Screening for Imported Diseases in an Immigrant Population: Experience from a Teaching Hospital in Barcelona, Spain

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Abstract. The objective of this study was to describe the screening for imported diseases among an immigrant population. This retrospective observational study was of all adult immigrants attended at the Tropical Medicine Unit of the Vall d'Hebron Teaching Hospital from September of 2007 to March of 2010. The screening strategy was adjusted by symptoms, country of origin, and length of residence in Europe. Overall, 927 patients were included. The median age was 34.5 years, and 42.1% of patients were male. A diagnosis was made in 419 (45.2%) patients. The most frequent diagnoses were Chagas disease, anemia, latent tuberculosis infection, intestinal parasitosis, hepatitis B virus (HBV) infection, and human immunodeficiency virus (HIV) infection. After screening, more diseases were identified in immigrants from sub-Saharan Africa (new diagnoses in 56.6% of patients) than patients from other geographic areas. The geographic origin and length of residence in a developed country determine the prevalence of diseases; hence, screening protocols must be based on this information.

INTRODUCTION

Human migration is a global phenomenon that has existed in every period of history and every part of the world. The magnitude and speed of these population movements have been increasing in the past few years, especially driven by the development of mass communication media and the growth of international travels. Nowadays, more than 214 million people live in a country other than the one in which they were born.¹ This situation possess a multitude of challenges to the migrant as well as governments and health providers, who must be made aware of migration patterns and global health problems, which are highly dynamic and shifting.²

Although migrants are usually healthy people, the likelihood of suffering health problems is higher. Several health determinants in their countries of origin, such as socioeconomic status or high rates of infectious diseases, condition the spectrum of illnesses. For this purpose, individualized screening programs have been recommended. The aim of these programs is to both offer early diagnosis and treatment to the patient and protect the health of the host community. Most of the diseases susceptible to screening can easily be diagnosed, but those with long latency periods or considered as tropical infections may require a specialized approach. Setting aside ethical considerations, these strategies significantly improve both the morbidity and the mortality of migrants, and in some cases, they are able to halt transmission of diseases to the host population.^{3–5}

Over the past few decades, Spain has shifted from experiencing net outward migration to managing net inward migration. Currently, the immigrant population represents 12% of the total population of Spain.⁶ This fact presents a challenge to Spanish public health authorities. Until 2012, the Spanish health system recognized the right to health protection and healthcare for all Spanish citizens as well as non-natives with established residence in the country. Nevertheless, in August of 2012, the current conservative government, enmeshed in the economic crisis, approved a law that

restricts access to healthcare for those without legal leave to remain in the country.⁷

The Tropical Medicine Unit of the Vall d'Hebron Teaching Hospital was created in 2007, and it provides specialized care to immigrants and travelers. The unit offers its own designed screening strategy for tropical and common diseases. The aims of this study were to evaluate this method, suggest a screening strategy that takes into account the geographic origin of immigrants with the final objective of providing equality of access to health services for immigrants, and contribute to addressing the health needs of immigrants and host communities alike.

METHODS

Study population and data collection. Retrospective observational study performed at the Tropical Medicine Unit (Infectious Diseases Department) of the Vall d'Hebron Teaching Hospital, included in the International Health Program of the Catalan Health Institute, Barcelona, Spain (PROSICS Barcelona). Adult immigrants (people migrating from outside the European Union who were over 18 years old) attended at the unit from September of 2007 to March of 2010 were included. Clinical and epidemiological data were collected from medical records: age, gender, country of origin, provenance, length of residence in Spain, clinical symptoms, diagnostic procedures performed, and diagnosis. The study protocol was approved by the institutional review board of the hospital.

The provenance of immigrant patients was recorded as follows: self-referrals or patients referred from different areas of the hospital, from general practitioners, from the Blood Bank, or by non-governmental organizations (NGOs), such as Asociación Comisión Católica Española de Migración (ACCEM), Comisión Española de Ayuda al Refugiado (CEAR), the Cepaim Foundation, and the Putxet Foundation. These NGOs referred patients to our unit when they first arrived in the country, for a routine screening, or to resolve clinical problems.

Screening strategy. Screening for imported diseases was offered to all immigrant patients who attended the Tropical Medicine outpatient service, regardless of the consultation motive. The screening strategy was adjusted by symptoms, country of origin, and length of residence in Europe. The tests

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performed in all patients were as follows: blood cell count, general biochemistry (including glucose, creatinine, albumin, and transaminases), detection of hepatitis B virus surface antigen (HBsAg), antibody against hepatitis B virus core antigen (HBcAb), antibody against hepatitis C virus (Ab anti-HCV), and *Treponema pallidum*, and human immunodeficiency virus (HIV) serology.

Stool samples from 3 different days were collected for parasitological examination from patients living in Spain for less than 3 years. Microscopic examination was performed using direct techniques (saline and iodine wet mounts) and later, Ritchie's formalin-ether concentration technique.

Patients living Spain for less than 5 years who were younger than 35 years old were tested for tuberculosis infection by the tuberculin skin test (TST); a positive TST was considered when the induration was > 10 mm. Patients with latent tuberculosis infection were offered treatment with isoniazid and rifampicin for 3 months. Chest X-ray was performed on all patients, regardless of their age and length of residence in Spain.

Thick and thin blood films for detection of malaria and microfilariae were performed on all immigrants from sub-Saharan Africa. Tests were performed on patients with other geographic origins depending on clinical symptoms and epidemiological factors. Moreover, a real-time polymerase chain reaction (rt-PCR) test was performed in peripheral blood samples; it is capable of identifying four different species of *Plasmodium* following the technique described by Rougemont and others.⁸

For schistosomiasis, patients arriving from schistosomiasis-endemic areas (sub-Saharan Africa and some Latin American regions) were tested with an enzyme-linked immunosorbent assay (ELISA) technique detecting IgG against *Schistosoma mansoni* (Novagnost *S. mansoni* IgG; Siemens Diagnostics, Marburg, Germany). When the results were positive, stool and urine samples were observed for parasite ova detection, and an abdominal ultrasound was performed.

Testing for Chagas disease included serological diagnosis with two ELISAs in parallel: one with a recombinant antigen (Bioelisa Chagas; Biokit, Barcelona, Spain), and one with a crude antigen (Ortho *Trypanosoma cruzi* ELISA; Johnson & Johnson, Piscataway, NJ). We considered results as positive or negative if both tests were concordant. All discordant sera were tested by a third serological diagnostic test (indirect immunofluorescence or Western blot technique). This test was offered to all South American patients considered at risk of being infected by *T. cruzi* (those coming from rural areas, those who recognized the triatomine bug, or those who were aware of the existence of the disease).

Statistical analysis. All data were analyzed with SPSS software for Windows (version 15.0; SPSS Inc., Chicago, IL). Categorical data are presented as absolute numbers and proportions, and continuous variables are expressed as medians and ranges. The χ^2 test or Fisher exact test, when appropriate, was used to compare the distribution of categorical variables, and the Mann-Whitney *U* test was used to compare the distribution of continuous variables. Results were considered statistically significant if the two-tailed *P* value was < 0.05.

RESULTS

Overall, 927 patients were included. The median age was 34.5 (18–78) years, and 390 (42.1%) patients were male. The

median time of residence in Spain before the screening was 2 (0–30) years. The origins of patients were as follows: 470 (50.7%) patients were from Central and South America, 362 (39.1%) patients were from sub-Saharan Africa, 52 (5.6%) patients were from the Indian subcontinent, 24 (2.6%) patients were from Eastern Europe, and 19 (2%) patients were from northern Africa. Bolivia was the most represented country with 359 (38.7%) patients.

In total, 271 (29.2%) patients attended on their own initiative, 215 (23.2%) patients were referred by NGOs, 164 (17.7%) patients attended after a consultation at the Emergency Department, 149 (16.1%) patients were referred by their general practitioner, 60 (6.5%) patients were referred by the Blood Bank, and 68 (7.3%) patients came after a consultation with other departments of the hospital.

Overall, a diagnosis was made in 419 (45.2%) patients: 84 (9%) patients had two simultaneous diseases, and 55 (5.9%) patients had three or more diseases. From all diagnoses, 540 were infections, and 72 were non-infectious pathologies. The most frequent diagnoses were Chagas disease (224 patients), anemia (116 patients), latent tuberculosis infection (100 patients), intestinal parasite infection (69 patients), and HBV infection (57 patients).

Chagas disease was the most frequent diagnosis (224 patients). Of these patients, 184 (82.1%) patients were in the indeterminate form of the disease, and 40 (17.9%) patients had cardiac or gastrointestinal involvement. Four patients had coinfection with HIV; 208 patients were offered treatment with benznidazole, although 36 patients did not receive treatment, because they were lost during follow-up.

Characteristics of patients and diagnoses by geographic areas are summarized in Table 1, which includes a comparison between the two most represented geographic areas (Central and South America and sub-Saharan Africa). Table 2 shows the intestinal parasites isolated. Figure 1 shows the profitability of screening imported diseases. After the screening was applied, more diseases were diagnosed among immigrants from sub-Saharan Africa compared with patients from Central and South America (*P* < 0.001).

DISCUSSION

People who emigrate for economic reasons could be considered especially vulnerable to contracting diseases. Several determinants, such as education, working conditions, housing, and economic status, could exacerbate existing inequalities in health. Strategies focused on this population could help to improve their health status and their integration into host communities.

The most frequent geographic origins of immigrant patients in our study were Bolivia and sub-Saharan Africa. These geographic areas are probably over-represented in our cohort for two reasons. Because of the increasing number of patients with Chagas disease, PROSICS has implemented different strategies with primary healthcare services to improve awareness of this disease.⁹ Second, many African patients are referred to our unit from NGOs very soon after their arrival to Spain to resolve clinical problems or undergo screening for different diseases.

Patients emigrating from sub-Saharan Africa had a greater proportion of infectious diseases (hepatitis B and C, syphilis, latent tuberculosis, HIV, intestinal parasites, and schistosomiasis)

TABLE 1

Characteristics and diagnoses of immigrants attended at the Tropical Medicine Unit of the Vall d'Hebron Teaching Hospital from September of 2007 to March of 2010

	Overall (N = 927)	Sub-Saharan Africa (N = 362)	Central and South America (N = 470)	P value*	Eastern Europe (N = 24)	Northern Africa (N = 19)	Indian subcontinent (N = 52)
Gender (male), n (%)	390/927 (42.1)	288/362 (79.6)	173/470 (36.8)	< 0.001	20/24 (83.3)	14/19 (73.6)	42/52 (80.8)
Age (years), median (range)	34.5 (18–78)	30 (18–78)	35 (18–78)	< 0.001	26.5 (19–53)	34 (19–74)	28.5 (18–76)
Time of residence (years), median (range)	2 (1–30)	1 (1–16)	5 (1–19)	< 0.001	1 (1–10)	1.5 (1–11)	3.5 (1–30)
Positive HBsAg, n (%)	57/857 (6.6)	48/349 (13.7)	7/419 (1.6)	< 0.001	1/23 (4.3)	1/18 (5.5)	0/48 (0)
Positive Ab anti-HCV, n (%)	36/859 (4.2)	27/351 (7.6)	4/418 (0.9)	< 0.001	3/23 (13)	0/18 (0)	2/49 (4.1)
Syphilis, n (%)	54/887 (6.1)	31/354 (8.7)	21/445 (4.7)	0.022	0/23 (0)	1/18 (5.5)	1/47 (2.1)
Active tuberculosis, n (%)	4/927 (0.4)	1/362 (0.3)	1/470 (0.2)	–	2/24 (8.3)	0/19 (0)	0/52 (0)
Latent tuberculosis infection, n (%)	100/230 (43.5)	65/142 (45.7)	19/49 (38.7)	0.395	7/12 (58.3)	3/7 (42.8)	6/20 (30)
HIV infection, n (%)	29/889 (3.3)	19/356 (5.3)	8/444 (1.8)	0.006	1/24 (4.1)	1/18 (5.5)	0/47 (0)
Intestinal parasites, n (%)	69/400 (17.2)	37/159 (23.2)	26/200 (13)	0.011	0/6 (0)	0/8 (0)	6/27 (22.2)
Schistosomiasis, n (%)	37/270 (13.7)	36/260 (13.8)	1/9 (11.1)	–	–	–	0/1 (0)
Malaria, n (%)	27/276 (9.8)	25/267 (9.3)	2/8 (25)	–	–	–	0/1 (0)
Filariasis, n (%)	7/205 (3.4)	7/205 (3.4)	–	–	–	–	–
Chagas disease, n (%)	224/416 (53.8)	–	224/416 (53.8)	–	–	–	–
Eosinophilia, n (%)	61/927 (6.6)	39/362 (10.8)	16/470 (3.4)	< 0.001	0/24 (0)	0/19 (0)	6/52 (11.5)
Anemia (hemoglobin < 11.5 mg/dL), n (%)	116/927 (12.5)	57/362 (15.7)	50/470 (10.6)	0.029	1/24 (4.1)	1/19 (5.2)	7/52 (13.5)
Adaptive disorders, n (%)	17/927 (1.8)	9/362 (2.4)	6/470 (1.3)	0.194	0/24 (0)	0/19 (0)	2/52 (3.8)

* Comparison between the two most represented geographic areas (Central and South America and sub-Saharan Africa).

compared with those emigrating from South America. Although both communities emigrated to Spain to seek new opportunities, the economic background or even the migratory process could be a significant differentiating factor.

Overall, 6.6% of immigrants from sub-Saharan Africa and 4.2% of immigrants from South America tested positive for HBsAg and Ab anti-HCV, and all of them were asymptomatic. These viral hepatitis infection rates were similar to those found in other studies performed in Spain.¹⁰ As expected, HBV infection was higher among immigrants from sub-Saharan Africa (13.7%) than immigrants from other geographic areas, reflecting the prevalence of HBV infection in these countries. Moreover, in this geographic area, most HBV infection cases occur through mother-to-child transmission or during childhood, facilitating chronicity of the infection.¹¹

Regarding sexually transmitted infections, 29 (3.3%) patients tested positive for HIV, and 54 (6.1%) patients had positive *T. pallidum* serology. Once again and as other studies have shown, prevalence of HIV infection is higher among

immigrants from sub-Saharan Africa, and the proportion of immigrants with recent HIV diagnoses is increasing.¹² This fact by itself could justify the screening program, especially when considering the substantial benefits that could be offered to the patient and the potential positive impact in terms of public health. Moreover, it is important to note that immigrant patients may have other infections that are prevalent in their countries of origin that can be reactivated or made manifest as severe forms because of the potential immunosuppression of HIV, such as *Strongyloides stercoralis* hyperinfection syndrome or myocarditis and meningoencephalitis caused by *T. cruzi*.¹³ In our study, all patients diagnosed with HIV infection were asymptomatic and did not have opportunistic infections.

Probably, tuberculosis is the disease most closely linked to immigration. Several studies show that, in developed countries, the immigrant population is one of the most at-risk populations for tuberculosis.^{14–16} In our study, a TST was performed on 230 patients, latent tuberculosis infection was diagnosed in 100 (43.5%) patients, and 4 patients were diagnosed with active tuberculosis (all of them were asymptomatic). This prevalence of latent tuberculosis infection is similar to that found in other Spanish studies, but it is probably overestimated because of the high percentage of people vaccinated with the Bacillus Calmette-Guérin (BCG) vaccine among the immigrant population (data not recorded in our study).^{5,10} It is important to point out that the number of TSTs performed and read is very low compared with the overall number of patients. Many factors, such as their temporary living situation or working conditions, make performing an adequate Mantoux test difficult. Taking into account these limitations of TST testing on immigrant patients, screening for latent tuberculosis infection in this population could be improved by the new interferon- γ release assays (IGRAs), because they are more specific tests in this population and returning to read the result is not required.¹⁷

In total, 416 Latin American patients were tested for Chagas disease, of which 224 (53.8%) patients tested positive.

TABLE 2
Intestinal parasites isolated

Intestinal parasite	Number of isolations
Pathogenic parasites	
<i>S. mansoni</i>	1
<i>S. stercoralis</i>	13
<i>Trichuris trichiura</i>	5
<i>Enterobius vermicularis</i>	2
<i>Ascaris lumbricoides</i>	9
<i>Hymenolepis nana</i>	1
<i>Giardia lamblia</i>	4
Hookworms	3
<i>Isospora belli</i>	2
<i>Cryptosporidium parvum</i>	1
Parasites of minor medical importance	
<i>Entamoeba histolytica/dispar</i>	20
<i>Endolimax nana</i>	7
<i>Iodamoeba bütschlii</i>	1
<i>Blastocystis hominis</i>	1
<i>Dientamoeba fragilis</i>	1

FIGURE 1. Profitability of the screening protocol by geographic regions. Asymptomatic indicates all patients who came or were referred to the hospital without complaining of any symptom or laboratory abnormalities. Diagnosed indicates all patients who came or were referred to the hospital because of any symptom, disease, or laboratory abnormality. New Dx indicates all patients in whom a diagnosis could be found after applying the screening program. No new Dx indicates all patients in whom a new diagnosis could not be found after applying the screening program.

As explained previously, most of these patients referred themselves to our unit searching for Chagas disease diagnosis after being informed about it by friends or relatives with Chagas disease. *T. cruzi* infection is being increasingly diagnosed in the tropical medicine units in Barcelona because of the high number of immigrants from endemic areas who have arrived in Spain over the past few years. Most of them are young people and have the indeterminate form of Chagas disease.⁹ Offering diagnosis and treatment to this population is crucial, because the risk of cardiac involvement progression and mother-to-child transmission can be reduced.

In relation to schistosomiasis, we chose serology as a first-step screening technique because of its higher sensitivity compared with urine direct examination as well as the mobility of our patients; on many occasions, we had only 1 day to complete the screening.¹⁸

Malaria was diagnosed in 27 patients, most of them complaining of fever and other symptoms. *P. falciparum* infection was diagnosed in four asymptomatic patients from sub-Saharan Africa through a positive rt-PCR, whereas the thick and thin blood films were negative. Other studies show this higher sensitivity of rt-PCR compared with thick and thin blood films in post-arrival screening for malaria in asymptomatic patients arriving from endemic areas.¹⁹

As Figure 1 shows, there is a huge number of patients with new diagnoses after screening for imported diseases. The effectiveness of the screening strategy depends on the geographic origin of the patients and the presence or absence of symptoms. The highest percentage of patients with new diagnoses is seen among patients from sub-Saharan Africa (56.6% of patients), even when they were asymptomatic (150 of 249 asymptomatic patients; 60.2%). This information probably reflects that this population originates from countries with high transmission rates of infectious diseases, poor socioeconomic conditions, and difficulties with access to healthcare.

This study has some limitations derived from its retrospective nature: information that does not appear in medical records is lost, and physicians may have changed the screening strategy in some patients depending on the clinical situation of the patient or availability of different tests. Moreover, our study population has specific social characteristics that make follow-up difficult, requiring greater effort by physicians.

Regarding ethical issues, screening programs for immigrants have been questioned, because they could be interpreted as a limitation of their human rights.²⁰ Probably, the screening programs by themselves do not constitute a threat but rather, the use that can be made of the results. With these results, we want to highlight the vulnerability of a specific population and how important it is to offer them appropriate medical care. Restrictions placed on access to the healthcare system may impact negatively on both the health of immigrants and their host communities.

In summary, as our study and other previously published studies have shown, immigrant populations are very vulnerable, because they carry a high number of undiagnosed and untreated health problems, some of which have public health implications, such as tuberculosis and sexually transmitted infections. Screening programs are useful and beneficial as long as they are based on impartiality and afford respect to the immigrants. Geographic origin and length of residence in a developed country determine the prevalence of diseases; hence, screening protocols must be based on this information. Other tests may be performed depending on the epidemiological and clinical characteristics of patients. To establish affordable and cost-effective screening protocols is a challenge for all countries hosting immigrant populations and represents an important public health issue.

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