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Chagas disease in the United Kingdom: A review of cases at the Hospital for Tropical Diseases London 1995–2018. The current state of detection of Chagas disease in the UK

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ABSTRACT

Background: Chagas disease (CD), is a parasitic disease endemic in Latin America. Presentation in non-endemic areas is either in the asymptomatic indeterminate phase or the chronic phase with cardiac and/or gastrointestinal complications.

Methods: The Hospital for Tropical Diseases (HTD) based in central London, provides tertiary care for the management of CD. We reviewed all cases managed at this centre between 1995 and 2018.

Results: Sixty patients with serologically proven CD were identified. Most were female (70%), with a median age at diagnosis of 41 years. Three quarters of the patients were originally from Bolivia. 62% of all patients were referred to the HTD by their GP. Nearly half of the patients were asymptomatic (47%). Twelve patients had signs of cardiac involvement secondary to CD. Evidence of gastrointestinal damage was established in three patients. Treatment was provided at HTD for 31 patients (47%). Most patients (29) received benznidazole, five of them did not tolerate the course and were switched to nifurtimox. Of the seven patients receiving this second line drug, five completed treatment, whilst two interrupted it due to side effects.

Conclusions: Despite the UK health system having all the resources required to diagnose, treat and follow up cases, there is lack of awareness of CD, such that the vast majority of cases remain undiagnosed and therefore do not receive treatment. We propose key interventions to improve the detection and management of this condition in the UK, especially in pregnant women and neonates.

1. Introduction

Chagas disease (CD) was described by the Brazilian physician and epidemiologist Carlos Chagas in 1909. Caused by the protozoan parasite *Trypanosoma cruzi*, (*T. cruzi*) transmitted by the bite of reduviid bugs, it is endemic to parts of North, Central and South America. Six to seven million individuals worldwide are infected [1,2].

In Europe, a non-endemic area, there were estimated to be between 68,000 and 122,000 infected individuals in 2009, with only 4290 diagnosed [3,4]. In 2015, the prevalence of Chagas disease in Latin American migrants living in Europe was estimated at 4.2% [5].

CD has an acute phase, which is amenable to treatment if detected early. It then enters an indeterminate (asymptomatic phase) for decades. 30–40% of those infected go on to develop cardiac or gastrointestinal complications [1]. The global economic cost of this disease is around $7 billion a year [6].

CD is primarily a disease of poverty and poor housing. However, *T. cruzi* is also transmitted by blood, organ donation, and vertically from mother to child. International migration patterns and these methods of potential transmission make vertical, blood-borne and organ-transmitted acquisition of *T. cruzi* a possibility in non-endemic countries [4].

The reasons for there being a low-detection rate are many-fold:

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Abbreviations

CD	Chagas Disease
HTD	Hospital for Tropical Diseases
T. cruzi	*Trypanosoma cruzi*

i. Lack of awareness among European specialists and general practitioners.
ii. Challenges in screening: lack of systems in place to request the initial serological test in primary health care and budgetary constraints.
iii. The affected communities may not access health services [7] or choose to limit their access to health care in some instances in fear of their illegal migration status being disclosed.
iv. Delay in diagnosis due to the asymptomatic nature of the chronic phase of the disease [3].

The Hospital for Tropical Diseases (HTD) London is a secondary and tertiary referral centre for *T. cruzi* cases linked with the UK National Parasitology Reference Laboratory. As a specialist centre, we reviewed all cases we diagnosed and managed between October 1995 and November 2018.

2. Materials and methods

Assessment of new patients with Chagas disease. Patients seen in the HTD clinics for *T. cruzi* infection may present as i) a self-referral with a previous diagnosis from their country of origin, ii) a referral from primary health care, iii) a referral from another speciality or from infectious diseases units elsewhere, following a positive serological test.

At presentation, a detailed travel, family and clinical history is taken. Patients' sera are tested first by ELISA. Any ELISA positive sera are tested by IFAT with titre. Those positive in both tests are considered confirmed cases. PCR for *T. cruzi*, an HIV test, chest x-ray, ECG and an echocardiogram are also offered. In the presence of cardiac or gastrointestinal complications, patients may be referred to the appropriate team for assessment. Antiparasitic treatment may also be offered when indicated [2].

Asymptomatic patients are reviewed annually with an ECG, *T. cruzi* serology (ELISA) and PCR. At 5-yearly follow-up, they are offered a repeat echocardiogram. Repeat chest x-rays are no longer requested routinely. Other tests e.g. 24 h Holter ECG monitoring, abdominal x-ray or specific gastrointestinal investigations are requested if symptoms warrant.

The initial laboratory diagnosis of chronic CD is made primarily by serological methods. At HTD, serum samples are screened using a commercial recombinant antigen-based ELISA assay and, if positive, the result is confirmed using an in-house indirect fluorescent antibody test (IFAT) using whole trypomastigotes. At subsequent follow-up appointments sera are tested by ELISA only [8]. PCR molecular testing is undertaken prior to commencing treatment and in subsequent follow-up clinic appointments. Treatment options are benznidazole as first line, or nifurtimox [2]. The treatment regimens in use at the Hospital for Tropical Diseases are benznidazole for 60 days (5 mg/kg/d in 2 divided doses) or nifurtimox for 60 days, (8 mg/kg/d in 3 divided doses). Full blood count and liver function tests are checked during treatment at two weekly intervals.

2.1. Data collection

Patients diagnosed as seropositive for *T. cruzi* between July 1995 and March 2018 were identified from the HTD Department of Clinical Parasitology laboratory database and data collected in a questionnaire designed for the audit. Information was extracted from patient notes and electronic records. Attempts to collect missing data were made by contacting patients' GPs and referring clinicians across the country.

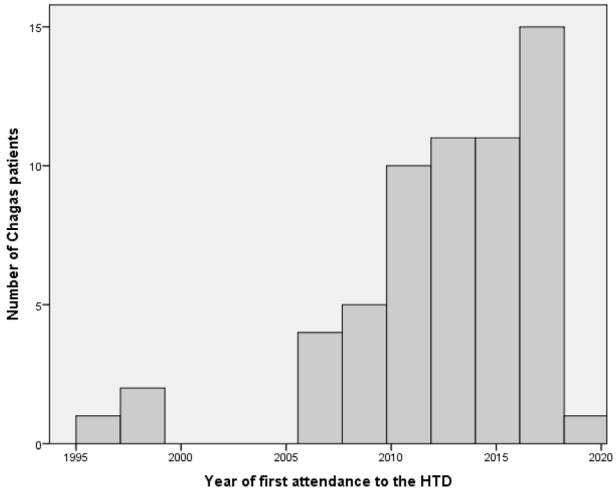

Fig. 1. Trend in presentation of CD cases at the Hospital for Tropical Diseases (1995–2018).

Audit data collected included age, sex, referral pathway, geographical origin, travel history, family history, clinical history, laboratory and radiology results, treatment and follow up. For female patients, data relating to children and pregnancies were also collated.

The clinical status of CD in seropositive patients was graded as indeterminate, cardiac, digestive or cardiodigestive according to Kuschnir (cardiac) [9] and Pinazo-Rezende (digestive) classifications [1,10,11].

3. Results

Between July 1995 and March 2018, 78 patients with positive *T. cruzi* serology results were identified, 16 were excluded from the analysis as they had never been seen at HTD; two patients were excluded as the serology results were thought to be false positives. The assessment and management by the HTD of 60 patients with serologically proven CD is presented below. The distribution of cases seen at HTD during the period reviewed is represented in Fig. 1.

Although there are more Latin American women (55%) than men living in England & Wales as a whole [12], this only partly explains our figures, as in our series, the percentage of patients who were female was greater, at 70% (n = 42). It points towards a difference in level of healthcare access by gender in Latin Americans in the UK, but is not explained by antenatal screening, as although 36/42 (86%) of our female patients were of child-bearing age, only three were pregnant when first seen. This is disappointing and may reflect the fact that there is no systematic antenatal screening programme for Chagas disease in the UK.

The median age at presentation at the HTD was 41 years (range: 18–67 years). In two cases, the country of origin was not recorded. The rest of the cohort was originally from CD endemic areas in South America. Most of patients were originally from Bolivia (45, 75%), followed by Brazil (4, 7%), Colombia (3, 5%), and the remaining 8 (15%) from Argentina, Chile, Ecuador, Uruguay and Venezuela. In the majority of patients (54, 90%) the country of birth of the patient, country of exposure and country of origin of patient's mother coincided. One patient did not know the country of origin of her biological mother as she was adopted, another patient was born in Uruguay from a Brazilian mother.

Two thirds of the cohort (40, 67%) were already aware of their CD diagnosis on arrival in the UK. Just over half of the patients were diagnosed in their home countries (31, 52%); followed by those diagnosed in Spain (9, 15%). Of the patients diagnosed in the UK (20, 33%),

the trigger for diagnosis was being originally from an endemic area (18, 90%), two patients from endemic areas were identified in specific situations (one on attending an antenatal clinic and another on screening for blood donation).

All women diagnosed with CD were older than 18 years when first presenting at the HTD; most (36/42; 86%) were of child bearing age (defined as 15–49 years old). Three patients were pregnant when first seen (3/42; 7%); for five women of child bearing age (5/42; 12%) there was no record of enquiring about pregnancy, offering or performing a pregnancy test.

More than half the female CD patients had offspring (26/42; 62%); testing or offering to test children was only documented for 22 of the 26 mothers with positive CD serology. In 6 cases (6/42; 14%) no information was available on whether or not the female CD patient had children.

Information regarding patients' relatives is presented in Table 1. Excluding one patient who was thought to have acquired the infection through blood transfusion, the mode of transmission for the rest of the patients was unclear. Nine patients reported their mother had been diagnosed with CD. Four patients reported their mother and at least one of their siblings had been diagnosed with CD making congenital infection a possible route of transmission, though in a region with active vectorial transmission, that route is also possible in the same household.

The patients accessed HTD through different pathways. Most patients were referred by their general practitioners (37, 62%), followed by patients transferred from specialist clinics (17, 28%), and one in ten patients self-presented (6, 10%). The majority of patients (50, 83%) were referred for consideration of treatment.

Just under half the patients were asymptomatic on their first visit to HTD (28, 47%). Among those with symptoms (32, 53%), half 16 (26.7%) reported cardiac symptoms (16/32, 50%) and 11 (18.3%) gastrointestinal symptoms (11/32, 34%), and five patients reported symptoms affecting both organ systems (5/32, 16%). However, reported symptoms such as constipation or palpitations may have other causes and not necessarily be related to Chagas disease. For example, 33% of patients with cardiac symptoms were Kuschnir grade 0 (Table 2) and 75% of patients with gastrointestinal symptoms were Rezende grade 0 (Table 3). No chagomas or acute CD presentations were identified.

HIV testing was not performed systematically for all patients but at the discretion of the treating physician. There was one case of co-infection in this cohort, but the patient was known to be HIV-positive at referral.

As per the audit inclusion criteria, patients had a positive ELISA antibody test for *T. cruzi*. Thirteen patients did not have an IFAT result recorded; for those who had a result available, both the median and mode IFAT titre was 1:160 (range 1:20 [the screening dilution] which is weakly positive to 1 > 2650 very strongly positive). Of eight PCR positive patients, seven had IFAT titres of greater than or equal to 1 in 320 and the eighth had a titre of 1 in 160, suggesting that higher IFAT titres were associated with PCR positivity, indicative of persisting parasite multiplication. Fifty six patients had a *T. cruzi* PCR performed. This test was positive in 8/56 (14%) and equivocal in 2/56 (4%). One of the patients with an equivocal test at initial diagnosis was retested post-treatment and was negative, the other patient was lost to follow up. More than three quarters of patients had a negative PCR (46/56, 82%). All previously treated patients were negative by PCR on first presentation to HTD. All positive PCR cases were among untreated patients and they had higher IFAT titres (1:160 and above). IFAT and PCR positivity are shown in Fig. 2.

Due to the retrospective nature of the study, the diagnostic tests were performed at the discretion of the treating physician, no systematic protocol was followed, but a unified policy for investigation and case management is now in place.

Routinely, patients would be screened for cardiac abnormalities, ECG and echocardiogram results were available for most patients (57/60, 95% and 52/60, 87%). The use of Chest X-ray is decreasing, whilst 24 h ECG tapes have been used more frequently in recent years. A third of patients with physician-diagnosed cardiac symptoms (7/21) had normal cardiac tests, whilst there was no correlation between the severity of symptoms reported and Kuschnir grading. Among asymptomatic patients (4/28, 14%) had incidental findings on ECG or echocardiogram. Over half of the patients (32/60, 53%) had an abdominal X-ray performed, upper and lower gastrointestinal studies were requested based on symptoms. Results of Kuschnir and Rezende grading of symptomatic patients are shown in Tables 2 and 3

Seven patients (7/60, 12%) had already been treated for CD when presenting to HTD, and were considered to be cured. Five patients (5/60, 8%) were lost to follow up before treatment could be discussed. Eight patients (8/60, 13%) were considered ineligible for antiparasitic drug treatment by age criteria, six (6/60, 10%) declined treatment and three (3/60, 5%) are on the waiting list to be treated. Initially, we were cautious and limited treatment to younger age groups (younger than 50 years) due to concern about drug toxicity in older patients. We now consider drug treatment in discussion with patients from any age group, balancing the potential benefits versus risk of side-effects [13].

Just over half of the cohort (31/60, 52%) received treatment at HTD. Most patients received benznidazole as first line (29/31, 94%), more than two thirds (20/29, 69%) reported side effects. The most common side effect from benznidazole therapy was a skin rash. This was treated with antihistamines and most patients were able to continue and complete the course of treatment.

However, five (5/29, 24%) did not complete the course and were switched to nifurtimox. In addition to those five, two patients were started directly on nifurtimox. Of the seven patients on nifurtimox, five (71%) reported side effects, four (57%) completed the course, but the other three (42.8%) discontinued treatment. Nifurtimox most commonly led to gastrointestinal side effects, but one patient developed high fever and myalgia, severe enough to require hospital admission.

Regarding access to treatment, cost is not a barrier to receiving antiparasitic drugs for Chagas disease. In the UK National Health Service, there is no charge for drugs received as an in-patient. As at May 2020, outpatients pay only GBP 9.15 for each drug prescribed so for example, a whole course of benznidazole would only cost them that amount. Furthermore, patients may claim exemption from the prescription charge as follows: Under 16, aged 16–18 and in full time education, aged 60 or over. Pregnant women and those who have had a baby in the last 12 months. Patients receiving benefits, tax credits, or on low income.

Two thirds of the patients (40/60; 66%) are still followed up routinely at HTD. Just over a quarter (16/60; 27%) were lost to follow up; 4 patients were discharged from clinic. The children of 10 women affected by CD were tested and were all negative. No cases of vertical transmission were identified.

4. Discussion

Due to the changing patterns of migration from Latin America, either directly or indirectly via Spain, CD is an increasing and under recognized public health problem in the UK, largely due to the fact that it is commonly asymptomatic. Funded by the European Union, COHEMI (COordinating resources to assess and improve HEalth status of MIgrants from Latin America) looked at health policies to control blood,

Table 1
Infection status in relatives of our Chagas disease patients.

	Mother	Siblings	Other family members
Known Positive	12/60 (20%)	15/60 (25%)	17/60 (28%)
Known Negative	9/60 (15%)	9/60 (15%)	7/60 (12%)
Not known/not recorded	39/60 (65%)	36/60 (60%)	36/60 (60%)

Table 2
Kuschnir classification for patients with cardiac symptoms.

ECG	Left Ventricular Size	CHF	Grade	Patients with cardiac symptoms N = 21
Normal	Normal	None	0	7 (33%)
Abnormal	Normal	None	I	8 (37%) (includes one patient with normal ECG but abnormal 24 h tape)
Abnormal	Enlarged	None	II	2 (10%) (based on echocardiogram)
NA	Enlarged	Present	III	2 (10%)

* There were no results available for 2 patients who had been lost to follow up.

organ and congenital transmission of CD. The recommendation was that all countries in Europe should have in place policies to ensure screening for CD in blood and transplant donation; and for antenatal and congenital cases; implementation of these policies should be monitored and regularly evaluated [4].

Basile et al. (2011) estimated that there were between 6111 and 12,201 *T. cruzi*-infected migrants in the United Kingdom [3]. Although the UK shows a relatively low number of Latin American migrants compared to other populations, the expected prevalence of the disease in this group is 1.3–2.4% [14]. This is slightly lower than a 2015 study in which the prevalence of Chagas disease in Latin American migrants living in Europe was estimated at 4.2% [5]. We believe this is due the UK having a lower proportion of people from the countries with higher Chagas disease prevalence, Bolivia, Honduras, El Salvador and Paraguay than other European countries. Based on the estimates of Basile et al. [3], there is 99% under-diagnosis of CD in the UK. Furthermore, there has been a surge in Latin American migration to the UK. There were an estimated 145,500 Latin Americans living in London in 2011, a four-fold increase since 2001, the main nationalities being Brazilian, Colombian, Ecuadorian, Peruvian and Bolivian. Most CD in Europe is found amongst Bolivians [15–19].

Since the global economic recession, increasing numbers of Latin American migrants have arrived in the UK from Spain. Latin Americans in London have up to 85% employment rates, but a large number do not access public services and a fifth have never been to a GP. Access to testing and care of *T. cruzi* infection is therefore a problem [7]. Latin Americans in London often work in manual/low-paid jobs and are not entitled to or do not claim sick pay. For this reason, attendance at clinic appointments may be difficult or impossible for them. Healthcare providers need to be aware of the magnitude of this problem, in order to access community groups and reach out to migrant communities. Disseminating information about testing and NHS services amongst this high-prevalence group would be an important public health intervention.

4.1. Blood and organ donation

Screening of CD in blood-banks has already been implemented in many European countries, such as Spain, Italy and Switzerland [4].

England was the first non-endemic country to introduce blood and organ screening for *T. cruzi* and implementing a programme of selective screening of high-risk individuals for antibodies has been successful [20]. Since the introduction of screening for *T. cruzi* infection in 1998, a total of 38,585 donors have been screened and only three positive cases

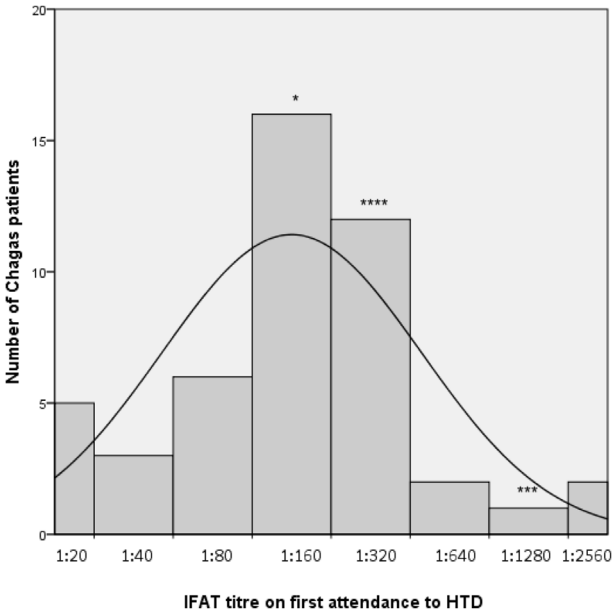

Fig. 2. IFAT titre distribution and positive PCR results.
*Number of positive PCR results at specified dilution.

identified. As well as minimising the risk of transmission, this screening process has a major benefit in reducing the loss of donors [20]. Prior to 1998, guidance suggested permanent deferral of at-risk individuals from blood donation. The Joint United Kingdom Blood Transfusion Services Professional Advisory Committee (JPAC) has implemented screening of at-risk blood products since 1999 [4].

Organ transplantation screening is recommended, but it is unclear whether it is universally applied [4]. The EU directive on solid organ transplantation does not specifically mention CD. National transplant organisations from Italy, Spain and the UK have sections on how to control *T. cruzi* transmission. According to the UK Department of Health's Advisory Committee on the Safety of Blood, Tissue and Organs (SaBTO) the patient assessment form includes a risk assessment for Chagas and subsequent serological testing [4].

4.2. Antenatal and congenital screening

When it comes to antenatal screening for CD in pregnant women

Table 3
Rezende classification for patients with gastrointestinal symptoms.

Oesophageal Diameter	Gross anatomy	Barium Swallow Study	Stage	Patients with GI symptoms N = 16
Normal	Normal	No retention	0	12(75%)
Normal	Tertiary contractions present	Small barium retention in lower oesophagus	I	2 (13%)
Mild to moderate dilatation	Greater number of tertiary contractions	Barium retention into mid-third of the oesophagus	II	0
Moderate to severe dilatation	Normal longitudinal axis maintained	Significant barium retention	III	1 (6%)
Severe dilatation	Longitudinal axis deviated		IV	0

*One patient was lost to follow up.

coming from endemic countries, this has also been shown to be cost-effective, but its implementation is still limited [21].

The Public Health England Migrant Health Guide states that healthcare practitioners should be aware of the risks of infectious and chronic disease in migrant groups. Serology should be requested if there is clinical suspicion of *T. cruzi* infection. Groups of particular concern include pregnant women and the infants of seropositive mothers [22].

The CD pooled prevalence rate among pregnant Latin American women living in Europe is 6.5% [23] with a transmission rate to newborns of 7.3% [24]. The prevalence of CD in pregnant Latin American women in the UK is not known, but thought to be similar to those European figures.

At present, routine antenatal screening for CD of at-risk mothers is not performed and most children who do become infected will follow an asymptomatic clinical course so remain undetected. Yet newborns with acute CD can be treated and cured easily. Furthermore, up to 30%–40% of vertically infected children will suffer cardiac, neurological and/or gastrointestinal disease, up to 5–15 years after infection [1]. Whilst treating patients with CD with anti parasitic treatment during the chronic phase has still not been clearly proven substantially to reduce the long-term complications related to the disease [18], treatment of infants within the first year of life results in almost 100% cure [25].

Even though it is estimated that about 3000 women per year from CD endemic areas receive maternity care in England, it seems that less than 6% of these women were tested in 2016 [26]. Despite the advice in the Migrant Health Guide, and in contrast to the situation of blood transfusion screening which is governed by law, in the UK there is currently no legislation and no targeted antenatal screening for diagnosis and treatment of vertically infected neonates—an intervention recommended by WHO because of its high treatment efficacy [27]. Screening programmes for Latin American migrants in antenatal care units and primary care centres in France, Germany, Italy, Switzerland and Spain have been shown to be cost-effective [28].

We strongly advocate a central directive to require those providing antenatal care to offer serological screening to pregnant women in at-risk groups. The *T. cruzi* antibody test is cheap and is available via the Public Health England Parasitology Reference Laboratory. Controlling vertical transmission of *T. cruzi* has been shown to be clinically and cost effective [21].

4.3. Screening of all asymptomatic individuals

Screening of asymptomatic individuals with latent CD has not yet been implemented, but recent cost-effectiveness studies suggest that screening and treating *T. cruzi*-seropositive individuals and following them up in the long term is a cost-effective strategy [28].

5. Future directions and unanswered questions

5.1. Treatment of the indeterminate phase

There are a number of unanswered questions relating to treatment of CD, not least which groups would benefit most from antiparasitic drug therapy, as there is variable uptake by our asymptomatic patients. The BENEFIT trial was the first large randomised controlled trial involving patients with CD, and examined whether trypanocidal therapy is efficacious in patients with early Chagas heart disease. The results showed no difference in cardiac deterioration in the treatment group compared to the placebo group [29]. There is no such trial for patients who have yet to develop CD-related complications, and most of our patients at HTD are in the indeterminate phase. Despite the lack of randomised controlled trials for patients in that phase, current data from smaller studies suggest some marginal beneficial effect of treatment of patients in the chronic phase [30]. Our aim at HTD is therefore to detect infection, offer antiparasitic drugs where appropriate and refer those with complications to specialist cardiac or gastrointestinal services before they reach an advanced stage of disease.

5.2. Co-infection with HIV and other immunosuppressed hosts

Concurrent infection with HIV can result in reactivation of asymptomatic CD [31] with individuals with CD4 T-cell counts below 200 cells/uL being at highest risk. Treatment must be considered in co-infected patients, hence serological testing is recommended [32,33]. Nonetheless, routine testing for *T. cruzi* infection in at-risk HIV positive patients has not been implemented in all centres in the UK.

The risk of reactivation is well established in solid organ transplantation. Case reports have been published regarding reactivation of CD with patients suffering from cancer or autoimmune diseases. However, the evidence is scarce and consensus guidelines for the management of these patients would be welcomed [34–36].

5.3. Chagas disease in travellers

So far, we have not identified any cases of *T. cruzi* infection in travellers to endemic areas. In Latin America, acai pulp and sugarcane juice have been associated with CD outbreaks [37]. This form of transmission is the one that potentially puts more travellers at risk. To minimise the risk of travel-acquired disease, we also suggest that clinicians and travel health specialists provide information regarding CD to those planning to travel to endemic areas, especially Bolivia and that clinicians include the differential diagnosis of CD in all migrants from and travellers to endemic areas, especially countries bordering the Gran Chaco region (Bolivia, Paraguay, Argentina) where there is significant ongoing transmission [38].

6. Conclusions

CD is an emerging, under-detected problem among Latin American migrants in the United Kingdom and there is a need to establish priorities to address the issue. We consider the following to be urgently required:

i. Implementation of antenatal screening for pregnant women from Latin America, particularly those from Bolivia. Women born in, or who have lived in, areas endemic for CD, or whose mothers were born in or lived in such areas, should be offered ante-natal serological screening.
ii. Implementation of post-natal monitoring of infants born to infected mothers, with treatment given if the child is found to be parasitaemic. Infants born to seropositive mothers should be closely monitored, including testing by PCR and microscopy at delivery and again at 6 weeks of age; if those tests are negative, repeat serology should be performed at 9 months of age
ii. To raise awareness of the disease among clinicians and in maternity clinics.
iv. Testing of Latin American migrants should be performed prior to undergoing immunosuppression and those found positive monitored for evidence of reactivation.
v. Offering screening for CD to HIV-positive patients of Latin-American origin or whose mother was born in an endemic area.
vi. Active case-detection from sentinel seropositive cases and instituting treatment.
vii. To assess the true epidemiological status of CD in the United Kingdom through surveillance (prevalence) studies.
vii. To set up an outreach programme to unearth undiagnosed cases among the Latin American migrant population, including strategies to reach the illegal migrants.
vii. A complete medical evaluation for those found to be seropositive, with referral to a tertiary centre for assessment and consideration of anti-parasitic treatment.

In summary, the Hospital for Tropical Diseases has specialist expertise in Chagas disease and is part of University College London Hospitals, a tertiary care centre incorporating advanced specialist cardiac and gastroenterology services and the Public Health England National Parasitology Reference Laboratory. Thus there is already appropriate provision of specialist services to look after patients with CD. The greater challenge is uptake of testing for this condition and access to care for those infected, as recommended in the Migrant Health Guide, but regrettably far from actioned. This situation requires urgent attention because of the risk of ongoing transmission and silent infection.

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CRediT authorship contribution statement

Marta González Sanz: Methodology, Validation, Data curation, Formal analysis, Writing - review & editing. **Valentina De Sario:** Methodology, Validation, Data curation, Formal analysis, Writing - review & editing. **Ana García-Mingo:** Methodology, Validation, Data curation, Formal analysis, Writing - review & editing. **Debbie Nolder:** Methodology, Validation, Data curation, Formal analysis, Writing - review & editing. **Naghum Dawood:** Methodology, Validation, Data curation, Formal analysis, Writing - review & editing. **Rosemarie Daly:** Validation, Data curation, Writing - review & editing. **Patricia Lowe:** Validation, Data curation, Writing - review & editing. **Sophie Yacoub:** Validation, Data curation, Writing - review & editing. **David AJ. Moore:** Methodology, Formal analysis, Writing - review & editing, Supervision. **Peter L. Chiodini:** Conceptualization, Methodology, Validation, Formal analysis, Writing - original draft, Writing - review & editing, Supervision.

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