Screening Program for Imported Diseases in Immigrant Women: Analysis and Implications from a Gender-Oriented Perspective

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Abstract. The female immigrant population is especially vulnerable to imported diseases. We describe the results of a prospective screening program for imported diseases performed in immigrant female patients. The protocol included tests for HIV, hepatitis B virus (HBV), hepatitis C virus (HCV), *Treponema pallidum*, *Trypanosoma cruzi*, *Strongyloides stercoralis* and *Schistosoma* spp., intestinal parasites, malaria, and the detection of microfilaremia, according to the patient's origin. Six hundred eleven patients were studied. The most frequent imported diseases were intestinal parasitosis (39.4%), followed by syphilis (14.6%), HIV infection (9%), chronic HCV (5%), and HBV (3.3%). Most of the cases of HIV (78%) and HBV (85%) were diagnosed in patients aged between 16 and 45 years. Hepatitis C virus appeared mostly in patients in the 46- to 65-year range ($P = 0.001$; odds ratio [OR]: 3.667 [1.741–7.724]) or older than 65 years ($P = 0.0001$; OR: 26.350 [7.509–92.463]). Syphilis was diagnosed more frequently in patients older than 46 years ($P = 0.0001$; OR: 4.273 [2.649–6.893]). Multivariate analysis confirmed a greater presence of HCV infection ($P = 0.049$) and syphilis ($P = 0.0001$) in patients aged between 46 and 65 years. In 15.4% of patients, screening did not find any pathology. These data show a high prevalence of imported diseases in the female immigrant population, which may have serious consequences in terms of morbimortality and vertical transmission. Our results encourage the establishment of policies of active screening both in women of childbearing age and within the specific pregnancy screening programs.

INTRODUCTION

Migration of people from developing areas to developed countries is a growing reality that has changed the epidemiological spectrum of infectious diseases in the host countries. In Spain, there are currently 5,025,264 foreign citizens, 9.5% of the total population, coming mostly from developing countries, of which approximately half are women of reproductive age.¹

Previous studies described a high prevalence of infectious diseases in the immigrant population, both in the case of infections of cosmopolitan distribution such as infection with HIV or hepatitis B virus (HBV) and infections with a geographical distribution, such as Chagas disease or malaria.^{2–5} The female immigrant population, especially the group of women of childbearing age, is especially vulnerable to these infections because of their possible consequences during pregnancy, such as prematurity, low birth weight, and even mortality in some cases, as well as the possibility of transmission to the fetus.

For these reasons, a program of systematic screening of both cosmopolitan and geographical infectious diseases was carried out in all the immigrant patients who visited the former Tropical Medicine Unit of the Central University Hospital of Asturias. The objective of this work was to describe the results of this screening program with respect to the female population, with special emphasis on women of childbearing age.

MATERIALS AND METHODS

A prospective screening program of infectious diseases in all female patients attending the Tropical Medicine Unit of the Central University Hospital of Asturias was performed between January 2009 and December 2017. Immigrants were defined as those patients born outside Spain who had come with the intention of settling permanently, regardless of their legal status. Patients who had temporarily returned to their places of origin, belonged to a European country, or who had not completed the protocol at the time of the end of the study were excluded.

In all patients, an epidemiological questionnaire including variables such as age, area and country of origin, and time spent in Spain before attending the Tropical Medicine Unit was carried out. Patients were classified according to their age into four groups: younger than 16 years, 16–45 years, 46–65 years, and older than 65 years. According to their origin, they were classified into seven geographical areas: Central Africa, East Africa, West Africa, North Africa, Mexico and Central America, South America, South Asia, and the Middle East.

In all patients, regardless of the presence or absence of symptoms, a screening protocol was performed that included a complete blood count and a biochemistry study; serological analysis for HIV infection, HBV, and hepatitis C virus (HCV); *Treponema pallidum* and *Strongyloides stercoralis*; screening for intestinal parasites; and chest X-ray and tuberculin skin testing (TST), with an intradermal injection of five international units of purified protein derivative test. HBsAg, anti-HBc, and anti-HBs were initially used for screening of HBV infection. In the case of HBsAg positivity, HBeAg and anti-HBe and the anti-HBc core IgM were also determined. All tests were performed by chemiluminescence (ARCHITECT, Abbott Diagnostic, Madrid, Spain). HIV-positive results were confirmed by the Western blot

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(BioRad, Madrid, Spain). In the case of hepatitis C, a strip immunoblot was used (INNO-LIA HVC Score[®], Innogenetics N.V., Ghent, Belgium). For screening of syphilis, a rapid plasma reagin (RPR) test (Reditest, Biokit) and ELISA G+M were performed (ARCHITECT, Abbott Diagnostic).

Three stool samples per patient, previously concentrated using the Copropack Extraction Kit C100 (Cromakit, Granada, Spain) according to the manufacturer's instructions, were stained with Lugol's solution and screened with a light microscope at low magnification. Diagnosis of malaria was made through microscopic examination of thick and thin blood smears, as well as by genomic detection using a semi-nested multiplex polymerase chain reaction (PCR).⁶

In sub-Saharan patients, qualitative detection of IgG antibodies against *S. stercoralis* and *Schistosoma* spp. was performed using an ELISA (DRG Diagnostics[®]) with micro-wells coated with *Strongyloides* antigen. Furthermore, a blood sample was taken for the detection of microfilaremia. The diagnosis of filariasis was made through observation of the parasite after a concentration technique with 2% formalin (Knott technique). The species identification was performed by Giemsa staining.

All patients from Central and South America were tested for Chagas disease. The ID-Chagas antibody test (particle gel immunoassay [PaGIA], DiaMed, Cressier, Switzerland) was used as a screening assay. All positive samples were sent to the National Microbiology Centre (Instituto Carlos III, Madrid, Spain) to confirm the result by determining anti-*Trypanosoma cruzi* antibodies by indirect immunofluorescent antibody test and by PCR.⁷

Definitions. The patient was considered to have active hepatitis B if HbsAg was positive, whereas a persistent carrier state was defined as the persistence of HbsAg in serum for more than six months. Past hepatitis was confirmed if anti-HBsAg or anti-HBc were positive. HIV or HCV infection was recognized in patients with positive western blot tests. Patients were considered to have syphilis if both RPR and syphilis G+M tests were positive. Syphilis was classified as latent in cases where only the syphilis G+M test was positive. The RPR test was considered to be positive when the titer was superior to 1/1.

Active tuberculosis was defined by a positive PCR test or Lowenstein culture from any sample. Latent tuberculosis was diagnosed when the TST caused an induration of more than 5 mm and the patient had a normal chest radiograph.

Malaria was diagnosed if asexual forms of the parasite were identified in peripheral blood in thin/thick films and/or the PCR test was positive.

Strongyloidiasis and schistosomiasis infections were considered to be established if microscopic visualization and/or the ELISA was positive. Patients were confirmed as having filariasis if the microscopic examination was positive.

Diagnosis of Chagas disease required positive serological tests with two different techniques.

Statistical analysis. The categorical variables were described by absolute and relative frequencies. Continuous variables were described as mean and SD. The qualitative variables were compared using Fisher's exact test or exact χ^2 -test, when necessary. Student's *t*-test, Welch's *t*-test, or the Mann-Whitney U test was used to compare quantitative variables. Significance was designated at $P < 0.05$. A binary logistic regression analysis using a stepwise method (Wald)

was applied to describe the diseases associated with each age-group.

Ethics statement. This study is a part of an overall project entitled "Study of prevalence of imported diseases in an immigrant population," which was approved by the Ethical Committee of Clinical Investigation of Asturias.

RESULTS

Six hundred eleven patients were studied, with an average age of $36 \pm (12)$ years. Three per cent were younger than 16 years, 62% were aged 16–45 years, 22.3% were from 46 to 65 years, and 2 were older than 65 years. The average time in Spain was $1,646 \pm (2,409)$ days. The areas of origin were Central Africa (44.5%), South America (37.6%), West Africa (8.2%), North Africa (3.4%), Mexico and Central America (3.3%), East Africa (1.5%), South Asia (1%), and the Middle East (0.5%). The characteristics of patients are summarized in Table 1. Twelve patients were pregnant at the time of consultation.

Among the cosmopolitan infections, the most frequently diagnosed were syphilis (14.6%) and HIV infection (9%), followed by chronic infection with hepatitis C (5%) and hepatitis B (3.3%) viruses. The analysis of distribution by age-groups is shown in Table 2. Although no women younger than 16 years were infected by HIV and most of the cases (78%) were diagnosed in those aged between 16 and 45 years, no significant differences were found between the groups. A similar result was observed in chronic HBV infection, where 85% of cases were diagnosed in women aged between 16 and 45 years, however without statistical significance ($P = 0.159$). In the case of hepatitis C, the disease appeared mostly in patients aged between 46 and 65 years (50%, 15/114 versus 15/418; $P = 0.001$; OR: 3.667 [1.741–7.724]) or older than 65 years (6/5 versus 24/527; $P = 0.0001$; OR: 26.350 [7.509–92.463]). Although syphilis was also diagnosed more frequently in patients aged between 16 and 45 years and in those older than 46 years (47% and 48% of the cases, respectively), statistical significance was only found in the older group (43/84 versus 46/384; $P = 0.0001$; OR: 4.273 [2.649–6.893]). Multivariate analysis confirmed a greater presence of HCV infection ($P = 0.049$) and syphilis ($P = 0.0001$) in patients aged between 46 and 65 years. Thirty-seven patients had latent tuberculosis, and nine had tuberculosis (six cases with lung involvement, two pleural cases, and one with lymph node involvement). The majority of patients with latent tuberculosis (56.7%) were in the 16- to 45-year group, however without significant differences ($P = 0.057$). Six of the tuberculosis cases also belonged to this age-group.

The most frequent imported diseases were intestinal parasitoses, which affected 39.4% of the patients. Of these, 101 patients had strongyloidiasis, 91 intestinal amoebiasis, 32 *Trichuris trichiura*, 22 *Blastocystis* spp., 19 *Giardia intestinalis*, and 9 *Ascaris lumbricoides*. No differences were found between the groups with respect to the appearance of intestinal parasitosis, except in the case of *A. lumbricoides*, which was more frequent in patients older than 65 years (3/9 versus 6/530; $P = 0.001$; OR: 29.444 [6.347–136.598]), and also in that of *T. trichiura* infection (3/9 versus 29/508; $P = 0.028$; OR: 5.839 [1.500–22.731]) but was not confirmed in the multivariable.

Of the 42 patients diagnosed with malaria (38 of them from sub-Saharan Africa), only 16 were detected by microscopic

TABLE 1
Characteristics of patients

Characteristic	Patients (n = 611)
Demographic characteristics	
Age-group (years), n (%)	36 ± (12)
≤ 15	18 (3)
16–45	444 (72.7)
46–65	136 (22.3)
≥ 65	13 (2)
Average time in Spain (days)	1,646 ± (2,409)
Areas of origin, n (%)	
Central Africa	272 (44.5)
West Africa	50 (8.2)
South America	230 (37.6)
North Africa	21 (3.4)
East Africa	9 (1.5)
Mexico and Central America	20 (3.3)
South Asia	6 (1)
Middle East	3 (0.5)
Most frequent countries of origin, n (%)	
Equatorial Guinea	267 (43.7)
Ecuador	77 (12.6)
Bolivia	42 (7)
Brazil	35 (5.7)
Colombia	28 (4.6)
Senegal	25 (4)
Nigeria	22 (3.6)
Paraguay	18 (2.9)
Venezuela	17 (2.8)
Reasons for consultation, n (%)	
Screening	268 (43.8)
Abdominal pain	89 (14.6)
Diarrhea	29 (4.7)
Fever	60 (9.8)
Skin diseases	49 (8)
Eosinophilia	157 (25.7)
Others	83 (13.5)
Cosmopolitan diseases, n (%)	
HIV infection	55 (9)
Chronic B hepatitis	20 (3.3)
Hepatitis C	30 (5)
Syphilis	89 (14.6)
Tuberculosis	9 (1.5)
HTLV	4 (0.7)
Geographical diseases, n (%)	
Filariasis*	36 (13.8)
Schistosomiasis*	44 (17)
Malaria	42 (7)
Chagas†	31 (12.4)
Intestinal parasitosis	241 (39.4)
Strongyloidiasis	101 (16.5)
Asymptomatic	293 (48)
Diagnostic, n (%)	
No parasite diseases	147 (24)
No diseases	94 (15.4)

* Percentage only in sub-Saharan patients.

† Percentage only in patients from Central and South America.

examination. Of the remainder, 16 were diagnosed by both antigen and genome detection, and only 10 by genome detection alone. Sixteen patients were asymptomatic. The most frequent type of plasmodium (81.8%) was *P. falciparum*. Although 64.2% of infections appeared in women aged between 16 and 45 years, there were no significant differences between the different groups. Eighty percent of the infections diagnosed only by genome detection also corresponded to this group, but again without statistical significance.

In the case of sub-Saharan patients, 44 patients presented with schistosomiasis and 36 with filariasis (58.3% of them with *Mansonella perstans*, and the rest with *Loa loa*). The presence of filariasis was significantly higher in patients aged between

46 and 65 years (9/51 versus 12/228; $P = 0.011$; OR: 3.353 [1.342–8.380]), but multivariate analysis did not confirm this relationship ($P = 0.854$).

Chagas disease was diagnosed in 31 patients. Although Chagas disease was more frequent in patients aged between 16 and 45 years, the distribution by groups did not achieve statistical significance.

One hundred fifty-seven patients (25.7%) had eosinophilia: this being the only symptom in 42 of them. Eosinophilia was significantly more frequent in patients with filariasis caused by *M. perstans* ($P = 0.013$; OR: 3.133 [1.274–7.704]) and *Loa loa* ($P = 0.001$; OR: 13.177 [3.569–48.656]) or in those with helminthiasis caused by *T. trichiura* ($P = 0.001$; OR: 3.679 [1.777–7.168]), hookworm ($P = 0.003$; OR: 5.333 [1.812–15.697]), and *S. stercoralis* ($P = 0.0001$; OR: 4.277 [2.723–6.719]).

Two hundred ninety-three patients (48%) reported being asymptomatic at the time of diagnosis, although only 78 of these showed no pathology on screening. A positive result on screening was significantly more frequent in the patients who reported symptoms (297/16 versus 215/78; $P = 0.0001$; OR: 6.73 [3.82–11.85]). Most patients were infected by a single parasite (215 cases), but there were also multiple infections: by two parasites (71 cases), three (11 cases), and four or more (11 cases). Only 24% of the patients did not present parasitic diseases, without differences between the groups and only in 15.4% did the screening not find any type of pathology. The absence of symptoms was more frequent in children younger than 16 years (14/3 versus 253/298; $P = 0.003$; OR: 5.497 [1.562–19.432]), as was also true for the absence of pathology (7/11 versus 87/495; $P = 0.014$; OR: 3.261 [1.366–9.596]), but the multivariate analysis only confirmed the relationship with the absence of symptoms ($P = 0.030$).

DISCUSSION

The appearance of diseases imported by the immigrant population is a common and growing phenomenon in European countries, to the point that the European Centre for Disease Prevention and Control (ECDC) has recently issued recommendations about the need to perform systematic screening in this population group.⁸ Several authors^{2–5} have described high prevalence of diseases of both cosmopolitan and geographical distribution in these population groups, but few refer only to the prevalence in the female population, despite the different repercussions of these pathologies in this group, especially in women of childbearing age.

About 15% of our patients had late latent syphilis, diagnosed more frequently in patients aged between 16 and 45 years. Immigrant women are a group especially vulnerable to STIs because they frequently suffer sexual violence, including rape; so screening in this population group is especially important. In Spain, testing for syphilis is part of the systematic screening performed during pregnancy, but, nonetheless, given the high prevalence in immigrant women of childbearing age, early screening and prompt treatment before pregnancy could be a cost-effective maneuver. According to data from the Ministry of Health in Spain, 36% of new HIV diagnoses were made on immigrants, especially of Latin American origin. In the case of women, this percentage increases to 57.3%, with a greater frequency in women aged between 20 and 40 years, as in our results.⁹ Screening for HIV infection is recommended almost universally in immigrant populations.

TABLE 2
Characteristics by age-group

Characteristic	Patients younger than 15 years	16–45 years	46–65 years	Older than 65 years
	N = 18	N = 444	N = 136	N = 13
Areas of origin, n (%)				
Central Africa	9 (50)	194 (43.6)	60 (44)	9 (69.2)
West Africa	1 (5.5)	47 (10.5)	2 (1.4)	0 (0)
South America	7 (38.8)	166 (37.3)	55 (40.4)	2 (15.3)
North Africa	0 (0)	10 (2.2)	11 (8)	0 (0)
East Africa	1 (5.5)	8 (1.8)	0 (0)	0 (0)
Central America	0 (0)	11 (2.47)	7 (5)	2 (15.3)
South Asia	0 (0)	5 (1)	1 (0.7)	0 (0)
Middle East	0 (0)	3 (0.6)	0 (0)	0 (0)
Cosmopolitan diseases, n (%)				
HIV infection	0 (0)	43 (9.6)	11 (8)	1 (7.6)
Chronic B hepatitis	0 (0)	17 (3.8)	3 (2.2)	0 (0)
Hepatitis C	0 (0)	9 (2)	15 (11)	6 (46)
Syphilis	0 (0)	42 (9.4)	43 (31.6)	4 (30.7)
Tuberculosis	0 (0)	4 (0.9)	4 (3)	1 (7.6)
HTLV	0 (0)	3 (0.6)	1 (0.7)	0 (0)
Latent TB	0 (0)	21 (4.72)	16 (11.7)	0 (0)
Geographical diseases, n (%)				
Filariasis	1 (5.5)	16 (3.6)	17 (12.5)	3 (23.7)
Schistosomiasis	3 (16.6)	32 (7.2)	9 (6.6)	0 (0)
Malaria	1 (5.5)	27 (6)	12 (8.8)	2 (15.3)
Chagas	0 (0)	19 (4)	11 (8)	1 (7.6)
Intestinal parasitosis	9 (50)	172 (38.7)	54 (39.7)	6 (46)
Strongyloidiasis	6 (33.3)	72 (16.2)	21 (15.4)	2 (15.3)
Asymptomatic	15 (83.3)	218 (49)	58 (42.6)	2 (15.3)
Diagnostic, n (%)				
No parasite diseases	7 (38.8)	103 (23)	33 (24.2)	4 (30.7)
No diseases	7 (38.8)	71 (16)	16 (11.7)	0 (0)

However, in the case of the female population, this screening should be especially proactive, because of the presence of associated factors of social vulnerability, such as commercial sex work, and the risk of vertical transmission in pregnancies with no medical supervision.^{10,11}

Chronic hepatitis B and/or C virus infections are associated with significant morbidity and mortality in the form of chronic hepatitis or liver neoplasm. In the case of hepatitis B, vertical transmission favors the development of chronic hepatitis of worse prognosis in those children infected at the time of birth. Several studies have shown that screening for hepatitis B is cost-effective in an immigrant population, including pregnant women, because it allows early diagnosis and treatment and slows down vertical transmission.^{12–17} The ECDC recommends the screening of immigrants from high prevalence areas but includes pregnant women as a priority group, regardless of the prevalence.⁸ However, given the high prevalence in women of childbearing age, the implementation of active screening measures for hepatitis B should be considered, to enable early diagnosis and treatment before the beginning of pregnancy.

Regarding hepatitis C, previous studies have shown that the screening of pregnant women is cost-effective, especially if it is subsequently accompanied by treatment. In our results, up to half of the infections appeared in patients of childbearing age, which supports the special importance of screening this population group.^{18–22} The best approach is screening for hepatitis B virus, hepatitis C virus, and HIV infections at the same time.

Only 7% of the patients had had malaria: most of these cases being diagnosed in women of childbearing age and frequently by submicroscopic methods. Malaria during pregnancy has been associated with fetal loss and low birth weight, and the possibility of congenital transmission arising

from these paucisymptomatic forms cannot be completely discounted. Malaria is unlike other imported diseases in that the need for systematic screening of the immigrant population has not been established. The results of this research indicate that the prevalence of malaria in women of childbearing age of sub-Saharan origin is far from negligible, especially that of cases involving submicroscopic diagnosis, and, therefore, the need for screening of this group, even with molecular biological techniques, should be reconsidered.^{23,24}

Positive serological tests for schistosomiasis were seen in 17% of the patients, with no differences in prevalence between the age-groups. Schistosomiasis is of especial importance in both women of childbearing age and in those who are pregnant and has serious consequences for children infected during pregnancy. Infection by *S. haematobium* leads to damage to the genital tract in 75% of infected women, and 20 million individuals are estimated to be infected at the present time. In the long term, these lesions lead to infertility, problems at childbirth, and may favor the transmission of HIV infection.^{25,26} Until 2002, the WHO excluded women of reproductive age from their mass treatment campaigns, which may explain the high prevalence of antibodies in this age-group and in the following one. Recently, the WHO recommended treatment with praziquantel even in pregnant and lactating mothers, although its safety in pregnancy is not altogether guaranteed and many authors reject such a policy. It is therefore fundamentally important to screen and provide early treatment, not only in pregnant women but also in those of childbearing age to avoid long-term morbidity and the consequences for the fetus of both the disease and its treatment.

Of all the imported diseases, Chagas disease is that which generates the widest consensus about the necessity for

screening in the female population.²⁷ The possibility of vertical transmission and the efficacy of the treatments available for children have made screening a highly effective strategy. However, because neither benznidazole nor nifurtimox can be used during pregnancy, some authors have advocated the need for early screening in women of reproductive age to permit diagnosis and treatment before pregnancy.

In conclusion, the data from this study show a high prevalence of imported diseases in the female immigrant population: diseases which may have serious consequences in terms of morbimortality and vertical transmission. The establishment of policies of active screening both in women of childbearing age and within the specific pregnancy screening programs would reduce the morbimortality of such diseases in this population group.

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