

# HIGH ALTITUDE IS ASSOCIATED WITH *HELICOBACTER PYLORI* INFECTION IN A POPULATION OF DYSPEPTIC PATIENTS IN NEPAL – A RESEARCH LETTER

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Dear Editor,

*Helicobacter pylori* (*H. pylori*) is a bacterium that infects the human stomach, leading to chronic inflammation, dyspepsia, and gastritis<sup>1</sup>. Eradication of *H. pylori* significantly reduces dyspeptic symptoms and, even in asymptomatic individuals, reduces the risk of developing gastric cancer (RR=0.55 95% CI 0.42-0.74)<sup>1</sup>.

Both the prevalence and clinical implications of *H. pylori* infection are known to vary widely between populations. A complex interaction between the host immune defense, the gastric microbiota, and the environment is suspected to underpin this heterogeneity<sup>2</sup>.

55% of patients who attend the MEDyARTE Foundation Clinic in the Himalayan Nar-Phu Valley, Nepal, seek treatment for dyspeptic symptoms. Previous studies in Nepal confirm a strong association between *H. pylori* infection and dyspeptic symptoms<sup>3-8</sup>. Endoscopic studies estimated the *H. pylori* prevalence in Nepalese regions at 24%-71%<sup>4</sup>.

Considering the health burden of dyspepsia in the Nar-Phu Valley, an *H. pylori* test and a treat strategy were employed as part of routine care. This work aimed to determine the prevalence of *H. pylori* infection in dyspeptic patients to facilitate the development of local treatment guidelines.

Four clinics were held in low-income Himalayan villages in the Manang District of Nepal as part of the routine services of MEDyARTE. Two villages, Manang (3,500 m) and Chame (2,700 m), were identified as 'high altitude' and two, Nar (4,200 m) and Phu (4,100 m), as 'ultra-high altitude'. Inhabitants were invited to attend with any medical problems. Clinical criteria for 'likely gastritis' were generated from the results of Du et al<sup>9</sup>, who collated the symptoms of 8,892 biopsy-proven gastritis patients. 'Likely gastritis' was diagnosed if patients met at least 1 major and 3 minor criteria (Table 1).

As per the standard of care, patients who met the criteria received a point-of-care *H. pylori* stool antigen test. In case of a positive stool antigen test, eradication therapy was given. The regimen was chosen according to local resistance patterns and cost: 7 days of amoxicillin 1 g twice daily, metronidazole 400 mg twice daily, and omeprazole 20 mg twice daily<sup>10</sup>. The study was submitted to the Oxford Tropical Research Ethics Committee (OxTREC), which declared it exempt from ethical review since it is a retrospective study of anonymized patients.



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**TABLE 1. CRITERIA FOR ‘CLINICALLY LIKELY GASTRITIS’ GENERATED FROM DU ET AL<sup>9</sup>. PATIENTS WERE CONSIDERED ‘CLINICALLY LIKELY GASTRITIS’ IF THEY REACHED 1 MAJOR AND AT LEAST 3 MINOR CRITERIA.**

Major criteria	Minor criteria
>3 months of epigastric pain or discomfort	Burning pain
	Abdominal bloating
	Nausea/vomiting
	Postprandial fullness
	Early satiety
	Loss of appetite
	Fluctuating severity according to food intake
	Belching
	Bloating

The Chi-squared test was used to assess differences in sex and *H. pylori* prevalence between ultra-high vs. high villages. Welch’s *t*-test was used to assess differences in age. *p*-values are reported after Bonferroni correction for multiple comparisons.

396 patients attended the clinics. 289 presented with clinically likely gastritis (73.0%). 193 of 289 presenting with likely gastritis, provided a stool sample, and were tested for *H. pylori* (Table 2).

There were no significant differences in the age or sex of patients in high- vs ultra-high-altitude villages. The total proportion of *H. pylori*-positive tests was 82.9%. A significantly higher proportion of patients from ultra-high- (98.1%) vs high-altitude (63.3%) villages were positive ( $p < 0.001$ ).

Patients from ultra-high-altitude villages lived in two-level wooden houses with an open fire, with their livestock living beneath them at ground level. Their water source was shared and came from streams a short distance from the villages. There was no sewage treatment, although some houses had outdoor toilets. Their diet consisted of rice, pickles, and daal, with little access to meat or fresh produce. Occupation was heavily weighted towards subsistence farming. The average income was around \$0.30 per day. Temperatures were around 5 degrees cooler at ultra-high altitude.

In contrast, patients from high villages lived in more modern houses, had access to treated water with gas heaters, and had a more varied diet with better access to fresh produce.

**TABLE 2. RESULTS TABLE.**

	Number of patients	Mean age (SD)	% male	% positive <i>H. pylori</i> stool antigen	Proportion subsistence farming (estimated)	Mean daily income (\$)	Treated water source?
High-altitude villages (~4000m)	90	48.3 (16.2)	37.8	63.3	<30%	3.00	Treated
Ultra-high-altitude villages (~4000m)	103	49.4 (14.4)	38.9	98.1	>80%	0.30	Untreated
Total	193	49.1 (15.3)	38.3	82.9	-	-	-
Statistic (degrees of freedom) comparing high to ultra-high	-	$t(179.6) = 0.700$	$\chi(1) = 5.320$	$\chi(1) = 36.708$	-	-	-
<i>p</i> -value	-	1.000	1.000	<0.001	-	-	-

Their villages were accessible by road, and most of the inhabitants had mopeds. Their drinking water was treated, and there was a sewage treatment plant. The average wages were around \$3 per day.

The prevalence of *H. pylori* in dyspeptic patients from four remote Nepalese villages was 82%. Patients from higher-altitude villages with lower socioeconomic status and harsher living conditions had a significantly increased prevalence of *H. pylori* compared to lower altitude villages with higher socio-economic status (98% vs. 63%).

Corroborating our results, previous observational work in China identified a link between high-altitude, *H. pylori* infection and gastric cancer<sup>11</sup>. Our prevalence estimate of 82% is slightly higher than that of previous work in other regions of Nepal<sup>3-8</sup>. Possible reasons include the Manang region being more remote and higher-altitude with lower socio-economic status; and our study design, in which only patients providing stool samples (whom may have had more severe and prolonged symptoms) were tested.

It is certainly likely that eradication of *H. pylori* in dyspeptic patients would lessen the financial burden on the local health system both by preventing gastric cancer and by reducing the need for prolonged dyspepsia treatment in symptomatic individuals<sup>12</sup>. Further large-scale prevalence studies are required in other regions of Nepal to build a more complete picture of the disease burden in the country.

### **Conflict of Interest**

The authors declare they have no conflict of interest.

### **Acknowledgments**

None.

### **Ethics Statement**

The Oxford Tropical Research Ethics Committee (OxTREC), upon notification, waived the need for ethics approval for this study due to the involvement of retrospective analysis of anonymized *H. pylori* testing data.

### **Authors' Contribution**

MT and MET collated data. MT conducted data analysis and produced the first draft. All authors edited and approved the final manuscript.

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### **AI Statement**

The authors declare they did not use any AI software to draft the manuscript.

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