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Migration and health: A retrospective study about the prevalence of HBV, HIV, HCV, tuberculosis and syphilis infections amongst newly arrived migrants screened at the Infectious Diseases Unit of Modena, Italy

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ABSTRACT

Introduction: Aim of the study is to evaluate the prevalence of HBV, HIV, HCV, tuberculosis and syphilis infection among immigrants assigned to the immigrant centre of the province of Modena.
Methods: At the time of arrival all immigrant were tested for: HBsAg, HBsAb, HBcAb, Ag p24/HIVAb, HCVAb, RPR, TPPA, Mantoux test (>10 mm diameter of induration was considered to be positive), Chest X-rays. In case of positive samples, second level tests were performed (HbeAg, HBeAb, HDVAb, and baseline management and treatment of the infection detected).
Results: A total of 304 immigrant people were enrolled in the study. HBsAg positivity was 12.2%, HCVAb 3.3%, HIVAb 1.6%, TPPA + RPR positivity in the 0.7%; 10.2% had a positive Mantoux test; 5.6% had Chest X-rays positive for signs of infection and 6 patients had an active tuberculosis. 83.8% HBsAg were HBeAb positive/HBeAg negative. HDVAb resulted positive in 1 patient (2.7%). Previous HBV infection was detected in 28.6% of cases, isolated HBcAb in 2.3%; 5.6% of patients resulted to be positive to HbsAb alone (probable vaccinated).
Conclusion: Our study confirms the high prevalence of HBsAg positivity and latent tuberculosis among immigrants, underlying the importance of screening for infections in this special population.

Introduction

Migration is nowadays a new global phenomenon, with a total of 244 million of international migrants, according to the UNDESA (United Nations Department of Economic and Social Affairs) data of the year 2015 [1]; 58% of them lived in developed countries. From 1990 to 2015 an increase of more than 60% in the total number of migrants was observed. Europe and Asia combined hosted nearly two-thirds of all international migrants worldwide in 2015. Migration should be recognized as a social determinant of health; mobility not only impacts upon an individual's physical vulnerability, but also on mental and social well-being [2]. According to the data for the year 2016, the number of immigrants in Italy was estimated to be around 6 million; data from Italian Ministry of Internal Affair reveal the presence of more than 174.000 new immigrant people residing in the reception centres spread through the national territory. European migrant crisis is a term given to identify the phenomenon in which rising numbers of people have been arriving in the European Union (EU), traveling across the Mediterranean Sea or overland through Southeast Europe. These people included asylum seekers, but also others, such as economic migrants. An asylum seeker is defined as a person fleeing persecution or conflict, and therefore seeking international protection under the 1951 Refugee Convention on the Status of Refugees; a refugee is an asylum seeker whose claim has been approved. However, the United Nations considers migrants fleeing war or persecution to be refugees, even before they officially receive asylum [3]. An economic migrant, by contrast, is a person whose primary motivation for leaving his or her home country is economic gain. Europe is currently witnessing a mixed-migration phenomenon, in which economic migrants and asylum seekers travel together. Con-

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Table 1
Characteristics of the immigrant population.

Characteristics	No (total = 304) — median (quantitative v.)	% (categorical) — range (quantitative)	95% CI
Age	21	16-44	
Gender (male)	285	93.8	
Nationality	78	25.7	
• Nigeria	71	23.4	
• Gambia	41	13.5	
• Mali	41	13.5	
• Pakistan	30	9.9	
• Ivory Coast	27	8.9	
• Senegal	16	5.1	
• Others			
Time from arrival in Italy (days)	74	15-213	
$HBsAg^+$	37	12.2	0.08–0.16
HBc Ab (isolated)	7	2.3	0.01–0.04
HBcAb/HBsAb (previous infection)	87	28.6	0.23–0.33
HBsAb (vaccinated)	17	5.6	0.03–0.08
$HCVAb^+$	10	3.3	0.01–0.05
$HIVAb^+$	5	1.6	0.00–0.03
$TPPA + RPR^+$	2	0.7	0.00–0.02
Mantoux (>10 mm)	31	10.2	0.07–0.14
Chest X-Rays (signs of infection)	17	5.6	0.03–0.08

sidering the very large number of migrants, a determination of the health status of the people at the arrival in the host countries is crucial, especially for transmittable infectious diseases. The prevalence of HIV infection according to the World Health Organization (WHO) data of 2015 is estimated to be 0.8% of adults aged 15–49 years worldwide. The burden of the epidemic varies considerably between countries. Sub-Saharan Africa remains the most affected region, with a prevalence of HIV infection of 4.4% and accounting for nearly 70% of the people living with HIV worldwide [4]. Hepatitis B infection is worldwide spread with about 240 million people infected (defined as Hepatitis B Surface antigen, HbsAg, positive), with a different geographical distribution; hepatitis B prevalence is highest in sub-Saharan Africa and East Asia, where between 5–10% of the adult population is chronically infected. In the Middle East and the Indian subcontinent, an estimated 2–5% of the general population is chronically infected. Less than 1% of the population of Western Europe and North America is chronically infected. Italy is a country with a low level of HBV prevalence, characterized by a global percentage of chronic carriers about 1.5% [5]. Hepatitis C sero-prevalence worldwide is estimated to be about 2.2%, with higher distribution among North African and east Asian countries [6]. In Italy the prevalence of HCV-positive (viremic or not) people is approximately 3% and almost 60% of them are older than 65 years [7]. The epidemiology of tuberculosis (TB) infection is closely connected to the social and economic condition of different countries, these related to diversified strategies of TB prevention. The global burden of TB is estimated to be 9.6 million new incident cases and 1.5 million deaths occurred in 2014 [8]; the large part of cases is localized in Asia and Africa. Migrants usually represent the mainly reservoir of TB in the developed countries with low prevalence rate of infection [9]. Syphilis continues to be a burden on the public health system, with the highest prevalence among men who have sex with men (MSM) and HIV positive people, but an increase also in sexually active women was observed [10]. The prevalence of different infections among migrant population usually reflects the one in the origin country, and it seems not to modify significantly the burden of each specific transmittable infectious disease in the host countries [11–13]. Aim of our study is to describe our screening of transmittable infectious diseases strategy among immigrant population, to analyse the prevalence HBV, HIV, HCV, tuberculosis and syphilis infection, in order to define the burden of certain infectious diseases in the province of Modena, during an observation period of nine months.

Methods

We conducted a cross-sectional descriptive study about the prevalence of different infectious diseases in all the immigrant population afferent to our centre from March 1st 2016 to December 31st 2016. Refugees, asylum seekers and economic migrants who arrived in Italy mainly through the flows in the Mediterranean Sea in accordance with Italian laws were filed at the point of arrival and then sent to various regional centers according to availability. At the arrival in the migration center of the province of Modena, all the immigrant people were referred to our clinic of Infectious Diseases in Modena in order to execute a primary screening of transmittable infection; all the subjects underwent to these exams: qualitative HBsAg, quantitative HbsAb, qualitative HBcAb (Abbott ARCHITET *i*1000*SR*®), Ag p24/HIVAb (Abbott ARCHITET *i*1000*SR*®), qualitative HCVAb (MUREX antiHCV version 4.0 DiaSorin®), RPR, TPPA (Abbott ARCHITET *i*1000*SR*®), Mantoux test, If Matoux test resulted positive, patients underwent Chest X-rays. HIV Ab positivity was confirmed by western blot assay (MP Diagnostics™ HIV BLOT 2.2). If HBsAg resulted positive, HBeAg, HbeAb, HDVAb (ETI-AB-DELTAK-2 (anti-HD) DiaSorin®) were requested. Chest X-rays suspicious of tuberculosis were considered: 1- Infiltrate or consolidation; 2- Any cavitary lesion; 3- Nodule with poorly defined margins; 4- Pleural effusion; 5- Hilar or mediastinal lymphadenopathy (bihilar lymphadenopathy); 6- Linear, interstitial disease (in children only); 7- Any other finding suggestive of active TB, such as miliary TB. Miliary findings are nodules of millet size (1–2 mm) distributed throughout the parenchyma [11]. The tuberculin test is based on the fact that infection with M. tuberculosis produces a delayed-type hypersensitivity reaction to certain antigenic components of the organism that are contained in extracts of culture filtrates called “tuberculins.” A standard dose of five tuberculin units (TU purified protein derivative, PPD, 0.1 ml) was injected intradermal (into the skin) in all the patients and read 48 to 72 h later). A diameter of induration at Mantoux test >10 mm was considered to be positive [12]. All the subjects underwent to a medical examination after the bloods exams; the patients that resulted positive to one or more on the infections screened were referred to specialist physicians in order to begin the management of the disease. All subjects who were sent to the Modena immigration centre during the study’s observation period were included in the analysis. All patients were given a questionnaire to collect demographic data. Patients expressed informed consent and the study was approved by the local ethics committee (Comitato

Table 2
Different distribution of infections according to Nationality.

Infection	Nationality [numer(%among the Country)]							P
	Nigeria	Gambia	Mali	Pakistan	Ivory Coast	Senegal	Others	
HBsAg+	8(10.3%)	11(15.5%)	11(25%)	0(0%)	3(10%)	3(11.1%)	1(7.7%)	0.031
HCVAb+	5(6.4%)	1(1.4%)	0(0%)	0(0%)	2(6.7%)	1(3.7%)	1(7.7%)	0.242
HIVAb+	1(1.3%)	0(0%)	0(0%)	0(0%)	4(13.3%)	0(0%)	0(0%)	**<0.001**
TPPA + RPR+	0(0%)	(0%)	0(0%)	0(0%)	0(0%)	0(0%)	2(15.4%)	**<0.001**
Mantoux (>10 mm)	4(5.1%)	10(14.1%)	6(13.6%)	9(22%)	1(3.7%)	1(3.7%)	1(7.7%)	**0.021**

The values in bold highlight the P < 0.05 and therefore statistically significant to the univariate analysis.

Etico Provinciale di Modena, protocol number 310/16). The ideal sample size considering a number of landings of immigrants in Italy during the observation period of about 150000 people, with a confidence interval of 95% and a margin of error of 5% would be 384 people. A sample size of 304 expresses a margin of error of 5.64% (according to the Survey System sample size calculator, https://www.surveysystem.com/sscalc.htm). Statistical analysis was made by the use of median and interquartile range (IQR) to summarize continuous variables and frequency for categorical variables. In univariate analysis between different groups, categorical variables were compared using the Chi-square test. A P-value less than 0.05 was considered to be statistically significant. All the statistical data were collected using IBM SPSS version 22.

Results

From March 1st to December 31st 2016 a total of 304 migrants were addressed to our clinic from the migration center of the province Modena in order to execute the first line screening of the infectious diseases. The study's target population was predominantly economic migrants (70%). The remaining part was of asylum seekers. No one had yet obtained refugee status at the time of the observation. General characteristics of the study population are reported in Table 1. Migrants were mostly male (285/304, 93.8%), median age was 21 years (range 16–44). People in the study came from: Nigeria in 25.7% of cases (78), Gambia in 23.4% (71), Mali and Pakistan in 13.5%, respectively (41), Ivory Coast in 9.9% (30), Senegal in 8.9% (27); other countries were represented in 5.1% (14) of cases. The median time from arrival in Italy was 74 days (range 15–213). HBsAg positivity was found in 37 patients (12.2%; CI 95% 0.08–0.16); 7 patients showed HbcAb isolated positivity (2.3%; CI 95% 0.01–0.04), other serological markers of HBV were negative. 87subjects (28.6%) had both HbcAb and HBsAb as a previous HBV infection, with HBsAg negative (28.6%; CI 95% 0.23–0.33), 17 patients (5.6%; CI 95% 0.03–0.08) were only HbsAb positive, probably due to previous vaccination, in absence of card of vaccinations. Other infections found were: HCVAb positivity in 10 cases (3.3%; CI 95% 0.01–0.05), Ag p24/HIVAb positivity in 5 cases (1.6%; CI 95% 0.00–0.03), TPPA positivity in 2 cases (0.7%; CI 95% 0.00–0.02). Regarding Tuberculosis 31 patients (10.2%; CI 95% 0.07–0.14) resulted to be positive at Mantoux test, 95%, 12 of them had chest X-rays compatible with signs of infection (5.6%; CI 95% 0.03–0.08) and finally 4 cases of active tuberculosis (2.1%, Fig. 1). Table 2 summarizes the different infections distribution in relation to the country of origin. There were no significant differences in the distribution of HCVAb. The distribution of HBsAg varied significantly between different nationalities (P = 0.031) with a higher prevalence in migrants from Mali. HIVAb showed significant differences in geographical distribution (P < 0.001); in fact, of the 5 cases found, 4 were from Ivory Coast and 1 from Nigeria. The 2 cases of RPR+/TPPA+ both came from less represented countries (P < 0.001). The geographical distribution of mantoux+ showed significant differences (P = 0.021), with a higher prevalence in Pakistani migrants. In Table 3 were summarized the characteristics of HBsAg positive patients: they were mostly male (34/37, 91.9%), median age was 20 (range 17–39). Countries of origin were: Mali and Gambia in 11 cases, respectively (29.7%), Nigeria in 8 (21.6%), Senegal and Ivory Coast in 3 cases, respectively (8.1%), Togo in one case (2.7%). Among HBsAg positive patients 6 cases (16,2%) were HBeAg positive, while the other 31 (83.8%) HBsAg positive patients resulted HBeAg negative and HBeAb positive. Regarding co-infections, HDVAb was found in 1 patient (2.7%), HCVAb in 3 (8.1%), and HIV Ab in 1 patient (2.7%).

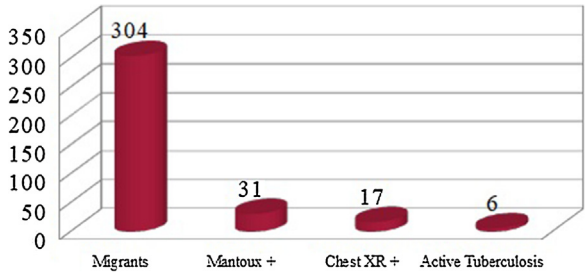

Fig. 1. Determination of tuberculosis infection.

Table 3
Characteristics of HBsAg positive patients.

HBsAg + Patients	N° (total = 37) — Median (quantitative v.)	% (categorical) — range (quantitative)
Age	20	17–39
Gender (male)	34	91.9
Nationality		
• Mali	11	29.7
• Gambia	11	29.7
• Nigeria	8	21.6
• Senegal	3	8.1
• Ivory Coast	3	8.1
• Togo	1	2.7
Time from arrival in Italy (days)	74	15–198
HBeAg	6	16.2
HBeAb	31	83.8
HDVAb	1	2.7
HCVAb	3	8.1
HIVAb	1	2.7

HBcAB: total hepatitis B core antibody; HBsAg; hepatitis B surface antigen; HbsAb: hepatitis B surface antibodies. HbeAg: hepatitis B e antigen: HbeAb: hepatitis B e antibodies; HCVAb: hepatitis C virus antibodies; HIV: human immunodeficiency virus Antibodies; RPR: Rapid Plasma Reagin test; TPPA: Treponema pallidum particle agglutination test.

Discussion

Infectious diseases represent an aspect of migration phenomenon that could change the pre-existing disease scenario of the host countries [2]. Migrants, especially coming from African regions, carry higher prevalence rates of HBV and HCV than European countries [14]. In our study the prevalence of HBV is consistently higher than the one observed in Italy, reflecting the HBV

distribution data on the countries of origin; this is supported also by the high percentage of people with HBV serology compatible with previous infection that we found. Therefore, migrants coming from countries with moderate-high prevalence of HBV and living in low prevalence nations are an important risk group; a systematic meta-analysis about the prevalence of HBV infection concludes that migrant could benefit from screening of HBV infection [15]. The results of our work on the prevalence of HBsAg can be compared to a recent Italian study with a larger number of cases than our own [16]. The vaccination coverage for HBV was very low in our study among the migrant population. This was exclusively deduced from the presence of HBsAb alone in the absence of the patient's vaccination card. The low vaccination coverage reflects the lack of effective vaccination campaigns in the countries of origin [17]. It is also very difficult to vaccinate the migrant population in relation to the frequent movements and the need for multiple doses [18].

HCV infection in migrants has a higher prevalence than the European host countries. A recent meta-analysis shows a quite variable rate of HCV sero-prevalence, the highest in Sub-Saharan Africa, Asia, and Eastern Europe, suggesting in conclusion the utility of HCVAb screening among migrants [19]. Our data reflect the HCV sero-prevalences of the origin countries, that are classified as moderate-high ones. Our data on the prevalence of HCV in the migrant population seems to reflect other previous studies in the same context (4.8% prevalence of HCVAb in Coppola et al.) [20]. HIV infection results to be endemic in many African regions: in our study the prevalence of HIV infection is similar to the one of the male population of many African nations [21]. The majority of the diagnosis of HIV infection among migrants are made in the host countries, but it is supposed the infection is home acquired, even if new post-migration HIV infection is possible, especially in some categories, like MSM [22]. Our study has not evaluated HCV-RNA. Our data overall underline the importance of screening among migrants, especially for HCV, HBV, HIV. Active screening campaigns among migrants have achieved appreciable results in similar contexts [23]. Our data show that tuberculosis can be a problem for the countries of arrival, both in terms of the spread of the disease and in terms of changing the local epidemiology. This figure is also closely related to the local epidemyology of the country of arrival of the migrants and to the extent of the migratory flow. In fact, a recent review has shown that in the European Union, migration flows do not seem to change the rates of incidence and prevalence of tuberculosis [24]. Migrants often present a sub-optimal state of health: this, associated with the poor conditions during the travel to other countries, could represent an important risk factor for reactivation of tuberculosis [25]. This is a very important issue if we consider that in our study more than 10% of the immigrants presented a positive mantoux test, marker of a previous contact with the Mycobacterium tuberculosis. None of our cases of active tuberculosis were caused by multi drugs resistant (MDR) strains, but other series showed an increase in percentage of MDR caused tuberculosis among migrants [26,27]. Syphilis infection and migration phenomenon is a not well characterized issue; in our study a low prevalence was observed. In an American cohort of refugees syphilis resulted to be associated to male sex, increasing age, and living in non-refugee camp [28]. It seems syphilis still remain a disease strictly related to sexual behaviour other than country origin or migration fluxes. Various studies have been carried out in Italy on the prevalence of infectious diseases among migrants, but not many consider hepatitis, HIV tuberculosis and syphilis at the same time [29,30]. This study has some limitations, mainly represented by the small sample of patients and the heterogeneity regarding the type of migrant. All patients who arrived at the immigration center of Modena were screened, so there is no potential refusal rate.

In conclusion, our study confirms that the prevalence rates of the infectious diseases analysed reflect those of the country of origin. Hepatitis B, and especially latent and active tuberculosis, can be a public health problem for the host nations by changing the local epidemiology. Our data underlines the importance of universal screening for infectious diseases for all newly arrived migrants, be they asylum seekers or economic migrants. With this in mind, it would be important for developed nations to adopt standardized protocols for the health of migrants.

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Competing interests

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