ORIGINAL

Helicobacter Pylori infection among asymptomatic schoolchildren: Link with parental educational level

Infección por Helicobacter Pylori en escolares asintomáticos: Relación con el nivel educativo de los padres

Pedro Antonio López Gutiérrez¹, Alexandra Marcela Palma Gonzáles¹, Sarah Angelly Membreño Soto², Gabriel Isaías Rodriguez Lagos¹, Wadia Marie Simón Andonie², Blanca Nelys Licona Hernández²

1. Catholic University of Honduras. Faculty of Medicine, General Practitioner 2. Catholic University of Honduras. Student of General Medicine

Corresponding author

Pedro Antonio López Gutiérrez E-mail: unicahinvestigacion20219@gmail.com **Received:** 8 - III - 2022 **Accepted:** 25 - IIII - 2022

doi: 10.3306/AJHS.2022.37.03.95

Abstract

Objectives: Helicobacter pylori is a bacterium that infects the gastric mucosa and causes both local and systemic diseases in children and adults. We aimed to establish Helicobacter pylori prevalence in the population studied and relate its presence with known risk factors for its infection, including parental educational level and nutritional variables.

Methods: This was an analytical cross-sectional study conducted in a public school in Tegucigalpa, Honduras, in August 2019, where 101 students between 6 and 12 years old were randomly selected after the signing of an informed consent form by their legal guardians and the child's own acceptance. Subsequently, a demographic survey was completed, and a stool sample was obtained from the participants to detect Helicobacter pylori antigen.

Results: Of the 101 schoolchildren studied, 18 (17.82%) tested positive. The mean age of participation was 8.9 ± 1.88 years, 58.4% female, 42.6% male. Educational level of the mother and father in relation to the prevalence of Helicobacter pylori had an odds ratio: 6.8 (Cl 95: 2.17 - 21.63) and odds ratio: 5.7 (1.45 - 23.8), respectively.

Conclusions: The prevalence of Helicobacter pylori was lower than in similar studies carried out in developing countries, and higher than in research on populations in developed countries. A relationship was identified with the educational level of both parents. No association was found with age, gender, body mass index, overcrowding, housing characteristics, access to basic services, pet ownership, family history of Helicobacter pylori infection or gastric cancer.

Key words: Helicobacter pylori, prevalence, education, body mass index.

Resumen

Objetivos: Helicobacter pylori es una bacteria que infecta la mucosa gástrica y que causa enfermedades tanto locales como sistémicas en niños y adultos. El objetivo fue establecer la prevalencia de su infección en la población estudiada y relacionar su presencia con factores de riesgo conocidos, incluyendo el nivel educativo de los progenitores.

Métodos: Estudio analítico, transversal, en una escuela pública de Tegucigalpa, Honduras, en agosto de 2019, donde se seleccionaron aleatoriamente 101 escolares entre 6 y 12 años, previa firma de un consentimiento informado por parte de sus tutores legales, y la aceptación del propio infante. Se completó una encuesta sociodemográfica y se obtuvo una muestra de heces de los participantes para detectar el antígeno de Helicobacter pylori.

Resultados: De 101 escolares estudiados, 18 (17.82%) dieron positivo. La edad media de participación fue de 8.9 ± 1.88 años, 58,4% mujeres y 42.6% hombres. El nivel educativo de la madre y del padre con respecto a la positividad de Helicobacter pylori tuvo un odds ratio: 6.8 (IC 95: 2.17 - 21.63) y odds ratio: 5.7 (1.45 - 23.8), respectivamente.

Conclusiones: La prevalencia de Helicobacter pylori fue inferior a la de estudios similares realizados en países en vías de desarrollo, y superior a la de investigaciones realizadas en poblaciones de países desarrollados. Se identificó una relación con el nivel educativo de ambos padres. No se encontró ninguna asociación con la edad, sexo, índice de masa corporal, hacinamiento, características de la vivienda, acceso a los servicios básicos, posesión de animales domésticos, antecedentes familiares de infección por Helicobacter pylori o de cáncer gástrico.

Palabras clave: Helicobacter pylori, prevalencia, educación, índice de masa corporal.

Introduction

Initially classified and described by a team of Australian physicians through gastroscopic biopsies of the antral muscosa¹, Helicobacter pylori (H.pylori) is a microaerophilic, 4- to 6-flagellated, urease-, catalaseand oxidase-producing, spiral-shaped, gram-negative bacillus-like bacterium², that has the capacity to invade the gastric mucosa and reduce the natural acidity of this tissue, thus enabling it to survive in this environment and contribute to the deterioration of human health^{3,4}.

Even though its infection can occur asymptomatically⁵, within the spectrum of diseases to which H. pylori has been related to, in the adult population, we encounter a span extending from chronic gastritis, gastroduodenal ulcer, and vitamin B12 deficiency⁶⁻⁸, all the way to esophageal and gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue lymphoma (MALT), being neoplasms its most feared consequence⁹⁻¹¹. In fact, the International Agency for Research on Cancer categorized it as a type I carcinogenic agent due to evidence that demonstrates both a correlative and etiological relationship with gastric cancer in human beings^{12,13}.

Then again, in children, idiopathic thrombocytopenic purpura has been described as a disease related to H. pylori infection¹⁴, as well as a decreased growth rate and the development of iron deficiency anemia due to the presence of the sabA gene, an encoder of one of the adhesin type proteins in H. pylori^{15,16}. In a literary review of international studies published between 1991 and 2014, researches from the University of Urmia, Iran, not only demonstrated the presence of iron deficiency anemia in infected individuals but also the resolution of refractory cases, of the aforementioned type of anemia, once H. pylori was eradicated¹⁷.

Its role as a carcinogenic agent and its connection with a multiplicity of diseases has motivated a variety of studies, including research on the extent of its worldwide presence. Regarding this, prevalence rates corresponding to 79.1% in the African region, 63.4% in Central America and the Caribbean, 54.7% in Asia, 47% in Europe, 37.7% in North America and 24.4% in Oceania have been exposed; figures derived from the analysis of data of studies in the general population from 1970 to 2016¹⁸. Then again, pediatric population data suggest prevalences higher than 80% in Oceania, higher than 50% in Africa, about 45% in Central America and the Caribbean, about 30% in Asia, less than 20% in Europe and close to 15% in North America¹⁹.

For both adults and infants the prevalence of H. pylori fluctuates widely depending on the characteristics of the population studied. Therefore, although the regions of Europe, North America, and Oceania present a low prevalence for the general population compared to Latin America, Africa and Asia, even within these territories there are significant variations according to the subpopulation studied¹⁹. Thus, we find in children figures as low as 3.4% in Iceland, close to 24% in Poland and over 40% in indigenous communities in Canada²⁰⁻²². In Latin American, Asian, and African countries, specific analyses of pediatric subpopulations have also shown results ranging from 14.2% in Ghana, 44.3% in Uganda, 41.2% in Ecuador, 77.3% in Colombia, and 31.7% in the United Arab Emirates²³⁻²⁷.

Regardless of the differences between subpopulations in countries with similar statistical background for Helicobacter pylori, it has been shown that the prevalence in the general population has decreased significantly since 2000 for the territories of Oceania, North America, and Europe; in contrast to Asia and Latin America, where it has remained constant as a plateau, and Africa, where the scarce amount of data prior to the year 2000 does not allow for comparison¹⁸.

Generally, the acquisition of the bacterium, whose onset is suggested to occur during infancy²⁸⁻³⁰, is explained by its apparent routes of transmission, being oral-fecal, oraloral and gastro-oral, the ones proposed³¹⁻³³. Although not necessarily mutually exclusive, the three of them are more likely to occur in conditions of overcrowding, poor hygiene, contact with domestic animals, parental low educational level in pediatric cases, open defecation, and ingestion of uncontrolled or poorly treated water, among other risk factors³⁴⁻³⁶, reaching prevalence figures close to 99% in these circumstances^{37,38}.

In Honduras, the data obtained estimates prevalences ranging from 84.7% in adults in the western part of the country³⁹, and between 61% and 64% in hospital-based studies in adults with gastric symptomatology^{40,41}.

In accordance with the information stated above, the present investigation aims to report the prevalence of Helicobacter pylori in schoolchildren ages 6 to 12 years from an urban school in the city of Tegucigalpa, capital of Honduras, and its association with known risk factors.

Methods

This is an analytical cross-sectional study carried out in August 2019 in asymptomatic children enrolled in the Escuela Mixta Los Robles, located in neighborhood Los Robles, in the urban area of Tegucigalpa. The inclusion criteria included age between 6 and 12 years old, active enrollment in Escuela Mixta Los Robles, Honduran nationality, and signature of informed consent by the legal guardians and assent of the ward. The exclusion criteria included having gastrointestinal symptoms in the last 15 days and ingestion of antibiotics, proton pump inhibitors, histamine 2 receptor antagonists or bismuth in the last 30 days, due to a decrease in the performance of the stool antigen detection test in these situations^{42,43}.

The project was approved by both the Institutional Review Board of the Catholic University of Honduras, complying with the Helsinki Declaration, and the local board of education. Meetings were held with the teachers and an informed consent form was sent to each parent explaining the details of the study so that they could evaluate the possibility of participating in the research. A total of 129 signed informed consents were received, after which 101 participants were randomly selected after sample size and sample method were determined using Epilnfo 7.2.4.0 and STATS 2.0, with 5% margin of error and 95% confidence interval.

Measurements of weight and height were taken with a calibrated analog body weight scale and a metal strip tape measure. Each child was given a survey to be answered at home by their legal guardians to be returned on the days of the stool sample collection. A total of 101 stool samples were obtained over 5 collection days. Two new children were included after two of the originally selected failed to provide the stool sample.

To obtain the stool sample parents were provided with a collection jar to deposit it in, instructing them that the sample should be obtained in the morning before the infant attended school or, failing that, to collect an overnight stool sample to be kept in an icebox or refrigerator for no more than 24 hours before its delivery to the research team.

Upon delivery, each sample was placed in an icebox at a temperature of 5 degrees and then transferred to the laboratory 4 hours later where tests were run by means of a qualitative enzyme adsorption immunoassay. The sensitivity and specificity reported for the Quantitative Fecal H. pylori Antigen ELISA Kit according to the manufacturer is, under the indicated conditions, 100% of both specificity and sensitivity⁴⁴.

101 stool samples were processed. A sample was considered positive when it was above the cut-off index suggested by the manufacturer, which was greater than 1.1 for the qualitative cut-off index.

The results were computed in Excel 365 and analyzed with Epilnfo 7.2.4.0 statistical software. For the association of H. pylori with categorical variables, the chi-square or Fisher test was used as appropriate, and for numerical variables, the T-student test was used. Statistical significance was considered p < 0.05.

Results

According to the sociodemographic variables of the schoolchildren participating in this study, it was evident that the prevailing sex was female, with 57.42% girls and 42.58% boys. The average age was 8.97 years old with a standard deviation of 1.88. The prevalence of Helicobacter Pylori infection in school children aged 6 to 12 years in an urban educational unit in Tegucigalpa, Honduras, was of 17.82 % (IC:95 10.92 % - 26.7%) due to 18 positive tests out of 101 samples analyzed, as shown in **table I**.

Open defecation was nonexistent among the infants studied, with 98.02% having access to a flush toilet and 1.98% having access to a latrine. All the children ingested drinking water in their homes and 96.04% of their homes also used it for cooking. The type of construction floor of each house was reported as 82.28% ceramic and 17.82% cement; no parent reported that the house they currently lived in had dirt floors. Exactly 47.52 % stated that their dwelling houses had brick walls, while 44.55 % reported they had block walls, 5.94 % wooden walls, and 1.98% adobe walls.

Regarding the relationship of risk factors with Helicobacter pylori infection, statistical significance was found, with p < 0.05, for the educational level of the parents as shown in **table II**; 36.1 % of the children of mothers with completed or incomplete primary school were positive compared to 8.33 % of the children of mothers with more than 9 years of schooling. On the other hand, 28.1 % of the children of fathers with complete primary schooling were positive compared to 6.25 % positivity for those whose fathers have more than 9 years of schooling.

 Table
 I: Frequency distribution of Helicobacter pylori presence among schoolchildren 6-12 years old.

Variable	Frequency	Percentage
Helicobacter pylori (+)	18	17.82 %
Helicobacter pylori (-)	83	82.18 %
Total	101	100 %

 Table II: Parent's educational level and its relationship to Helicobacter pylori

 prevalence among schoolchildren 6-12 years old.

Evaluated factors		Presence of H. pylori		OR (IC:95)	p - value	
		Yes	No			
Mother's educational	More than 9 years of schooling	5	60	6.8		
level	9 years of schooling or less	13	23	(2.17-21.63)	0.000351	
Father's educational	More than 9 years of schooling	3	45	5.7	0.0105	
level	9 years of schooling or less	9	23	(1.45-23.8)		

Table III: Relationship between other risk factors and Helicobacter pylori prevalence among schoolchildren 6-12 years old.

Other risk factors studied		Presence of H. pylori		OR (IC:95)	p - value
		Si No			
Age	6 to 8 years 9 to 12 years	5 13	30 53	0.68 (0.22-2.09)	0. 498
Sex	Male Female	8 10	35 48	1.1 (0.39-3.06)	0.859
School grade	1 - 3 4 - 6	6 12	31 52	0.84 (0.29-2.46)	0.748
Abnormal BMI	Yes No	10 8	35 48	1.71 (0.61-4.69)	0.3
Shares sleeping room	Yes No	16 2	66 17	2.06 (0.43-9.84)	0.513
Shares bed	Yes No	11 7	42 41	1.53 (0.54-4.34)	0.418
Has pets at home	Yes No	10 8	41 42	1.28 (0.46-3.57)	0.636
Number of adults at home	More than 3 3 or less	7 11	40 43	0.68 (0.24-1.94)	0.473
Number of children at home	More than 3 3 or less	6 12	27 56	1.04 (0.35-3.06)	0.947
Overcrowding	Yes No	4 14	23 60	0.75 (0.22-2.5)	0.774
Monthly economic income	More than 10,000 L.* Less than 10,000 L.	9 9	60 23	2.61 (0.92-7.39)	0.065
Family history of Helicobacter pylori	Yes No	6 12	23 60	1.3 (0.44-3.89)	0.633
Family history of gastric cancer	Yes No	1 17	11 72	0.39 (0.05-3.19)	0.688

* L. Stands for Honduran currency: Lempira. As of August 2019: L. 24.4 = 1 USD https://www.bch.hn/estadisticos/GIE/_layouts/15/WopiFrame. aspx?sourcedoc=%7B90EEBD7C-D458-446A-AB96-FF39D6D7CB00%7D&file=Precio%20Promedio%20del%20D%C3%B3lar%20-%20Serie%20Mensual. xlsx&action=default

 $\begin{tabular}{ll} \begin{tabular}{ll} Table IV: Frequency distribution of nutritional variables regarding Helicobacter pylori presence among schoolchildren 6-12 years old. \end{tabular}$

Studied variat	bles	Helicobacter pylori (+)	Total (%)
BMI for age	Normal Risk of overweight Overweight Obesity	8 / 56 (14.28) 5 / 24 (20.8) 4 / 18 (22.2) 1 / 3 (33.3)	56 /101 (55.4) 24/101 (23.8) 18/101 (17.8) 3/101 (3)
Height for age	Normal	18 /101 (17.8)	101 /101 (100)

For the other risk factors evaluated in **table III**, such as age, sex, school grade, BMI, room sharing, bed sharing, pets at home, adults at home, children at home, overcrowding, economic income, family history of H. pylori, and family history of gastric cancer, no statistically significant association was found.

As height for age and BMI for age are nutritional variables, they were evaluated according to the WHO growth charts for children and adolescents between 5 and 19 years of age, the results are shown in **table IV**. No statistically significant difference was shown for BMI and Helicobacter Pylori.

Discussion

The prevalence of H. pylori obtained in this study was obtained by stool antigen detection due to its wide

application in microbiology, cost, high sensitivity and specificity, and because it is a non-invasive method⁴⁵. El-Shabrawi et al. demonstrated in Cairo, Egypt the applicability of the stool antigen test in children, detecting a sensitivity between 89% and 98% and a specificity between 94 and 100%; only slightly lower than the C-13 urea breath test whose operation implies higher economic costs for laboratories and less tolerance by infants⁴⁶. Other non-invasive methods include serological tests and molecular tests on saliva and stool samples⁴⁷.

Regarding the results obtained according to the objectives of the study, the prevalence of H. pylori in the population studied, 17.8%, contrasts considerably with other national results in which a higher prevalence of H. pylori than that reported in our study has been stated. In 2006, Morgan et al. identified that 85% of the asymptomatic adult population participating in their study in the western part of the country had a positive seroprevalence⁴⁰ Subsequently, in 2013, through positive cultures of gastric biopsies, Morgan et al. also reported 61.4% of 189 adult patients with gastric symptomatology in Hospital de Occidente, as carriers of Helicobacter pylori³⁹.

In both cases, the conditions of space, time, and population in which the study was carried out should be considered, since although the decline in the prevalence of H. pylori has been demonstrated mainly in the inhabitants of socioeconomically developed territories ⁴⁸⁻⁵⁰, similar behavior has also been observed in increasingly industrialized countries such as China and Brazil, where its decrease has been attributed to better living conditions^{51,52}. Therefore, the high percentage coverage of flush toilets, the absence of open defecation, the construction materials used in dwellings, the high consumption of drinking water, and the pediatric study population probably explain the low prevalence found.

Similarly, in Jordan, a developing country, Eyad Altamimi et al. found in 2019 that the prevalence of H. pylori for asymptomatic pediatric patients, probed by carbon 13 breath test, stood at 14.6 % for infants aged 4 to 17 years, and 25% for those aged 6 to 11 years⁵³. In sub-Saharan Africa, in 2017, a study conducted in Ghana by Awuku et al. demonstrated a prevalence, by stool antigen, of 14.2 percent in pediatric villagers aged 5 to 16 years and 14.5 percent in patients aged 5 to 10 years. In those positive patients, open defecation, female gender, and source of drinking water represented risk factors²³.

Regarding the educational level of the mother, at least since 2001 information has been obtained identifying it as a risk factor for H. pylori infection, as demonstrated by Malaty et al. when they studied 356 children between 2 and 16 years of age from the Houston area in the United States between 1996 and 1998, obtaining statistically significant results regarding maternal education as a risk factor with p<0.001 for mothers who had not completed at least 12 years of education⁵⁴. Later Galal et al. examined 630 Egyptian children with gastric symptomatology and found a prevalence of 64.9 % by stool antigen detection and an association between illiterate mothers and stool antigen positivity for H. pylori⁵⁵.

In our study, statistically significant differences were found for H. pylori positivity according to the educational level of both parents, not only the mother, taking 9 school years as the cut-off educational level, since in Honduras, according to article 22 of the Fundamental Law of Education published in 2012, basic education consists of 9 years of compulsory schooling⁵⁶. Similarly, in Portugal, Bastos et al. found a lower prevalence in adolescents whose parents had a higher level of education⁵⁷. Wangda et al. also found a similar association in children from 8 public schools in Bhutan where H. pylori positivity reflected a statistically significant difference when comparing children of college-educated mothers with those of non-college educated mothers⁵⁸. Muhsen et al. obtained, in 2012, an association between the fathers' educational level and H. pylori positivity by dividing male parents into 2 groups: those with more than nine grades of schooling and those with less than nine grades of schooling. With respect to the mothers' education, no significant differences were found in that study⁵⁹.

The statistical results between the association of Helicobacter pylori and body mass index has sometimes proven to show contradictory data. Previously, Arslan et al. had shown some association in their analysis of 103 obese adult patients and 111 controls, regarding Helicobacter pylori infection and BMI, obtaining results with statistical significance p <0.01 and odds ratio greater than two⁶⁰. Chen et al. also obtained results showing an association between body mass index and H. pylori infection, specifically in adult patients under 50 years of age⁶¹. However, in pediatric patients, associations inversely proportional to BMI have been found, where after H. pylori eradication this parameter increases⁶², even reaching morbid obesity levels⁶³. Moran - Lev et al. showed the same phenomenon in symptomatic Israeli children diagnosed by means of gastric biopsies; 31% of the non-infected children presented obesity or overweight, in contrast to the infected children, of only whom 11% presented obesity, generating a statistically significant difference, suggesting an inverse relationship between the ordinal value of BMI and H. pylori positivity⁶⁴. The results of our project have yielded data with no significant statistical difference between BMI, both in its ordinal and numerical values, and H. pylori infection, as can be seen in the publications of Pundak et al. and Choi et al. where, in the former, they report the lack of relationship between obesity or overweight and infection by H. pylori infection⁶⁵ whereas in the latter they report that after eradication of the bacteria, the treated infants presented a significantly greater weight gain than those who were not treated, without specifying whether or not the magnitude of the weight gain caused them to move from one BMI category to another⁶⁶. The present investigation did not have the scope to treat infants with positive results.

Conclusions

More studies covering larger populations will be needed to confirm H. pylori's prevalence in children. Nonetheless, within the scope of the present report, a lower prevalence was found when compared to similar studies. Moreover, a particular association was observed between the lower educational level of both parents and Helicobacter pylori stool antigen positivity.

Acknowledgements

The authors thank Nissi Laboratories for donating the total amount of the antigen stool tests used during this investigation; all other research expenses were self-financed.

Conflict of Interests

The authors have no conflict of interest.

References

1. Marshall B, Warren R. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. The Lancet. 1984 Jun; 323(8390):1311-15.

2. Burkitt MD, Duckworth C, Williams JM, Pritchard DM. Helicobacter pylori-induced gastric pathology: insights from in vivo and ex vivo models. Disease Models & Mechanisms. 2017 Feb; 10(2):89-104.

3. Crowe SE. Helicobacter pylori Infection. New England Journal of Medicine. 2019 Mar; 380(12):1158-65.

4. Blanchard TG, Czinn JS. Identification of Helicobacter pylori and the evolution of an efficacious childhood vaccine to protect against gastritis and peptic ulcer disease. Pediatric Research. 2017 Jan; 81(1):170-76.

5. Ford AC, Forman D, Hunt RH, Yuhong Y, Moayyedi P. Helicobacter pylori eradication therapy to prevent gastric cancer in healthy asymptomatic infected individuals: systematic review and meta-analysis of randomised controlled trials. The BMJ. 2014 May; 348:1-13.

6. Sugano K, Tack J, Kuipers EJ, Graham DY, El-Omar EM, Miura S, et al. Kyoto global consensus report on Helicobacter pylori gastritis. BMJ journal. 2015 Sep; 64(9):1353-67.

7. Ravi K, Joseph J, Thomas D. Helicobacter pylori infection and vitamin B-12 deficiency- A cross sectional study. Asian Journal of Medical Sciences. 2017 Jul; 8(4):16-20.

8. Ulasoglu C, Temiz H, Sağlam Z. The Relation of Cytotoxin-Associated Gene-A Seropositivity with Vitamin B12 Deficiency in Helicobacter pylori-Positive Patients. BioMed Research International. 2019 Dec; 2019: 1450536.

9. Polyzos SA, Zeglinas C, Artemaki F, Doulberis M, Kazakos E, Katsinelos P, et al. Helicobacter pylori infection and esophageal adenocarcinoma: a review and a personal view. Annals of Gastroenterology. 2018 Jan - Feb; 31(1):8-13.

10. Santambrogio O. Helicobacter pylori and hematological disorders. Minerva Gastroenterologica e Dietologica. 2019 Apr; 65(3).

11. Floch P, Mégraud F, Lehours P. Helicobacter pylori Strains and Gastric MALT Lymphoma. Toxins. 2017 Apr; 9(4):132.

12. World Health Organization. Helicobacter pylori Eradication as a Strategy for preventing Gastric Cancer. Scientific report. Lyon: World Health Organization, International Agency for Research on Cancer ; 2014. Report No.: ISBN 978-92-832-2454-9.

Diaconu S, Predescu A, Moldoveanu A, Pop C, Fierbinţeanu-Braticevici
 C. Helicobacter pylori infection: old and new. Journal of Medicine and Life.
 2017 Apr - Jun; 10(2):112-17.

14. Hanai H, Pellegrini J, Loggetto S, Strehl R, Hernandes C, Kawakami E. Helicobacter pylori infection & immune thrombocytopenic purpura in children and adolescents: A randomized controlled trial. Platelets. 2015 May; 26(4):336-41.

15. Dror G, Muhsen K. Helicobacter pylori Infection and Children's Growth. Journal of PEdiatric Gastroenterology and Nutrition. 2016 Jun; 62(6):48 -59.

16. Kato S, Osaki T, Kamiya S, Zhang XS, Blaser MJ. Helicobacter pylori sabA gene is associated with iron deficiency anemia in childhood and adolescence. PLOS One. 2017 Aug; 12(8):1-15.

17. Gheibi S, Farrokh-Eslamlou H, Noroozi M, Pakniyat A. Refractory iron deficiency anemia and HelicobacterPylori Infection in pediatrics: A review. Iranian Journal of Pediatric Hematology Oncology. 2015 Mar; 15(1):50-64.

18. Hooi JKY, Lai WY, Khoon Ng W, Suen MMY, Underwood FE, Tanyingoh D, et al. Global Prevalence of Helicobacter pylori Infection: Systematic Review and Meta-Analysis. Gastroenterology. 2017 Aug; 153(2):420-29.

19. Zamani M, Ebrahimtabarm F, Zamani V, Miller VH, Alizadeh-Navaei R, Shokri-Shirvani J, et al. Systematic review with meta-analysis: the worldwide prevalence of Helicobacter pylori infection. Alimentary Pharmacology & Therapeutics. 2018 Jan; 47(7):868-76.

20. Asgeirsdottir GA, Kjartansdottir I, Olafsdottir AS, Hreinsson JP, Hrafnkelsson H, Johannsson E, et al. Helicobacter pylori infection in Icelandic children. Scandinavian Journal of Gastroenterology. 2017 Mar; 52(6-7):686-90.

21. Anna Szaflarska-Poplawska AS. Prevalence of Helicobacter pylori infection among junior high school students in Grudziadz, Poland. Helicobcater. 2018 Oct; 24(1).

22. Fagan-Garcia K, Geary J, Chang HJ, McAlpine L, Walker E, Colquhoun A, et al. Burden of disease from Helicobacter pylori infection in western Canadian Arctic communities. BMC Public Health. 2019 June; 730(19).

23. Awuku YA, Simpong DL, Alhassan IK, Anamaale D, Afaa TT, Adu P. Prevalence of helicobacter pylori infection among children living in a rural setting in Sub Saharian Africa. BMC Public Health. 2017 Apr; 17(1).

24. Hestvik E, Tylleskar T, H Kaddu-Mulindwa D, Ndeezi G, Grahnquist L, Olafsdottir E, et al. Helicobacter pyloriin apparently healthy children aged 0-12 years in urban Kampala, Uganda: a community-based cross sectional survey. BMC Gastroenterology. 2016 Jun; 10(62).

25. Pico Mawyin TL, Galarza SN, Barzola C, Arcadio G, Saavedra Aguilar ÁM. Comportamiento de infección por Helicobacter pylori en pacientes pediátricos detectados mediante prueba de aliento con urea-c13. Revista Científica Mundo de la Investigacion y el Conocimineto. 2019 Apr; 3(2):785-800.

26. Bohórquez MS, Liévano M, Campuzano G, Bolívar T, Rozo A. Prevalencia de Helicobacter pylori en escolares: factores nutricionales y socio-culturales en Bogotá. Pediatria. 2012 Jun; 45(2):81-93.

27. Khoder G, Muhammad JS, Mahmoud I, Soliman SSM, Burucoa C. Prevalence of Helicobacter pylori and Its Associated Factors among Healthy Asymptomatic Residents in the United Arab Emirates. Pathogens. 2019 Apr; 8(2):44.

28. Castro-Muñoz LJ, González-Díaz C, Muñoz-Escobara A, Tovar-Ayonad B, Aguilar L, Anguiano , et al. Prevalence of Helicobacter pylori from the oral cavity of Mexican asymptomatic children under 5 years of age through PCR. Archives of Oral Biology. 2017 January; 73(2017):55-59.

29. Coelho LG, Minho J, Genta R, Tenório L, Friche Pasos MdC, Zaterka C. IVth Brazilian Consensus Conference On Helicobater Pylori Infection. Archives of Gastroeneterology. 2018 Apr-Jun; 55(2): 97-121.

30. Kienesberger S, Perez-Perez GI, Olivares AZ, Bardhan P, Sarker SA, Hasan KH, et al. When is Helicobacter pylori acquired in populations in developing countries? A birth-cohort study in Bangladeshi children. Gut Microbes. 2018 March; 9(3):252-63.

31. Kayali S, Manfredi M, Gaiani FBL, Bizzarri B, Leandro G, di Mario F, et al. Helicobacter pylori, transmission routes and recurrence of of infection; state of the art. Acta Biomedica. 2018 Dec; 89(8): 72-6.

32. Bui D, Brown HE, Harris BR, Oren E. Serologic Evidence for Fecal-Oral Transmission of Helicobacter pylori. The American Journal of Tropical medicine and Hygiene. 2016 Jan; 94(1):82-8.

33. Zakrzewska M, Zakrzewski M, Gladka A, Czarniecka-Barglowska K, Maciorkowska E. Saliva testing for Helicobacter pylori infection in children and adolescents – a literature review. Polish Journal of Paediatrics. 2019 Aug; 94(4):255-8.

34. Krueger WS, Hilborn ED, Converse R, Wade TJ. Environmental risk factors associated with Helicobacter pylori seroprevalence in the United

States: a cross-sectional analysis of NHANES data. Epidemiology & Inection. 2015 Jan; 143(12):2520-31.

35. Ozbeycorresponding G, Hanafiah A. Epidemiology, Diagnosis, and Risk Factors of Helicobacter pylori Infection in Children. Eurasian Journal of Hepato - Gastroenterology. 2017 May; 7(1):34-9.

36. Eshraghian A. Epidemiology of Helicobacter pylori infection among the healthy population in Iran and countries of the Eastern Mediterranean Region: A systematic review of prevalence and risk factors. World Journal of Gastroenterology. 2014 Dec; 20(46).

37. Goodman KJ, Correa P, Tenganá Aux HJ, Ramírez H, DeLany JP, Guerrero O, et al. Helicobacter pylori infection in the Colombian Andes: a population-based study of transmission pathways. Americna Journal of epidemiology. 1996 Aug; 144(3):290-9.

38. Arboleda RN, Schneider BG, Bravo LE, Romero-Gallo J, Peek RM, Jr MR, et al. Use of a Non-invasive Test (Entero-test) in the Detection of Helicobacter pylori in Children in an Endemic Area in Colombia. Journal of Pediatric Gastroenterology and Nutrition. 2013 Aug; 57(2):192-6.

39. Morgan D, Dominguez R, O. Keku T, Heidt P, F. Martin C, Galanko J, et al. Gastric Cancer and the High Combination Prevalence of Host Cytokine Genotypesand Helicobacter pylori in Honduras. Clinical Gastroenterology and Hepatology. 2006 Sep; 4(9):1103-11.

40. Ortiz V, Estevez-Ordonez D, Montalvan-Sanchez E, Urrutia-Argueta S, Israel D, Krishna US, et al. Helicobacter pylori antimicrobial resistance and antibiotic consumption in the low-resource Central America setting. Helicobacter. 2019 May; 24(4): p. e19525.

41. Durón RA, Zuniga GA, Zelaya , Jose F, Amador L, de Aviles M, et al. Incidencia de Helicobacter. Revista MEdica Hondureña. 1990 Aug;58(2).

42. Calik Z, Karamesea M, Acar O, Karamese S, Dicle Y, Albayrak F, et al. Investigation of Helicobacter pylori antigen in stool samples of patients with upper gastrointestinal complaints. Brazilian Journal of Microbiology. 2016 Jan - Mar; 47(1):167-71.

43. Sánchez Delgadoa J, García-Iglesias P, Titó L, Puig I, Planella M, Gené E, et al. Update on the management of Helicobacter pylori infection. Position paper from the Catalan Society of Digestology. Gastroenterologia y Hepatologia. 2018 Apr; 41(4):272-80.

44. Epitope Diagnostics, Inc. Epitope Diagnistics. [Online].; 2017 [cited 2021 Feb 12. Available from: https://static1.squarespace.com/ static/52545951e4b021818110f9cf/t/592f110d8419c2ffb83d7 bf6/1496256787481/KT+826+Fecal+H.+Pylori+Antigen+Elisa_v11_IVD.pdf.

45. Cardinali L, Rocha G, Rocha A, de Moura S, de Figueiredo Soares T, Esteves A et al. Evaluation of [13 C]Urea Breath Test and Helicobacter pylori Stool Antigen Test for Diagnosis of H. pylori Infection in Children from a Developing Country. Journal of Clinical Microbiology. 2003;41(7):3334-5.

46. El-Shabrawi M, Abd El-Aziz N, Zakaria El-Adly T, Hassanin F, Eskander A, Abou-Zekri M, et al. Stool antigen detection versus 13C-urea breath test for non-invasive diagnosis of pediatric Helicobacter pylori infection in a limited resource setting. Archives of Medical Science. 2018 Jan; 14(1):69-73.

47. Kalali B, Formichella L, Gerhand M. Diagnosis of Helicobacter pylori: Changes towards the Future. Diseases. 2015 Jun; 3(3):122-35.

48. Miyamoto R, Okuda M, Lin Y, Murotani K, Okumura A, Kikuchi S. Rapidly decreasing prevalence of Helicobacter pylori among Japanese children and adolescents. Journal of Infection and Chemotherapy. 2019 Jul; 25(7):526-30.

49. Sonnenberg A, Turner KO, Genta RM. Low Prevalence of Helicobacter pylori-Positive Peptic Ulcers in Private Outpatient Endoscopy Centers in the United States. The American Journal of Gastroenterology. 2020 Feb; 115(2):244-50.

50. Roberts SE, Morrison-Rees S, Samuel DG, Thome K, Akbari A, Williams JG. Review article: the prevalence of Helicobacter pylori and the incidence of gastric cancer across Europe. Alimentary Pharmacology and Therapeutics. 2015 Nov; 43(3):334-45.

51. Yu X, Yang X, Yang T, Dong Q, Wang L, Feng L. Decreasing prevalence of Helicobacter pylori according to birth cohorts in urban China. The Turiskh Journal of Gastroenterology. 2017 Mar; 28(2):94-97.

52. Toscano E, Fernandes F, Dutra-Rulli M, Maia L, Alcântara M, Silva V, et al. Epidemiological and Clinical-Pathological Aspects of Helicobacter pylori Infection in Brazilian Children and Adults. Gastroenterology Research and Practice. 2018 Sep; 2018.

53. Altamimi E, Alsharkhat NAA, Abu Hamad MR, Abu Assi A, Alawneh S, Al-Ahmad M. Declining prevalence of Helicobacter pylori infection in Jordanian children. Heylon. 2020 Jul; 6(7): p. e04416.

54. Malaty HM, Logan ND, Graham DY, Ramchatesingh JE. Helicobacter pylori Infection in Preschool and School-Aged Minority Children: Effect of Socioeconomic Indicators and Breast-Feeding Practices. Clinical Infectius Diseases. 2001 May; 32(10):1387-92.

55. Galal YS, Ghobrial CM, Labib JR, Abou-Zekri ME. Helicobacter pylori among symptomatic Egyptian children: prevalence, risk factors, and effect on growth. Journal of Egyptina Public Health Association. 2019 May; 94(17).

56. Congreso Nacional de Honduras. Ley Fundamental de Educación. Diario Oficial La Gaceta. 2012 Feb: 1-6.

57. Bastos J, Peleteiro B, Pinto H, Marinho A, T.Guimarães J, Ramosa E, et al. Prevalence, incidence and risk factors for Helicobacter pylori infection in a cohort of Portuguese adolescents (EpiTeen). Digestive and Liver Disease. 2013 Apr; 45(4):290-5.

58. Wangda S, Richter JM, Kuenzang P, Wangchuk K, Choden T, Tenzin K, et al. Epidemiology of Helicobacter pylori infection in asymptomatic schoolchildren in Bhutan. Helicobacter. 2017 Dec; 6(22).

59. Muhsen K, Jurban M, Goren S, Cohen D. Incidence, Age of Acquisition and Risk Factors of Helicobacter pylori Infection among Israeli Arab Infants. Journal of Tropical Pediatrics. 2012 Jun; 58(3):208-13.

60. Arslan E, Atılgan H, Yavaşoğlu I. The prevalence of Helicobacter pylori in obese subjects. European Jornal of Internal Medicine. 2009 Nov; 20(7):695-7.

61. Chen LW, Kuo SF, Chen CH, Chien CH, Lin CL, Chien RN. A community-based study on the association between Helicobacter pylori Infection and obesity. Scientific Reports 8. 2018 Jul; 10746(2018).

62. Pacifico L, Anania C, Osborn J, Schiavo E, Bonamico M, Chiesa C. Long-term effects of Helicobacter pylori eradication on circulating ghrelin and leptin concentrations and body composition in prepubertal children. European Journal of Endocrinology. 2008 Mar; 158(3):323-32.

63. Wu MS, Lee WJ, Wang HH. A Case-Control Study of Association of Helicobacter pylori Infection With Morbid Obesity in Taiwan. Archives of Internal Medicine. 2005 Jul; 165(13):1552-5.

64. Moran-Lev H, Lubetzky R, Mandel D, Yerushalmy-Feler A, Cohen S. Inverse Correlation between Helicobacter pylori Colonization and Pediatric Overweight: A Preliminary Study. Childhood Obesity. 2017 Aug; 13(4):267-71.

65. Pundak OY, Olivestone CT, Hofi L, Kori M. Lack of association between Helicobacter pylori infection and childhood overweight/obesity. Helicobacter. 2020 Jul; 25(5): p. e12728.

66. Choi JS, Ko KO, Lim JW, Cheon EJ, Min Lee G, Min Yoon J. The Association between Helicobacter pylori Infection and Body Weight among Children. Pediatric Gastroenterology, Hepatology & Nutrition. 2016 Jun; 19(2):110-5.