

Prevalence of latent tuberculosis, syphilis, hepatitis B and C among asylum seekers in Malta

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ABSTRACT

Background In the last few years, Malta has witnessed increasing immigration flows from the Libyan coasts. Public health policies are focused on screening migrants for tuberculosis, whereas no systematic actions against STIs are implemented. The aim of this study is to define the epidemiological profile of asylum seekers in Malta as regards syphilis, hepatitis B, C and latent tuberculosis, thus supporting screening policies.

Methods Five hundred migrants living in open centres were screened between December 2010 and June 2011.

Results 83.2% of people was from Somalia, 81.2% males, average age 26.5 years. The tuberculin skin test (TST) was positive in 225 migrants (45%). Latent syphilis was diagnosed in 11 migrants, hepatitis C in 3 and 31 migrants were HBsAg positive.

Conclusion Systematic screening for asymptomatic migrants in Malta is not recommended for hepatitis C and syphilis, given the low prevalence observed. On the contrary, it should be considered for hepatitis B. TST could be indicated as the first step of a two step screening for migrants from countries with high TB incidence. Efficacy and cost-effectiveness could be achieved by further targeting screening to specific subgroups at higher risk of reactivation, such as people living with HIV and subjects affected by chronic diseases.

Keywords hepatitis, migrants, Malta, sexually transmitted infections, tuberculosis

Background

Inward migration to Southern European countries has increased over the past years. Malta, situated in the middle of the Mediterranean Sea, is constantly interested by massive influxes of immigrants who leave poor African countries to escape from social conflict, civil and political unrest and to seek asylum in Europe.¹ Malta has a total area of 316 km² and about 404 000 inhabitants, resulting as the most densely populated country in Europe. The phenomenon of ‘boat migration’ began in 2001 and increased throughout the years affecting local resources and the population. In 2010, the number of migrants in Malta was estimated around 3000 individuals, with a predominance of people from the Horn of Africa, followed by Western Africans and other nationalities. The number of migrants continuously changes due to new arrivals and departures of people who are resettled after obtaining refugee status.

In this study, the term asylum seeker refers to migrants with refugee status or humanitarian protection, and those whose application was rejected or still pending.

Malta adopts administrative detention measures: upon arrival, migrants can be detained for a maximum of 18 months. After release, they are generally accommodated in one of the 10 open centres on the main island and grouped

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by age, marital status, gender and vulnerability conditions. There are three largest open centres with a maximum capacity of 800 people where serious problems concerning living conditions, hygiene and lodging are usually reported. The migrants hosted, who include a majority of young, sexually active, single men, share a common room or tent with a maximum of 25 persons. These conditions favour the spreading of skin infections and communicable diseases.

Public health policies adopted in Detention and open centres provide radiological screening for active and latent TB only in case of pulmonary changes compatible with past untreated disease. During the first days after arrival and before release from detention, asylum seekers undergo chest X-ray. In open centres, TB identification is based on passive case finding and contact tracing. If affected by active pulmonary TB, patients are started on treatment; preventive treatment is offered to latent TB infection (LTBI)-positive subjects.

TB prevalence in Malta is low (12/100 000).² Nevertheless, migrants from countries with high TB endemicity^{3,4} are a risk group requiring targeted actions. No consensus has been reached in Europe on the public health impact of latent TB prevention in immigrants.^{5–7} Despite this, also considering that a small percentage of migrants arriving in Malta leaves the country within the following 5 years and that only some of them live in private accommodations, TB infection screening and prevention represent an important public health measure.

Contrary to the systematic approach adopted for TB, no screening activities are provided for HIV/STIs among asylum seekers. Few data are available on the incidence of STIs in Malta⁸ and the numbers actually seen are undoubtedly underestimated. STIs are rather common in Africa. Studies from the Horn of Africa, particularly Ethiopia, report a HBsAg carriage rate between 5.4 and 15% and anti-hepatitis C virus (HCV) positivity between 0.8 and 5.1% in the different groups considered.^{9,10} Therefore, the arrival of asylum seekers may influence the prevalence of STIs among the Maltese population, especially if no appropriate preventive programmes are planned.

A pilot study, aimed at assessing the prevalence of latent TB, Hepatitis B and C, syphilis and abnormal liver function in 500 asylum seekers hosted in the open centres was conducted to provide data and support the development of sound public health policies. The study was conducted in the framework of the EU project 'Mare Nostrum: Common approach to upgrade asylum facilities in Italy and Malta', implemented by the National Institute for Health, Migration and Poverty of Rome in partnership with Maltese health authorities. According to the knowledge of the authors, this is

the first large-scale study on the epidemiological profile of migrants in Malta.

Methods

Five hundred migrants hosted in Maltese Open Centres, representing about one-sixth of the migrants in the country, were recruited on a voluntary basis for 6 months from December 2010 to June 2011. Screening was performed by a team of doctors and cultural mediators in the three open centres hosting higher numbers of migrants (500–800). Under-18 people, pregnant women and migrants with past history of treated latent or active TB were excluded from the study. Screening was offered to migrants who had arrived in Malta after 2007, with the aim of targeting migrants at higher risk of TB reactivation and who would have benefited more from screening and prophylactic treatment.⁵

A standardized, pre-coded questionnaire was administered by a dermatologist and an infectious disease specialist supported by cultural mediators. A medical history focused on socio-demographic data, particularly chronic liver diseases, medications, alcohol consumption (type, quantity, duration and mean daily intake), drug use, sexual health and possible risk factors for Hepatitis B and C. Clinical examination for assessing the presence of active TB was also performed. Data were collected in a purpose-specific database; migrants were registered with a double identification code corresponding to the Identity Card (ID) number and a Police number assigned by the immigration office upon arrival. Diagnoses were recorded according to the International Classification of Diseases (ICD-9).

A written multilingual informed consent was created with the support of cultural mediators; contact details and telephone numbers were collected in a separate file.

A tuberculin skin test (TST)—intradermal injection of 2-TU of PPD RT 23 (Statens Serum Institute, Copenhagen, Denmark) on the volar aspect of the forearm—was performed during the first examination as provided by standard procedures.¹¹ Induration was measured by palpation 72 h later, and the TST was considered positive if the transverse induration diameter was at least 10 mm. In the case of HIV-positive patients or subjects with impaired immunity, the cut-off point was set at 5 mm.¹¹ TST-positive subjects were referred for chest X-ray. Asymptomatic patients with positive Mantoux test and chest X-ray abnormalities (fibrosis, mediastinal and/or hilar lymphadenopathy, signs compatible with inactive or past TB or apical fibronodular diseases) were referred to the chest clinic for assessment and interferon- γ release assays (IGRA; Quantiferon TB Gold, Cellestis, USA) in order to exclude active TB and further

investigate for LTBI.¹² Sputum of IGRA-positive migrants was observed by direct microscopy and in culture for *Mycobacterium tuberculosis*. Culture always resulted negative. IGRA-positive migrants were therefore considered as LTBI carriers and standard prophylactic treatment (INH + RIF for 3 months) was offered.

Blood samples for hepatitis, syphilis and liver chronic diseases screening were collected in the open centres and processed by a local private laboratory. All subjects were tested for Hepatitis B surface antigen- HBsAg (method: ECLIA—electrochemiluminescence immunoassay; cut-off index: <0.90 = negative; >0.90–<1.0 = borderline; >1.0 = positive), HCV total antibodies (method: ELISA, enzyme-linked immunosorbent assay; cut-off index: average negative control + 0.12, result issued positive or negative), aspartate aminotransferase—AST (method: IFCC—International Federation of Clinical Chemistry without pyridoxal phosphate; reference range: males < 38 U/l, females < 32 U/l), alanine aminotransferase—ALT (method: IFCC—International Federation of Clinical Chemistry without pyridoxal phosphate; reference range: males < 41 U/l, females < 31 U/l), VDRL—Venereal Disease Research Laboratory /RPR—rapid plasma Reagin (method: macroscopic non-treponemal flocculation test; threshold : <2 = non reactive, >2 = reactive) and TPHA—treponema pallidum haemagglutination assay (method : indirect haemagglutination; threshold: <80 = negative, >80 = positive).

Patients testing positive for one or more infections were referred for treatment, follow-up and completion of STIs screening to the Genito-Urinary Clinic at Boffa Hospital.

Table 1 Screening results in a sample of 500 migrants

Test	Negative	Positive	Total
VDRL	491 (98.2%)	9 (1.8%)	500 (100%)
TPHA	489 (97.8%)	11 (2.2%)	500 (100%)
HBsAg	469 (93.8%)	31 (6.2%)	500 (100%)
HCV Ab	497 (99.6%)	3 (0.6%)	500 (100%)
AST	450 (90%)	50 (10%)	500 (100%)
ALT	471 (94.2%)	29 (5.8%)	500 (100%)
IDR	252 (51.4%)	248 (49.6%)	500 (100%)

Latent syphilis was detected in 2.2% of migrants (VDRL negative/TPHA positive or VDRL positive/TPHA negative; 72.7% males); HCV antibodies were found in 0.6% ($n = 3$) and 6.2% ($n = 31$) resulted HBsAg positive (93.5% males; 83.8% from Somalia; 67.7% in the age group 20–30 years); 10% ($n = 50$) had increased ALT levels (average 60 U/l) and 5.8% ($n = 29$) raised AST levels (average 53.1 U/l). 49.6% ($n = 248$) were TST positive. The mean size of induration in Mantoux-positive patients at 72 h was 17.3 mm.

Patients with AST or ALT abnormalities testing negative for hepatitis were further examined and referred for confirmation.

The study was approved by the Maltese Ethic Committee.

'Mare Nostrum' project funds (ERF-European Refugees Fund) covered the costs of laboratory tests for hepatitis, syphilis and liver diseases screening; chest radiographies, PPD-S and IGRA tests were provided by the Maltese National Health Service.

Results

From December 2010 to June 2011, 500 migrants hosted in Maltese Open Centres were screened for latent TB, hepatitis B, C and syphilis. Among them, 83.2% ($n = 416$) were from Somalia, 8.2% ($n = 44$) from Eritrea, 2.4% ($n = 12$) from Ethiopia and 5.6% ($n = 28$) from West African countries. 81.2% ($n = 406$) were males and the mean age was 26.5 years.

All subjects spent an average period of 5 months and a half in a detention centre, and 9 months in an open centre. As regards their legal status, 81.4% ($n = 407$) had obtained some form of international protection, whereas 9% ($n = 45$) of applications had been rejected. Only 0.4% ($n = 2$) had been recognized as refugees and in 9.2% of cases ($n = 46$) the application was still pending. 52.8% ($n = 264$) declared to be married and to have their family and children in the origin country, 42% ($n = 210$) were single, 3% ($n = 15$) divorced and 2.2% ($n = 11$) widowed; as for religious beliefs, 92% ($n = 460$) declared to be Muslim, 7% ($n = 35$) Orthodox and 1% ($n = 5$) Catholic. Only 9.6% ($n = 48$) declared they consumed tobacco, 2.4% ($n = 12$) drugs, particularly *kebat*, and 2.4% ($n = 12$) alcohol. BCG vaccination scars were observed in 18.6% ($n = 93$) of the total sample.

According to STIs risk assessment, 96.8% ($n = 484$) of the considered subjects referred that they had less than five sexual partners in their lifetime; 1.6% ($n = 8$) persons reported that they had an STI, 10% ($n = 50$) declared that they performed a HIV test at least once in their lives and 3.2% ($n = 16$) they tested negative in the previous 6 months. 0.4% of men ($n = 2$) reported having sex with sexual workers in Malta.

Out of 94 women included in the study, 73.4% ($n = 69$) were from Somalia, 18% ($n = 17$) from Eritrea, 7.4% ($n = 7$) from Ethiopia and 1% ($n = 1$) from Nigeria; 35% ($n = 33$) were single, 53% ($n = 50$) married and 12% ($n = 11$) divorced. 96% ($n = 90$) referred they had undergone some type of Female Genital Mutilation (FGM), half of them had a type III FGM.

Screening results are reported in Table 1. Five hundred and twenty-two migrants underwent a Mantoux test; out of them, 22 (4.2%) did not attend follow-up visits and dropped out of the study. Such a low rate of drop outs can be explained with the particular setting where the study was conducted, as all participants were hosted in reception centers and tracking was easily performed.

Out of TST positive migrants, 214 (86%) underwent a chest X-ray. Lung abnormalities, including fibrosis, fibronodular changes, pleural thickness or pinching suspicious for latent or past TB, were observed in 32 patients (14.9%); they were referred to the Chest Clinic for follow-up and possible IGRA testing. 19 (60%) of them resulted positive to IGRA test and treatment was offered.

Discussion

Main findings of this study

The objective of this study was to define the epidemiology of hepatitis B and C, syphilis and latent TB among asylum seekers in Malta, to improve screening policies and to verify the feasibility of systematic screening.

The sample was mainly composed of young men from Sub Saharan Africa who had left Libya by boat after 2007. Their majority had fled political persecution (Eritreans) and war (Somali). Only a few of them had migrated for economic reasons, mainly from West Africa. Before arrival, many of them had spent several years in transit countries, such as Sudan or Libya. Differences in behavioural risk factors for STIs were observed within the two groups, according to cultural and religious beliefs. Most of them were Muslim; they declared a very low number of sexual partners in their lifetime, not to use condom and to have austere sexual habits due to religious restrictions. Most of people included in the sample denied alcohol and recreational drug consumption, except for *kebat*, which is culturally acceptable in the Horn of Africa. STI screening revealed low prevalence of HBsAg carriage and latent syphilis, and very low prevalence of hepatitis C antibodies, as expected on the basis of the self-reported risk assessment and the target group's ethnic composition (Somali people with conservative sexual habits and low behavioural risk for STIs). STIs-positive migrants were referred to the Genitourinary Clinic and further tested for HIV infection with negative results. Other STIs such as chlamydia and gonorrhoea, which can be asymptomatic, were not investigated. Clinical examination did not evidence other STIs. In the considered sample, only a few migrants testing positive for hepatitis had increased AST and ALT levels, thus suggesting, in

most cases, inactive carrier status; this result is in line with findings of other authors.^{13,14}

AST and ALT levels resulted abnormal in 70 patients despite hepatitis markers were negative. Alcohol consumption, drug abuse and food habits were investigated: out of them, only three patients declared alcohol or *kebat* abuse. Oily food and drugs intake was put in relation with transitory increase in liver enzymes. In particular, *kebat* chewing is being studied as possible cause of hepatotoxicity.^{15,16}

As regards latent TB screening, almost half of the sample was TST positive and 32 people showed chest X-ray changes, suggesting past or latent TB and therefore at higher risk of reactivation. The study group had already undergone radiographic TB screening upon arrival and just before leaving Detention Centres. After this, healthy migrants were moved to overcrowd open centres where 20 or more people shared the same living space, under conditions of bad general hygiene and poor dietary intake, which favour TB reactivation and susceptibility to infectious diseases. It is also recognized that the risk of TB transmission is higher within ethnic communities from high prevalence countries.¹⁷ The above-mentioned factors may lead to new infections and reactivation of latent TB acquired before migration.^{18,19}

What is already known on this topic

Screening was provided on a voluntary basis and the sample was randomly recruited among healthy individuals corresponding to the established selection criteria. The possibility to extend the same policy to the entire community is debatable, both in terms of feasibility, ethics and cost-effectiveness.^{20,21} A few recent studies on Somali migrants showed substantial, even though not alarming, HBV circulation in the general population and among migrant groups in Europe, thus suggesting the possible usefulness of applying preventive policies among this community.²² Two recent studies, which evaluated the cost-effectiveness of adopting chronic hepatitis B screening policies for migrants,^{23,24} showed that screening programmes, together with provision of antiviral treatment to chronic infected people, can be optimized by targeting specific ethnic groups. This confirms the importance of considering ethnic composition when planning surveillance and preventive measures.

As described in the literature, ~50% of foreign-born TB cases are diagnosed in the first 5 years after arrival in the host country, then prevalence rapidly decreases over time.^{25–27}

National TB screening protocols for asylum seekers and migrants entering Europe vary from country to country. They are mostly aimed at screening for active TB and are mainly based on chest radiography; nevertheless, little is known about the efficacy and cost-effectiveness of these policies. A recent analysis showed that radiographic screening has limited impact, is not cost-effective and requires high levels of investment.²⁸

No one-step, low cost, easy to administer and sensitive screening test for LTBI exists which is specific enough to be considered reliable without a confirmatory test. A TST is usually used for LTBI screening but it has a number of limitations, including high rates of cross-reactivity with BCG vaccination and environmental non-tuberculous mycobacteria and possible influence on results due to operators' bias.²⁹

Chest radiography is useful for identifying LTBI cases with increased risk of reactivation but, when used alone, this screening tool reveals a high number of false-negative results. More recently, IGRAs have been used as an alternative method for LTBI screening, but they require higher costs and technical investment.

Studies showed that a limited number of migrants normally accept to undergo LTBI screening and prophylaxis and that only ~60% complete treatment.²⁹ Optimization could be reached by improving follow-up and treatment programmes and by targeting specific subgroups of migrants at higher risk of reactivation (i.e. HIV-positive subjects, people affected by chronic diseases or who had recent contact with an active case).^{5,30}

What this study adds

Based on the results of this study, systematic screening of healthy asymptomatic asylum seekers recently arrived in Malta results unsuitable for hepatitis C and syphilis, given the low prevalence observed. On the contrary, systematic screening should be considered for hepatitis B, since early detection and treatment of this infection substantially reduces liver-related health outcomes. Systematic screening for chronic HBV infection among migrants is likely to be cost-effective, even estimating low HBV prevalence, participation, referral and treatment compliance.^{23,31,32} Furthermore, early detection of HBsAg-positive subjects could have important public health impact if preventive measures such as education and vaccination of contacts and groups at risk are implemented.

As regards tuberculosis, optimization of screening protocols is needed for increasing cost-effectiveness and reducing unnecessary tests. A generalised use of TST for diagnosis of latent infection appears to have low specificity and limited

effectiveness; it could be indicated as the first test of a two-step screening for migrants from countries with high TB incidence. Efficacy and cost-effectiveness can also be achieved by targeting screening to specific subgroups at higher risk of reactivation, such as people living with HIV, subjects with radiographic changes compatible with past TB and people affected by chronic diseases.

Limitations of this study

Due to the existence of ethnic, religious and cultural differences among migrant groups, which should be carefully considered in the interpretation of results, the outcomes of this study cannot be generalized. Other limitations include the small sample size, its inhomogeneous ethnic composition, the exclusion of under-18 and the self-reporting of sexual behaviours. Moreover, a direct link between ethnic origin and epidemiological risk cannot be defined because there is an increased exposure to infection in transit countries, during migrants' movements within Europe and to their native countries.³³

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