ЧАСТОТА ВСТРЕЧАЕМОСТИ АНТИТЕЛ К *HELICOBACTER PYLORI* СРЕДИ НАСЕЛЕНИЯ АЗЕРБАЙДЖАНА (ИРАН)

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Резюме. *Helicobacter pylori* (*H. pylori*) является частой инфекцией, которая может приводить к развитию гастрита, язвы желудка и злокачественнных опухолей в этой области. В данном исследовании мы изучали серопозитивность в отношении *H. pylori* по каждому классу иммуноглобулинов, а также их ассоциацию с полом и возрастом в выборке генеральной популяции Табриза (Иран).

В рамках этой работы обследованы 3733 участника, направленных в нашу лабораторию для тестирования в течение 2019-2022 гг. Иммуноферментная диагностика (ИФА) применялась для количественного выявления антител классов IgG, IgM и IgA к *H. pylori*. Статистический анализ проводили с помощью версии 20 пакета программ SPSS.

Из 3733 обследованных лиц 1235 (33,1%) были мужского пола и 2498 (66,9%) – женского. 57,9% участников имели позитивные тесты на антитела класса IgG. Для антител классов IgM и IgA к *H. pylori* этот показатель составил, соответственно, 0,3% и 11,6%. Средний возраст (±SD) составлял 40,72±16,91 года. Не выявлено достоверной связи между полом и позитивностью тестов по IgG и IgA ($p = 0,11$ и 0,08 соответственно). При исследовании антител класса IgM показана более высокая частота позитивных тестов у женщин (0,4% среди женщин и 0,2% среди мужчин; $p = 0,009$). Частота встречаемости положительных тестов по IgG также достоверно возрастала (p-value < 0,001). При анализе частот антител классов IgM и IgA отмечено значительное повышение числа серопозитивных лиц с возрастом ($p = 0,005$ и < 0,001 соответственно).

Данное исследование показало, что частота выявления антител к *H. pylori* в Табризе составляет около 57%, что находится в пределах значений по Ирану в целом, но она выше, чем в развитых странах. Встречаемость всех классов антител против *H. pylori* достоверно увеличивается с возрастом.

Ключевые слова: Helicobacter pylori, антитела, серопозитивность, Табриз, Иран

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SEROPREVALENCE OF ANTI-*HELICOBACTER PYLORI* ANTIBODIES IN POPULATION OF AZERBAIJAN, IRAN

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Abstract. *Helicobacter pylori* (*H. pylori*) is a common infection which can lead to gastritis, peptic ulcer disease and gastric-originated malignancies. In this study prevalence of seropositivity of each immunoglobulins against *H. pylori* and also, their association with sex and age were evaluated in a sample of the ordinary population from Tabriz, Iran.

In this study, 3733 individuals referred to the laboratory for Para clinical tests between 2019 and 2022, participated. Enzyme-linked immunosorbent assay (ELISA) was utilized to detect the quantity of anti-*H. pylori* Immunoglobulin G (IgG), Immunoglobulin M (IgM), and Immunoglobulin A (IgA). The statistical analysis was conducted using the 20th version of SPSS software.

Out of 3733 participants, 1235 (33.1%) were male and 2498 (66.9%) were female. 57.9% of the participants have positive IgG serology. Also, this index was 0.3% and 11.6% for IgM and IgA, respectively. The mean (SD) age was 40.72 (16.91). There was no significant relationship between gender and IgG and IgA positiveness (p-values = 0.11 and 0.08 respectively). For IgM, serum positiveness was higher in females (0.4% for females and 0.2% for males; p-value: 0.009). The prevalence of positive IgG was increasing significantly (p-value < 0.001). For IgM and IgA there was a significant increase in the number of seropositive individuals with an increase in age (p-value = 0.005; and < 0.001 respectively).

This study reveals that the prevalence of *H. pylori* in Tabriz is approximately 57% which is in the range estimated to be in Iran, but in comparison to developed countries, it was higher. The prevalence of anti-*H. pylori* immunoglobulins increases significantly with age.

Keywords: Helicobacter pylori, Immunoglobulins, seroprevalence, Tabriz, Iran

Introduction

Helicobacter pylori (*H. pylori*) is a common infection that affects gastric tissue and can lead to gastritis, peptic ulcer disease [11], and gastric-originated malignancies such as gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma (MALToma) [1, 6]. *H. pylori* infection is usually asymptomatic; therefore, most epidemiologic information originates from serologic-based studies [2]. There are several invasive and non-invasive methods to diagnose *H. pylori*. Invasive methods depend on endoscopic specimens that are used for histologic staining, polymerase chain reaction (PCR) testing, bacterial culture, and urease testing. Non-invasive methods include urea breath tests and anti-*H. pylori* serologic assays (qualitative or quantitative) stool antigen detecting [4, 14].

The prevalence of *H. pylori* infection depends on geographic area, age, race, and socioeconomic status [5, 12]. The distribution of *H. pylori* among various populations depends on the standards of public hygiene. It is imagined that in childhood *H. pylori* is transferred by the orofecal route from parents [16]. In developing countries, the infection commonly accrues in children and chronic infection continues into adulthood; however, in the developed world infection is less in children and develops more commonly in adulthood [2]. Risk factors for *H. pylori* transmission encompass living in crowded places, living with infected individuals, and living in places with an unreliable supply of water [8, 12]. Age and sex are also suggested as factors associated with *H. pylori* infection [9]. A meta-analysis was conducted to quantify the relationship between sex and *H. pylori* infection and reported a male predominance of *H. pylori* infection both in children and adults; however, the need for future studies was also mentioned [7]. More prevalence of the infection in adults was also mentioned in previous studies [19]; however, the is limited evidence regards the rate of infection in different age groups in Iran.

For overcoming the mentioned limitations; in this study prevalence of seropositivity of each immunoglobulin against *H. pylori* and also, their association with sex and age were evaluated in a sample of the ordinary population from Tabriz, Iran.

Materials and methods

Ethical considerations

This study was conducted following the ethical principles mentioned in the Helsinki declaration. The ethics committee of Tabriz University of Medical

Sciences reviewed and approved all aspects of the study (n; 28577).

Participants

During this study from 2019 to 2022, 3733 individuals (either asymptomatic or symptomatic) referred to the laboratory for paraclinical tests, participated. All individuals were residents of Tabriz or nearby rural areas. Before sampling demographic information including sex and age was registered.

Sampling

Three milliliters of venous blood were drawn and stored in a refrigerator until laboratory evaluation. Enzyme-linked immunosorbent assay (ELISA, Immunolab, German) method was utilized to detect the quantity of anti-*H. pylori* Immunoglobulin G (IgG), Immunoglobulin M (IgM), and Immunoglobulin A (IgA). The cut-off values were considered as following: negative (< 8), equivalent (8-12), and positive (> 12) results.

Statistics

The statistical analysis was conducted using the SPSS software version 25. The prevalence of seropositivity for each immunoglobulin was calculated and compared between males and females. Also, the trend of seropositivity in age groups was examined. To evaluate the relationship between age and the results of immunoglobulin assessments, individuals' age is divided into subgroups with 10 years intervals. The chi-square test and linear trend test were utilized to evaluate association between the prevalence of seropositivity and the sex and age groups respectively with a 0.05 level of significance for the p-value.

Results

In this study, 3733 individuals participated. The mean age of the patients was 40.72 and their median was 41.00 and 33.1 percentage of them were male. As it is shown in Table 1, 57.9% of the participants have positive IgG serology. Also, this index was 0.3% and 11.6% for IgM and IgA, respectively.

As presented in Table 2, the prevalence of positive IgG and IgA, was higher in males; however, there was no significant relationship between gender and IgG and IgA positiveness (p-values: 0.11 and 0.08 respectively). For IgM, serum positiveness was higher in females (0.4% for females and 0.2% for males) and there was a significant association (p-value: 0.009).

As it is shown in Table 3, the prevalence of positive IgG was increasing significantly with an increase in age (p-value < 0.001). For IgM, there was a significant increase in the number of seropositive individuals (p-value = 0.005). For IgA, also there was a significant increase in the number of seropositive participants with an increase in age (p-value < 0.001).

Also, we examine sex impact on seropositiveness in each age subgroups. For IgG, in some subgroups (for instance: 20-30, 60-70, > 70) we see significant difference between male and female in which seropositiveness is higher in males than females.

For IgM, we see significant difference between males and females in some age subgroups (for instance: For IgA, there is no positive case in some age subgroups, also, in other subgroups, there isn`t significant difference between male and female.

TABLE 1. NUMBER AND RATE OF POSITIVE, EQUIVALENT, AND NEGATIVE RESULTS OF IMMUNOGLOBULIN ASSESSMENTS

Test result	IgG	IgM	IgA
Positive	1949 (57.9%)	8 (0.3%)	83 (11.6%)
Equivalent	417 (12.4%)	250 (10.1%)	97 (13.6%)
Negative	999 (29.7%)	2208 (89.5%)	533 (74.8%)

Note. IgG, Immunoglobulin G; IgM, Immunoglobulin M; IgA, Immunoglobulin A.

TABLE 2. NUMBER AND RATE OF POSITIVE, EQUIVALENT, AND NEGATIVE RESULTS OF IMMUNOGLOBULIN ASSESSMENTS IN MALES AND FEMALES

Test result	Sex subgroup	IgG	IgM	IgA
Positive	Male	634 (60.2%)	2 (0.2%)	44 (14.7%)
	Female	1315 (56.9%)	6 (0.4%)	39 (9.4%)
Equivalent	Male	115 (10.9%)	63 (7.6%)	41 (13.7%)
	Female	302 (13.1%)	187 (11.5%)	56 (13.5%)
Negative	Male	305 (28.9%)	768 (92.2%)	214 (71.6%)
	Female	694 (30.0%)	1440 (88.2%)	319 (77.1%)
p-value		0.11	< 0.01	0.08

Note. As for Table 1.

TABLE 3. NUMBER AND RATE OF POSITIVE, EQUIVALENT, AND NEGATIVE RESULTS OF IMMUNOGLOBULIN ASSESSMENTS IN DIFFERENT AGE GROUPS

Age group	Test result	IgG	IgM	IgA
≤ 10	Negative	101 (70.1%)	138 (88.5%)	61 (98.4%)
	Equivalent	15 (10.4%)	18 (11.5%)	1 (1.6%)
	Positive	28 (19.4%)	0 (0.0%)	0 (0.0%)
11-20	Negative	165 (57.9%)	201 (84.8%)	50 (86.2%)
	Equivalent	32 (11.2%)	36 (15.2%)	6 (10.6%)
	Positive	88 (19.4%)	0 (0.0%)	2 (3.4%)
21-30	Negative	137 (32.3%)	254 (84.9%)	71 (84.5%)
	Equivalent	50 (11.8%)	43 (14.4%)	7 (8.3%)
	Positive	237 (55.9%)	2 (0.7%)	6 (7.1%)
31-40	Negative	190 (24.4%)	525 (88.8%)	100 (72.5%)
	Equivalent	84 (10.8%)	63 (10.7%)	18 (13.0%)
	Positive	504 (64.8%)	3 (0.5%)	20 (14.5%)
41-50	Negative	174 (22.5%)	498 (90.7%)	117 (73.6%)
	Equivalent	113 (14.6%)	50 (9.1%)	27 (17.0%)
	Positive	486 (62.9%)	1 (0.2%)	15 (9.4%)
51-60	Negative	121 (22.8%)	334 (93.3%)	71 (61.2%)
	Equivalent	79 (14.9%)	24 (6.7%)	25 (21.6%)
	Positive	330 (62.3%)	0 (0.0%)	20 (17.2%)
61-70	Negative	80 (25.1%)	187 (93.0%)	53 (66.3%)
	Equivalent	28 (8.8%)	13 (6.5%)	11 (13.8%)
	Positive	211 (66.1%)	1 (0.5%)	16 (20.0%)
≥ 71	Negative	31 (27.7%)	71 (94.7%)	10 (62.5%)
	Equivalent	16 (14.3%)	3 (4.0%)	2 (12.5%)
	positive	65 (58.0%)	1 (1.3%)	4 (25.0%)
p-value		< 0.01	< 0.01	< 0.01

Note. As for Table 1.

Discussion

This study was conducted to assess the rate of *H. pylori* immunoglobulin seropositivity in a sample of people in Tabriz, the capital city of East Azerbaijan Province in northwestern Iran. We found a significant association between positive IgM results and sex, which was more prevalent in females. Also, this study demonstrated an increasing number of seropositive individuals with aging.

Similar to our study, a study of *H. pylori* serology in 21,429 individuals during 2 years (2012 to 2014) in Tabriz city [13], revealed that seropositivity of *H. pylori* infection in Tabriz was 63.9% which is approximately compatible with our findings. Also, in the mentioned study, there wasn't a significant difference between males and females and it was indicated that by increasing age, the prevalence of IgG positiveness grows progressively which is compatible with our results.

By searching among other investigations all over the world, it can be concluded that age has a positive correlation with IgG positiveness which is known as the "cohort effect". This positive correlation is confirmed in our and other similar studies [17]. We must notice that the sampling of this study was taken from the ordinary population, not from highly probable gastric patients, which can affect the result.

Many studies were designed to determine the prevalence of *H. pylori* in Iran, also there is various conclusion among these studies. This rate is reported as 36.5% in Kurdistan [18], 44.5% in Sari [11], and 41% in patients with gastrointestinal disorders in Birjand [15]. According to a systematic review performed by Zamani in 2018 [19], the prevalence of *H. pylori* infection is estimated to be in the range of 55 to 69.9% in Iran. Our results were in this range (57%) too. This rate is higher than in developed countries which ranged between 30 to 50% [3]. Also, it was higher than in previous studies in other middle-eastern

counties such as the United Arab Emirates which was 41% in a sample of asymptomatic residents [10].

Our study demonstrated a significant association between sex and seropositivity of *H. pylori* IgM. A higher prevalence of *H. pylori* infection was mentioned in previous studies, too [10]. These results contradict a recent systematic review of the prevalence of *H. pylori*, which found no variations in *H. pylori* infection between males and females [19]. To comprehend the mechanisms through which sex may affect the acquisition and persistence of infection, future studies are required.

The prominent strength of our study is the high number of participants in comparison to similar studies, also, in this study, samples were selected from an general population. Other strengths were age- and sex-based analysis of all available Immunoglobulins distinctly. Unfortunately, because of lack of data for participant's occupation, hygiene, smoking, and socio-economic status, the correlation between these items and *H. pylori* is not evaluated in this study.

Conclusion

In conclusion, our study reveals that the prevalence of *H. pylori* in Tabriz is approximately 57% which is in the range estimated to be in Iran, but in comparison to developed countries, it was higher. The prevalence of anti-*H. pylori* immunoglobulins increases significantly with age.

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