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Incidence of *Rodentolepis nana* infection within people seeking asylum and refugees attending health screening at an integrated refugee health service

Kieran Killington[1,2*], Nicky Longley[1,2,3], Katherine Bowers[1,4], Humayra Chowdhury[1,2], Paola Cinardo[1,2], Laura Nabarro[2,4] and Sarah Eisen[2,3,5]

Abstract

Background *Rodentolepis (Hymenolepis) nana (R. nana)* is the most common cestode to infect humans, and whilst most infections are asymptomatic, those with a high burden of infection can present with abdominal pain, diarrhoea, or growth stunting. The Respond service, London, offers screening and treatment for common infections to people seeking asylum and refugees (PSAR), including testing for gastrointestinal parasites such as *R. nana*.

Methods We present a retrospective observational analysis of all positive *R. nana* results in patients screened by the Respond service between April 2016 and July 2023. A positive result was defined by the presence of *R. nana* ova on stool microscopy for ova, cysts and parasites (OCP) or *R. nana* DNA detection using the Novodiag® Stool Parasite assay (NSP), a cartridge based multiplex molecular assay. We explore incidence of *R. nana* infection and efficacy of treatment in PSAR presenting to an integrated refugee health service.

Results *R. nana* was identified in 54/1797 (3%) of patients who had a stool sample collected in the Respond service. Median age of patients was 15 years (interquartile range [IQR] 9–17), and 38/54 (70%) were male, reflecting the sex demographic of the cohort. Coinfection with other parasites occurred in 28/54 (52%) of the cohort. Of the 27 patients who tested positive for *R. nana* where their family members were also tested, 11 patients (41%) had family members who were also infected with *R. nana*. Treatment failure (defined as failure to clear *R. nana* detected by OCP/NSP after treatment with praziquantel) occurred in 43% of the patients for whom a clearance sample was returned.

Conclusions We show a significant prevalence of *R. nana* in people seeking asylum screened within the Respond cohort. We show significant clustering within family units and a relatively high treatment failure rate. We propose prompt treatment of positive cases to prevent transmission within families, and consideration of treatment of family units simultaneously to prevent re-infection.

Keywords Hymenolepis nana, Rodentolepis nana, refugees, migrant health

Background

Rodentolepis nana is the most common cestode infecting humans, particularly young children. It is commonly known as the "dwarf tapeworm" due to its small size, only 2–4 cm long and 1 mm wide, and differs from all other human tapeworms by being able to complete its entire lifecycle in a single host [1, 2]. *R. nana* is considered a

*Correspondence:
Kieran Killington
kieran.killington@nhs.net
Full list of author information is available at the end of the article

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zoonotic infection, as infected rodents and arthropod intermediate hosts represent a reservoir of infection; however, the commonest route of infection is via direct human-to-human contact [3, 4]. *R. nana* is found worldwide, in both resource-rich and resource-limited settings [5]. In the Western United States, prevalence was as high as 1.5% in patients experiencing gastrointestinal symptoms [6]. Increased prevalence is seen in those living in temperate climates, low socioeconomic status, crowded living conditions, and poor access to sanitation [7, 8]. Prevalence in refugee populations has been reported to be as high as 31–32%, in those living in Pakistan and South Sudan [8, 9].

R. nana tapeworms produce double-walled eggs (Fig. 1), which are immediately infectious after excretion, facilitating direct person-to-person transmission and reinfection within households [10, 11]. The eggs can survive up to 10 days in the external environment [12], and are able to contaminate food and water supplies, causing infection in the community [13]. *R. nana* is the only human-infecting cestode capable of autoinfection without an intermediate host, either due to eggs hatching in the gastrointestinal tract prior to reaching the external environment, or autoinfection from contaminated hands, so although each tapeworm has a short lifespan of 4–6 weeks, internal autoinfection allows the infection to persist for years [5, 12].

Most carriers are asymptomatic; however, those with high burden of infection can present with abdominal pain, diarrhoea, weakness, and growth stunting [14]. In exceptionally rare circumstances with concomitant immunosuppression, lethal invasive cases have been described, as well as malignant transformation [15, 16]. Epidemiological evidence shows that co-infection with other parasites is common, especially with *Giardia duodenalis* [17, 18] and that *R. nana* may contribute to poor development and nutritional deficiency seen in co-carriers of other infections [3].

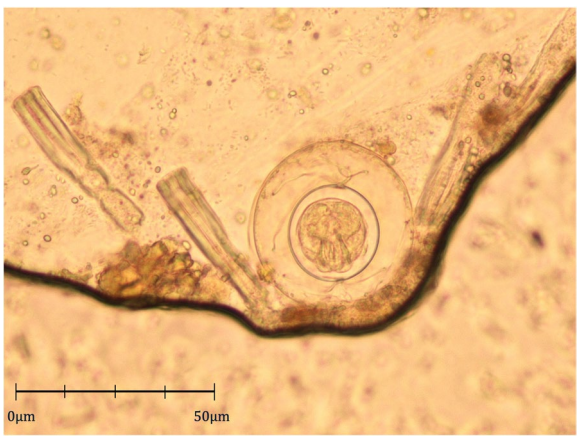

Fig. 1 Microscopy image of R. nana egg with scale bar (0-50 microns)

Those migrating from countries of high prevalence are recognised to be disproportionately affected by parasitic infections compared to the general UK population [19–23]. Recommendations for helminth screening vary, even between UK guidelines [24, 25]. Generally, stool testing for ova, cysts, and parasites (OCP) is recommended either routinely or based on risk in UK and European guidelines [20, 26] but implementation is often variable [21] The Respond service, London, (https://www.uclh.nhs.uk/our-services/find-service/children-and-young-peoples-services/respond-integrated-refugee-health-service) offers screening and treatment for common infections to people seeking asylum and refugees (PSAR), including children (accompanied and unaccompanied), adults and family groups. Respond is designed to meet the complex needs of people seeking asylum and refugees. Appointments with an infection and inclusion health practitioner are offered to patients following general practitioner (GP) registration, where a holistic, integrated care assessment is undertaken [27]. This includes testing for gastrointestinal parasites, including *R. nana*. Treatment is provided if diagnosed, and a follow up stool sample checked after 1 month to ensure clearance. We explore incidence of *R. nana* infection and efficacy of treatment in PSAR presenting to the 'Respond' integrated refugee health service.

Methods

Stool samples positive for *R. nana* within the Respond patient cohort between April 2016 and July 2023 were identified as follows. All positive results for *R. nana* from the parasitology lab within the relevant time period were identified using the search function of Winpath software from CliniSys [28], a laboratory information management system used at our NHS Foundation Trust. A positive result was defined as either detection of ova on concentrated stool microscopy for OCP or deoxyribonucleic acid (DNA) detection using a Novodiag® Stool Parasite assay (NSP) [29] Stool concentration is performed using the Apacor Midi Parasep® Faecal Parasite Concentrator system, as per manufacturer's instructions [30], following which two wet prep coverslips were examined. The NSP is a cartridge-based multiplex molecular assay which detects 26 distinct targets, encompassing protozoans, helminths and microsporidia in stool samples, which was performed according to manufacturer's instructions [29]. Testing strategy changed, unrelated to this work, in October 2022 when OCP was replaced by NSP, but all positives by NSP continued to be confirmed by OCP. The NSP was introduced, following a rigorous verification process, to address a rise in demand of testing samples

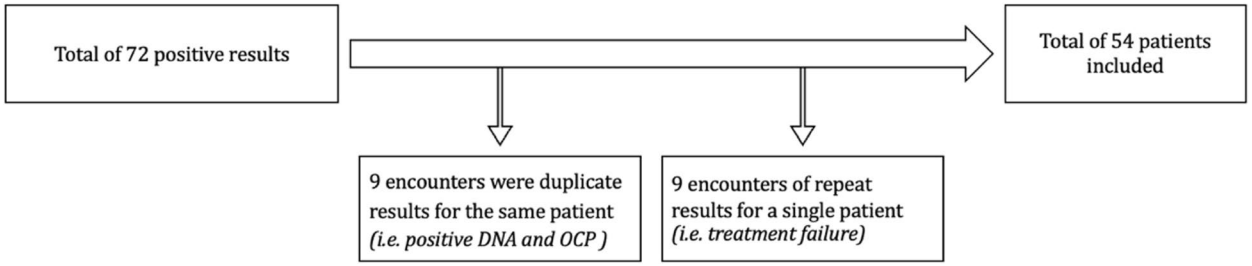

Fig. 2 Flow diagram to show identification of those patients seen within Respond who were positive for R. nana

by concentrated stool microscopy due to an increase in migrant screening. Where cysts of *Entamoeba histolytica/dispar* were identified on stool OCP, samples were sent for confirmatory polymerase chain reaction (PCR) testing to speciate. *Helicobacter pylori* was identified using a stool antigen assay. Pathology testing for this work was delivered by Health Services Laboratories, a joint venture between The Doctors Laboratory (TDL), the Royal Free London NHS Foundation Trust and University College London Hospitals NHS Foundation Trust. All positive results were then manually matched to electronic patient demographic and clinical data using the electronic patient healthcare record, to enable identification of those within the Respond cohort. Clinical and demographic data were anonymised at the point of collection and stored securely. Descriptive statistics were undertaken using Microsoft Excel (Version 16.86) [31].

Results

A total of 1797 patients within the Respond cohort provided stool for infection screening during the study time period. Seventy-two positive results for *R. nana* were identified, reflecting results of 54 individual patients (Fig. 2) and a prevalence of 3% in our cohort. Of 54 positive samples included in the study, 1 was from 2017, 5 from 2018, 5 from 2019, 4 from 2020, 5 from 2021, 25 from 2022 and 9 from 2023 (data until June). Of the 54 patients within the Respond cohort found to be positive for *R. nana*, 44/54 (81%) were under the age of 18 years; for these paediatric patients, median age was 13 years (IQR 8–16). Ten patients (19%) were over the age of 18 years; of these adults, the median age is 27 (IQR 19–32). The median time since arrival to the UK at the time samples were taken was 5 months (IQR 2–10 months). At the time of sampling, 22 patients were in hotel or hostel accommodation, 14 in foster care, and 18 in unknown accommodation types. Twenty-five out of 54 (46%) patients were unaccompanied by family members in the UK, 27/54 (50%) had family members who were tested as part of routine screening, 2/54 (4%) did not have any information regarding family contacts. Baseline characteristics are shown in Table 1.

Baseline characteristics in the study population were generally reflective of the Respond population, of which 75% are male. Those testing positive for *R. nana* tended to be younger, with median age of the Respond population of 21 years (IQR 11–26). Afghanistan and Eritrea as a country of origin were over-represented in our cohort, with 29% of the total Respond cohort originating from Afghanistan and 9% from Eritrea.

All those with positive *R. nana* results were provided treatment with 30 mg/kg praziquantel as a single dose. Concomitant gastrointestinal infections were common in those infected with *R. nana*. 16/54 (30%) of patients had concurrent infection with *G. duodenalis*, 10/54 (19%) with *Helicobacter pylori*, 1/54 (2%) had each of *Entamoeba histolytica*, *Schistosoma* spp., and *Strongyloides* spp. DNA targets of Schistosoma

Table 1 Baseline characteristics of study population

Characteristic	Population ($n = 54$)
Age, years, median (IQR)	15 (9–17)
Male, *n* (%)	38 (70)
Country of origin	
Afghanistan, *n* (%)	39 (72)
Eritrea, *n* (%	6 (11)
Sudan, *n* (%)	3 (6)
Ethiopia, *n* (%)	2 (4)
Iraq, *n* (%)	2 (4)
Iran, *n* (%)	1 (2)
Namibia, *n* (%)	1 (2)
Accommodation type	
Hostel or hotel, *n* (%)	22 (41)
Foster care, *n* (%)	14 (26)
Unknown, *n* (%)	18 (33)
Time to review from arrival to the UK, months, median (IQR)	5 (2–10)

and Strongyloides are detected by NSP, although both cases were prior to NSP introduction, and were identified using serological tests. One patient had co-infection with both *E. histolytica* and *G. duodenalis*.

Of the 72 test results positive for *R. nana*, 41/72 (57%) of samples were diagnosed only by microscopy prior to the introduction of the NSP. Since introduction of the NSP in October 2022, a further 31 samples were positive. Of these 21/31 (68%) had a positive OCP and NSP result, 6/31 (19%) had a positive NSP with a negative OCP, and 4/31 (13%) had only a positive NSP result (insufficient stool for OCP to be performed).

Of the 27 patients who tested positive for *R. nana* where their family members were also tested, 11 patients (41%) had family members who were also infected with *R. nana* (4 of 5 positive family units). Of these, 2 families were advised to be treated empirically due to multiple positive family members—one family of 7 with 4 members positive for infection, and one family of 8 with 2 members positive for infection.

Regarding treatment failure and test of with follow-up stool sample, 21 patients returned stool for clearance checking after treatment. One was lost to follow up, and 1 further had a planned delay in treatment due to completing TB treatment first. Nine out of 21 clearance samples (43%) still tested positive for *R. nana* at least 1 month post-treatment. Two of these were repeat failures in the same 2 patients (7 patients with treatment failure overall). Seven of 9 repeat samples were OCP/OCP +NSP positive. Two samples were PCR positive only with no *R. nana* identified by microscopy. *R. nana* DNA was detected in these samples 5 and 6 months after treatment.

All 7 patients with treatment failure were children. Six out of 7 were from Afghanistan, 1 was from Eritrea. Six out of 7 patients were in family groups, and two of these had another family member who had also tested positive for *R. nana*. Of the two patients who failed treatment more than once, one was a 15-year-old young person seeking asylum living in foster care, who was treated successfully on the third attempt using two 30 mg/kg doses of praziquantel, 7 days apart. Another patient was a 13-year-old child seeking asylum who attended with 6 family members, one of whom was also positive for infection with *R. nana* but was treated successfully with a single dose of praziquantel. The index patient required three doses of praziquantel 30 mg/kg for treatment, with the third dose being supervised. The whole family was offered repeat treatment. Five out of 7 (71%) of treatment failures occurred at the same location. The number of those who failed treatment is over-represented at this location, with only 16/54 (30%) patients staying at this site.

Discussion

Fifty-four out of 1797 (3%) of those who provided stool samples within the Respond cohort were positive for *R. nana*. Concomitant gastrointestinal parasitic infection was common, as was clustering of *R. nana* within family groups. Treatment failure was common and occurred in a third of the cohort where a repeat stool test post-treatment was available. It is unclear whether this represents failure of treatment to eradicate infection or reinfection from the home environment. Use of Novodiag as a diagnostic test for *R. nana* infection appears to be corroborate well with traditional microscopy findings. Sensitivity may be greater than that of OCP testing alone, with 6/31 (19%) tests positive for PCR had a negative microscopy result.

The prevalence of *R. nana* in our cohort matches the reported prevalence in endemic countries [22, 23, 32], although is lower than some reports of up to 30% prevalence in PSAR in temperate regions [8, 9]. This high prevalence is perhaps not surprising, given the circumstances of our cohort, who had travelled from countries of high endemicity, and likely experienced poor living conditions, including overcrowding, inadequate sanitation, and poor hygiene prior to and during their journey to the UK, resulting in high risk of acquisition [2]. Co-infection is to be expected with other infections which are spread through faecal-oral transmission, with *R. nana* infection acting as a proxy for exposure to unclean food and water supplies and thus predicting risk of co-infection with other pathogens [33]. Other studies have shown that co-infection is common, and in some cohorts is more common than infection with a single parasite [34].

Family clustering of *R. nana* infection in our cohort is not unexpected, given likely shared exposures in country of origin and during the journey to the UK. Direct transmission between family members may also play a role. Our cohort were almost all residing in shared accommodation, and in relative proximity to other family members with limited facilities, increasing risk of transmission [2]. Infection within the family has been reported as a risk factor for infection in previous studies, especially in urban settings [35]. Reported prevalence is high in children, attributed to poorer personal hygiene, and overcrowding, such as in day care centres or schools [33, 35, 36]. It is interesting that in infected family units in our cohort, infection tended to be of siblings and not of parents, which may point towards behaviourally influenced direct transmission rather than (or in addition to) shared exposures (parents and children would likely have consumed the same food and water). A survey of UK asylum seekers has shown that accommodation is often crowded, with kitchens and bathrooms shared between many individuals [37]. In our cohort, even beyond family clustering,

30% of individuals were in the same accommodation location. This presents a likely further increased risk of *R. nana* transmission, although genomic analysis would be required to confirm that transmission had occurred between individuals in shared accommodation.

Treatment failure occurred in 43% of instances, where a clearance stool sample was returned at least 1 month later, in our study. Treatment failure has been seen in up to 16% of individuals treated with a single 30 mg/kg dose of praziquantel in previous studies and is more likely in settings where another family member has been infected [35]. Treatment failure may be due to failure of praziquantel to eliminate parasites from the GI tract (underdosing or resistance), poor treatment adherence, or re-infection (autoinfection or from the home environment or another family member).

Resistance to praziquantel has not been documented in the literature in human cestode infection, although praziquantel resistance in parasitic infection has been described [38].

Nitazoxanide and albendazole have both shown efficacy at treating *R. nana* and have been proposed as an alternative treatment strategy [39, 40]. Although nitazoxanide cleared 82% of infections compared to 96% clearance with praziquantel and albendazole combination therapy in one trial [40], it has never been compared to praziquantel alone. There is no trial evidence comparing treatment efficacy for albendazole to praziquantel. Behavioural factors likely remain key to treatment failure; although praziquantel, nitazoxanide, and albendazole are effective at treating infections with R. nana, they are unable to control the parasite in areas of high prevalence, where rapid re-infection occurs, without behavioural change [39]. In our cohort, all patients who failed treatment were children. Six of 7 children were in large family units ($\geq$ 6 family members) and 2 of these families had more than one sibling positive for *R. nana*, indicating a possibility for cross-infection, which is a prominent route of transmission for *R. nana*, as demonstrated by prior molecular phylogenetic analysis [10]. Previous studies have similarly highlighted positive correlations between parasitic intestinal infections, household size, and number of children [41]. The high treatment failure in our cohort most likely reflects difficulty in implementing public health measures in crowded environments, often without access to adequate facilities for washing and cooking, and consequent reinfection from other family members whose infection may have not been detected. Education, improved hygiene and sanitation are required to prevent reinfection.

Treatment adherence may also have contributed to treatment failure in our study. All patients were treated with a single dose of oral praziquantel (30 mg/kg), and patients were not directly supervised when taking treatment. One patient with two episodes of treatment failure cleared the infection following supervised administration, suggesting that treatment adherence may have contributed to failure in this case at least.

Techniques to manage treatment failure in our cohort included repeating treatment, offering two doses of praziquantel 7 days apart, supervised treatment, and suggesting treatment to families where one member tested positive. Counselling on the importance of taking medication and addressing barriers and concerns to taking treatment is paramount but may be resource intensive, requiring use of interpreters and trained staff.

Given the high prevalence of *R. nana* in our cohort, and the presence of significant risk factors for transmission and treatment failure, diagnosis and appropriate treatment is important. Asymptomatic infection, however, may often go undiagnosed. Further, access to appropriate healthcare remains challenging for this population, due to multiple barriers, including language, awareness, financial and digital poverty and stigma, compounded by frequent short notice relocations [42]. It is therefore important to take a proactive approach, and we propose opportunistic screening for *R. nana* in populations seeking asylum and refugees to prevent the risk of faltering growth in children from untreated infections.

Our study has several limitations, including its relatively small sample size. A core limitation of our study is the inability to determine transmission routes and cause of treatment failure. Family clustering and shared accommodation settings suggest possible person-to-person transmission. However, genomic sequencing was not performed to confirm direct transmission, limiting conclusions about infection dynamics within family units and communal living spaces. No direct assessment of hygiene practices or sanitation access was conducted. Further work should consider the use of whole genome sequencing or molecular phenotyping to interpret if recurrent infections are from the same organism or new infection.

Treatment adherence was not directly monitored in this study, and one case of successful clearance occurred after supervised administration, suggesting that adherence may have influenced treatment outcomes. Follow-up stool testing was not universally performed, and repeat testing post-treatment was only available for a subset of the cohort. This limits the ability to comprehensively evaluate treatment efficacy and reinfection rates. Significant barriers limit accurate follow-up in this cohort, including difficulty for PSAR to access care due to frequent relocations.

Conclusions

R. nana has been identified in 3% of our cohort of people seeking asylum and refugees screened at an integrated refugee health service in London, with significant familial clustering and relatively high treatment failure rates. We suggest that, given the prevalence, opportunistic testing for *R. nana* in people seeking asylum and refugee populations is appropriate, to prevent the risk of onward transmission and potential for contributing to faltering growth in children in severe cases. Given the risk of familial transmission, families should ideally be tested and treated together, and in families where more than one member tests positive for *R. nana*, we would recommend treatment of family members testing negative, to reduce risk of undetected reinfection.

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Authors' contributions
SE LN and NL developed the concept of the manuscript. HC PC and KB all contributed to data collection and extraction. KK summarised and interpreted the data with support of SE LN AND NL, who all contributed to the discussion and provided guidance to the interpretation of the results. KK developed the first and subsequent drafts of the manuscript. All authors contributed to the revision and editing the manuscript. All authors read and approved the final manuscript.

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Data availability
The dataset generated and analysed during this study contains information on a small cohort of individuals from a vulnerable population. While all data have been anonymised to the greatest extent possible, details such as clinic location, year of positive sample, and family size could pose a risk of re-identification. Given these considerations, the raw data cannot be made publicly available. However, summary data supporting the findings of this study are included within the manuscript. Further details may be available upon reasonable request to the corresponding author, subject to local ethics and research governance criteria.

Declarations

Ethics approval and consent to participate
The project was reviewed by the UCLH Divisional Governance committee, who deemed that no formal ethics approval was required as the work was classified as service evaluation rather than research and used routine clinical data only. The work was therefore registered as a service evaluation within the Division, according to local governance processes. All data were collected and stored in concordance with the Data Protection Act and the General Data Protection Regulation. Research confirmed to the principles set out in the Declarations of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]University College London Hospital, London NW1 2BU, UK. [2]Hospital for Tropical Diseases, London, WC1E 6JD, UK. [3]London School of Hygiene & Tropical Medicine, London, WC1E 7HT, UK. [4]Health Services Laboratories, Halo Building, London WC1H 9AX, UK. [5]Department of Paediatrics, University College London Hospital, London, UK.

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