Original paper

Imported diseases in the emergency room

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Abstract

Introduction: the increase in migratory movements and travel to low-resource countries in recent years has led to an increase in the incidence of infectious diseases that are uncommon in Spain. The objective of the study was to describe the characteristics of patients with imported disease in the emergency room.

Methods: a retrospective study was conducted between 2012-2019. The study included children under 16 years of age with a history of international travel in the past 3 months managed in the emergency department of the Hospital de Torrejón. We collected demographic and clinical data. Diagnoses were grouped into three categories: tropical infection (typically imported from tropical areas), communicable infections (including infections with global distribution and a greater prevalence in tropical areas, such as tuberculosis) and common infections.

Results: the sample included 100 children were included. The median age was 3 years, and 53% were female. Eighty-seven percent had visited sub-Saharan Africa. The reason for the trip was to visit friends and relatives in 43% of cases, immigration in 45% and tourism in 9%. Four percent received prophylaxis against malaria. Twenty-four received a diagnosis of malaria, without a history of fever in 6. Other tropical infections included dengue, chikungunya and liver abscess. Five children received diagnoses of communicable infections (HIV, tuberculosis, meningitis, hepatitis A, giardiasis), and 67 children of common infections.

Conclusions: malaria was the second most frequent diagnosis in children with fever following travel to an endemic area, after common infections. In our study, the initial presentation of life-threatening imported diseases were indistinguishable from those banal infections.

Key words:
• Immigrants
• Malaria
• Traveller
• Tropical infections

Patología importada en urgencias

Resumen

Introducción: el incremento en los últimos años de los movimientos migratorios y de viajeros a países de escasos recursos ha producido un repunte en la incidencia de enfermedades infecciosas raras en nuestro medio. El objetivo del estudio fue describir las características de los pacientes con patología infecciosa importada en urgencias.

Métodos: se realizó un estudio retrospectivo entre 2012 y 2019. Se incluyeron los menores de 16 años atendidos en el Servicio de Urgencias del Hospital de Torrejón, con antecedentes de viaje internacional tres meses antes de la visita. Se recogieron datos demográficos y clínicos. Los diagnósticos se agruparon en tres categorías: infección tropical (típicamente importada de áreas tropicales), infecciones transmisibles (incluyendo infecciones de distribución global más prevalentes en áreas tropicales, como la tuberculosis) e infecciones comunes.

Resultados: se incluyeron 100 niños. La mediana de edad fue de 3 años y el 53% fueron mujeres. El 87% habían viajado desde África subsahariana. El motivo del viaje fue visitar a familiares y conocidos (43%), inmigrantes (45%), turistas (9%). Recibieron profilaxis contra la malaria (paludismo) un 4%. Fueron diagnosticados de malaria 24 niños, 6 sin historia de fiebre. Otras infecciones tropicales fueron dengue, *chikungunya*, absceso hepático. Cinco niños fueron diagnosticados de infecciones transmisibles (VIH, tuberculosis, meningitis, hepatitis A, giardiasis) y 67 niños, de infecciones comunes.

Conclusiones: la malaria fue el diagnóstico más frecuente en niños con fiebre después de un viaje a zona endémica, tras las infecciones comunes. En nuestro estudio, los síntomas iniciales de las enfermedades importadas potencialmente mortales eran indistinguibles de las infecciones banales.

Palabras clave:
• Infecciones tropicales
• Inmigrantes
• Malaria
• Paludismo
• Viajero

INTRODUCTION

The increase in migratory movements combined and the exponential growth of international travel in recent years, from 25 million in 1950 to 1.4 billion in 2018,[1] have contributed to an upsurge in the incidence of infectious diseases that are uncommon in Spain. In addition, the current speed of travel makes it possible for diseases with a short incubation period to be diagnosed and treated in Spain after arrival. Ensuring adequate knowledge and management of these diseases is one of the possible strategies to prevent their emergence.[2,3]

According to data from the Instituto Nacional de Estadística (National Institute of Statistics of Spain), the immigrant population in Spain has experienced an exponential increase, growing from 719 647 in 1998 to 6 373 463 as of October 1, 2023, currently amounting to 10% of the total population of Spain. Out of the total immigrant population, one million individuals are younger than 16 years, and most reside in large cities, such as Madrid.[4]

The largest group of traveling minors are those who travel to visit family in the country of origin, a group known as *visiting friends and relatives* (VFR), in which seeking care before travel to take preventive measures is uncommon.[5] In addition, these minors tend to be younger, travel for longer periods, visit areas with higher risk and live in conditions similar to those of their country of origin. This exposes them to diseases that are rare or nonexistent in Spain and, absent vaccination, may lead to the development of severe disease.

The aim of our study was to describe the clinical and epidemiological characteristics of children who visited the pediatric emergency department of our hospital following international travel.

PATIENTS AND METHODS

We conducted a retrospective study between March 2012 and December 2019. The study was approved by the Regional Research and Ethics Committee of the Community of Madrid with the study code PED-IMPORT-2019. The study was conducted in a secondary care hospital within the public health system of the Community of Madrid that manages approximately 29 000 pediatric emergency care visits a year. The sample included children aged less than 16 years who visited the emergency department with a history of international travel in the past 3 months.

The hospital is located in a city in eastern Madrid and serves a health area with a catchment population of 136 331 inhabitants, of who 25 993 (19%) are immigrants.[6]

We collected data on demographic and clinical variables: age, sex, travel destination (country), reason for traveling (categorized into VFR, tourism, immigration), duration of travel, prophylaxis, specific vaccination before travel, symptoms, diagnostic tests, diagnosis, treatment and outcomes.

The duration of travel was categorized into short (< 30 days), intermediate (30-180 days) and long (> 180 days).

We grouped patients according to the presenting complaint as follows: febrile illness, gastrointestinal illness, other. We also grouped them by disease category: tropical disease (infectious disease typically imported from tropical areas, such as malaria), communicable disease (including infections with a global distribution, but more prevalent in tropical areas, such as tuberculosis or human immunodeficiency virus [HIV]) and common infectious disease (with similar distributions in tropical and nontropical countries).

Diagnostic tests were performed depending on the country of origin and, if the patient came from a region endemic for malaria, included: malaria rapid diagnostic test (RDT), thick blood film and malaria polymerase chain reaction (PCR) test.

Serologic tests for detection of *chikungunya*, dengue y *zika*, among others, were used according to the guidelines presented in the yellow book of the CDC.[7] In some patients, serologic tests for detection of syphilis, HIV, hepatitis b (HPV) and hepatitis C (HCV) were also performed based on the judgment of the clinician in charge.

The case definition of malaria was direct visualization of the parasite on examination of a thick blood smear and/or positive malaria RDT and/or PCR test. The severity of malaria was graded according to the recommendations of the Sociedad Española de Infectología Pediátrica (SEIP, Spanish Society of Pediatric Infectious Disease).[8]

The case definition of HIV infection was a positive ELISA test confirmed by PCR detection of HIV or a detectable viral load in patients aged less than 18 months (in 2 separate measurements); or a positive ELISA test confirmed by western blot in patients aged more than 18 months.

In the case of infection by dengue, zika or chikungunya, the diagnosis was based on a positive IgM antibody test confirmed in a second specimen.

The remaining diagnoses were defined based on commonly used methods, such as radiological features or the findings of microbial culture, serology tests or PCR.

The statistical analysis was performed with the software package SPSS 15.0 for Windows. We calculated the median and interquartile range (IQR) for quantitative variables. For qualitative variables, we obtained the absolute frequency and percentage distributions of the categories in each variable. We used the Fisher exact test to analyze qualitative variables.

RESULTS

During the study period, the pediatric emergency department received 200 909 visits from children aged less than 16 years. Of this total, we included 100 patients who reported international travel in the past three months.

Table 1 summarizes the general characteristics of the sample. Fifty-three percent of the patients were female, and the median age was 36 months (IQR: 18.2-105.0). The median time elapsed between returning from the trip and the emergency department visit was 8 days (IQR: 5-160), with a majority of cases clustering in September.

Fifty-one percent of the children were born in Sub-Saharan Africa, while 43.5% were born in Spain. In 87% of the sample, the travel destination was sub-Saharan Africa.

With respect to the reason for traveling, 43% were VFR travelers and 45% were immigrants. Four children received malaria prophylaxis during the trip.

Table 2 presents the clinical characteristics of the patients. The chief presenting complaints were fever (72%), respiratory symptoms (6%), diarrhea (5%), cutaneous symptoms (4%) and other (13%). Sixty-four percent of the patients received a diagnosis of common infectious diseases, 27% of tropical diseases and 9% of communicable diseases.

Thirty-four percent of the children required admission, and 38% of admitted patients were VRF travelers. The most frequent diagnosis in hospitalized children was malaria (44%). None of the children died or developed long-term sequelae. The outcome was favorable in every case.

Table 3 presents the results of the analysis by infection category.

Tropical infectious diseases

- **Malaria** (Table 4). Twenty-four patients received a diagnosis of malaria. In 75% of cases, fever was the cardinal symptom. Sixty-two percent of the children diagnosed with malaria were immigrants and 33% VFR travelers. The physical examination revealed hepatomegaly in 13% and splenomegaly in 17%.

- In the laboratory tests, 3 children had hemoglobin levels below 10 g/dL. The RDT was positive for *Plasmodium falciparum* in 23 patients, one of whom had coinfection with *Plasmodium vivax*. The thick blood smear was positive in 14 patients. The median parasite concentration was less than 1% (IQR <1-1%).

Of these patients, 63% required hospital admission. Five of them required intravenous treatment, 4 due to oral intolerance, one due to severe disease. Five received quinine plus clindamycin, which was switched to IV artesunate during the

Table 1. General characteristics of the patients (n = 100)		
Age	Median: 36 months (IQR: 18.2-105)	
Sex	53/100 female	
	47/100 male	
Reason for travel	VRF	43/100
	Immigrant	45/100
	Tourism	9/100
	Not documented	3/100
Days elapsed from returning from travel and emergency department visit	8 days (IQR 5-160)	
Place of birth of the child	Sub-Saharan Africa:	51/100
	• Equatorial Guinea	42
	• Nigeria	2
	• Cameroon	1
	• Ivory Coast	1
	• Guinea Bissau	1
	• Sub-Saharan Africa, country not specified	4
	Spain	43/100
	Other:	6/100
	• Venezuela	1
	• Dominican Republic	1
	• Not specified	4
Travel destination	Sub-Saharan Africa:	87/100
	• Equatorial Guinea	64
	• Nigeria	8
	• Guinea Bissau	1
	• Ivory Coast	1
	• Sub-Saharan Africa, country not specified	13
	Others:	13/100
	• Dominican Republic	8
	• Venezuela	2
	• Costa Rica	1
	• Morocco	1
	• Paraguay	1
Duration of travel (documented in n = 40 patients)	>60 days: 28 patients	
	30-60 days: 5 patients	
	<30 days: 7 patients	
	Median: 60 days (IQR: 30-272.5)	

VFR: visiting friends and relatives.

hospital stay in two of them. Sixteen percent (4/24) of these patients received antibiotherapy for suspected associated bacteremia. Two children required transfusion of blood products.

An infant aged 8 months required transfer to the intensive care unit (ICU) due to hypotension and altered level of consciousness, where she received supportive care and antimalarial treatment (artesunate), which achieved improvement.

Table 2. Presenting complaints, diagnoses and hospital admission (n = 100)		
Presenting complaint	Fever	72/100
	Respiratory symptoms	6/100
	Diarrhea	5/100
	Cutaneous symptoms	4/100
	Others	13/100
Diagnosis after evaluation	Common infections	67/100
	Imported infections	27/100 (24 malaria)
	Communicable infections	5/100
Hospital admission • Age • Most frequent diagnosis	34/100 Median age: 36 months Malaria 13/34	
	None of the children died or developed sequelae	

- **Other tropical diseases.** Diagnosed in 4 patients. Two received a diagnosis of infection by dengue virus, without complications. Infection by chikungunya virus was diagnosed in a child after travel to the Dominican Republic. One child received a diagnosis of amoebic liver abscess.

Communicable diseases

Diagnosed in 5 patients: HIV infection, pulmonary tuberculosis, meningitis secondary to group W meningococcus infection, hepatitis A virus infection and *Giardia* infection. Here were no cases of HCV infection, HCB infection or syphilis.

Common infections

Diagnosed in 67 patients: upper respiratory tract infection (48), acute diarrhea (9), cutaneous infection (3), pneumonia (3), pyelonephritis (2), bacteremia caused by nontyphoidal *Salmonella* (1) and pneumococcus (1).

DISCUSSION

The frequency of imported diseases is increasing in Spain, and diseases associated with travel and immigration are becoming common in clinical practice.

Table 3. Analysis by infection category (n = 100)	
Common infections:	**67/100**
• Upper respiratory tract infection	48/100
• Diarrhea	9/100
• Cutaneous infection	3/100
• Pneumonia	3/100
• Pyelonephritis	2/100
• Bacteremia by nontyphoidal *Salmonella*	1/100
• Pneumococcal bacteremia	1/100
Communicable infections:	**5/100**
• HIV	1/100
• Pulmonary tuberculosis	1/100
• Meningitis due to group W meningococcus	1/100
• Hepatitis A infection	1/100
• *Giardia* infection	1/100
No cases of HCV, HBV or syphilis were detected	
Tropical infections	**28/100**

HBV: hepatitis B virus; **HCV:** hepatitis C virus; **HIV:** human immunodeficiency virus.

Table 4. Characteristics of patients with a diagnosis of malaria (n= 24)		
Malaria		**24/100**
Presenting symptoms	Fever	18/24 (75%)
	Afebrile, visited ED for other reasons:	6/24 (5 immigrants/1 VRF) (25%)
	• Exanthema	2
	• Vomiting	1
	• Cold symptoms	1
	• Asymptomatic	2
Patient characteristics	Immigrant	15/24 (62.5%)
	VRF	8/24 (33.5%)
	Reason for travel not documented	1/24 (4%)
Physical examination	Hepatomegaly	3/24 (13%)
	Splenomegaly	4/24 (17%)
Laboratory tests	Hb <10 g/dL	3/24 (13%)
	Positive RDT:	
	• *Plasmodium falciparum*	23/24 (95%)
	• *P. falciparum/P. vivax* coinfection	1/24 (4%)
	Positive thick blood smear	14/24 (58%)
	Median parasite concentration in blood < 1%	
	Plasmodium falciparum PCR test:	
	• *P. falciparum*	15
	• *P. falciparum/P. vivax* coinfection	1
	• No detection	8
Malaria-related admissions	Required admission	15/24 (63%)
	Median age: 6.5 years	
	Intravenous treatment:	5/24 (20%)
	• Oral intolerance	4/24 (16%)
	• Malaria with indicators of severity	1/24 (4%)
	Intravenous treatment received:	
	• Quinine + clindamycin	5/24 (20%)
	• Switch to artesunate IV	2 of the above 5
	Oral treatment:	
	• Atovaquone-proguanil	12
	• Oral artemisin	2
	• No oral pharmacotherapy (fully intravenous regimen)	1
	• Oral treatment + primaquine for *P. vivax*	2
	Suspected associated bacteremia	4/24 (16%)
	Transfusion of blood products	2/24 (8%)
	Admission to PICU	1/24 (4%)

PCR: polymerase chain reaction; **PICU:** intensive care unit; **RDT:** rapid diagnostic test (malaria); **VFR:** visiting friends and relatives.

Immigrant children from low-income countries are a particularly vulnerable group due to nutritional deficiencies, crowded living conditions, lack of access to drinking water and absent or incomplete vaccination. This increases their risk for infectious diseases such as tuberculosis, measles or hepatitis A or B.[9] On the other hand, VFR travelers lack immunity due to the lack of exposure to these diseases in their countries of origin and usually do not take preventive measures, so they are at risk of more severe forms of disease.[10,11] Most patients in our study were immigrants and VFR travelers (88%).

In the cohort under study, respiratory infection was the most frequent diagnosis in children who presented to the emergency department following international travel. However, it is worth noting

that one third of travelers (33%) received diagnoses of tropical and communicable diseases associated with a high morbidity and mortality if they are not treated appropriately, so one third of travelers required hospital admission.

We ought to highlight the considerable number of patients with a diagnosis of malaria, all caused by *P. falciparum*, which carries a risk of severe disease and cerebral involvement. This high percentage is partly explained by the fact that the travel destination was Sub-Saharan Africa in 87% of the sample. According to the World Health Organization, up to 20% of imported malaria cases affect children, of who up to 10% develop severe forms of disease, underscoring the importance of early diagnosis and treatment.[12] In agreement with the description of other cohorts, in most children with malaria the findings of the physical examination were normal and the initial symptoms similar to those of common infections.[13]

Children with malaria may present with nonspecific symptoms, such as vomiting, diarrhea or abdominal pain, which may be interpreted as gastroenteritis; they may also experience respiratory symptoms suggestive of pneumonia. In addition, in our group, 25% of patients with malaria did not develop fever, so travel history, not just the presence of fever, should alert clinicians to the possibility of malaria.

A boy who received a diagnosis of malaria had returned from Africa approximately 3 months earlier. Although 98% of malaria cases are diagnosed within 3 months of travel, 2% are detected up to six months later.[14]

Diagnosis was easy thanks to the availability of rapid testing, with a sensitivity of 99%, compared to the thick blood film, which had a sensitivity of 58% in our cohort. The observed difference in sensitivity was probably due to a low parasite density in our patients, as none had received treatment in the preceding days. The use of RDTs is a simple and observer-independent technique that allows early initiation of treatment.[15,16]

Ninety-six percent of the patients included in our study had not taken preventive measures during the trip. These missed opportunities for the health system to prevent disease have been described in similar studies. The most significant barriers include difficulty accessing health care prior to travel and the cost of prophylaxis. Identifying potential travelers and promoting the use of prophylaxis at the primary care level could have a positive impact on imported disease.[17,18]

There are limitations to our study, such as the small sample size or the risk of selection bias, as we excluded patients presenting to the emergency department with banal diseases, in whom the history of travel was not specifically addressed.

CONCLUSION

In conclusion, following common infectious diseases, malaria was the most frequent disease in this cohort of febrile children following travel to endemic areas. The initial symptoms of potentially lethal imported diseases were indistinguishable from those of banal infections. Most children in our study had not taken preventive measures before or during travel, which highlights the missed opportunities for disease prevention in the health care system.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare in relation to the preparation and publication of this article.

AUTHORSHIP

All authors contributed equally to the development of the published manuscript.

ABBREVIATIONS

ICU: intensive care unit • **HBV:** hepatitis B virus • **HCV:** hepatitis C virus • **HIV:** human immunodeficiency virus • **IQR:** interquartile range • **PCR:** polymerase chain reaction • **RDT:** rapid diagnostic test • **SEIP:** Sociedad Española de Infectología Pediátrica • **VFR:** visiting friends and relatives.

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