Disparity in *Helicobacter pylori* Positivity among Israeli Adults with Uninvestigated Dyspepsia in an Urban Setting with Mixed Ethnicity

Ibrahim Zvidi MD[1], Ram Dickman MD[2,3], and Doron Boltin MBBS[2,3]

[1]Clalit Health Services, Lod, Israel
[2]Division of Gastroenterology, Rabin Medical Center (Beilinson Campus), Petah Tikva, Israel
[3]Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ABSTRACT **Background:** *Helicobacter pylori* (*H. pylori*) prevalence varies according to both geographical region and ethnicity. The interplay between these two factors has been poorly studied.

Objectives: To determine the positivity rate of *H. pylori* infection among Jewish and Arab patients who live in a mixed urban center in Israel.

Methods: Between November 2009 and September 2014, dyspeptic patients referred to a gastroenterology clinic in Lod, Israel, were enrolled in a prospective study. For each patient, clinical and epidemiological data were collected and a noninvasive or endoscopy-based test for *H. pylori* was performed.

Results: A total of 429 consecutive patients (322 Jewish and 107 Arabs), mean age 45 years (range 15–91 years) were included; 130 males. Overall positivity for *H. pylori* was 42.4% (182/429). The positivity rate of *H. pylori* was 38.8% for Jews (125/322) and 53.2% for Arabs (57/107) in Lod ($P < 0.01$). When immigrants were excluded, the difference in *H. pylori* positivity did not reach statistical significance (45.0% [77/171] vs. 53.2% [57/107], $P = 0.217$, in Jews and Arabs, respectively).

Conclusions: *H. pylori* infection was more common in Arabs that Jews in the mixed city of Lod, Israel. This finding may suggest that non-environmental factors were responsible for the observed difference in *H. pylori* positivity.

IMAJ 2023; 25: 729–733

KEY WORDS: dyspepsia, endoscopic findings, ethnic origin, *Helicobacter pylori* (*H. pylori*), Israel

Helicobacter pylori (*H. pylori*) is the causative organism in the development of peptic ulcer disease and gastric adenocarcinoma [1]. Although the prevalence of infection is decreasing in developed countries, there are still discrepancies within Western countries related to age, socioeconomic status, and country of birth [2]. In the United States, the prevalence of *H. pylori* in the middle- and upper-class populations is only 10–15% [3]. However, *H. pylori* infection is more common among socially disadvantaged populations and among immigrants [4]. Differences in prevalence among ethnic groups of similar socioeconomic status [4] reflect components of environment and possibly host genetics.

Environmental factors that have been associated with *H. pylori* positivity include poor sanitation, crowding, bore water use, and contact with farm animals [5-6]. However, prior exposure to antibiotics and proton pump inhibitors may be associated with lower *H. pylori* positivity [7,8]. Proton pump inhibitors may be associated with lower *H. pylori* positivity [7].

Data for *H. pylori* prevalence in Israel are scarce and are biased by heterogeneous study populations and variability in the diagnostic tests used. Annual infection rates among Israeli adults remains low (0–1%) [2,9,10]. Some studies have found that the overall seroprevalence of *H. pylori* is similar among Jews and Arabs [7,11]. However, while prevalence among Jewish Israelis is decreasing, the prevalence among Arab Israelis appears to be on the rise [7]. The diverging trends in *H. pylori* prevalence between the Jewish and Arab populations in Israel warrants further study. It is unclear whether the trend toward a higher prevalence in Arab Israelis is attributable to en-

vironmental factors such as non-urban living, crowding, and alternate water sources. Perhaps genetic host factors determine immune response to infection.

To address these questions, we performed a prospective study of *H. pylori* positivity in the city of Lod, where Jewish and Arab Israelis share similar living conditions. We hypothesized that if environmental and socioeconomic factors alone were responsible for *H. pylori* infection, then Jewish and Arab Israelis in Lod would have a similar prevalence of *H. pylori* infection.

PATIENTS AND METHODS

PATIENTS

We conducted a prospective study between November 2009 and September 2014, including consecutive patients who were referred from primary care clinics in Lod to the Lod Gastroesophageal Clinic belonging to Clalit Health Services.

All patients reported dyspepsia at least 30 days before presentation. In addition, patients reported symptoms such as nausea, vomiting, heartburn, and abdominal pain not localized to the epigastrium. History of nonsteroidal anti-inflammatory drug ingestion, smoking, and alcohol consumption were documented. A single biopsy from the antrum of the stomach can detect H. pylori in more than 90% of cases [12].

Upper gastrointestinal endoscopy using a short-acting sedative (5–10 mg midazolam) was performed when clinically indicated. During endoscopy, findings such as hiatus hernia, esophagitis and its grade, gastritis, and gastric or duodenal ulcers as well as any gross esophageal, gastric, or duodenal pathology were documented. At least three biopsies were taken from the antrum of the stomach and placed in a formalin-containing tube. These biopsies were sent to the pathology department for histological examination. The presence of *H. pylori* was determined by modified Giemsa stain.

Additional staining to aid the diagnosis of H. pylori was standard practice at the laboratory that processed all of the biopsy specimens. Modified Giemsa has been used for as long as *H pylori* has been known to exist [13] It is considered the method of choice because it is sensitive, cheap, easy to perform, and reproducible [14].

Patients with a macroscopically normal endoscopic examination underwent a rapid urease test to assess for *H. pylori* infection. Patients who did not have a clinical indication for endoscopic examination underwent a 13C-urea breath test for *H. pylori.* Cutoff for positivity was 3.0 delta over baseline. All patients were instructed to discontinue treatment with proton pump inhibitor for 2 weeks and antibiotics or bismuth salts for 4 weeks prior to first endoscopy or C13-urea breath test. Failure to do so resulted in screening failure.

Exclusion criteria included previous diagnosis or treatment for *H. pylori* infection, bleeding, dyscrasia, inability to provide informed consent, pregnancy, suspected upper gastrointestinal bleeding, previous upper gastrointestinal tract surgery, and severe systemic disease in addition to patients who were not expected to benefit from *H. pylori* treatment due to poor general condition. Patients who were found to have a positive test for *H. pylori* were referred to their primary care physician for treatment. We did not provide treatment for *H. pylori.*

ETHICS APPROVAL

This study was conducted in accordance with the principles of the Declaration of Helsinki and good clinical practice and was approved by the Human Subjects Protection Program of the Rabin Medical Center (Beilinson Campus), Petah Tikva, Israel.

STATISTICAL ANALYSIS

Continuous variables were presented as mean ± standard deviation. Qualitative variables were presented as percentages and 95% confidence intervals (95%CI). Fisher's exact test was used to compare the value of categorical variables between study groups. Significance was considered at $P < 0.05$.

RESULTS

CLINICAL FACTORS

Of the 429 patients referred to our clinic, 322 were Jewish and 107 were Arab. Mean age was 45 years (47 years for Jews; 41 years for Arabs). Males accounted for 130 patients (99 Jews; 31 Arabs); 64 (14.9%) were smokers (47 Jews [14.5%]; 17 Arabs [15.8%]). Alcohol consumption was reported by 7 patients (1.6%) (6 Jews [1.8%] and 1 Arab [0.93%]) [Table 1]. Of the 322 Jewish patients, 171 were born in Israel, 25 originated from North Africa, 102 were European born, and 24 were of Ethiopian origin [Table 1].

Patients were referred to our department for further investigation of the following symptoms: 404 patients pre-

Table 1. Socio-demographic characteristics

	Jewish (n=322)	Arab (n=107)	Total (N=429)	*P*-value
Mean age in years, n ± SD	47 ± 18.5	41 ± 15.7	45 ± 17.9	0.0027
Sex				
Male, n (%)	99 (30.7)	31 (28.9)	130 (30.3)	0.8084
Birthplace				
Israel, n (%)	171 (53.1)	107 (100)	278 (64.8)	0.0001
North Africa, n (%)	25 (7.7)	–	–	
Europe, n (%)	102 (31.6)	–	–	
Ethiopia, n (%)	24 (7.4)	–	–	
Smoking status, n (%)	47 (14.5)	17 (15.8)	64 (14.9)	0.7551
Alcohol consumption, n (%)	6 (1.8)	1 (0.93)	7 (1.6)	0.6861

SD = standard deviation

Table 2. Clinical characteristics

	Jewish (n=322)	Arab (n=107)	All (N=429)	*P*-value
Abdominal pain, n (%)	305 (94.7)	99 (92.5)	404 (94.1)	0.4741
Nausea, n (%)	29 (9.0)	7 (6.5)	36 (8.3)	0.5471
Bloating, n (%)	33 (10.2)	7 (6.5)	40 (9.3)	0.3373
Vomiting, n (%)	26 (8.0)	8 (7.4)	34 (7.9)	1.0000
Proton pump inhibitor use, n (%)	46 (14.2)	12 (11.2)	58 (13.5)	0.5146

sented with upper abdominal pain (305 Jews; 99 Arabs), 36 presented with nausea, 40 with bloating, 34 with vomiting, and 3 with a history of gastric cancer. In addition, 58 (13.5%) were on proton pump inhibitor treatment (46 Jews [14.2%]; 12 Arabs [11.2%]) [Table 2].

DIAGNOSTIC TESTS

In our cohort, 279 patients (65%) underwent gastroscopy and subsequent urease test or biopsy (210 Jews [65.6%]; 69 Arabs [64.4%]); 105 patients (65 Jews and 40 Arabs) had an urease test. Biopsy was performed on 174 patients, and 150 patients (114 Jewish and 36 Arabs) had a breath test.

HELICOBACTER PYLORI POSITIVITY

In our study, 182 patients (42.4%) tested positive for *H. pylori*: 125 (38.8%) were Jewish and 57 (53.2%) were Arab. Of the Jewish patients, 8 (32%) originated from North Africa, 6 (25%) were of Ethiopian origin, 34 (33.3%) were born in Europe, and 77 (45%) were born in Israel [Table 3].

ENDOSCOPIC FINDINGS

Endoscopy was abnormal in 122 (28.2%) patients (82 Jews [39.0%]; 40 Arabs [58.0%]. Gastritis was the main pathologic finding in 68 (32.3%) Jews and 24 (34.7%) Arabs. Eighteen patients had esophagitis (13 Jews [6.1%]; 5 Arabs [7.2%]). There were 37 patients with diaphragmatic hernia (26 Jews [12.3%]; 11 Arabs [15.9%]). Five Jewish patients were diagnosed with a malignancy (2 patients with MALToma, 1 esophageal cancer, 1 gastric cancer, and 1 gastrointestinal stromal tumor. Three Jewish patients had gastric ulcer, 3 had duodenal ulcer, and 1 had celiac disease [Table 4].

DISCUSSION

Studying the epidemiology of *H. pylori* in Israel is necessary, since accurate and up-to-date prevalence and incidence data may facilitate public health initiatives to decrease transmission of the organism and to aid in planning community-based treatment programs [15]. Prevalence rates of *H. pylori* have been shown to correlate with age and low socioeconomic status, but not gender [15]. The socioeconomic status in the city of Lod is rated 4 out of 10 (1 being the lowest). There are several mixed neighborhoods where Arabs and Jews live together.

Our findings showed that the positivity of *H. pylori* is higher in the Arab population of Lod than the Jewish population (53.2% vs. 38.8%, $P < 0.01$, respectively). Since Jewish and Arab Israelis in Lod share a unique and uniform socioeconomic setting, our findings suggest that non-environmental factors could be responsible for the difference in *H. pylori* positivity. *H. pylori* positivity was lowest in the Jews born outside of Israel who later moved to Lod (31.8% [48/151]). Jews born outside of Israel also had a significantly lower *H. pylori* positivity compared to Israeli-born Jews in Lod (31.8% [48/151] and 45.0% [77/171], $P = 0.0164$, respectively). The positivity rate of *H. pylori* among Jews born outside of Israel is like *H. pylori* prevalence in developed countries [16].

Although the prevalence of *H. pylori* in Arabs in Lod appears high, it remains lower that other Arab populations in the region. Two studies of *H. pylori* prevalence in Jordan showed this trend. Latif and colleagues [17] reported that *H. pylori* was present in 68% of patients regardless of the pathology found during endoscopy. Shen-

Table 3. *Helicobacter pylori* (*H. pylori*) positivity

	H. pylori positivity*	*P*-value
Total, n (%)	182/429 (42.4)	
Jew, n (%)	125/322 (38.8)	0.0096
Arab, n (%)	57/107 (53.2)	
Ethnicity of total cohort		
Israeli-born Jew, n (%)	77/171 (45.0)	0.2174
Arab, n (%)	57/107 (53.2)	
Ethnicity of Jewish patients		
Israeli-born Jew, n (%)	77/171 (45.0)	0.0164
Immigrant Jew, n (%)	48/151 (31.8)	

*Number of patients out of the total population

Table 4. Endoscopic findings

	Jewish	Arab	*P*-value
Normal endoscopy, n (%)	128 (61.0)	29 (42.0)	
Abnormal endoscopy, n (%)	82 (39.0)	40 (58.0)	0.0077
Gastritis, n (%)	68 (32.3)	24 (34.7)	0.7683
Malignancy*, n (%)	5 (2.3)	0 (0)	0.3375
Esophagitis, n (%)	13 (6.1)	5 (7.2)	0.7793
Diaphragmatic hernia, n (%)	26 (12.3)	11 (15.9)	0.5392
Gastric ulcer, n (%)	3 (1.4)	0 (0)	1.0000
Duodenal ulcer, n (%)	3 (1.4)	0 (0)	1.0000
Celiac disease, n (%)	1 (0.4)	0 (0)	1.0000
Total, n (%)	**210 (100)**	**69 (100)**	

*Type of malignancy: MALToma (2 patients), esophageal cancer (1 patient), gastric cancer (1 patient), gastrointestinal stromal tumor (GIST) (1 patient)

nak and Kilani [18] reported that *H. pylori* was present in more than 90% of dyspeptic patients. Similar results were reported from other developing countries. In India it was found that the frequency of *H. pylori* increased with age and reached more than 80% by the age of 20 years. This high prevalence was also reported in the Kingdom of Saudi Arabia where it was found that *H. pylori* affected approximately 40% of children aged 5–10 years and 70% of individuals aged 20 years or older [9]. These high percentages, more than 70% of the general population in developing countries such as Arab countries or India, differ from those in developed countries where only up to one-half of adults are infected [11].

H. pylori was detected in 52% of the asymptomatic population in the United States [7]. This rate is falling in the United Kingdom and the United States [19], where the rate of acquisition is only 0–0.5% per patient per year [19]. The difference in the prevalence rate between developed and developing countries can be mainly attributed to inadequate living conditions, poor sanitation, inadequate hygiene, and overcrowding [15].

Epidemiological studies among asymptomatic adults generally use serology for *H. pylori* diagnosis. Serological tests have suboptimal performance when compared to other noninvasive and invasive diagnostic tests. The prevalence of *H. pylori* in asymptomatic Israeli adults is unknown since there is no indication for screening of asymptomatic individuals in Israel.

Interestingly, we did not find a statistically significant difference between *H. pylori* positivity among the Israeli-born Jews and Arabs in Lod (45.0% vs. 53.2%, $P = 0.217$, respectively). This is noteworthy, since acquisition of the organism typically occurs in childhood. Therefore, exclusion of immigrants may provide a more representative population in which to assess *H. pylori* positivity in Lod. Nevertheless, the lack of significance should not be taken to mean that the prevalence of *H. pylori* in Israeli-born Jews and Arabs is similar, rather only that the difference was not statistically significant. The absolute difference in *H. pylori* positivity between Israeli-born Jews and Arabs in Lod was large (8.2%). If the sample size was greater, it would be possible to interpret the absolute difference in positivity with more confidence. While we cannot know for certain what the difference would be, we can presume that *H. pylori* positivity in Israeli-born Jews would remain lower than in Arabs. If so, this suggests that environmental and socioeconomic factors are not the only factors responsible.

There a several possible explanations for the disparate rate of *H. pylori* positivity that we observed in the Jews and Arabs of Lod who share a unique and uniform social setting. First, the difference in *H. pylori* prevalence could be related to different behaviors in seeking and utilizing healthcare services among Jews and Arabs. For example, a lower prevalence of *H. pylori* in the Jewish population may be due to greater antibiotic consumption in childhood or prior use of proton pump inhibitors.

Second, since the study population consisted of patients with dyspepsia, it is possible that the disparity simply reflected a greater proportion of dyspepsia functional disease among Jews than Arabs. This result is supported by our finding that Jews had significantly fewer pathological endoscopic findings compared to Arabs (82/210 [39.0%] vs. 40/69 [58.0%], $P = 0.008$, respectively) [Table 4].

Third, the disparity could be caused by genetic factors, which may impact host immune defenses and the ability of the organism to establish chronic active gastritis. For example, HLA allele associations (in particular, HLA-DQB1*05:01) and single nucleotide polymorphisms (such as rs35030589 on chromosome 6) have been associated with *H. pylori* infection [20]. Last, it is possible that even though Jews and Arabs in Lod live in the same urban setting and receive the same social services, Arabs in Lod live in more crowded conditions.

Limitations of our study include the use of different diagnostic tests, the inclusion of symptomatic (rather than healthy) patients, and the lack of children in our cohort. These differences limit the applicability of our data to the general population.

The use of a single antral biopsy rather than multiple biopsies from the gastric corpus and antrum may have led to underestimation of *H. pylori* prevalence. Furthermore, since *H. pylori* is generally acquired during childhood, it would have been useful to compare *H. pylori* prevalence in Jewish and Arab children in Lod, rather than just adults, who may have previously lived in another city. Similarly, although we know that the overall socioeconomic level of Lod is 4 of 10, the socioeconomic level of individual patients is unknown. The strength of our study is its prospective design and unique single center setting, which allowed us to standardize the impact of environmental and socioeconomic factors on *H. pylori* prevalence.

CONCLUSIONS

H. pylori infection is common and was found in 49.2% of the population studied in Lod, Israel. The infection was more frequent in the Arab compared to the Jewish population. Non-environmental factors should be further studied to better understand the reason for our findings.

Correspondence

Dr I. Zvidi
Clalit Health Services, Lod, Israel
Phone: (972-8) 977-0002
Fax: (972-8) 977-0001
Email: zbidieb@clalit.org.il

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