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Geographic, symptomatic and laboratory predictors of parasitic and bacterial causes of diarrhoea in travellers

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ABSTRACT

An observational study of patients presenting with diarrhoea to a walk-in service for returning travellers was conducted with the aim of identifying features that would help predict whether pathogens were bacterial or parasitic. In total, 509 cases were included, of which a bacterial aetiology was found in 55/440 (12.5%) and a parasitic cause in 51/428 (11.9%). Patients with symptoms of ≤14 days were significantly more likely to have a bacterial diagnosis than those with longer symptoms ($p < 0.001$), whereas parasitic causes of diarrhoea were not associated with length of symptoms and became proportionately more likely with time. Raised CRP, faecal white cells and fever were all predictive of positive bacterial culture ($p<0.001$, $p = 0.001$ and $p = 0.001$, respectively) but did not predict parasitic infection. Travellers to South and Southeast Asia were more likely to have parasites detected in their stool than travellers to other tropical areas (OR = 1.96; $p = 0.041$). Gender, ethnicity, reason for travel and length of stay abroad were not significantly associated with the faecal pathogen identified. These findings should help guide appropriate antimicrobials when empirical therapy is indicated.

1. Introduction

Diarrhoeal disease is one of the most common health problems encountered by travellers to low-resource countries who are unwell on their return.[1,2] The risk of developing diarrhoea has been found to be as high as 60% in some studies.[3] Bacteria such as *Escherichia coli*, *Salmonella* spp., *Shigella* spp. and *Campylobacter* spp. are responsible for most acute infectious diarrhoea, but parasites such as *Giardia lamblia* and others of the genera *Cryptosporidium*, *Isospora* and *Cyclospora* are also found.[4] Although other bacteria such as enterotoxigenic *Bacteroides fragilis* and *Arcobacter* spp. are increasingly implicated in travel-associated diarrhoea,[5] the diagnostic capabilities of most laboratories generally remain limited to species of *Salmonella*, *Shigella*, *Campylobacter*, *E. coli* 0157 and the common parasites. The median length of symptoms of travel-associated diarrhoea is 4 days, although episodes resolve within 48 h in up to 50% of cases. Travel-associated diarrhoea with prolonged symptoms is well recognised[6–8] and these cases predominate in clinics in the developed world.

Laboratory testing of stool samples may identify a treatable cause of diarrhoea, but this information is generally not available for several hours (longer in the case of stool culture) and is not useful in guiding initial therapy. Identification of clinical pointers to parasitic or bacterial infection is therefore helpful since first-line treatment is different. Despite a number of studies reporting absolute numbers and proportions of parasitic infections, few data exist that examine clinical pointers usable by clinicians. In particular, although parasites are known to persist in stool longer than

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bacterial pathogens, we have found few comparisons in the literature of infectious causes of diarrhoea with respect to length of illness and there are sparse data on temporal and geographical associations that cover both parasitic and bacterial causes of diarrhoea.

The Hospital for Tropical Diseases in London (UK) has a walk-in clinic for unwell travellers returning from low-resource countries where diarrhoea is common. Treatment is free for all, removing a financial barrier to attendance. We set out to identify predictors of parasitic or bacterial disease in patients with a history of diarrhoea, concentrating on symptoms and tests that could help initial management. In addition, we aimed to examine the usefulness of two further simple and rapid tests: microscopy for faecal leukocytes, which can be undertaken more rapidly than culture; and CRP. We also looked at the culture positivity rate against stool consistency.

2. Methods

Consecutive patients seen in the clinic between 1 January 2009 and 31 December 2009 who complained of gastrointestinal problems were potentially eligible for inclusion. Demographic and clinical information about each patient episode was prospectively entered into a database at the time of presentation together with the area of travel, presence and length of symptoms, systems affected, and baseline clinical observations. Symptoms were categorised as acute (≤14 days) or persistent (>14 days). Cases were defined as patients who attended the clinic with a complaint of at least one loose stool over the preceding 3 days, with or without constitutional symptoms. Where the symptoms had not been clearly recorded in the database, the request to the laboratory and the clinical notes were scrutinised and individuals with no documented evidence of a diarrhoeal illness were excluded from the analysis.

Stool was cultured for *Salmonella* and *Shigella* spp. on XLD agar and triple sugar iron agar slopes at 37 °C in a microbiology laboratory. All samples were also incubated on CAMP agar at 42 °C in microaerophilic conditions for the isolation of *Campylobacter* spp. Identification of presumptive pathogens was performed using biochemical tests and serum agglutination reactions according to standard methods.[9] *Aeromonas* and *Plesiomonas* spp. were only identified in cases where they were the predominant organism at 24 h of culture. Anaerobic culture of stool and antigen detection by ELISA for *Clostridium difficile* toxin as well as faecal culture on TCBS agar for *Vibrio* spp. were performed if specifically requested by the clinician. Microscopy of stool samples for pathogenic faecal parasites was performed after concentration with formol–ether using the Ridley–Allen technique in a specialised parasitology laboratory (Hospital for Tropical Diseases).[10] In the case of morphological *Entamoeba histolytica*/*dispar*, an 'in-house' adhesin ELISA was performed to distinguish *E. histolytica* from the non-pathogenic *E. dispar*. Examination of wet preparations of stool to look for faecal leukocytes was performed on unformed specimens. The results were recorded as 'seen' (≥1 leukocyte/high power field) or 'not seen' (<1 leukocyte/high power field). When tested, the peripheral white cell count and CRP levels were recorded. Stool consistency was recorded by experienced parasitology technicians as formed, semi-formed (initially intact but readily disrupted), unformed (pourable but thick) or liquid (watery). The latter three categories were grouped as 'not formed'.

Clinical and laboratory data were entered using Microsoft Access (Microsoft Corp., Redmond, WA, USA) and analysed with STATA 11.0 (StataCorp LP, College Station, TX, USA). The travel history was categorised into geographical regions visited in the preceding 6 months. Some travellers had complex travel schedules, making it difficult to ascribe their conditions to one specific area, and these were excluded from the analysis of pathogen against region visited. Pathogens were grouped into bacteria (*E. coli* 0157, *Salmonella*, *Shigella*, *Campylobacter*, *Aeromonas* and *Plesiomonas*) and parasites (*Giardia*, *Cryptosporidium*, *Isospora* and *Cyclospora*). ORs were calculated for positive stool culture or microscopy against raised CRP, faecal leukocytes and history of fever as well as for travel to South and Southeast Asia compared with other tropical areas. The proportion of positive bacterial cultures and parasitic isolates was determined for patients with acute and chronic symptoms.

3. Results

A total of 509 patients with diarrhoea were included in the initial analysis, of whom 266 (52.3%) were men. The mean age was 35.1 years (SD 12.1 years). The majority of individuals stated their ethnicity as White (419; 82.3%); other ethnicities included South Asian (32; 6.3%), Black Caribbean (9; 1.8%) Chinese/other Asian (13; 2.6%), Black African (16; 3.1%) and Hispanic (4; 0.8%). In total, 440 individuals (86.4%) submitted stool samples for culture, 428 (84.1%) had stool analysed for parasites and 238 (46.8%) had blood tests performed. The presence or absence of a history of fever (as reported by the patient) was recorded in 421 cases (82.7%) and the length of symptoms in 479 cases (94.1%). Information on travel area was considered reliable and unambiguous in 494 cases (97.1%). The demographic and travel background of patients is summarised in Table 1. In 368 individuals, samples were examined both by microscopy and bacterial culture and the comparison of positive results to length of symptoms was restricted to this group.

A bacterial cause of diarrhoea was identified in 55/440 cases (12.5%) and a parasitic cause in 51/428 (11.9%). The commonest bacterial pathogens (see Table 2) were *Shigella* spp. (18 cases), *Campylobacter* spp. (17 cases) and non-Typhi *Salmonella* spp. (13 cases). *Giardia* was by far the most common parasite (35/51 cases). Helminth eggs were only seen in one stool sample (*Schistosoma mansoni*). The length of symptoms was strongly correlated with bacterial culture results but, by contrast, the prevalence of parasitic infections remained stable (Table 3). In patients with >14 days of symptoms, significantly fewer cases (10/186; 5.4%) had a positive bacterial stool culture compared with those with shorter symptoms (36/182; 19.8%) (OR = 4.34; $p<0.001$). Only 1/89 patients with symptoms of >28 days had a positive culture. However, there was