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REGULAR ARTICLE

Italian multicentre study found infectious and vaccine-preventable diseases in children adopted from Africa and recommends prompt medical screening

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ABSTRACT

Aim: This study evaluated the prevalence of infectious diseases and immunisation status of children adopted from Africa.

Methods: We studied 762 African children referred to 11 Italian paediatric centres in 2009–2015. Clinical and laboratory data were retrospectively collected and analysed.

Results: The median age of the children (60.3% males) was 3 years and 6 months, 52.6% came from Ethiopia and 50.1% had at least one infectious disease. Parasitic infections accounted for the majority of the infectious diseases (409 of 715), and the most common were *Giardia lamblia* (n = 239), *Toxocara canis* (n = 65) and skin infections (n = 205), notably *Tinea capitis/corporis* (n = 134) and *Molluscum contagiosum* (n = 56) Active tuberculosis (TB) was diagnosed in nine children (1.2%). Latent TB infections were diagnosed in 52 (6.8%) children, and only 23 had concordant positive tuberculin skin tests and Quantiferon Gold In-Tube results. Discordant results were associated with Bacille de Calmette-Guérin vaccinations (odd ratio 6.30 and 95% confidence interval of 1.01–39.20, p = 0.011). Nonprotective antitetanus or antihepatitis B antibody titres were documented in 266 (34.9%) and 396 (51.9%) of the 762 children.

Conclusion: The prevalence of infectious conditions and not-protective titres for vaccine-preventable diseases observed in our population underlines the need for prompt and complete medical screening of children adopted from Africa.

INTRODUCTION

More than 2000 children are internationally adopted in Italy every year (1). Although internationally adopted children are often declared healthy in their native countries, medical disorders are often missed and diagnosed after adoption (2–6). As medical preadoption information can be incomplete, wrongly translated and, or discordant, medical care on arrival is a fundamental requirement so that the child's health status can be assessed (7–9). Early identification of infectious disorders, such as tuberculosis (TB), acute or chronic viral diseases and parasitic infections (2–6), and the evaluation of antibody serum levels towards vaccine-preventable diseases allow clinicians to treat potential

Abbreviations
BCG, Bacille de Calmette-Guérin; HIV 1-2, Human immunodeficiency virus type I e II; IQR, Interquartile range; OR, Odds ratio; QFT-G-IT, Quantiferon Gold In-Tube; TB, Tuberculosis; TST, Tuberculin skin test.

Key notes

- We evaluated the prevalence of infectious diseases and immunisation status of children adopted from Africa and referred to 11 Italian paediatric centres in 2009–2015.
- The median age of the children was 3 years and 6 months and 50.1% had at least one infectious disease, with the most common being parasitic infections.
- The prevalence of infectious conditions and not-protective titres for vaccine-preventable diseases underlines the need for prompt and complete medical screening.

transmittable diseases and update the child's immunisation status (10–13).

Few previous studies have investigated the health status of internationally adopted children (2,12,14–16). Intestinal parasitic and dermatological infections have been described as the most frequent infectious diseases, with prevalence rates of up to 42.7% and 35.0%, respectively (2,7,10,12,15,16). Since 2005, African adoptions have increased significantly in Italy, rising from 9.3% of total adoptions in 2005 to 20.3% in 2013 (1). The available literature on children adopted from Africa is limited (9,17–21). To date, only one study has investigated the global health status of adopted African children (22). This study retrospectively evaluated the global health status of a large cohort of internationally adopted African children referred to 11 Italian paediatric centres.

MATERIALS AND METHODS

Study design

A retrospective multicentre study was performed, involving 11 paediatric infectious disease centres who took care of internationally adopted children and were members of the Italian Working Group for Immigrant and Adopted Children. They were located in 11 Italian cities: Firenze, Novara, Roma, Milano, Torino, Ancona, Pordenone, Palermo, Lecce, Verbania and Tradate.

Study group

All the children up to 18 years of age who were adopted from any African country and consecutively referred to the participating Centres over a 7-year period (January 2009–December 2015) underwent their first screening for internationally adopted children and were enrolled in the study (12). The only exclusion criterion was being adopted from non-African countries. Medical records were collected and entered into an electronic database. The study was approved by the local Ethics Committee for Human Investigation.

Screening protocol

All the children underwent a standard operative protocol, developed by National Working Group for Immigrant Children following international recommendations (13–23). The sociodemographic data that were collected included their age on arrival in Italy, their age at their first evaluation, their sex and their country of origin. Medical history and preadoption immunisation records were reviewed, when available. Children were classified as having special need when conditions included in the American Academy of Pediatrics' definition were evident (24). Children were considered to have been vaccinated with Bacille de Calmette-Guérin (BCG) when clear documentation was available and, or, a BCG scar was noted. All the children were clinically evaluated. At the first evaluation, all the children underwent a venipunture and laboratory assessment that included a complete blood count. Other tests carried out included serological tests for several infectious diseases, and, in particular, the hepatitis B virus, the hepatitis C virus, the hepatitis A virus, the human immunodeficiency virus, types I e II (HIV 1-2), *Treponema pallidum* and *Toxocara canis*. A tuberculin skin test (TST) and Quantiferon-TB Gold in-tube assay (QFT-G-IT) were performed, and a chest radiograph was carried out if either of these were positive, according to the international guideline definitions (24–26). In addition, three stool samples were collected to search for ova and parasites and for the *Giardia lamblia* antigen test.

Laboratory tests

All the laboratory examinations were performed in the laboratories of each National Working Group for Immigrant Children centre, using standardised techniques and according to the manufacturers' instructions. Following the American Academy of Pediatrics' guidelines (24), a positive TST was defined as an induration size of up to 10 mm (24–26).

The QFT-G-IT assay (QIAGEN, Hilden, Germany) was performed according to the manufacturer's instructions (24). After subtracting the value from the negative control, the result was positive if the antigen-dependent response was ≥0.35 IU, negative if the mitogen-induced response was ≥0.5 IU/mL and the antigen-dependent response was <0.35 IU/mL and indeterminate if both the mitogen-induced and antigen-dependent responses were below cut-off or the mitogen-induced response >8 IU/mL. The test was repeated if the test was indeterminate (24).

TB definition

Study children were classified as not infected, latent TB infection cases or active TB disease cases, following the definitions in the American Academy of Pediatrics' guidelines (24). In particular, asymptomatic children with negative TST and QFT-G-IT tests were defined as uninfected. A confirmed latent TB infection diagnosis was assigned to any child with positive TST and QFT-G-IT tests and no clinical or radiographic evidence of active TB (24).

Statistical analysis

The nonparametric Mann–Whitney test was used to compare continuous variables. Fisher's exact test and the chi-squared tests were used to compare categorical variables, as appropriate. Univariate and multivariate analyses were performed to evaluate possible predictors of positive TST and negative QFT-G-IT discordant results and odds ratios (OR) and 95% confidence intervals (95% CI) were calculated. All statistical analyses were carried out using the SPSS for Windows version 19 (IBM Corp, New York, NY, USA). A p value of <0.05 was considered significant.

RESULTS

Characteristics of the study population

We included 762 children (60.3% males) in the study, and the median age at the time of the first evaluation was 3 years and 6 months with an interquartile range (IQR) of

3.5–5.7. The majority came from Ethiopia (52.6%), the Democratic Republic of Congo (21.3%) and Burkina Faso (11.3%). Other children came from Mali (3.7%), Benin (2.6%), Senegal (2.0%) and other African countries (6.5%). The age distribution of the children according to country of origin is shown in Figure 1, and the characteristics of the study population are described in Table 1.

Table 1 Characteristics of the study population

Characteristic	Number or median	Percentage or interquartile range
Age (years)	3,6 (median)	3.5–5.7 (Interquartile range)
Sex		
Male	460	60.3%
Female	302	39.7%
Country of origin		
Ethiopia	401	52.6%
Democratic Republic of Congo	162	21.3%
Burkina Faso	86	11.3%
Mali	28	3.7%
Benin	20	2.6%
Senegal	15	2%
Other African States	50	6.5%
Centre		
Firenze	286	37.5%
Roma	138	18.1%
Torino	138	18.1%
Novara	62	8.2%
Milano	41	5.4%
Other centres	97	12.7%
BCG/scar	411	53.9%

BCG, Bacille de Calmette-Guérin.

Prevalence of infectious diseases

Overall, 382 of the 762 children (50.1%) presented with at least one infectious disease: 44.5 had at least one parasitic infection and 8.0% had active or latent TB. The prevalence of infectious diseases is shown in Figure 2.

The most frequent infections were parasitic infections, which accounted for 409 of the 715 infectious diagnoses (57.2%), followed by skin infections (28.7%) (Figure 2).

Of the 339 children diagnosed with at least one parasitic infection, 76.4% had one parasitic infection, 16.8% had two simultaneous parasitic infections, 5.4% had three and 1.5% had four. The most frequent of the 409 parasitic infections were *G. lamblia* (61.4%) and *T. canis* (16.7%). In 85 (21.9%) cases, other parasites were involved, in particular *Hymenolepis nana* (n = 24, 6.2%), *Ascaris lumbricoides* (n = 11, 2.8%), *Entamoeba histolytica* (n = 11, 2.8%), *Blastocystis hominis* (n = 10, 2.6%), *Strongyloides stercoralis* (n = 8, 2.0%), *Taenia solium/cisticerco* (n = 6, 1.5%) *Trichuris trichiura* (n = 5, 1.3%), *Schistosoma spp* (n = 4, 1.0%), *Ancylostoma duodenale* (n = 3, 0.8%), *Dientamoeba fragilis* (n = 2, 0.5%) and *Enterobius vermicularis* (n = 1, 0.3%).

The total number of cutaneous infections was 205, and the most frequently observed were *Tinea capitis/corporis* (n = 134, 65.4%) and *Molluscum contagiosum* (n = 56, 27.3%). Lice and scabies were diagnosed in eight (3.9%) and seven (3.4%) children, respectively (Figure 2).

Viral hepatitis was rarely observed as follows: the hepatitis B virus was diagnosed in 26 of 715 cases with an infectious diagnosis (3.6%), the hepatitis A virus in 11 cases (1.5%) and the hepatitis C virus in two cases (0.3%). One child had HIV-1 infected (0.1%) (Figure 2).

Tuberculosis

Active TB pulmonary disease was diagnosed in nine children (1.2%) and latent TB in 52 children (6.8%). Of note, 23 of 52 (44.2%) of the children with latent TB had concordant positive TST and QFT-G-IT results, while 29 of 52 (55.7%) had discordant results, namely a positive TST

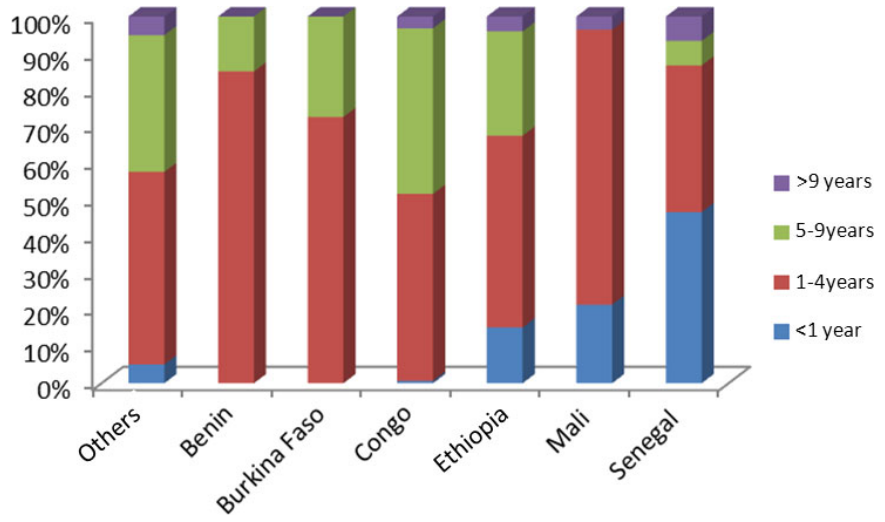

Figure 1 The study population of 762 children classified according to age and country of origin.

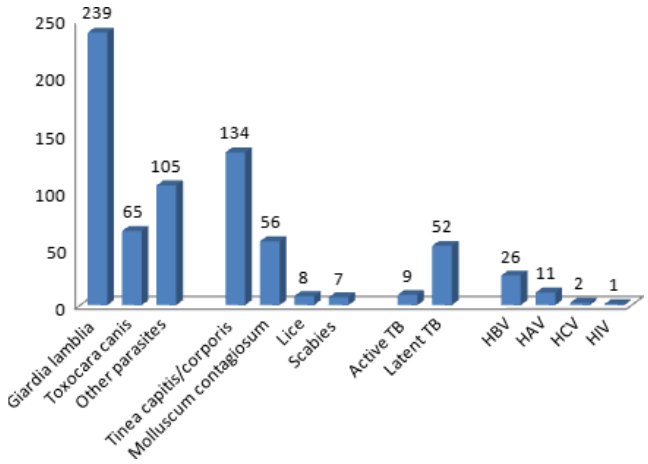

Figure 2 Selected infectious diseases in the study population: hepatitis A, B and C viruses and tuberculosis.

and a negative QFT-G-IT. No indeterminate QFT-TB-IT results were observed.

The prevalence of latent TB was the same in the two subgroups of children under 5 years of age and 5 years of age or older (13.0%). We observed a higher frequency (8% versus 6%) of positive TST and negative QFT-G-IT discordant results in children under 5 years of age, than in the older children, but these data were not statistically significant (p = 0.428).

Information regarding BCG status and scars is collected for 732 of the 762 children: 411 had received the BGC immunisation (56.1%) and 321 children (43.9%) were BCG/scar negative.

A multivariate analysis was performed to evaluate possible predictors of positive TST and negative QFT-G-IT discordant results and this showed a significantly higher risk of the TST and QFT-G-IT tests and prior BCG vaccination (OR 6.30, 95% CI 1.01–39.20, p = 0.011). There was no association with age or gender (Table 2).

Immunisation status

Serological tests showed a nonprotective antibody titre versus tetanus in 266 of 762 (35.0%) and versus the hepatitis B virus in 396 of 762 (52.0%) children. Other serological tests were carried out on a minority of children.

Table 2 Risk factors for discordant results at multivariate analysis (positive tuberculin skin test and negative Quantiferon Gold In-Tube)

	aOR	95% CI	p
Age			
<5 years	1		
>5 years	0.23	0.45–1.188	0.800
BCG			
No	1		
Yes	6.30	1.01–39.20	0.011
Gender			
Female	1		
Male	2.45	0.53–11.42	0.247

Missing data: Age n = 2; BCG n = 30; Gender n = 0.
BCG, Bacille de Calmette-Guérin.

DISCUSSION

This study evaluated the health status of 762 children adopted from Africa from 2009 to 2015, making this the largest cohort of African adopted children ever reported. In agreement with data from previous studies of internationally adopted children, infectious diseases were diagnosed in a high percentage of the children in our study: 44.5% of them had at least one parasitic infection and 15.3% had active or latent TB. Until now, only one study published in 2007 analysed the health status of adopted children coming from an African country, namely Ethiopia (22), and this reported that the incidence of parasitic infections in the 50 study children was a much higher 72%. As in our study, the most frequently identified parasitic pathogen was *G. lamblia* (40%). Other parasites were found in percentages similar to those observed in our study (22).

Active TB was diagnosed in nine children in our study. Latent TB infections, defined as a positive result from either or both of the TST and QFT-G-IT tests, was diagnosed in 52 children – 13.1% of those tested – similar to previously published data (22). Only 5.8% children had concordant TST and QFT-G-IT results that were both positive, while 7.3% had a positive TST test but a negative QFT-G-IT test. Similar data were reported by Howley et al. (27) in 2520 immigrant children screened for latent TB. Children with discordant results were classified as having latent TB infection, following the recommendations in the American Academy of Pediatrics' guidelines. However, we may speculate that discordant positive TST and negative QFT-G-IT results may be due to a falsely negative QFT-G-IT result. We noted that a discordant result was more frequent, but not significantly, in children under 5 years of age than older ones (8% versus 6%), suggesting that the QFT-G-IT test may be less reliable in younger children. An alternative, and opposite, explanation is that latent TB infection may be overestimated in positive TST and negative QFT-G-IT cases because of poor TST specificity, due to a cross-reaction with the BCG vaccination, the booster effect of previous TST tests and the possibility of nontuberculous mycobacterial infections. The fact that the multivariate analysis found a significant association between discordant positive TST and negative QFT-G-IT results and prior BCG vaccinations (adjusted OR 6.30, 95% CI 1.01–39.20, p = 0.011) (Table 1), but no association with age or gender, suggests that the discordant results in our cohort were more likely to be due to a false-positive TST, related to BCG vaccination, than to a false-negative QFT-G-IT. Accordingly, a strong association between BCG and positive TST results in children has been widely confirmed (28,29).

Vaccine documentation for tetanus, diphtheria, the hepatitis B virus, poliomyelitis and BCG was only available in just over half of the patients (58%), similar to previous studies (30). Percentages ranging from 35% to 52% displayed nonprotective antibody levels, confirming the

insufficient protection of children adopted from Africa with regard to vaccine-preventable diseases, the lack of reliability of immunisation records and possible discrepancies between the available documentation and test results (10,11,13).

Our cross-sectional study had some limitations. First of all, the study group only represented approximately one-third of the total number of African adopted children in Italy during the study period, leading to the possible suboptimal representativeness of our results. Furthermore, during the 7-year study period, some investigations included in the screening protocol changed and some tests were not performed in the whole population. This could have been partly related to an inhomogeneous collection of data in the different centres.

CONCLUSION

About a half of our study population was diagnosed with at least one infectious disease: TB infections were observed in approximately 15% of the children and parasitic infection in 50%. TB diagnoses appeared to be particularly difficult in our data set, due to the high rate of discordant TST and QFT-G-IT results, which were probably related to previous BCG vaccinations. Serological screening for vaccine-preventable diseases is crucial to update the immunisation status of these adopted children. Our data confirm the need for prompt, careful and complete screening for children adopted from Africa.

CONFLICTS OF INTERESTS

The authors have no conflicts of interests to disclose.

FINANCE

This study did not receive any external funding.

References

1. Italian Presidency of the Council of Ministers, Commission for International Adoptions. International Adoptions. Available at: http://www.commissioneadozioni.it/it/notizie/2016/dati-adozioni.aspx. (accessed on June 10, 2017).
2. Hénaff F, Hazart I, Picherot G, Baqué F, Gras-Le Guen C, Launay E. Frequency and characteristics of infectious diseases in internationally adopted children: a retrospective study in Nantes from 2010 to 2012. *J Travel Med* 2015; 22: 179–85.
3. Eckerle JK, Howard CR, John CC. Infections in internationally adopted children. *Pediatr Clin North Am* 2013; 60: 487–505.
4. Ampofo K. Infectious disease issues in adoption of young children. *Curr Opin Pediatr* 2013; 25: 78–87.
5. Baldwin S. Initial infectious disease screening evaluation of the international adoptee. *J Ark Med Soc* 2009; 106: 137–9.
6. Barnett ED. Immunizations and infectious disease screening for internationally adopted children. *Pediatr Clin North Am* 2005; 52: 1287–309.
7. Sciauvaud J, Rigal E, Pascal J, Nourrisson C, Poirier P, Poirier V, et al. Transmission of infectious diseases from internationally adopted children to their adoptive families. *Clin Microbiol Infect* 2014; 20: 746–51.
8. Tandé D, Boisramé-Gastrin S, Münck MR, Héry-Arnaud G, Gouriou S, Jallot N, et al. Intrafamilial transmission of extended-spectrum-betalactamase-producing Escherichia coli and Salmonella enterica Babelsberg among the families of internationally adopted children. *J Antimicrob Chemother* 2010; 65: 859–65.
9. Vanhoof R, Gillis P, Stévart O, Boland C, Vandenberg O, Fux F, et al. Transmission of multiple resistant Salmonella Concord from internationally adopted children to their adoptive families and social environment: proposition of guidelines. *Eur J Clin Microbiol Infect Dis* 2012; 31: 491–7.
10. van Schaik R, Wolfs TF, Geelen SP. Improved general health of international adoptees, but immunization status still insufficient. *Eur J Pediatr* 2009; 168: 1101–6.
11. Tchidjou HK, Gargiullo L, Vescio F, Giampaolo R, Nicolosi L, Finocchi A. Immunization status of internationally adopted children in Rome, Italy. *Niger J Clin Pract* 2015; 18: 307–11.
12. Valentini P, Gargiullo L, Ceccarelli M, Ranno O. Health status of internationally adopted children. The experience of an Italian GLNBI paediatric centre. *Ital J Pub Health* 2012; 9: e7527–2.
13. Veronesi L, Virdis R, Bizzoco S, Colucci ME, Affanni P, Paganuzzi F, et al. Vaccination status and prevalence of enteric viruses in internationally adopted children. The case of Parma, Italy. *Acta Biomed* 2011; 82: 208–13.
14. Martínez Ortiz A, Domínguez Pinilla N, Wudineh M, González-Granado LI. International adoption from Ethiopia in a 5-year period. *An Pediatr (Barc)* 2015; 82: 302–7.
15. Pedersen TM, Poulsen A, Pedersen FK. The risk of infections in internationally adopted children is real. *Ugeskr Laeger* 2013; 175: 1789–93.
16. Piñeiro-Pérez R, García-Hortelano M, José Mellado M, García-Ascaso M, Medina-Claros A, Fernández N, et al. Is there interference in the interpretation of the tuberculin skin test in children with intestinal parasitic infestation? *Pathog Glob Health* 2012; 106: 172–6.
17. Stadler LP, Mezoff AG, Staat MA. Hepatitis B virus screening for internationally adopted children. *Pediatrics* 2008; 122: 1223–8.
18. Staat MA, Rice M, Donauer S, Mukkada S, Holloway M, Cassedy A, et al. Intestinal parasite screening in internationally adopted children: importance of multiple stool specimens. *Pediatrics* 2011; 128: e613–22.
19. Lee Y, Allen PJ. Infectious diseases in international adoptees from South Korea. *Pediatr Nurs* 2008; 34: 480–5.
20. Spicer KB, Turner J, Wang SH, Koranyi K, Powell DA. Tuberculin skin testing and T-SPOT.TB in internationally adopted children. *Pediatr Infect Dis J* 2015; 34: 599–603.
21. Staat MA, Stadler LP, Donauer S, Trehan I, Rice M, Salisbury S. Serologic testing to verify the immune status of internationally adopted children against vaccine preventable diseases. *Vaccine* 2010; 28: 7947–55.
22. Miller LC, Tseng B, Tirella LG, Chan W, Feig E. Health of children adopted from Ethiopia. *Matern Child Health J* 2008; 12: 599–605.
23. Jones VF, Committee on Early Childhood, Adoption, and Dependent Care. Comprehensive health evaluation of the newly adopted child. *Pediatrics* 2012; 129: e214–23.
24. American Academy of Pediatrics. Tuberculosis. In: DW Kimberlin, MT Brady, MA Jackson, SS Long, editors. *Red book: 2015 report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2015: 805–30.

25. Starke JR. Tuberculosis in children. *Semin Respir Crit Care Med* 2004; 25: 353–64.
26. American Thoracic Society. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Resp Crit Care Med* 2000; 161: 1376–95.
27. Howley MM, Painter JA, Katz DJ, Graviss EA, Reves R, Beavers SF, et al. Evaluation of QuantiFERON-TB gold in-tube and tuberculin skin tests among immigrant children being screened for latent tuberculosis infection. *Pediatr Infect Dis J* 2015; 34: 35–9.
28. Wang L, Turner MO, Elwood RK, Schulzer M, FitzGerald JM. A meta-analysis of the effect of Bacille Calmette Guérin vaccination on tuberculin skin test measurements. *Thorax* 2002; 57: 804–9.
29. Méndez-Echevarría A, Sainz T, García-Hortelano M, Baquero-Artigao F, Mellado MJ. Usefulness of interferon-gamma release assays in the screening of latent tuberculosis infection in immigrant and internationally adopted children. *Pediatr Infect Dis J* 2015; 34: 1141–2.
30. Verla-Tebit E, Zhu X, Holsinger E, Mandalakas AM. Predictive value of immunization records and risk factors for immunization failure in internationally adopted children. *Arch Pediatr Adolesc Med* 2009; 163: 473–9.

