

Microbiology Research Journal International

30(7): 80-91, 2020; Article no.MRJI.58186 ISSN: 2456-7043 (Past name: British Microbiology Research Journal, Past ISSN: 2231-0886, NLM ID: 101608140)

Burden of *Helicobacter pylori* Infections and Associated Risk Factors among Cases of Iron Deficiency Anaemia in Egypt

Hadir M. El-Kady¹, Waiel Al-Kahiry² and Hadeel Said Tawfik Abdelsalam^{1*}

¹Medical Laboratory Department, Pharos University in Alexandria, Egypt. ²Department of Hematology, Faculty of Medicine and Health Sciences, University of Aden, Yemen.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/MRJI/2020/v30i730241 <u>Editor(s):</u> (1) Dr. Kai Zhang, State University of New York at Buffalo, USA. (2) Dr. Lachhman Das Singla, Guru Angad Dev Veterinary and Animal Sciences University, India. <u>Reviewers:</u> (1) Josue Jesus Aliaga Ramos, Cayetano Heredia University, Peru. (2) P. N. Remya, SRM Institute of Science and Technology, India. Complete Peer review History: <u>http://www.sdiarticle4.com/review-history/58186</u>

Original Research Article

Received 28 May 2020 Accepted 04 August 2020 Published 19 August 2020

ABSTRACT

Introduction: Iron deficiency anaemia (IDA) is a worldwide nutritional problem; it accounts for about half of the world's anaemia burden. Globally, *Helicobacter pylori (H. pylori)* is becoming an increasingly troublesome economic and public health problem. The colonization of the organism in gastric mucosa may impair iron uptake and increase iron loss, potentially leading to iron deficiency anaemia. The mechanisms by which *H. pylori* is postulated to cause IDA are *H. pylori* -associated chronic gastritis resulting in hypo/or achlorhydria, reduced ascorbic acid secretion and reduced intestinal iron absorption, occult blood loss due to chronic erosive gastritis, and sequestration and utilization of iron by *Helicobacter pylori*.

Aims: To detect *H. pylori*–related IDA prevalence among asymptomatic cases of anaemia and to address the possibility that such infection may play a detrimental role in their blood picture, serum iron and ferritin levels and total iron binding capacity (TIBC)

Study Design & Methods: Facility based cross-sectional study was conducted in the period from December 2018 to May 2019. Screening was done for asymptomatic attendants of a number of private laboratories in Beheira, Alexandria and Gharbiya governorates. Three

hundreds of whom were proved to be cases of IDA and were further tested for *H. pylori* antigen in stool.

Results: *Helicobacter pylori* Ag test in stool was positive in 180 out of 300 cases of iron deficiency anaemia. The infection significantly affected the haemoglobin level, MCV, MCH and RDW in studied cases (p<0.05). Infection with *H. pylori* also significantly affected the serum iron, serum ferritin and TIBC in the studied cases of IDA (p<0.05).

Conclusion: A significant association between *H. pylori* infection and IDA. Screening for *H. pylori* among unexplained cases of IDA is recommended.

Keywords: H. pylori; H. pylori stool AG test; Iron deficiency anaemia; serum iron; TIBC.

1. INTRODUCTION

Anemia is a medical condition associated with increased or decreased RBCs characterized by inadequate oxygen-carrying capacity to meet physiological needs [1]. Iron deficiency is the most common cause of anemia globally. Iron deficiency anemia (IDA) is caused by deranged synthesis of haemoglobin, resulting in red cells that are include reduced amounts of hemoglobin (hypochromic) and smaller than normal (microcytic) [2]. Iron deficiency evolves through three stages: iron depletion is the earliest stage of iron deficiency in which storage iron is decreased or absent but serum iron concentration and blood hemoglobin levels are normal, the second stage is iron deficiency without anemia then iron deficiency anemia [3].

Helicobacter pylori (*H. pylori*) infection is the most common chronic infection involving half of the population worldwide [4]. *H. pylori* is a microaerophilic, Gram-negative, spiral-shaped bacterium [5].Numerous researchers have focused on the role of *H. pylori* infection on a wide range of gastrointestinal disorders that vary from asymptomatic gastritis to peptic ulcer, and also gastric carcinoma and lymphoma [6]. It has been reported that *H. pylori* may influence some extra-gastrointestinal diseases including iron deficiency (ID), and iron deficiency anemia [4].

The major cause of iron deficiency (ID) in developed countries is overt or occult gastrointestinal blood loss [3]. The mechanisms by which Hp infection is postulated to cause IDA are Hp-associated chronic gastritis resulting in hypo or achlorhydria, reduced ascorbic acid secretion and reduced intestinal iron absorption, occult blood loss due to chronic erosive gastritis, and sequestration and utilization of iron by *Helicobacter pylori* [4].

This study aimed to detect *H. pylori*–related IDA prevalence among cases of anaemia who are asymptomatic regards GIT complaints and to address the possibility that such infection may

play a detrimental role in their blood picture, serum iron and ferritin levels and total iron binding capacity (TIBC).

2. MATERIALS AND METHODS

A facility based descriptive cross-sectional study design was conducted in the period from December 2018 to May 2019 in some private laboratories in Beheira, Alexandria and Gharbiya governorates. Screened subjects included all the attendance seeking a routine check up blood picture and those indicated for follow up of cases of anaemia. Selected participants in the study were those 300 cases proved to be cases of IDA; 200 subjects were newly diagnosed as IDA and the remaining were on iron supplements. All the 300 subjects were asymptomatic regards GIT manifestations of *H. pylori* infection.

Patients with malignancies, chronic diseases, dimorphic anemia, obvious causes of IDA, obvious non-GI causes of blood loss, chronic renal failure and acute infections were excluded from the study. Also patients who were on nonsteroidal anti-inflammatory drugs for long periods were excluded. None of the patients enrolled mentioned previous diagnosis, endoscopic examination or receiving treatment for H. pylori infection.

2.1 Questionnaire

Participants were asked to fill in a questionnaire covering personal and demographic data and dietary habits; personally or by the parents.

2.2 Blood Sample

2.2.1 Complete Blood Count (CBC)

Blood sampling was done for all screened subjects throughout the duration of the study and were examined for complete blood count (CBC) done by (Sysmex-XS 500i).

It was measured using the Elecsys 2010 system using a Roche diagnostics kit by the electrochemiluminescence immunoassay (ELISA) method.

2.2.3 Serum levels of iron

Serum levels of iron were measured by the colorimetric method with a Roche modular analyzer.

2.2.4 TIBC

TIBC was measured with the Roche modular analyzer.

2.3 Stool Samples

2.3.1 Helicobacter pylori stool antigen

Stool samples were provided by participants and were tested for H. pylori stool antigen (H. pylori Antigen ELISA Diagnostic Kit; CTK Biotech HpSA kit, San Diego, CA 92121 Inc., USA). The test was done on fresh stool samples. A random stool specimen in a clean, dry receptacle was collected .The stool collection device with the specimen's ID number (patient ID sticker) was labeled. The stool collection device was opened by unscrewing the top and using the collection stick to randomly pierce in 2-5 different sites, twisting the collection stick into the stool specimens to help collection if necessary. All inner grooves of the collection stick were filled with the stool specimen. However, excess stool specimen on the outside of grooves was scraped off the collection stick and the stool collection device was tightened securely to close. According to the manufacturer leaflet provided with the H. pylori test kits the relative sensitivity, relative specificity, and overall agreement were 96.7%, 93.8%, and 94.9%, respectively. Its analytical sensitivity was 100% positive detection rate at 1 ng/mL of pylori lysate antigen in fecal specimens.

3. RESULTS

Three hundred participants suffering from IDA were recruited in this study. The age of the participants ranged from 3 to 68 years old with a mean of $31.2 \pm$ SD10.3, *H. pylori* Ag test was positive in 180/ 300 (60%) of the participants.

In this study although the prevalence was highest among participants > 50 years old (62%) compared to all other younger participants; yet no statistically significant difference between age groups was reported (p=0.077) [Table 1].

In this work the prevalence rate of *H. pylori* was significantly higher among females (62.2%) than among males (57%). (p=0.001) [Table 1].

One hundred and thirty four out of the 300 cases of IDA studied in this study (44.7%) were residents of urban areas while 166 (55.3%) were residents of rural areas. Prevalence rate of *H. pylori* infection among urban dwellers was 57.5% (77/134) compared to 62% (103/166) in rural dwellers .Residence was not significantly associated with prevalence of *H. pylori* [Table1].

Family history of *H. pylori* infection significantly affected the prevalence rate of *H. pylori* among the participants. (p=0.037). Prevalence rate among those with positive family history was 71.4% compared to 57% among those with no family history. It is worth mentioning that in the 63 cases with positive family history; it was the mother who had *H. pylori* infection [Table 1].

An inverse association between the level of education and *H. pylori* infection among the studied cases was reported in this study. *H. pylori* prevalence recorded among those who were illiterate or had only primary school education was 73.55 and 78.4%, respectively compared to 51.8% among those who had high school education and to only 30.8% among those who achieved university education or higher. This variance was highly statistically significant (p=0.001) [Table 1].

Smoking and eating spicy food had no statistically significant effect on the prevalence of *H. pylori* among the participants. (p > 0.05) [Table 2]. Intake of high protein diet and skipping meals were significantly implicated to increase the risk of *H. pylori* infection among the enrolled cases of IDA. (p<0.05) [Table 2].

In addition, drinking coffee and tea significantly increased the prevalence rate of *H. pylori* among participants compared to those who didn't have such dietary habits. (p < 0.05)[Table 2].

Helicobacter pylori infection significantly affected the haemoglobin level, MCV, MCH and RDW in the studied cases (p<0.05). [Table 3]. On the other hand no statistically significant

Parameter	Helicobacter Pylori (Stool antigen test)				Total		<i>p</i> -value
	Positive (n = 180)		Negative (n = 120)		(n = 300)		
	N⁰	%	N⁰	%	N⁰	%#	—
- Sex:							
Male	73	57.0	55	43.0	128	42.7	0.001
Female	107	62.2	65	37.8	172	57.3	
-Mean age ± SD (years):	30.2 ±	9.6	32.4 ±	11.8	31.2 ±	10.3	0.077
(MinMax.)	(3 - 68))	(3 - 65	5)	(3 - 68	3)	
- Age group: (years)							
< 10	3	60.0	2	40.0	5	1.7	0.984
10 – 29	98	60.1	65	39.9	163	54.3	
30 – 49	48	58.5	34	41.5	82	27.3	
≥ 50	31	62.0	19	38.0	50	16.7	
- Residence:							
Urban	77	57.5	57	42.5	134	44.7	0.420
Rural	103	62.0	63	38.0	166	55.3	
- Family history of H.pylor	i infectio	n:					
Yes	45	71.4	18	28.6	63	21.0	0.037
No	135	57.0	102	43.0	237	79.0	
- Education:##							
Illiterate	10	55.6	8	44.4	18	6.0	0.003
Primary	71	62.8	42	37.2	113	37.7	
Secondary	63	71.6	25	28.4	88	29.3	
University	36	44.4	45	55.6	81	27.0	

Table 1. Sociodemographic data of the studied patients with IDA in relation to Helicobacter pylori infection

^{*}Percentages were calculated from the total sample size, while other by the total of each row. [#]For children, the educational level of mother was considered. *p-value <0.05 is statistically significant

Table 2. Smoking and dietary habits of the studied patients with IDA in relation to Helicobacter pylori infection

Habits	Helicobacter pylori (Stool antigen test)				Total		<i>p</i> -value
	Positive (n = 180)		Negative (n = 120)		(n = 300)		•
	N⁰	%	N⁰	%	N⁰	%#	-
- Smoking:							
Yes	64	67.4	31	32.6	95	31.7	0.076
No	116	56.6	89	43.4	205	68.3	
- Protein rich diets:							
Yes	168	63.6	96	36.4	264	88.0	0.001
No	12	33.3	24	66.7	36	12.0	
- Skipping meals:							
Yes	174	62.4	105	37.6	279	93.0	0.002*
No	6	28.6	15	71.4	21	7.0	
 Eating spicy food 							
Yes	76	65.0	41	35.0	117	39.0	0.161
No	104	56.8	79	43.2	183	61.0	
- Drinking coffee:							
Yes	175	65.5	92	34.5	267	89.0	0.001*
No	5	15.2	28	84.8	33	11.0	
- Drinking Tea:							
Yes	178	61.0	114	39.0	292	97.3	0.041
No	2	25.0	6	75.0	8	2.7	

[#]Percentages were calculated from the total sample size, while other by the total of each row. *p-value <0.05 is statistically significant

Parameter	Unit	Helico	p-value	
		Positive (n=180) (Mean ± SD)	Negative (n=120) (Mean ± SD)	
Hemoglobin	g/dl	10.1 ±1.6	10.6 ±1.5	0.007*
Hematocrit	%	33.4±4.1	33.1 ±4.0	0.531
MCV	FI	72.3 ±5.9	74.1± 3.8	0.003*
MCH	Pg	22.3 ±2.8	23.1±2.6	0.013*
MCHC	g/dl	29.9 ± 1.2	30.1 ±1.3	0.172
RDW	%	16.0 ±1.3	15.7±1.2	0.044*
RBC's count	x10 ¹² /L	3.7 ±0.45	3.8 ±0.51	0.075
WBC's count	x10 ⁹ /L	6.3±2.4	6.0±2.3	0.282
Platelets count	x10 ⁹ /L	306.9±78.4	305.1±79.5	0.847
ESR	mm/hr	19.9±17.4	18.7±16.6	0.552

Table 3. The main hematological parameters for the studied patients with iron deficiency anemia in relation to Helicobacter pylori

MCV: Mean corpuscular volume MCH: Mean corpuscular hemoglobin RDW: Red cells distribution widthMCH: Mean corpuscular hemoglobin concentration RBC: Red blood cells ESR: Erythrocytes sedimentation rate WBC: white blood cells p-values> 0.05 are statistically insignificant

difference between both positive and negative groups for H. pylori regards their hematocrit level, MCHC, RBCs count, WBCs count, platelets count and ESR was recorded (p>0.05).

Meanwhile, H. pylori infection significantly affected the serum iron, serum ferritin and TIBC in studied cases of IDA (p<0.05). [Table 4].

4. DISCUSSION

Iron (Fe) is an essential element for hemoglobin synthesis, oxidation-reduction reactions, and cellular proliferation. The term iron deficiency (ID) describes a deficit in total body iron, resulting in reduction of serum ferritin levels below normal limit [7]. Iron deficiency may occur due to dietary deficiency or chronic blood loss [8] .

Based on the WHO estimation, iron deficiency is responsible for 50 percent of all anemias. The prevalence of anemia during infancy and early childhood is higher than at any other time in the life cycle such as pregnancy [9].

IDA is defined as low hemoglobin and plasma ferritin values caused by further decrease in iron stores. IDA is the most common form of anemia worldwide with a prevalence varying from 2% to 8% in developed countries. IDA may occur at all stages of the life cycle, but it is more prevalent in mothers and young children [10].

Refractory IDA accounts for 4%-13% of referrals to gastroenterologists and in 5%-10% of patients with IDA without aastrointestinal bleeding the diagnosis remains obscure in spite of extensive examination [11].

Helicobacter pylori possesses microbiological characteristics that allow it to survive in extremely adverse conditions such as the gastric acidic environment. Transmission of the infection occurs mainly through the oral-fecal route. Oral-oral transmission is also possible, as shown by the isolation of the bacterium in saliva and dental plaque [12].

Several studies including meta-analysis have indicated an association between H. pylori infection and ID, and IDA [11-13]. Evidences to support the likelihood causative association between H. pylori

Table 4. Iron profile for the studied patients with IDA in relation to H. pylori

Parameter	Unit	H. pylori				
		Positive (n=180) (Mean ± SD)	Negative (n=120) (Mean ± SD)	Total (n=300) (Mean ± SD)		
Serum iron	µmol/L	12.4 ± 7.3	18.3 ± 6.4	15.4 ± 6.8	0.001*	
TIBC	µmol/L	75.1 ± 11.5	71.0 ± 11.0	73.1 ± 11.2	0.002*	
Serum ferritin	ng/ml	19.2 ± 10.1	24.6 ± 12.3	21.9 ± 11.2	0.001*	

Serum iron : Reference range: 13 – 36 µmol/L; TIBC: Total iron binding capacity Reference range: 45-78 µmol/L; Serum ferritin : Reference range: M : 30 – 400 ng/ml , F : 15 – 150 ng/mL

*p-values< 0.05 are statistically significant

gastritis and decreased iron stores comes also from case reports, epidemiologic studies and clinical trials [14].

The Maastricht IV Consensus on the management of Hp infection recommends testing and treatment of Hp infection in patients with unexplained IDA [3]. These guidelines may be applicable in countries with high prevalence for Hp infection.

Results of the present study revealed a prevalence rate of 60% for *H. pylori* infection among asymptomatic cases of IDA. Different results were reported among Egyptians as those reported by Hassanein et al., 2017: 24% [15] and by Sabah et al., 2015: 69.4% [16]. The present prevalence rate was in line with results reported in previous studies carried out in African countries as that in Nigeria :52.5% [17] in Libyia: 54.4% [18] and 56.5% [19] . Higher percentages were reported in Ethiopia: 70% [20], Libyia: 76% [21], Nigeria: 80% [22], Tunis: 83% [23], Morocco: 92.65% [24] and in a public survey carried out also in Nigeria 93.6% [25].

The recorded percentages in studies carried out in Asian countries, for screening for *H. pylori* infection among asymptomatic subjects, varied from as low as 13.1% in Iran [26], Lebanon (21%) [27], India (46%) [28], Saudi Arabia (51%) [29], Korea (54.4%) [30], China (63.4%) [31], Oman (69.5%) [32] to as high as82.5% in Turkey [33].

Even in developed countries variable rates of *H. pylori* infection were reported among asymptomatic subjects as in Portugal: 84.2% [34] Mexico: 52.2% [35], Brazil: 41.1% [36], Canada: 37.9% [37], Netherlands: 32% [38], USA: 25.4% [39] and Belgium: 11% [40].

It is actually difficult to compare the prevalence rates in different studies due to variations in age and the sector of population studied. This difference in reported rates could be attributed to the different methodology, prevalence of common risk factors, criteria of the sample, as well as the specificities of techniques employed in studies.

A number of studies have suggested *H. pylori* infection as a reason of refractory IDA (IDA that does not respond properly to oral iron supplementation) in patients with no obvious other cause of anemia. [41,42] In one study, 58% of cases with IDA were *H. pylori* positive at endoscopy. [43] Another study showed that 61.9% of patients with IDA had *H. pylori* infection [44]

A different study showed that 62% of patients with IDA were *H. pylori* positive. [45] It has been obviously demonstrated in earlier studies that H pylori eradication can reverse the negative influence of *H. pylori* infection on iron absorption and lead to improvement of IDA in case series and in clinical trials in both children and adults. [11,43]

In this research, age of the participants didn't significantly influence the prevalence rate of *H. pylori* among them. On the other hand, other studies as that carried out in 2019 in Egypt by Youssef et al., highlighted a very high significant statistical association of age with *H. pylori* positive antibody, the highest proportion was at the age more than 65 years old, then the prevalence shows decrease gradually with deceasing the age groups. [46] This result was in line with the results in our region (EMRO) and most of developing countries, which regarded the increasing in the age as a risk factor for *H. pylori* infection. [47]

In this study the prevalence rate of H. pylori was significantly higher among females (62.2%) than (57%). Significantly hiaher among males prevalence rates among females were also previously reported in many studies worldwide. [17,19,38] The relationship between gender and H. pylori infection has been controversial in other studies [46.48.49]. The role of sex to put males at significantly higher risk of H. pylori infection compared to females was observed in many previous studies [17,50,51]. Nevertheless, such trend contradicted other studies; where gender was not significantly associated with H. pylori infection [52-54]. In addition, a systematic review with metaanalysis carried out in 2018 reported that no significant difference was observed between the two genders in worldwide H. pylori prevalence [55].

In this piece of work, prevalence rate of H. pylori infection among urban dwellers was 57.5% compared to 62% in rural dwellers. Residence was not significantly associated with prevalence of H. pylori. This finding is in line with previous studies carried out in Egypt, Mexico and Lybia [19,56,57]. On the other hand, several researchers reported a positive correlation between rural life and H. pylori infection [30,58,59]. This could be attributed to inadequate sanitary conditions and to personal absence or poor hygiene [60]. Urbanization and educational level are in fact major determinants of H. pylori prevalence [27,61,62].

In the present study, *H. pylori* prevalence among those with family history of *H. pylori* (especially

infection of the mother) was 71.4% compared to 57% among others. The difference between both groups was statistically significant

Fathers tend to have less contact with their siblings than mothers, so they are less involved in the transmission. It was reported that the relative risk of a person becoming infected with H. pylori is approximately four or eight times greater; when the father or the mother is infected, respectively [63]. Molecular studies carried out to trace intrafamilial transmssion confirmed the mother-to-child transmission in most cases and further reported a grandmother-to-child transmission. It seems that mothers could transmit the infection through mouth secretions; using common spoons or tasting the food. [64]

Furthermore, interfamilial transmission may be also responsible for re-infection with *H. pylori* as its presence among asymptomatic family members may facilitate the transmission among households. Several previous studies consistently supported infected siblings as a risk factor for *H. pylori* infection among families. [64-66]

An inverse association between the level of education and *H. pylori* infection among the studied students was reported in the current work. The same association was reported in other similar studies [34,40]. Unlikely, Youssef et al., (2019) in Egypt reported no significant association between level of education and prevalence of H.pylori infection. [46]

Smoking showed no significant association with *H. pylori* infection among the cases screened in this research. This is in line with several previous reports [19,31,67]. The absence of association in such studies may be due to less number of smokers screened, besides the type of tobacco and the frequency of smoking. On the other hand,other researchers reported that smokers were at higher risk of acquiring *H. pylori* infection. [20,33,46,60]

As regards the dietary habits of the participants in the current work; drinking coffee and tea, intake of high protein diet and skipping meals were significantly implicated to increase the risk of *H. pylori* infection. (p<0.05) This finding coincided with the results of a study carried out in Ethiopia [20] and another in Egypt. [68]

As for protein rich food stuffs, it was postulated that *H. pylori* could survive in some animal products rich in protein, including meat and dairy products at

temperature below 30°C. Moreover, such foods could serve as source of amino acids which support the growth of this bacterium in the stomach [69] Drinking coffee supports the growth of *H. pylori* by suppressing acid production in the stomach. Coffee drinking was also claimed to be involved in hyper stimulation and increased levels of stress related hormones such as cortisol, adrenaline and norepinephrine [18]; which in turn could negatively influence the activity of the immune system supposed to combat *H. pylori*. On the other hand, Rana (2007) reported tea consumption as a protective factor against *H. pylori* infection. [70]

On the other hand, eating spicy food was not significantly associated with a higher *H. pylori* prevalence in the present work. This is in line with the findings of a Libyan study [19]

H. pylori infection remains the most frequent and persistent bacterial infection worldwide; thus the need for an accurate diagnosis of infection is imperative. The ideal test for detection of *H. pylori* infection should be non-invasive, highly accurate, widely available and inexpensive [71].

The invasive techniques for diagnosis of *H. pylori* are difficult, expensive and not preferred by the patients, therefore; a rapid and cost-effective detection method for diagnosis of *H. pylori* infection is required. Therefore, non-invasive testing for *H. pylori* has been strongly recommended as it is cheaper, more patient friendly than invasive methods and does not require very complicated laboratory facilities [72].

In the current study, H. pylori infection significantly affected the haemoglobin level, MCV, MCH and RDW in studied cases (p<0.05). On the other hand no statistically significant difference between both positive and negative groups for *H. pylori* regards their hematocrit level, MCHC, RBCs count, WBCs count, platelets count and ESR was recorded. Meanwhile, H. pylori infection significantly affected the serum iron, serum ferritin and TIBC in studied cases of IDA. Several studies highlighted that after confirmation of eradication of *H. pylori*, the mean values of hemoglobin and iron indices including ferritin have improved significantly without the use of iron supplementation which indicates improved absorption of dietary iron with subsequent improvement of IDA [72,73]

Stool Ag test is one of the non-invasive methods that is broadly used in the diagnosis of *H. pylori* infection and had been known for the accuracy of its results and comparability to invasive methods. In the current research, *H. pylori* stool Ag test was considered the gold standard method for diagnosis of *H. pylori* infection. This is attributed to its previously reported high sensitivity and specificity (up to 97%) [74,75] and its excellent positive and negative predictive values regardless of *H. pylori* prevalence [74].

Compared to UBT, stool Ag test was reported by Frenck et al., [76] at Cairo University to be equivalent to its sensitivity and specificity. They concluded that UBT and stool Ag test had comparable high sensitivity (98 and 94%, respectively) and specificity (89% and 81%, respectively) and thus the stool Ag test has been evaluated as equivalent to the UBT.

H. pylori can be tested for using stool antigen test (HPSA) which is an enzymatic immunoassay to detect bacterial antigen of actual ongoing infection in stool is a reliable noninvasive marker in the primary diagnosis and in the monitoring of post treatment outcome. [77]

5. CONCLUSION

- Helicobacter pylori is highly associated risk factor with cases of iron deficiency anaemia
- Family history of *H. pylori* infection, limited level of education and some dietary habits as eating high protein diet, skipping meals, drinking coffee and tea are considered as risk factors for acquiring *H. pylori* infection.
- Helicobacter pylori infection significantly affects haemoglobin level, blood indices, serum iron and ferritin and TIBC.

6. RECOMMENDATIONS

- This study is small and did not exclude other causes of IDA by extensive laboratory work and interventions including upper and lower endoscopy. Therefore, further large scale case control studies are warranted among study participants to evaluate the relationship between *H. pylori* infection and IDA and to set successful management regimens for treatment of cases.
- Effective treatment strategies must be applied for treatment of *H. pylori* infection to guard against development of IDA.

CONSENT

A written consent was signed for approval to be part of this research work.

ETHICAL APPROVAL

This study was fully funded by the authors only. Author identifying information are present on the title page that is separate from the manuscript.

This study received ethical approval from the High Institute of Public Health (HIPH) Ethics Committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- 1. Marks PW. Anemia: Clinical approach. In concise guide to hematology. Springer, Cham. 2019;21-27.
- 2. Lopez A, Cacoub P, Macdougall IC, Peyrin-Biroulet L. Iron deficiency anaemia. The Lancet. 201627;387(10021):907-16.
- Longo DL, Camaschella C. Iron-deficiency anemia. N Engl J Med. 20157;372(19): 1832-43.
- Marshall B, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. The Lancet. 1984;323(8390):1311-5.
- 5. Moretti E, Figura N, Collodel G, Ponzetto A. Can helicobacter pylori infection influence human reproduction? World J Gastroenterol. 2014;20(19):5567-74.
- Kandulski A, Selgrad M, Malfertheiner P. Helicobacter pylori infection: A clinical overview. Digestive and Liver Disease. 2008;40(8):619-26.
- Andrews NC. Disorders of iron metabolism. New England Journal of Medicine. 1999;341(26):1986-95.
- Means RT. Iron deficiency anemia. Hematology. Means RT. Iron deficiency anemia. Hematology (Amsterdam, Netherlands). 2013;18(5):305-6
- 9. Lutter CK. Iron deficiency in young children in low-income countries and new approaches for its prevention. The Journal of nutrition. 2008;138(12):2523-8.
- 10. Goddard AF, James MW, McIntyre AS, Scott BB. Guidelines for the management of iron deficiency anaemia. Gut. 2011; 2010: 2-8.
- Qu XH, Huang XL, Xiong P, Zhu CY, Huang YL, Lu LG, Sun X, Rong L, Zhong L, Sun DY, Lin H. Does *Helicobacter pylori* infection play a role in iron deficiency anemia? A meta-analysis. World

journal of gastroenterology: WJG. 2010; 16(7):886.

- Mladenova I, Durazzo M. Transmission of Helicobacter pylori. E dietologica. 2018; 64(3):251-4.
- Webb PM, Knight T, Greaves S, Wilson A, Newell DG, Elder J, Forman D. Relation between infection with Helicobacter pylori and living conditions in childhood: Evidence for person to person transmission in early life. Bmj. 1994; 308(6931):750-3.
- Diop S, Aouba A, Varet B. Reversal of iron deficiency anaemia after eradication of *Helicobacter pylori* infection. Presse medicale (Paris, France: 1983). 2004; 33(21):1517-8.
- 15. Hassanein FI, Shehata AI, Abdul-Ghani RG. lamblia *H. pylori* infections among mentally challenged individuals in rehabilitation centers in Alexandria, Egypt. The Journal of Infection in Developing Countries. 2017;11(07):577-82.
- Sabah AA, Gneidy MR, Saleh NM. Prevalence of *Helicobacter pylori* infection among adult patients with different gastrointestinal parasites in Tanta City district. Journal of the Egyptian Society of Parasitology. 2015;45(1):101-6.
- Omosor KI, Omosor OH, Ibeh IN, Adejumo BI, Abdulkadir UI, Dimkpa U, Uchuno GA, Oke OM, Abdulkadir RL, Hamidu MV, Emmanuel AM. Seroprevalence of Helicobacter pylori infection and risk factors among asymptomatic subjects in Delta state, Nigeria. Advances in Microbiology. 2017;7(9):641-52.
- Almadi MA, Aljebreen AM, Tounesi FA, Abdo AA. *Helicobacter pylori* prevalence among medical students in a high endemic area. Saudi medical journal. 2007; 28(6):896.
- 19. Almehdawi KA, Ali RH. The prevalence of *Helicobacter Pylori* infection in Benghazi, Libya. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2016;16(04).
- 20. Alebie G, Kaba D. Prevalence of *Helicobacter pylori* infection and associated factors among gastritis students in Jigjiga University, Jigjiga, Somali regional state of Ethiopia. J Bacteriol Mycol. 2016;3(3):00060.
- Bakka AS, Salih BA. Prevalence of Helicobacter pylori infection in asymptomatic subjects in Libya. Diagnostic Microbiology and Infectious Disease. 2002; 43(4):265-8.

- 22. Oluwasola AO, Ola SO, Saliu L, Solanke TF. *Helicobacter pylori* infection in South Nigerians: A serological study of dyspeptic patients and healthy individuals. West African Journal of Medicine. 2002;21(2): 138-41.
- Ben AA, Cheikh I, Kchaou M, Chouaib S, Ouerghi H, Chaâbouni H. Prevalence of *Helicobacter pylori* infection in normal or asymptomatic patients. La Tunisie Medicale. 2003;81(3):200-4.
- Bounder G, Boura H, Saloua Nadifiyine MR, Bensassi M, Kadi M, Eljihad M, Badre W, Benomar H, Kettani A, Lebrazi H, Maachi F. Epidemiology of *Helicobacter pylori* infection and related gastric pathologies in Moroccan population. J Life Sci. 2017;11:211-8.
- Olokoba AB, Gashau W, Bwala S, Adamu A, Salawu FK. *Helicabacter pylori* Infection in Nigerians with Dyspepsia. Ghana Medical Journal. 2013;47(2):79-81.
- 26. Namakin, K., Nejad FB. Prevalence of *Helicobacter Pylori* Infection in Asymptomatic Children in Birjand, Eastern Iran. Int. J. Pediatr. 2014;2(6):4-2.
- Naous A, Al-Tannir M, Naja Z, Ziade F, El-Rajab M. Fecoprevalence and determinants of *Helicobacter pylori* infection among asymptomatic children in Lebanon. Le Journal medical libanais. The Lebanese medical journal. 2007;55(3):138-44.
- Rastogi M, Rastogi D, Singh S, Agarwal A, Priyadarshi BP, Middha T. Prevalence of *Helicobacter pylori* in asymptomatic adult patients in a tertiary care hospital: A cross sectional study. Biomed. Res. 2014;25(4): 117-122.
- 29. Khan MA, Ghazi HO. Helicobacter pylori infection in asymptomatic subjects in Makkah, Saudi Arabia. JPMA. The Journal of the Pakistan Medical Association. 2007; 57(3):114.
- Lim SH, Kwon JW, Kim N, Kim GH, Kang JM, Park MJ, Yim JY, Kim HU, Baik GH, Seo GS, Shin JE. Prevalence and risk factors of *Helicobacter pylori* infection in Korea: Nationwide multicenter study over 13 years. BMC gastroenterology. 2013; 13(1):104.
- 31. Zhu Y, Zhou X, Wu J, Su J, Zhang G. Risk factors and prevalence of *Helicobacter pylori* infection in persistent high incidence area of gastric carcinoma in Yangzhong city. Gastroenterology Research and Practice; 2014.

- Al-Balushi MS, Al-Busaidi JZ, Al-Daihani MS, Shafeeq MO, Hasson SS. Seroprevalence of *Helicobacter pylori* infection among asymptomatic healthy Omani blood donors. Asian Pacific Journal of Tropical Disease. 2013;3(2):146-9.
- Ozaydin N, Turkyilmaz SA, Cali S. Prevalence and risk factors of *helicobacter pylori* in Turkey: A nationallyrepresentative, cross-sectional, screening with the 13 C-Urea breath test. BMC Public Health. 2013;13(1):1215.
- Bastos J, Peleteiro B, Barros R, Alves L, Severo M, de Fátima Pina M, Pinto H, Carvalho S, Marinho A, Guimarães JT, Azevedo A. Sociodemographic determinants of prevalence and incidence of *Helicobacter pylori* infection in Portuguese adults. Helicobacter. 2013; 18(6):413-22.
- 35. Alvarado-Esquivel C. Seroepidemiology of *Helicobacter pylori* infection in pregnant women in rural Durango, Mexico. International Journal of Biomedical Science: IJBS. 2013;9(4):224.
- Pacheco SL, Ogata SK, Machado RS, da Silva Patrício FR, Pardo ML, Kawakami E. Diagnosis of *Helicobacter pylori* infection by means of reduced-dose 13Curea breath test and early sampling of exhaled breath. Journal of Pediatric Gastroentero-logy and Nutrition. 2013; 57(5):607-11.
- Sethi A, Chaudhuri M, Kelly L, Hopman W. Prevalence of *Helicobacter pylori* in a first nations population in northwestern Ontario. Canadian Family Physician. 2013;59(4): 182-7.
- Van Blankenstein M, van Vuuren AJ, Looman CW, Ouwendijk M, Kuipers EJ. The prevalence of *Helicobacter pylori* infection in the Netherlands. Scandinavian journal of gastroenterology. 2013;48(7): 794-800.
- Krueger WS, Hilborn ED, Converse RR, Wade TJ. Environmental risk factors associated with *Helicobacter pylori* seroprevalence in the United States: A cross-sectional analysis of NHANES data. Epidemiology & Infection. 2015;143(12): 2520-31.
- 40. Mana F, Vandebosch S, Deyi VM, Haentjens P, Urbain D. Prevalence of and risk factors for *H. pylori* infection in healthy children and young adults in Belgium anno 2010/2011. Acta Gastro-Enterologica BELGICA. 2013;76(4):381-5.

- Gheibi SH, Farrokh-Eslamlou HR, Noroozi M, Pakniyat A. Refractory iron deficiency anemia and *Helicobacter Pylori* Infection in pediatrics: A review. Iranian Journal of Pediatric Hematology and Oncology. 2015; 5(1):50.
- 42. Barabino A. *Helicobacter pylori* related iron deficiency anemia: A review. Helicobacter 2002;7:71-5. 3.
- 43. Choe YH, Kim SK, Son BK, Lee DH, Hong YC, Pai SH. Randomized placebocontrolled trial of *Helicobacter pylori* eradication for iron-deficiency anemia in preadolescent children and adolescents. Helicobacter. 1999;4:135-9.
- Choe YH, Lee JE, Kim SK. Effect of 44. Helicobacter pylori eradication on sideropenic refractory anaemia in adolescent girls with Helicobacter pylori infection. Acta Paediatr. 2000:89:154-7.
- Valiyaveettil AN, Hamide A, Zachariah B, Krishnan R. Effect of anti-*Helicobacter pylori* therapy on outcome of irondeficiency anemia: A randomized, controlled study. Indian J Gastroenterol. 2005;24: 155-7.
- Yousif MK, Al-Ghuzi AAS, Al Jaberry AJ, Yassin SJ. Seroprevalence and determinants of *Helicobacter Pylori* among primary health care centers attendants in AL-Nassiryia City at 2017. Journal of Global Pharma Technology. 2018;10(03): 736-745
- 47. Nouraie M, Latifi-Navid S, Rezvan H, Radmard AR, Maghsudlu M, Zaer-Rezaii H, Amini S, Siavoshi F, Malekzadeh R. Childhood hygienic practice and family education status determine the prevalence of *Helicobacter pylori* infection in Iran. Helicobacter. 2009;14(1):40-6.
- 48. Yordanov D, Boyanova L, Markovska R, Ilieva J, Andreev N, Gergova G, Mitov I. Influence of dietary factors on *Helicobacter pylori* and CagA seroprevalence in Bulgaria. Gastroenterology Research and Practice. 2017;2017.
- 49. Yu X, Yang X, Yang T, Dong Q, Wang L, Feng L. Decreasing prevalence of *Helicobacter pylori* according to birth cohorts in urban China. Turk J Gastroenterol. 2017;28(2):94-7.
- 50. Ibrahim A, Morais S, Ferro A, Lunet N, Peleteiro B. Sex-differences in the prevalence of *Helicobacter pylori* infection in pediatric and adult populations: Systematic review and meta-analysis of

244 studies. Digestive and Liver Disease. 2017;49(7):742-9.

- Valliani A, Khan F, Chagani B, Khuwaja AK, Majid S, Hashmi S, Nanji K, Valliani S. Factors associated with *Helicobacter pylori* infection, results from a developing country-Pakistan. Asian Pacific Journal of Cancer Prevention. 2013;14(1):53-6.
- 52. Şeyda T, Derya Ç, Füsun A, Meliha K. The relationship of *Helicobacter pylori* positivity with age, sex, and ABO/Rhesus blood groups in patients with gastrointestinal complaints in Turkey. Helicobacter. 2007; 12(3):244-50.
- 53. Mathewos, B., Moges, B, Dagnew M. Seroprevalence and trend of *Helicobacter pylori* infection in Gondar University Hospital among dyspeptic patients, Gondar, North West Ethiopia. BMC. Res. Notes. 2013;6(1):346.
- 54. Tadege T, Mengistu Y, Desta K, Asrat D. Serioprevalence of *Helicobacter pylori* infection in and its relationship with ABO blood groups. Ethiopian Journal of Health Development. 2005;19(1):55-9.
- 55. Zamani M, Ebrahimtabar F, Zamani V, Miller WH, Alizadeh-Navaei R, Shokri-Shirvani J, Derakhshan MH. Systematic review with meta-analysis: The worldwide prevalence of *Helicobacter pylori* infection. Alimentary Pharmacology & Therapeutics. 2018;47(7):868-76.
- Mohamed ON, El Zalabany MM, Abaza AF, El Kady MA. Diagnosis of *Helicobacter pylori* infection in children and their mothers using some noninvasive techniques. Afr J Microbiol Res. 2016; 10(31):1194-202.
- Łaszewicz W, Iwańczak F, Iwańczak B, Annabhani A, Bała G, Bąk-Romaniszyn L, Budzyńska A, Cader J, Celiński K, Cichy W, Czerwionka-Szaflarska M. Seroprevalence of *Helicobacter pylori* infection in Polish children and adults depending on socioeconomic status and living conditions. Advances in Medical Sciences. 2014; 59(1):147-50.
- Abdallah TM, Mohammed HB, Mohammed MH, Ali AA. Sero-prevalence and factors associated with *Helicobacter pylori* infection in Eastern Sudan. Asian Pacific Journal of Tropical Disease. 2014; 4(2):115-9.
- 59. Vilaichone RK, Mahachai V, Shiota S, Uchida T, Ratanachu-ek T, Tshering L, Tung NL, Fujioka T, Moriyama M, Yamaoka Y. Extremely high prevalence of

Helicobacter pylori infection in Bhutan. World journal of gastroenterology: WJG. 2013;19(18):2806.

- 60. Hanafi MI, Mohamed AM. *Helicobacter pylori* infection: Seroprevalence and predictors among healthy individuals in Al Madinah, Saudi Arabia. The Journal of the Egyptian Public Health Association. 2013; 88(1):40-5..
- 61. Khalifa MM, Sharaf RR, Aziz RK. *Helicobacter pylori*: A poor man's gut pathogen?. Gut Pathogens. 2010;2(1):2.
- 62. 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: WJG. 2014;20(46):17618.
- Manfredi M, Iuliano S, Gismondi P, Bizzarri B, Gaiani F, Ghiselli A, De'Angelis GL. *Helicobacter pylori* infection: We should always verify the intrafamilial transmission. Biol Med (Aligarh). 2016;9(366):2.
- Dattoli VC, Veiga RV, Da Cunha SS, Pontes-de-Carvalho LC, Barreto ML, Alcântara-Neves NM. Seroprevalence and potential risk factors for *Helicobacter pylori* infection in Brazilian children. Helicobacter. 2010;15(4):273-8.
- Muhsen K, Athamna A, Bialik A, Alpert G, Cohen D. Presence of *Helicobacter pylori* in a sibling is associated with a long-term increased risk of *H. pylori* infection in Israeli Arab children. Helicobacter. 2010; 15(2):108-13.
- Nam JH, Choi IJ, Cho SJ, Kim CG, Lee JY, Nam SY, Park SR, Kook MC, Nam BH, Kim YW. *Helicobacter pylori* infection and histological changes in siblings of young gastric cancer patients. Journal of Gastroenterology and Hepatology. 2011; 26(7):1157-63.
- Den Hollander WJ, Holster IL, den Hoed CM, van Deurzen F, van Vuuren AJ, Jaddoe VW, Hofman A, Perez Perez GI, Blaser MJ, Moll HA, Kuipers EJ. Ethnicity is a strong predictor for *Helicobacter pylori* infection in young women in a multi-ethnic E uropean city. Journal of Gastroenterology and Hepatology. 2013;28(11):1705-11.
- 68. El Kady H. Screening for *Helicobacter pylori* Infection among Asymptomatic University Students in Alexandria, Egypt, Using Non Invasive Laboratory

Techniques. Int. J. Curr. Microbiol. App. Sci. 20187(6):2136-2155.

- 69. Farsakh NA. Risk factors for duodenal ulcer disease. Saudi Medical Journal. 2002;23(2):168-72.
- Rana M. Risk factors associated with *Helicobacter pylori* infection in Gaza. master thesis, science in biological science: Medical technology. Egypt; 2007.
- Soltani J, Amirzadeh J, Nahedi S, Shahsavari S. Prevalence of *Helicobacter pylori* infection in children, a populationbased cross-sectional study in west iran. Iranian Journal of Pediatrics. 2013;23(1): 13.
- 72. Osman HA, Hasan H, Suppian R, Bahar N, Hussin NS, Rahim AA, Hassan S, Andee DZ, Zilfalil BA. Evaluation of the Atlas *Helicobacter pylori* stool antigen test for diagnosis of infection in adult patients. Asian Pac J Cancer Prev. 2014;15(13): 5245-7.
- 73. Shatla MM. Treatment of *Helicobacter Pylori* associated iron deficiency anemia: Does iron supplementation make

difference. European Journal of Preventive Medicine. 2016;4(2):50-55

- 74. Bakri MM. Evaluation of non-invasive diagnostic tests for *Helicobacter pylori* infection in symptomatic patients and healthy volunteers. Pak J Physiol. 2015;8: 10-2.
- Garza-González E, Perez-Perez GI, Maldonado-Garza HJ, Bosques-Padilla FJ. A review of *Helicobacter pylori* diagnosis, treatment, and methods to detect eradication. World Journal of Gastroenterology: WJG. 2014;20(6):1438.
- 76. Frenck RW, Fathy HM, Sherif M, Mohran Z, El Mohammedy H, Francis W, Rockabrand D, Mounir BI, Rozmajzl P, Frierson HF. Sensitivity and specificity of various tests for the diagnosis of *Helicobacter pylori* in Egyptian children. Pediatrics. 2006;118(4):1195-202.
- 77. M. Azami, Parizad Nasirkandy M, Mansouri A, et al., "Global Prevalence of *Helicobacter pylori* infection in pregnant women: A Systematic Review and Metaanalysis Study, "International Journal of Women's Health and Reproduction Sciences. 2017;5(1)30–36.

© 2020 El-Kady et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history: The peer review history for this paper can be accessed here: http://www.sdiarticle4.com/review-history/58186