The epidemiology of *Helicobacter pylori* infection in African refugee children resettled in Australia

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ABSTRACT

Objective: To determine the prevalence and associated epidemiological features of *Helicobacter pylori* infection in child refugees in Western Australia.

Design and participants: Cross-sectional study of 193 eligible African refugee children (aged < 16 years) at their initial health assessment after resettlement in Australia between 1 February and 30 November 2006.

Main outcome measures: (i) Prevalence of *H. pylori* infection determined by monoclonal faecal antigen enzyme immunoassay testing (MFAT); (ii) associations of *H. pylori* infection with epidemiological factors (age, sex, transit through refugee camps, comorbidities and treatment interventions).

Results: MFAT was performed in 182 of the 193 children; 149 of these 182 (82%) had *H. pylori* infection. Age was an independent predictor of *H. pylori* infection (odds ratio [OR], 1.18; 95% CI, 1.07–1.31). No sex differences were observed. Premigration antimalarial therapy (with sulfadoxine–pyrimethamine and artesunate) significantly reduced the prevalence of *H. pylori* infection (age-adjusted OR, 0.33; 95% CI, 0.15–0.75).

Conclusion: African refugee children have a high prevalence of *H. pylori* infection. Increasing age is a strong predictor of infection and antimalarial treatment may have a protective effect.

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Helicobacter pylori infection is usually acquired in childhood.[1,2] Acute infection is often silent, with symptoms and disease manifesting later in life, as does an increased risk of *H. pylori*-related malignancy.

The prevalence of *H. pylori* infection is markedly increased in developing countries,[3,4] and risk factors include increasing age, large family size and socioeconomic deprivation.[5-7] Refugees resettled in developed countries generally come from regions of high *H. pylori* prevalence, whereas those who have grown up in industrialised nations have a lower prevalence of *H. pylori* infection.[3,8] Increased prevalence is also found in migrants and indigenous populations; adverse socioeconomic conditions in these groups account for some of the excess risk.[7,9,10]

Western Australia resettles about 1300 humanitarian refugees annually, representing over 10% of Australia's refugee intake.[11] Currently, many families are African, and about half the refugees are children.[12]

In this study, we investigated the prevalence and epidemiological associations of *H. pylori* infection in a high-risk paediatric population. The main outcome measure was *H. pylori* infection diagnosed by monoclonal faecal antigen enzyme immunoassay testing (MFAT). The effects of age, sex, transit through refugee camps, comorbidities and treatment interventions were investigated.

METHODS

We conducted a cross-sectional study at the Migrant Health Unit (MHU) in Perth, WA, the sole screening unit for humanitarian refugees resettled in WA. About 80% of targeted refugees in WA receive an initial health assessment at the MHU.[12] African children (aged less than 16 years) who presented for initial health assessment between 1 February and 30 November 2006 were included. Blood samples were obtained for routine screening investigations at the first clinic visit as part of standard clinical care and stool samples were collected 1 week later. Children were excluded from our study if they had received antibiotics or proton-pump inhibitors in the preceding month, if they had an immunodeficiency or active tuberculosis. Ethical approval was obtained from the Women and Children's Ethics Committee, Princess Margaret Hospital for Children. Informed consent was obtained in the presence of trained interpreters, as appropriate.

Data on age, sex, ethnicity, country of last transit, transit period, country of birth, type of dwelling in country of transit, and recent drug administration were obtained at the first visit by means of a structured questionnaire. Breastfeeding history was recorded for children under 2 years of age. Details of premigration antihelminthic and antimalarial treatment were obtained from accompanying International Office of Migration documentation.

1 Ethnicity, country of birth and transit profiles of the 193 African refugee children in the study

Ethnicity		Country of birth		Country of last transit		
Group	No.	Country	No.	Country	No.	Median transit time (IQR)
Sudanese	66 (34%)	Sudan	54 (28%)	Tanzania	64 (33%)	6.1 years (3.0–9.0)
Burundian	55 (29%)	Tanzania	40 (21%)	Kenya	33 (17%)	5.5 years (4.0–9.4)
Liberian	23 (12%)	Kenya	21 (11%)	Egypt	28 (15%)	2.0 years (1.2–2.9)
Congolese	22 (11%)	Burundi	14 (7%)	Guinea	26 (13%)	5.8 years (4.0–7.3)
Eritrean	20 (10%)	Democratic Republic of Congo	13 (7%)	Sudan	19 (10%)	6.4 years (3.3–9.4)
Other*	7 (4%)	Other†	51 (26%)	Other‡	23 (12%)	7.0 years (3.3–10.0)

IQR = interquartile range. * Other ethnicity: Sierra Leonian (7). † Other countries of birth: Liberia (11); Egypt (9); Guinea (9); Zambia (8); Sierra Leone (6); Ethiopia (2); Ghana (2); Zimbabwe (2); Ivory Coast (1); Nigeria (1). ‡ Other transit countries: Zambia (11); Ghana (3); Ethiopia (3); Uganda (3); Zimbabwe (2); Nigeria (1). ◆

2 Adjusted odds ratios for factors tested for independent associations with *Helicobacter pylori* infection

Variable	No. of children	No. infected with *H. pylori*	Odds ratio* (95% CI)	*P*
Age (years)	182	149 (82%)	1.17 (1.07–1.28)	0.002
Age strata (sex-adjusted)				0.013
< 5 years	51	35 (69%)	1.0	
5–10 years	67	56 (84%)	2.29 (0.95–5.53)	0.064
> 10 years	64	58 (91%)	4.35 (1.55–12.19)	0.005
Sex (age-adjusted)				
Female	89	70 (79%)	1.0	
Male	93	79 (85%)	1.51 (0.69–3.31)	0.3
Protracted refugee stay (> 5 years)				
Yes	98	85 (87%)	1.0	
No	84	64 (76%)	1.03 (0.38–2.80)	0.95
Type of dwelling				0.42
Refugee camp	123	99 (81%)	1.0	
Apartment	28	22 (79%)	0.96 (0.33–2.74)	0.93
House	31	28 (90%)	2.34 (0.65–8.63)	0.2
Ethnicity				0.35
Sudanese	61	54 (89%)	1.0	
Liberian	23	19 (89%)	0.48 (0.12–1.94)	0.3
Congolese	19	16 (84%)	0.61 (0.13–2.28)	0.53
Burundian	52	37 (71%)	0.30 (0.11–0.85)	0.023
Eritrean	20	17 (85%)	0.73 (0.16–3.22)	0.68
Sierra Leonian	7	6 (86%)	0.61 (0.06–6.29)	0.68
Last transit country				0.23
Tanzania	61	45 (74%)	1.0	
Kenya	32	31 (97%)	11.3 (1.40–91.28)	0.023
Guinea	26	23 (88%)	2.34 (0.59–9.30)	0.23
Egypt	24	19 (79%)	1.61 (0.49–5.27)	0.44
Sudan	19	16 (84%)	2.02 (0.49–8.20)	0.33
Other†	20	15 (75%)	0.96 (0.28–3.24)	0.95
Breastfeeding				
Yes	16	10 (63%)	1.0	
No	166	139 (84%)	1.12 (0.30–4.21)	0.87
Premigration antihelminthic treatment				
Yes	144	119 (83%)	1.0	
No	38	30 (79%)	1.05 (0.41–2.68)	0.92
Premigration antimalarial treatment				
No	103	91 (88%)	1.0	
Yes	79	58 (73%)	0.31 (0.14–0.72)	0.006
Helminth infection				
Yes	76	66 (87%)	1.0	
No	106	83 (78%)	1.01 (0.40–2.55)	0.98
QuantiFERON-TB Gold test result				
Negative	120	99 (83%)	1.0	
Positive‡	11	11 (100%)		
Indeterminate	22	17 (77%)	0.85 (0.27–2.71)	0.79
Plasmodium falciparum infection				
Yes	16	12 (75%)	1.0	
No	166	137 (83%)	2.06 (0.57–7.23)	0.26
Tinea capitis				
Yes	15	11 (73%)	1.0	
No	167	138 (83%)	1.84 (0.52–6.46)	0.34

* Odds ratios are age- and sex-adjusted by logistic regression. † Other transit countries: Zambia (11); Ghana (3); Ethiopia (3); Uganda (3); Zimbabwe (2); Nigeria (1). ‡ No odds ratio reported for positive QuantiFERON-TB Gold test results because of small numbers. ◆

Helicobacter pylori diagnosis

Fresh faecal samples were obtained from each child and frozen at −20°C for batch analyses. We assessed *H. pylori* status using Amplified IDEIA HpStAR kits (Dako, Glostrup, Denmark) following the manufacturer's instructions and as previously reported.[13]

Identification of other infections

Details of helminth infection, tinea capitis, tuberculosis and malaria were obtained for each child. Helminth infection was defined as the presence of any of the following results: positive serological test for schistosomiasis and/or strongyloidiasis, positive stool microscopy for ova, cysts or parasites of pathogenic helminths, peripheral eosinophilia ($\geq 0.7 \times 10^9$/L) or elevated immunoglobulin E (IgE) levels (> 280 kU/L). Premigration administration of albendazole was documented in 80% of children, with the remainder receiving empiric albendazole at the first health assessment visit.

A clinical diagnosis of tinea capitis was made at the initial visit based on skin examination. Latent or active tuberculosis infection was diagnosed by QuantiFERON-TB Gold testing (Cellestis International, Melbourne, Vic) in children over 2 years of age, with chest radiographs as indicated. All children had a single blood film and smears and rapid immunochromatographic testing (BinaxNOW, Portland, Ore, USA), irrespective of symptoms or premigration antimalarial treatment.

Statistical analyses

All data were analysed with SPSS, version 14.0 for Windows (SPSS Inc, Chicago, Ill, USA). Continuous variables were compared by independent *t* tests or Mann–Whitney tests, as appropriate. Associations between categorical variables and *H. pylori* infection were initially analysed by Pearson χ^2 or Fisher's exact tests. Logistic regression was used to determine the effect of independent variables separately on *H. pylori* infection, adjusting only for age and sex. Multivariate logistic regression was used to evaluate the effect of covariates on *H. pylori* infection. Statistical significance was set at the 5% level and two-sided *P* values were calculated.

RESULTS

Two-hundred and one African refugee children presenting for screening at the MHU were recruited consecutively, with a 100% response rate. Eight children were excluded

3 Multivariate logistic regression model of variables associated with *Helicobacter pylori* infection

Variable	No. of children	No. infected with *H. pylori*	Odds ratio (95% CI)	*P*
Age (years)	182	149 (82%)	1.18 (1.07–1.31)	< 0.05
Premigration antimalarial treatment				
No	103	91 (88%)	1.0	
Yes	79	58 (73%)	0.33 (0.15–0.75)	< 0.05

(five received antibiotics before screening and three were of non-African ethnicity). Of the 193 eligible children, 100 (52%) were male. The mean age was 7.9 years (SD, 4.4 years). Box 1 shows the main demographic features of the cohort.

Eighteen children (9%) were breastfeeding at the time of enrolment (mean age of breastfeeding children, 11.3 months; SD, 5.2 months). There were 116 children (60%) who had lived in refugee camps, with the remainder living in urban dwellings (apartments or houses). Almost all children who transited through Tanzania or Kenya (96 of 97; 99%) had lived in refugee camps, while all 28 who transited through Egypt had lived in apartments. The overall median transit time before resettlement in WA was 5.5 years (interquartile range [IQR], 3.0–8.4). Protracted refugee stays (more than 5 years in transit) were common (98 of 193; 51%); the median transit time for these 98 children was 8.0 years (IQR, 6.5–10.0).

Helicobacter pylori infection

MFAT was performed in 182 children, and *H. pylori* infection was diagnosed in 149 (82%). MFAT results clearly discriminated between populations that were infected (median positive optical density [OD], 2.85; IQR, 1.18–3.61) and uninfected (median negative OD, 0.10; IQR, 0.08–0.18), with no equivocal results ($P < 0.001$).

Children with *H. pylori* infection were significantly older (mean age, 8.5 years [SD, 4.2] v mean age, 5.8 years [SD, 4.5]; $P < 0.001$) with no sex differences. The prevalence of *H. pylori* infection was 63% for children under 2 years of age, rising to 95% for those older than 14 years. When analysed by age strata, the odds of infection were more than fourfold higher for children aged over 10 years compared with those aged less than 5 years (odds ratio [OR], 4.42; 95% CI, 1.58–12.35). Where two or more children in a family were enrolled (51 families), 45 of the 51 oldest siblings (88%) had *H. pylori* infection compared with 35 of the youngest siblings (69%; OR 3.43; 95% CI, 1.21–9.67).

Logistic regression was used to assess the effect of various factors on the odds of *H. pylori* infection (Box 2). Age was a significant predictor of *H. pylori* infection, with the odds of infection increasing by 17% for each year of age (OR, 1.17; 95% CI, 1.07–1.28). While the odds of infection were numerically largest for children transiting through Kenya, the overall relationship between country of transit and infection was not significant after adjusting for age and sex. Premigration antimalarial treatment (79 of 182 children; 43%) significantly reduced the odds of *H. pylori* infection after adjusting for age and sex (OR, 0.31; 95% CI, 0.14–0.72). Multivariate regression showed that only age and premigration antimalarial treatment were significantly associated with *H. pylori* infection (Box 3).

Effect of other infectious diseases on *Helicobacter pylori* infection

In total, 76 of the 182 children (42%) had evidence of helminth infection, 15 (8%) had tinea capitis, 16 (9%) had *Plasmodium falciparum* infection, and 11 of the 153 children (7%) tested had positive QuantiFERON-TB Gold results (with normal chest radiographs), indicative of latent tuberculosis infection. After adjusting for age and sex, the prevalence of *H. pylori* infection was not affected by the presence any of these infections (Box 2). No difference in IgE levels or peripheral eosinophilia counts were found in children with or without *H. pylori* infection (data not shown).

DISCUSSION

Our study shows a high prevalence of *H. pylori* infection in African refugee children, confirming that children from developing countries are at greater risk of infection.[14] Our results support the observation that early childhood is the main period of acquisition of *H. pylori* infection in high-prevalence populations.[1,2,4] *H. pylori* infection was present in 82% of this cohort, and the odds of infection increased significantly with age. In comparison, the prevalence of *H. pylori* infection in Australian children is low,[8] although the prevalence in Australian Aboriginal children is significantly higher, especially in those from remote areas,[9] reflecting differences in socioeconomic status.

The protective effect of antimalarial treatment on *H. pylori* infection is a potentially important and unexpected finding. In children who received empirical premigration antimalarial treatment, this was given about 6 weeks before study enrolment. This correlated with the median time between arrival in Australia and the MHU health screening (Dr A Thambiran, Medical Director, MHU, Perth, WA, personal communication). Empirical premigration antimalarial treatment was ceased in mid 2006 because of concerns about efficacy and coverage.[15]

The antimalarial therapy may have eradicated existing *H. pylori* infection. The period between administration of antimalarial drugs and collection of faecal samples was short, and so reacquisition of *H. pylori* infection during this intervening period is unlikely. The elimination half-lives of pyrimethamine and sulfadoxine are relatively long (3–4 and 6–9 days, respectively) and that of dihydroartemisinin, the active metabolite of artesunate, is less than 1 hour.[16] Antimalarial therapy is unlikely to have affected MFAT performance. The effect of antimalarial therapy remained significant in our final regression analyses, and was independent of albendazole therapy. To our knowledge, this in-vivo association has not been previously reported, although artemisinins are known to have antibacterial properties.[17] It has been postulated that artemisinin derivatives may interact with iron-dependent bacteria (such as *H. pylori*) and potentially provide a mechanism for targeted bacterial death.[18] The possible therapeutic role of artemisinins, which are cheap and well tolerated, in *H. pylori* eradication warrants further investigation.

A limitation of our study is the lack of a traditional "gold standard" for the diagnosis of *H. pylori* infection. Methods based on endoscopy and biopsy, or urea breath testing, are neither practical nor ethical for population-based screening of children, particularly in non-English speaking and often traumatised families. Recent international guidelines now recommend MFAT as an alternative in both adult and paediatric populations.[19,20]

In this study, we investigated potential epidemiological risk factors that may predispose refugee children to *H. pylori* infection. Surprisingly, transit through refugee camps did not place children at increased risk of infection, despite harsh environmental and nutritional conditions. The ubiquitous deprivation and overcrowding that characterise urban refugee conditions (eg, Egyptian apartments) may instead contribute to the non-significant association between dwelling type and *H. pylori* infection.

Intrafamilial spread of *H. pylori*, particularly mother-to-child transmission[2,21,22] or from infected older siblings,[2,23] is a potentially important mechanism for acquisition. In our cohort, older siblings had odds of *H. pylori* infection three times higher than those of their youngest siblings, supporting this premise. Parental *H. pylori* infection was not assessed in this study, but a high prevalence would be expected, in keeping with analogous published results.[22-24] Reliable data on family size could not be obtained, as many siblings and/or parents were displaced in transit.

The relationship between breastfeeding and infection was not found to be statistically significant; however, the number of children being breastfed at the time of enrolment was small. Our study did not address the phenomenon of transient *H. pylori* infections.[25] Over 60% of children aged under 2 years had *H. pylori* infection, which is similar to other reports of African infants.[4] Given the high levels of overall infection in this cohort, reinfection is likely even if there were cases of transient infection in infancy.

Clinicians should be aware of the high prevalence of *H. pylori* infection in resettled refugee children, including the potential development of chronic complications. Longitudinal studies of this population are warranted.

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COMPETING INTERESTS

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