Prevalence of parasitic infections in migrants: do official symptom-driven guidelines apply to the current situation?

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SUMMARY

In recent years, migration has become a significant challenge in Western countries. Migrant populations, coming from hyper-endemic areas, may present parasitic infections that remain latent and asymptomatic even for years, eventually leading to severe complications. Italian guidelines have been established to perform screening guided by the presence of symptoms and/or hypereosinophilia. Parasitological screening was conducted in a migrant population to carry out preventative measures. All migrants were asked to report any symptoms suggesting parasitic infections and list any previous treatment received. Travel data were recorded. Parasitological examination of stools and urine were conducted in all patients regardless of symptoms. In all, 208 consecutive patients were enrolled in our outpatient clinic from November 2016 to August 2017. Thirty-four patients were excluded due to the previous assumption of albendazole or because they did not exhibit suitable samples. Prevalence of parasitic infections was 33/174 (18.9%). A statistically significant difference for the prevalence of parasitic infections was not found between patients who were asymptomatic and without hypereosinophilia compared to those who presented symptoms and/or hypereosinophilia (27/151 [17.9%] vs. 6/23 [26.0%]; p=0.39). By contrast, a statistically significant difference was found for the length of time between arrival in Italy and parasitological examinations (4/51 [7.8%] migrants who arrived in Italy more than six months prior to screening vs. 29/123 [23.6%] migrants who arrived within six months; p=0.016). Our results did not demonstrate any significant differences in prevalence of parasitic infections between symptomatic or hypereosinophilic and asymptomatic migrants. Thus we feel it inappropriate to support recent guidelines recommending parasitological examinations only in migrants with symptoms and/or hypereosinophilia. By contrast, it would appear important to perform parasitological screening in migrants as soon as possible after their arrival. Since such infestations, if untreated, could result in chronic diseases and complications, and could be transmitted in the host countries, our results have potential implications for public health.

Keywords: migrant population, parasitic infections, prevalence, screening, asymptomatic migrants.

INTRODUCTION

In recent years, migration has become a significant challenge in Western Countries. More than 350,000 migrants arrived in Italy in 2017, including many unaccompanied minors [1]. Most of

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them came from Africa (Nigeria, Eritrea, Guinea, Ivory Coast, Gambia, Senegal, Mali, Sudan, and Somalia) and Asia (especially from Syria, Iraq, Bangladesh, Pakistan) [2, 3].
Most migrants come from areas hyper-endemic for parasitic infections. Some parasitic infections such as those due to *Ascaris lumbricoides*, *Ancylostoma duodenale*, *Schistosoma* species (spp.). *Trichuris*, *Taenia* spp., may be entirely asymptomatic, remaining latent even for years and eventually leading to severe complications (*i.e.*, malignancies and neurological complications) [4-8]. The presence of infestations and their interaction with the host immune system may also predispose patients to develop bacterial infections [9-11]. Paediatric populations in particular are affected by a greater risk of growth impairment and delayed cognitive development, related to the loss of micronutrients caused by parasites [12-14].
Recent Italian Guidelines suggest performing a parasitological examination of stools and urine only in presence of suggestive symptoms and/or hypereosinophilia. In this work, we evaluated results of a screening program in a migrant population, to guide policies for preventive programs. Our main objective was to evaluate whether prevalence and distribution of parasitic infections may support recent Italian recommendations [15].

MATERIALS, POPULATION AND METHODS

The Infectious and Tropical Diseases Unit, in collaboration with the Microbiology and Virology Unit, conducted this prospective observational study at "*Mater Domini*" University Hospital in Catanzaro (Calabria, Southern Italy). The study procedures were in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice. The Ethical Committee of Calabria Region (Central) approved the study protocol and patients and their legal representatives (in case of?? minor age) signed an informed consent for participation.
Our study population consisted of migrants living in 4 centers for the asylum and refugee protection coming to our outpatient clinic (Centers of Africo, Vibo Valentia and Camini cities in Calabria Region).
We contacted centers hosting migrants offering them to revise the results of or to perform a screening for chronic infections, including parasitic ones. Serological tests were considered as needed (screening for HIV, HBV, HCV viruses and active or latent tuberculosis) [15].
Patients were screened for parasitic infections by parasitological examination of stools and urine. Moreover, the length of time lasting from their arrival in Italy to the parasitological exams was recorded. All migrants were asked to report presence of any symptoms with a particular attention to those suggestive of parasitic infections (*i.e.*, nausea, vomiting, itching, rash, weight loss, diarrhoea and abdominal pain), as well as previous assumption of antimicrobial agents and for which reason (for example antibiotics or anti-helminthic drugs). Complete blood count was recorded in order to evaluate the presence of hypereosinophilia, anaemia or other haematological abnormalities. According to reference values of our laboratory, a count of 500 total eosinophils per microliter or more (or more than 7%) was considered as a cut-off to define hypereosinophia. Patients who reported hypereosinophilia were managed according to the international guidelines, thus once parasitic infections were excluded, haematological consult was requested [16].
Although good clinical practice recommends to perform parasitological examination at least on three samples to rule out the presence of parasitic infections, unfortunately, for economic reasons and possible adherence constrains in this population only one microscopic ova and parasite (O&P) examination per patient was performed. The O&P examination is generally considered a gold standard method for stool parasite testing and it remains the cornerstone of diagnosis for intestinal protozoa and helminthic infections [17, 18].
Stool samples were collected from patients in the morning and parasite search and microscopic evaluation were carried out by direct methods (saline and iodine wet mounts) and also by Ritchie's concentration technique with formalin-ether [19].
Urine samples were collected from patients in the morning and centrifuged within two hours. The pellet from urine specimen was observed by direct microscopy for worm ova and protozoa trophozoites.
To establish differences by relevant factors (time spent in Italy, nationality, age and prevalence of

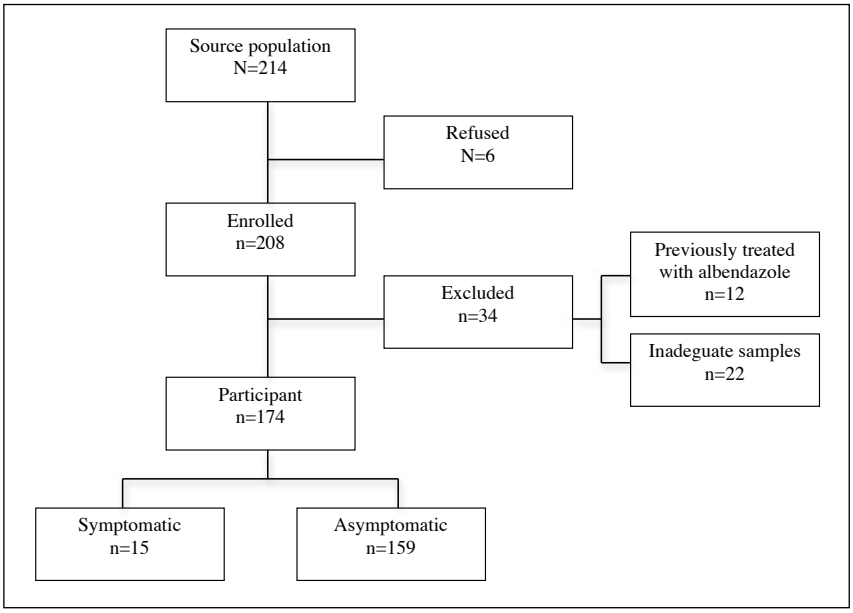

Figure 1 - Patient flow.

parasitic infections), statistical analyses were performed by Chi-square test. All data have been reported as percentages, or as mean (standard deviation, SD), as appropriate. All statistical tests were two-sided, assuming a level of significance of 0.05 for p value.

RESULTS

From November 2016 to August 2017, 214 migrants came to our outpatient clinic. Patient flow is depicted in Figure 1. Six patients refused to participate to the study. Two hundred and eight patients were enrolled but 34 were excluded from the study since 12 migrants were previously treated with albendazole and 22 did not provide adequate samples of urine and/or stools. Among 174 migrants who provided both urine and stool samples, 15 presented typical symptoms of infestations, while 159 were asymptomatic. Among symptomatic patients, two coming from Mali with dysuria and lower abdominal pain were diagnosed urinary schistosomiasis; one male, coming from Pakistan, with abdominal pain and abnormal liver function was diagnosed autoimmune hepatitis. Parasitic infections were excluded in the other 12 patients and notwithstanding symptoms alternative diagnoses were not found.

Patient characteristics are represented in Table 1. Among 174 patients, 153 (87.9%) were males and 21/174 (12.1%) were females. Mean age was 18.6 years (SD 8.5). One hundred and twenty-three (70.7%) patients were minor than 18 years of age. Seventy eight out of 174 migrants (44.8%) arrived in Italy within 12 weeks before the screening. Migrants came mostly from Gambia (20.1%), Bangladesh (18.4%), Syria (12.6%), Ivory Coast (7.5) and Nigeria (6.9%).

With regard to major chronic viral infections, eleven patients (11/174, 6.3%) left their centers before serological tests were performed. As for the other 163 patients, none of them was HIV positive, one patient was HCV positive, but with a negative HCV RNA. Thirteen patients (13/163, 8%) were found to be positive for HBsAg. Ninety one out of 163 (55.8%) were sero-negative for all HBV markers, so HBV vaccination was suggested. Only 17 (17/163, 10.4%) were previously vaccinated. Thirteen migrants (8%) presented positivity only for anti-HBc antibodies.

Concerning tuberculosis, 34/163 (20.9%) migrants had a latent tuberculosis infection (LTBI). Among them, 16/34 patients were assessed with tuberculin skin test (TST), 13/34 patients assessed with interferon gamma release assay (IGRA) test and 5/34 patients assessed with both. Patients with positive results at TST and/or IGRA tests

Table 1 - Epidemiological and demographical characteristics of the studied population.

Characteristic	*Overall (n=174)*	*Asymptomatic (n=159)*	*Symptomatic (n=15)*
Quantitative variables, mean (standard deviation)			
Age, years	18.6 (8.5)	18.5 (8.5)	18.6 (8.6)
Qualitative variables (n, %)			
Age			
More than 18 years	51 (29.3)	44 (27.7)	7 (46.7)
Less than 18 years	123 (70.7)	115 (72.3)	8 (53.3)
Gender			
Male	153 (87.9)	139 (82.4)	14 (93.4)
Female	21 (12.1)	20 (17.6)	1 (6.6)
Nationality			
Bangladesh	32 (18.4)	26 (16.3)	6 (40)
Camerun	2 (1.2)	1 (0.6)	1 (6.6)
Eritrea	2 (1.2)	2 (1.2)	0 (0)
Ethiopia	1 (0.6)	1 (0.6)	0 (0)
Gambia	35 (20.1)	31 (19.5)	4 (26.8)
Ghana	2 (1.2)	2 (1.2)	0 (0)
Guinea	10 (5.7)	10 (6.3)	0 (0)
Guinea Bissau	2 (1.2)	2 (1.2)	0 (0)
Iraq	10 (5.7)	10 (6.3)	0 (0)
Ivory Coast	13 (7.5)	13 (8.6)	0 (0)
Mali	13 (7.5)	10 (6.3)	3 (20)
Niger	1 (0.6)	0 (0)	1 (6.6)
Nigeria	16 (9.2)	16 (10.1)	0 (0)
Pakistan	6 (3.5)	6 (3.8)	0 (0)
Senegal	11 (6.3)	11 (6.9)	0 (0)
Sierra Leone	1 (0.6)	1 (0.6)	0 (0)
Syria	11 (6.3)	11 (6.9)	0 (0)
Sudan	3 (1.6)	3 (1.8)	0 (0)
Ukraine	3 (1.6)	3 (1.8)	0 (0)
Time arrival-observation			
Within 4 weeks	8 (4.6)	8 (4.7)	0 (0)
Fom 5 to 11 weeks	70 (40.2)	65 (40.9)	5 (33)
From 12 weeks to 23 weeks	17 (9.5)	13 (8.6)	4 (26.8)
From 24 to 47 weeks	28 (16.1)	24 (15.1)	4 (26.8)
From 48 weeks to 52 weeks	2 (1.1)	2 (1.2)	0 (0)
Beyond 52 weeks	49 (28.2)	47 (29.5)	2 (13.4)
Presence of hypereosinophilia			
Yes	10 (5.7)	8 (4.7)	2 (13.4)
No	164 (94.3)	151 (95.3)	13 (86.6)

underwent chest X-rays. No active tuberculosis was found and treatment for LTBI was prescribed using isoniazide 300 mg daily for 6 months.

Overall, 33/174 (18.9%) patients were affected by one or more parasitic infections. A complete description of patients affected by parasitic infections and treatments prescribed (drugs and dosing) is available in Table 2. Eight out of 33 (24.3%) migrants were affected by schistosomiasis (4 *S. mansoni* and 4 *S. haematobium*). Among those 8 cases, only two patients (patient #32 and #33) coming from Mali were symptomatic and one presented hypereosinophilia (patient #32), while the other did not.

A further O&P examination of stools and urine was performed to check the efficacy of treatment prescribed after diagnosis. In two cases ova of *Schistosoma haematobium* and in one case ova of *Schistosoma mansoni* were excreted up to three months after the end of treatment, so a further treatment course was administered. Patient #30 refused to be treated for schistosomiasis.

In the post-therapeutic follow-up, at O&P examination, two patients exhibited *Entamoeba histolytica/dispar/moshkovskii* as a new parasitic infection, not detected before (patient #3 and patient #15).

When rate of parasitic infections was concerned, statistically significant differences were not found between asymptomatic (29/159, 18.2%) compared to symptomatic migrants (4/15, 26.6%); p=0.42. Also differences in prevalence of parasitic infections were not found to be statistically significant when asymptomatic migrants without hypereosinophilia were compared to those with symptoms and/or hypereosinophilia (6/23 [26.1%] vs. 27/151[18.5%]; p=0.34).

Among 113 patients coming from Africa, prevalence of parasitic infections was 23% (26/113), while among 61 migrants coming from other Countries it was 11.5% (7/61), p=0.06.

Table 2 - Clinical characteristics of patients affected by parasitic infections and prescribed treatment (n=33).

Patient ID	*Age (years)*	*Sex*	*Country of origin*	*Time from arrival to parassitological tests (weeks)*	*Symptoms (Yes- No)*	*Hypereosinophilia (Yes – No), If Yes (value, %)*	*Results of parasitological tests Form – Parasite - sample*	*Treatment*
1	17	M	Senegal	8	No	No	Cystis of *Giardia lamblia* stools Eggs of *Ascaris lumbricoides* stools	Metronidazole 250 mg per os twice daily for 5 days Mebendazole 500 mg per os, single dose
2	15	M	Senegal	8	No	Yes (11.2%)	Cystis of *Entamoeba hystolica* stools	Tinidazole 2 g per os daily for 3 days
3	14	M	Gambia	8	No	Yes (7.7%)	Eggs of *Ancylostoma duodenalis* stools	Mebendazole 500 mg per os, single dose
4	16	M	Senegal	8	No	No	Eggs of *Ascaris lumbricoides* stools	Mebendazole 500 mg per os, single dose
5	16	M	Gambia	8	No	No	Eggs of *Ascaris lumbricoides* stools	Mebendazole 500 mg per os, single dose
6	16	M	Gambia	4	No	No	Eggs of *Schistosoma mansoni* stools	Praziquantel 60 mg /kg per os in two divided doses
7	16	M	Gambia	8	No	No	Eggs of *Ascaris lumbricoides* stools	Mebendazole 500 mg per os, single dose
8	12	M	Syria	24	No	No	Cystis of *Giardia lamblia* stools	Metronidazole 250 mg per os twice daily for 5 days
9	8	M	Syria	24	No	No	Cystis of *Giardia lamblia* stools	Metronidazole 250 mg per os twice daily for 5 days
10	6	M	Syria	24	No	No	Cystis of *Giardia lamblia* stools	Metronidazole 250 mg per os twice daily for 5 days
11	17	M	Nigeria	24	No	No	Eggs of *Ancylostoma duodenalis* stools	Mebendazole 500 mg per os, single dose

Patient ID	*Age (years)*	*Sex*	*Country of origin*	*Time from arrival to parassitological tests (weeks)*	*Symptoms (Yes- No)*	*Hypereosinophilia (Yes – No), If Yes (value, %)*	*Results of parasitological tests Form – Parasite - sample*	*Treatment*
12	16	M	Nigeria	24	No	No	Eggs of *Ancylostoma duodenalis* stools	Mebendazole 500 mg per os, single dose
13	16	M	Bangladesh	12	No	No	Eggs of *Ascaris lumbricoides* stools	Mebendazole 500 mg per os, single dose
14	16	M	Gambia	8	No	No	Cystis of *Giardia lamblia* stools	Metronidazole 250 mg per os twice daily for 5 days
15	16	M	Senegal	12	No	No	Eggs of *Ancylostoma duodenalis* stools	Mebendazole 500 mg per os, single dose
16	16	M	Guinea	8	No	No	Eggs of *Schistosoma mansoni* stools	Praziquantel 60 mg/ kg per os in two divided doses
17	14	M	Guinea	12	No	No	Eggs of *Schistosoma mansoni* stools	Praziquantel 60 mg /kg per os in two divided doses
18	17	M	Senegal	8	No	No	Cystis of *Giardia lamblia* stools	Metronidazole 250 mg per os twice daily for 5 days
19	15	M	Senegal	8	No	No	Eggs of *Trichiuris trichiura* stools	Mebendazole 500 mg per os, single dose
20	17	M	Gambia	8	Yes	No	Cystis of *Entamoeba hystolica* stools	Tinidazole 2 g per os daily for 3 days
21	17	M	Gambia	8	No	No	Cystis of *Entamoeba hystolica* stools	Tinidazole 2 g per os daily for 3 days
22	18	M	Sudan	52	No	No	Cystis of *Giardia lamblia* stools	Metronidazole 250 mg per os twice daily for 5 days
23	18	M	Bangladesh	8	No	No	Cystis of *Giardia lamblia* stools	Metronidazole 250 mg per os twice daily for 5 days
24	17	M	Bangladesh	12	Yes	No	Cystis of *Giardia lamblia* stools	Metronidazole 250 mg per os twice daily for 5 days
25	17	M	Bangladesh	12	No	No	Cystis of *Giardia lamblia* stools	Metronidazole 250 mg per os twice daily for 5 days
26	14	M	Guinea Bissau	12	No	No	Cystis of *Giardia lamblia* stools	Metronidazole 250 mg per os twice daily for 5 days
27	18	M	Ghana	52	No	No	Eggs of *Ancylostoma duodenalis*	Mebendazole 500 mg per os, single dose
28	18	M	Guinea Bissau	52	No	No	Eggs of *Ancylostoma duodenalis* stools	Mebendazole 500 mg per os, single dose
29	16	M	Gambia	52	No	No	Eggs of *Schistosoma mansoni* stools Eggs of *Ancylostoma duodenalis* stools	Praziquantel 60 mg /kg per os in two divided doses Mebendazole 500 mg per os, single dose
30	16	M	Guinea	8	No	No	Eggs of *Schistosoma haematobium* urine	Refuse treatment
31	17	M	Mali	4	No	No	Eggs of *Schistosoma haematobium* urine	Praziquantel 60 mg /kg per os in two divided doses
32	21	F	Mali	24	Yes	Yes (12%)	Eggs of *Schistosoma haematobium* urine	Praziquantel 60 mg /kg per os in two divided doses
33	22	M	Mali	24	Yes	No	Eggs of *Schistosoma haematobium* urine	Praziquantel 60 mg /kg per os in two divided doses

Even considering prevalence of parasitic infections in minors compared to adults, a statistically significant difference was not found (27/123 [21,9%] vs. 6/51 [11.8%]; p=0.23). By contrast, a statistically significant difference was found considering the length of time in between arrival to Italy and parasitological examination, with a prevalence of parasitic infections in patients tested in the six months after arrival higher than in patients tested after more than six months (29/123 [23.6%] vs. 4/51 [7.8%], p=0.016).

DISCUSSION

Almost 1 out of five migrants coming to Calabria showed at least one parasitic infections. Although our results need to be confirmed with a greater number of patients, we confirmed a high prevalence of parasitic infections in this population. Moreover, in our opinion, a screening strategy, which combines parasitological, virological, and tuberculosis testing would be more cost-effective.

Recent Italian recommendations suggest performing parasitological examination only in presence of symptoms or hypereosinophilia [15]. However, in our study no statistically significant difference was found in the prevalence of parasitic infections between asymptomatic and symptomatic patients. Importantly, if the current recommendation had been applied, 27/151 (18.5%) asymptomatic patients not presenting hypereosinophilia would have been left undiagnosed, and therefore untreated [15]. In other terms, we believe that an evaluation based on presumptive symptoms or hypereosinophilia may be a nonsense in the field of imported chronic diseases and does not fit with many parasitic infections.

The highest percentage of parasitic infections was found in minors who recently arrived in Italy within six months before the screening. The percentage of positive cases was higher in migrants coming from African Countries. It is difficult to explain why prevalence was higher in those who arrived more recently, but the most likely explanation is that a reduction of parasites and eggs excretion over time occurs for a spontaneous clearance in setting where the risk of re-infestation is low [20]. In any cases, our results suggest that a window of opportunity should not be missed to test migrants as soon as possible after their arrival since, along time, diagnosis could become more difficult precluding prevention of complications and/or secondary infections in the host population. Indeed, patients carrying an untreated parasitic disease would progress to a chronic stage with further complications (*e.g.*, amebic abscess of the liver) and spreading of the infection in the environment would occur. Moreover, camps where migrants reside for many weeks or months are usually overcrowded, thus outbreaks of parasitic diseases may occasionally happen [21]. Possible circulation of imported protozoa and helminths should therefore be seriously taken into account by the health authorities in the hosting Countries. With regard to schistosomiasis, the risk of autochthonous transmission in the host Countries has already been reported [22, 23]. This emerging disease should be diagnosed early because its diagnosis and treatment would allow to prevent serious complications such as portal hypertension and varices bleeding by *S. mansoni* or bladder cancer by *S. haematobium*.

Even if a mass treatment, rather than a test and treat strategy, is applied to control parasitic infections in migrants, this would not be necessary useful and applicable to schistosomiasis. In fact, while albendazole, used for a mass treatment, would be active for the other parasitic infections, for schistosomiasis its efficacy has been suggested only in one study and only for the treatment of *S. haematobium* [24]. Also, for schistosomiasis, even in absence of hypereosinophilia and symptoms, screening should be performed, since we found that one out of four patients were affected and only two out of eight were symptomatic. Particularly, the screening should be implemented also for migrant women during pregnancy, since schistosomiasis may exert negative effects on the foetus [27].

The present study is affected by several limitations. First, we included a limited number of patients. Second, we did not perform any interventions to implement screening or improve adherence to treatment recommendations. Third, only a single stool or urine sample was examined for parasitological tests with direct microscopy [25, 26]. Indeed, the investigations carried out are very likely to be characterized by a non-optimal sensitivity. In fact, the real prevalence of parasitic infections is probably much higher. If underestimation could be a problem, our conclusion may be even more sup-

ported by data. Moreover, in hyperendemic countries the analysis of a single sample is fair, even if the diagnosis of intestinal parasitic infections should generally request at least three samples of stools to reduce false negative results [17, 18, 28].
In conclusion, our results suggest that all recently arrived migrants, including those asymptomatic and without hypereosinophilia, should be carefully screened for parasitic infections, especially minors and those coming from Africa. This conclusion, if our results will be confirmed by larger studies, should modify recent guidelines that suggest performing parasitological examination only in presence of symptoms or hypereosinophilia [15]. Lastly, combined screening for chronic viral infections and latent tuberculosis may further increase the cost-effectiveness of the screening procedures.

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Competing interests
All the authors declare that there is no conflict of interests regarding the publication of this paper.

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