 or liver stiffness > 9.5 kPa).

2.7 | Data Analysis

The HepBC*link* strategy was evaluated using a series of indicators in order to evaluate the quality of this community-based action and compare it to other screening programmes:

- Effectiveness indicators: percentage of people who accepted to participate in the study (degree of participation), number of people attending educational sessions, number of people tested, percentage of people who reported to have been previously tested, percentage of people with an HBsAg or HCV-Ab positive result among those tested, percentage of people who received test results among those tested (complete screening), percentage of people who tested HBV-DNA positive who visited the hepatologist or HCV-RNA positive who attended doctor's appointment at the IHU among all viremic cases (linkage to care), and percentage of people among the latter who started and completed treatment (retention in care). The number of participants needed to screen in order to detect one new HBV or HCV diagnosis was also calculated by dividing the number of people tested by the number of new diagnoses of viremic HBV or HCV infection.
- Impact indicator: percentage of people who tested HBV or HCV positive and presented late, as defined above.

Additionally, we measured acceptability as to what extent the new intervention was judged as suitable and satisfying by programme recipients, by asking the following two closed questions (5-point Likert scale): "do you agree with HBV and HCV testing being carried out within a community intervention?" and "are you satisfied with HBV and HCV testing during the intervention?"

Prevalence was calculated for HBsAg, HCV-Ab, and HCV-RNA, and 95% confidence intervals (CIs) were estimated using the Clopper-Pearson exact method. Self-knowledge of disease status was evaluated by comparing test results with self-reported data.

Descriptive analyses were conducted using frequency tables for categorical data and medians with interquartile ranges (IQRs) for numerical data. Statistical comparisons employed chi-square tests for categorical variables and the Mann–Whitney U test for continuous measures. The analysis was performed with R version 4.0.3.

3 | Results

3.1 | Study Feasibility and Characteristics of Participants

Among all migrants approached ($N = 849$), 786 (92.6%) agreed to participate in the study: 85.2% (346/406) for migrants from Pakistan, 99.7% (304/305) for those from Senegal, and 98.6% (136/138) for those from Romania. Among those who refused to participate, the main reasons were fear of results ($n = 42$, 66.7%) and no time to get tested at that moment ($n = 21$, 33.3%); 3 (4.7%) reported an active infection for HBV and 3 (4.7%) for HCV; all six were from Pakistan (three women and three men).

Overall, 68 community actions were carried out in different settings. For the Pakistani population, these actions were carried out in the consulate ($n = 177$, 51.2%), mosque ($n = 91$, 26.3%) and taxi driving schools ($n = 78$, 22.5%); for the Senegalese population in civil associations ($n = 297$, 97.7%) and a settlement ($n = 7$, 2.3%); and for the Romanian population in a church ($n = 101$, 74.3%), households ($n = 24$, 17.6%) and institutional places ($n = 11$, 8.1%). For the latter, it was not possible to reach the intended sample size of 300 due to: (i) the complexity in finding individuals from this country who could be trained as CHW and had a continuing dedication; (ii) the difficulty in diversifying testing sites other than the Orthodox church; and (iii) the conflict between Russia and Ukraine, which made creating links with the community more difficult.

Table 1 summarises the characteristics of participants. We found significant differences between migrants from Pakistan, Senegal and Romania. Pakistani migrants were younger (median age of 38.4 years), had been living in Spain for less time (median of 11.2 years), and had the lowest percentage of participants who spoke Catalan and/or Spanish (62.1%). Actually, recent immigration to Spain (≤ 5 years) was 29.4% in Pakistani migrants, 16.9% in Senegalese migrants and 9.1% in Romanian

TABLE 1 | Socio-demographic characteristics of the HepBC*link* participants.

	Pakistan (*N* = 346)		Senegal (*N* = 304)		Romania (*N* = 136)		
	N	**%**	***N***	**%**	***N***	**%**	***p***
Socio-demographic characteristics							
Women	84	24.3	65	21.4	79	60.8	< 0.001
Median age (IQR), years.	38.4	(12.0)	42.0	(10.5)	47.0	(13.8)	< 0.001
Median time of residency in Spain (IQR), years.	11.2	(7.18)	15.8	(8.73)	16.1	(5.63)	< 0.001
Recent migrant (≤ 5 year)	101	29.5	51	16.9	12	9.1	< 0.001
Speaks Spanish and/or Catalan	211	62.1	279	93.6	106	80.3	< 0.001
Education							
None	17	4.9	43	14.3	6	4.7	
Primary	137	39.8	107	35.7	16	12.4	
Secondary	123	35.8	119	39.7	83	64.3	
University	67	19.5	28	9.3	21	16.3	
Current remunerated job	192	55.8	205	68.3	70	58.3	—
Previous consume of drugs injected	4	1.16	4	1.36	0	0	0.005
Access to healthcare services							
Public healthcare card	317	92.7	280	95.9	112	84.2	< 0.001
At least one medical visit during the previous year	256	80.3	213	86.6	95	82.6	0.139
HBV							
Knowledge of HBV	163	47.7	109	36.1	94	71.2	< 0.001
Previously tested for HBV	19	5.5	27	8.9	16	12.1	0.044
Previously diagnosed with HBV	2	10.5	4	14.8	5	31.25	0.376
Treatment for HBV							1.000
Previously treated	1	50	2	50	1	20	
In treatment	1	50	1	25	2	40	
Linked to HBV care	1	50	1	25	1	20	0.245
Previously HBV vaccinated							0.008
Yes	57	16.8	23	8.3	9	8.5	
No	143	42.2	117	42.2	51	48.1	
Don't know	139	41.0	137	49.5	46	43.4	
Any relative with HBV							—
Yes	32	9.28	8	2.69	20	15.62	
No	177	51.3	89	29.9	57	44.5	
Don't Know	136	39.4	201	67.4	51	39.8	
HCV							
Knowledge of HCV	164	48.0	103	34.1	93	70.5	< 0.001
Previously tested for HCV	22	6.4	25	8.3	13	9.9	0.405
Previously diagnosed with HCV	6	27.3	1	4.0	2	15.4	0.018
Previously treated for HCV	3	50.0	1	4.0	1	7.7	1.000

Note: Percentages were calculated excluding missing values.
Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus.

migrants ($p < 0.001$). The majority of Romanian participants were female (60.8%) and they had the lowest percentage of participants who had the public healthcare card (84.2%), however, they had a better understanding of what hepatitis B and C were (71.2% and 70.5%, respectively) and a higher percentage of previous screening for HBV and HCV (12.1% and 9.9%, respectively). Participants from Pakistan and Senegal were predominantly male and reported previous consumption of injected drugs in a similar low proportion.

Overall, an understanding of what HBV and HCV were was significantly higher among women than it was among men (62.1% in women vs. 40.7% in men for HBV, and 61.9% vs. 39.7% in women and men for HCV, with a p-value < 0.001 for both variables). Eleven out of the 54 participants previously tested reported a previous diagnosis of HBV infection, four of them had been under treatment, and another three reported that they were currently linked to the healthcare system.

In terms of HBV vaccination status, Pakistani participants reported a significantly higher vaccination rate than those from the other countries. Senegalese participants demonstrated poorer knowledge of HBV infection in any relatives. For HCV, nine out of the 60 participants who had been previously tested reported a previous positive result, and five of them reported having received antiviral treatment.

3.2 | HBV Community Testing and Linkage to Care

Figure 2 shows the flow of participants through testing, linkage to care, and treatment, and Table 2 shows the observed HBsAg prevalence according to country of origin. In the Pakistani group, 3 (men) of 346 participants were positive for the HBsAg RDT (0.9% prevalence; 95% CI: 0.2%–2.7%) and two of them were unaware of having been infected (2/3 new diagnoses). These two participants were LTFU after they had been referred to the hospital, and the participant previously diagnosed and linked to care was under treatment (HBeAg negative chronic infection). The number of people needed to screen to detect a new hepatitis B diagnosis was 173 (Figure 3).

In the Senegalese group, 25 of 304 participants were HBsAg positive (8.2% prevalence; 95% CI: 5.5%–12.1%; 88% were men and 12% women). Eight (32%) had been previously diagnosed and linked to care, and 17 (68%) were unaware of having been infected (newly diagnosed). Twelve out of 17 new diagnoses (70.6%) were linked to the IHU, and the presence of viremia was confirmed in all of them through routine testing. Among them, 7 (58.3%) participants were referred to the hepatologist, and none of them met treatment initiation criteria. The other ten newly diagnosed participants were LTFU: five did not attend the visit to the IHU (one moved to France, two were not interested, and two for unknown causes); four attended the IHU visit but did not return for the blood work results (and, therefore, could not be referred to the specialist), and the last one was referred to the hepatologist but did not attend (Figure 2). Of all 25 HBV-infected participants, eleven could be categorised, and all of them had a HBeAg-negative chronic infection. The number of people needed to screen to detect a new HBV diagnosis was 18 (Figure 3).

In the Romanian group, 2 (both were women) of 136 participants were HBsAg positive (1.47% prevalence; 95% CI: 0.3%–5.8%) and one of them was unaware of having been infected (1/2 newly diagnosed). Both of them were linked to the specialist but did not meet treatment initiation criteria (HBeAg negative chronic

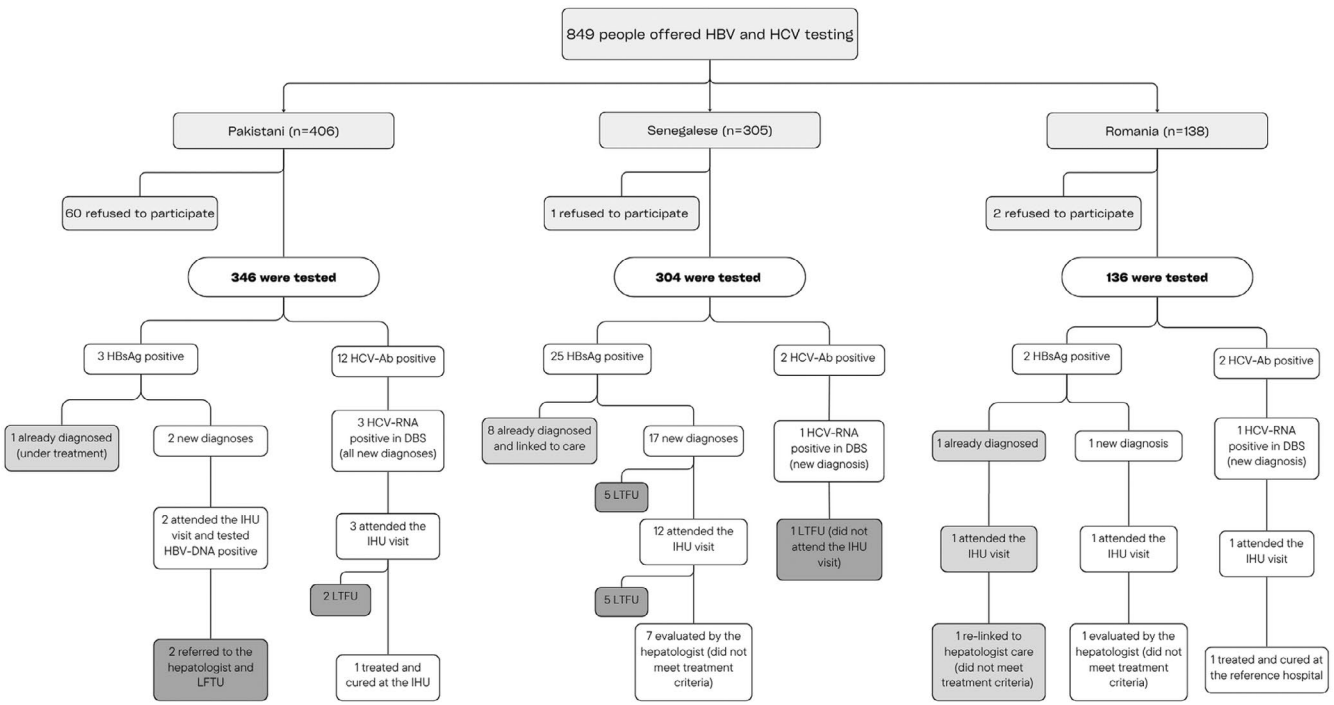

FIGURE 2 | Flowchart depicting the recruitment, testing, linkage to care and follow-up for HBV and HCV according to country of origin. HBV, hepatitis B virus; HCV, hepatitis C virus; IHU, International Health Unit; LFTU, lost to follow-up; HBsAg, hepatitis B virus surface antigen; HCV-Ab, antibodies against hepatitis C virus.

TABLE 2 | Observed prevalence for HBV and HCV according to country of origin.

	Prevalence, % (95% CI)		
	Pakistan	**Senegal**	**Romania**
HBsAg	0.9 (0.2–2.7)	8.2 (5.5–12.1)	1.4 (0.3–5.8)
HCV-Ab	3.5 (1.9–6.1)	0.65 (0.1–2.6)	1.47 (0.3–5.8)
HCV-RNA	0.86 (0.2–2.7)	0.32 (0.2–2.1)	0.73 (0.4–4.6)

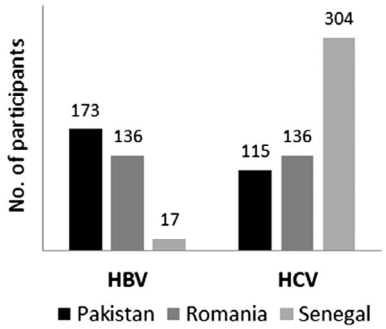

FIGURE 3 | Number of persons needed to screen to find a new diagnosis of viremic HBV or HCV infection. HBV, hepatitis B virus; HCV, hepatitis C virus.

infection) (Figure 2). The number of people needed to screen to detect a new HBV diagnosis was 68 (Figure 3).

Characteristics of all participants newly diagnosed of either viremic HCV ($n=5$) or HBV infection ($n=20$) are described in Table S1, both for those successfully linked to care ($n=10$; 2 for HCV and 8 for HBV) and for those LTFU ($n=15$; 3 for HCV and 12 for HBV). No statistically significant differences between groups were found.

Regarding HBV-DNA detection in DBS, these samples were obtained in 25 out of 30 cases (83.3%; the other five were already linked to care). However, routine viral load testing was only possible in 16 cases for comparison (the others were LTFU). HBV-DNA was detected in 8/16 (50%) DBS samples (these participants had viral loads of 331–14 454 IU/mL in plasma). No amplification was detected in the rest of the DBS samples (corresponding to participants with viral loads of 33–2089 IU/mL in plasma).

Overall, none of the HBV-DNA positive participants presented co-infection with HDV or HIV.

3.3 | HCV Community Testing, Linkage to Care and Treatment

The observed HCV prevalence according to country of origin is shown in Table 2. In the Pakistani group, 12 of 346 participants were HCV-Ab positive (3.5% seroprevalence; 95% CI: 1.9%–6.1%; 91.7% were men and 8.3% women) and 66.6% ($n=8$) were unaware of having been infected. All 12 cases (100%) accepted the DBS collection and 3 were HCV-RNA positive (3/3 all newly diagnosed and HCV genotype 3a; all men), which represents a viremic infection prevalence of 0.87% (3/346; 95% CI: 0.2%–2.72%). One of them received treatment at the IHU during the study. The remaining two were considered LTFU after their first IHU visit (Figure 2). The number of people needed to screen to detect a new hepatitis C diagnosis was 115 (Figure 3).

In the Senegalese group, 2 (both men) out of 304 participants were HCV-Ab positive (0.65%; 95% CI: 0.1%–2.6%), and both were unaware of having been infected. Viremia was positive in one of them (1/304 with HCV genotype 2d; 0.32% viremic infection prevalence; 95% CI: 0.02%–2.1%), who did not attend the visit at IHU and was thus considered LTFU (Figure 2). The number of people needed to screen to detect a new hepatitis C diagnosis was 304 (Figure 3).

In the Romanian group, 2 (a man and a woman) of 136 participants were HCV-Ab positive (1.47% seroprevalence; 95% CI: 0.3%–5.8%) and both (100%) were unaware of having been infected. Both accepted the DBS collection and one was viremic (newly diagnosed with HCV genotype 1b), which represents a viremic infection prevalence of 0.74% (1/136; 95% CI: 0.4%–4.6%) (Table 2). This case was considered a late diagnosis, with a liver stiffness of 18.1 kPa, which received treatment with direct-acting antivirals at the hospital and achieved cure (SVR12) (Figure 2). The number of people needed to screen to detect a new hepatitis C diagnosis was 136 (Figure 3).

Overall, none of the HCV-RNA-positive participants presented co-infection with HIV.

3.4 | Quality Indicators for the HepBC*link* Intervention

Overall, the degree of agreement and satisfaction is shown in Figure 4. Participants from Pakistan and Senegal presented a higher percentage strongly agreeing to be tested during community action (341/346, 98.6% and 282/304, 92.8% respectively) compared to those from Romania (112/136; 82.4%), and participants from Pakistan and Senegal were also very satisfied with the community action more frequently than Romania (313/346, 90.5%; 259/304, 85.2%; and 95/136, 69.9%, respectively). The other quality indicators of effectiveness and impact are summarised in Tables S2 and S3.

4 | Discussion

Migrants are key populations affected by HBV and HCV in Europe, and their targeted screening has been recommended. Bringing screening into the community with engagement of these populations in raising awareness and service delivery breaks the main barriers that migrant communities face when accessing mainstream healthcare services. The HepBC*link* builds on previous experience with migrants [14], expanding HBV and HCV education and screening through a community action carried out by CHW from both genders and from the same country of origin as participants (Pakistan, Senegal and Romania), creating a climate of trust, as well as empowering and resourcing a variety of civil society organisations. This

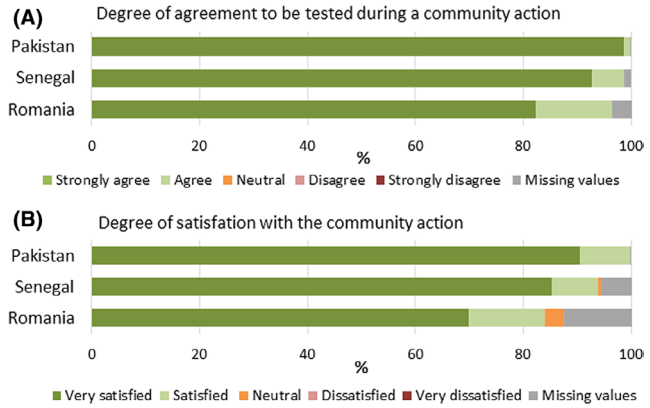

FIGURE 4 | Degree of agreement (A) and satisfaction (B) of participants with the community action.

community-based, person-centred action further promoted health equity by providing participants with simplified access to care and treatment and, despite inevitable losses to follow-up, showed feasibility and high acceptability even during the COVID-19 pandemic.

Regarding the degree of participation in this community action carried out by CHW, 92.6% of the 849 migrants approached agreed to participate and undergo HBV and HCV screening. This proportion is in line with other strategies; a study in Sicily found 95.9% of African migrants agreed to be screened for HBV, HCV, and HIV [22] and a study carried out in an International Medicine Service in Northern Italy among undocumented migrants from non-EU countries, in which 91.4% agreed to be screened for HBV [23]. In the Netherlands, only 57% of undocumented migrants from diverse origins and uninsured legal residents agreed to participate in HBV, HCV, and HIV screening in NGO centres [24]. Besides the high rates of participation, 100% of HepBC*link* participants tested agreed and 99.1% were satisfied with getting tested during the community action. CHW played an essential role in the recruitment and acceptance of the screening test, as it has been shown that health promotion and screening strategies carried out with agents from the same country of origin as participants help to remove barriers and increase acceptability [25].

The knowledge of hepatitis B and C among the participants was limited, especially among Senegalese participants (about one-third), compared to participants from Pakistan (about half) and Romania (about two-thirds). These differences might also be related to gender, as knowledge was greater among women, and they predominated among Romanian participants (as screening was mostly carried out in a church), while male participants predominated among the other two countries of origin. A study in Germany in migrants from sub-Saharan Africa found similar results, with the proportion of participants with knowledge about HBV and HCV varying from 40% to 58%, but they did not find differences between men and women [26]. The lack of knowledge of HBV and HCV among migrant groups makes them more vulnerable to infections, due to a lack of awareness of the risks [27]. The Spanish Strategic Plan includes the promotion of viral hepatitis diagnosis in priority populations when they attend primary care among its objectives; however, overall, less than 10% (71/777) of the participants reported having been tested before, even though 78.9% had been living in Spain for more than 5 years and 92.4% had a health card. These numbers are lower than those found in the greater Barcelona area study in West African migrants (mostly from Ghana), where 18.2% of the participants had been tested before for HBV [28], and in a study in the Netherlands (30% for HBV and 16.6% for HCV) in migrants mostly from Africa and Asia [24]. Our results evidence that viral hepatitis screening of migrants from endemic countries accessing primary care should also be reinforced.

The three countries included in this study were chosen due to their representation among migrants in Catalonia and their high HBV and/or HCV prevalence at the time of study design. Pakistan is the fifth most common country of origin for migrants in Catalonia and had the fourth largest number of HCV infections globally, with a 5.5% HCV seroprevalence and 4.2% HBV prevalence [29, 30]. Romania, with an estimated prevalence for HBsAg and HCV-Ab of 5.2%–5.7% and 3.2%, respectively [29, 30], is the second most represented country among migrants in Catalonia. Finally, Senegal is a country with a high endemicity, especially for HBV, with an estimated HBsAg prevalence of 10.1%–15.2% and 5.3% HCV seroprevalence [29, 30]. Nevertheless, current prevalence estimates have decreased due to elimination efforts in these countries: the HBsAg prevalence was 2.2% for Pakistan, 10% for Senegal, and 3.0% for Romania in 2022 [31], and the estimated viremic HCV prevalence was 3.3% for Pakistan, 0.75% for Senegal, and 2.3% for Romania in 2020 [32].

The HBsAg prevalence observed in HepBC*link* was 8.2% (95% CI: 5.5%–12.1%), 1.4% (95% CI: 0.3%–5.8%) and 0.9% (95% CI: 0.2%–2.7%) for Senegalese, Romanian, and Pakistani migrants, respectively. These values are 37.2, 6.3, and 4.1 times higher than in the general population in Spain (0.22%; 95% CI: 0.10%–0.34%) [33], which justifies screening and linkage to care in order to achieve the elimination goals. The prevalence observed in this study is in line with a study in Northern Italy in undocumented migrants from non-EU countries between 2006 and 2010 (13%, 3.7% and 2.1% in participants from Senegal, Romania and Pakistan, respectively) [23]. Another study in Sicily in African migrants (2015–2017) found 9.7% HBsAg prevalence in Senegalese migrants, and no co-infection with HDV was identified [22].

Regarding linkage to care of HBV cases newly diagnosed in the community, most of them attended the IHU visit (15/20; 75.0%), while seven of them were subsequently LTFU during the process of referral from the IHU to the specialist. Therefore, 12 out of 20 (60%) HBV newly diagnosed cases, 10 (83.3%) of them being of Senegalese origin, did not reach the specialist, even though CHWs tried to call or visit these participants to minimise losses to follow-up. Additionally, chronic HBV infection requires monitoring over time, and this engagement in long-term care may be even more difficult among highly mobile populations such as migrants. When all participants newly diagnosed of either viremic HCV or HBV infection were considered ($n = 25$), while differences were not statistically significant due to the small numbers, those lost to follow-up tended to be more frequently younger, recent migrants, and spoke Spanish and/or Catalan less frequently; additionally, two of them did not have the health card issued. Although this

study was performed over the COVID-19 pandemic, which probably had an impact on attendance to healthcare centres, strategies to minimise losses to follow-up should be further refined by increasing simplified treatment access, such as direct referral to the specialist [28] or treatment decentralisation in primary care. Furthermore, qualitative studies with these migrant communities could help us to identify unmet needs. Among HBsAg-positive participants who were linked to care, none fulfilled treatment criteria. In fact, fewer than 1 in 5 West African people with chronic HBV infection are eligible for treatment [34]. This scenario may change in the future with the new HBV treatment guidelines [35].

Regarding the use of DBS for HBV-DNA detection, positivity was observed in half of the cases with detectable viral load in plasma. Similarly, 44% of viremic participants in a community screening study in Barcelona were detected using plasma separation cards [36]. With these results, DBS testing would identify most patients who could potentially require antiviral treatment (viral load > 2000 IU/mL) for reinforced linkage to care for liver function tests and treatment evaluation. Therefore, DBS testing could complement rapid HBsAg testing for the screening of HBV infection in these migrant populations.

Vaccination at birth is the most effective way of decreasing HBV infection [3]; in lower- and middle-income countries, vaccination rates have increased over the last years, but there is a lag time before this protective effect can be observed in migrants from these countries [37]. Most HepBC*link* participants did not know their vaccination status (41.2%) or had not been vaccinated (39.8%), similar to findings in African communities in Barcelona, with 70.1% of the participants reporting not being vaccinated [36]. Therefore, screening and vaccination programmes in migrants should be strengthened.

The HCV seroprevalence observed in HepBC*link* was 3.6% (95% CI: 1.9%–6.1%), 1.47% (95% CI: 0.3%–5.8%) and 0.65% (95% CI: 0.1%–2.6%) for Pakistan, Romania, and Senegal, respectively. In comparison with the general population in Spain (0.85% seroprevalence, 95% CI: 0.64%–1.08%) [33], the Pakistani and Romanian populations present a seroprevalence 4.2 and 1.8-fold higher, respectively, while the prevalence in migrants from Senegal is comparable. The prevalence of viremic HCV infection was 0.87% (95% CI: 0.2%–2.7%), 0.74% (95% CI: 0.4%–4.6%), and 0.32% (95% CI: 0.2%–2.1%) for migrants from Pakistan, Romania, and Senegal. Therefore, for Pakistani and Romanian migrants, it is 4 and 3-fold higher, respectively, compared to the general population (0.22%; 95% CI: 0.12%–0.32%) [33], while for Senegal, it is similar. As with HBV, the observed HCV seroprevalence was lower than previous estimates in Spain (5.0%, 5.3% and 3.2% for Pakistan, Senegal and Romania) [30]. The HCV seroprevalence observed in Senegalese migrants is in line with a study in Sicily (0.9%) [22] and that observed in the Pakistani community is similar to our previous study in the same area before the COVID-19 pandemic (4.6% seroprevalence and 1.2% viremic infection prevalence) [14]. Although HCV prevalence data in the general population in Romania is scarce, the prevalence of viremic HCV infection observed in this study is similar to that reported in a national survey between 2020 to 2023 (0.96%, with no significant differences among men and women) [38].

While viral hepatitis screening is recommended in all migrants from intermediate and high prevalence countries, case-finding by the HepBC*link* community action is especially effective for HBV in migrants from Senegal, as 17 people need to be screened to find a new diagnosis, and this is followed by HCV in the Pakistani population, with 115 people screened to find a new diagnosis, and by HBV and HCV in people from Romania (136 people screened to find a new diagnosis).

This study has several limitations. Firstly, since participants were recruited by convenience sampling, these results may not be generalisable to the whole migrant population from the tested countries or to migrants from the same origin living in other countries. In particular, the study was conducted during the COVID-19 pandemic, which made community outreach activities challenging due to the national restrictions at the time. This issue was particularly challenging for the Romanian population (particularly men) and prevented us from reaching the initially planned sample size of 900 people to be screened, linked to care and possibly treated. Future studies should try to ensure engagement of both male and female participants; even though both attended church events on weekends, women were generally more willing to participate than men. It is also noteworthy that Romanian community leaders expressed that this population group, being of European origin, oftentimes did not feel the need for differentiated treatment. Secondly, self-reported data regarding previous HBV and HCV testing and diagnosis may not be completely reliable due to limited recall. Thirdly, the use of RDTs for screening may have led to an underestimation of prevalence due to limited sensitivity in comparison with standard diagnostic tests; additionally, three HCV viremic cases and another three HBV viremic cases from Pakistan refused to participate and, therefore, were not computed for prevalence calculations. Finally, this study was mostly descriptive, and the relatively small number of participants who tested positive precluded us from identifying independent factors for loss to follow-up in the linkage to care process.

In conclusion, the HepBC*link* model of HBV and HCV care has been proven to successfully reach migrant populations from Pakistan, Senegal, and Romania in a situation of vulnerability and provide them with education on viral hepatitis and access to testing and care. The high prevalence observed in the different groups and the limited self-knowledge of their HBV and HCV status justify their targeting screening in agreement with recommendations by the WHO and ECDC. However, access to treatment should be further simplified to minimise losses to follow-up. This decentralised care model was also piloted in other regions in Catalonia [39] to assess scaling up this intervention and its usefulness in reaching the WHO elimination targets. Finally, the low vaccination rate and lack of knowledge of HBV vaccination status were remarkable, for which HBV vaccination should also be reinforced, ideally in the community setting.

Author Contributions

E.M. designed and coordinated this study and obtained the funding. E.M. and J.G.P. developed the methodology behind it. H.O.E. and J.G.P. organised and supervised the community action and questionnaire

administration, and obtained follow-up information. A.N. analysed the dried blood spots (DBS) samples, informed test results, performed data entry from questionnaires and supervised patient inclusion and follow-up. B.T., M.B. and R.M.M. provided care and treatment to participants with hepatitis B or C and obtained follow-up information. M.M. and C.F. performed the statistical analysis. A.N. and A.E.B. prepared the figures. X.M. and J.C. provided resources. All authors contributed to the interpretation of results. A.N. and E.M. wrote the first manuscript draft and incorporated revisions from all authors. All authors read and approved the final version of the manuscript.

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Ethics Statement

This project was approved by the ethics committees at Germans Trias i Pujol and Vall d'Hebron Hospitals. A signed informed consent was obtained from all study participants.

Consent

The authors have nothing to report.

Conflicts of Interest

E.M. has received lecture fees and research grants from Abbott GmbH & Co.K.G., Gilead Sciences, Cepheid and Abbvie, outside of the submitted work. M.B. received fees and research grants from Gilead and Abbvie.

Data Availability Statement

The data that support the findings of the HepBC*link* study are available from the corresponding author, E.M., upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.