

THE PREVALENCE OF IRON DEFICIENCY ANEMIA IN PATIENTS WITH HELICOBACTER PYLORI INFECTION IN MISAN, IRAQ.

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ABSTRACT

Since iron deficiency anemia being the most common type of anemia all over the world, studying its different aspect (including the etiologies) been an area of interest since decades. In certain situations, no exact cause can be found, and the patient not respond optimally to iron therapy (refractory anemia). In these situations, several studies found a strong association between Helicobacter pylori and iron deficiency anemia. In this study, we try to compare the prevalence of IDA between those with or without H. pylori infection.

Methods

A cross-sectional observational study was performed on 447 individuals who attended the consultation clinic at Al-Sadr Teaching Hospital, Misan-Southern Iraq, from January to December 2019, for different digestive complaints. The study enrolled 290 women and 157 men. For each subject, demographic data, stool antigen test for H. pylori, complete blood count and serum ferritin done.

Results

Out of the 447 subjects included in our study, there are 290 women, and 157 men. The average age of the participant is 36 (± 16) years. Subjects with positive tests for H. pylori were 249 (55.7%) of them 75 (30.1%) subject have iron deficiency anemia. Of the control group (subject with negative tests for H. pylori n=198), 49 (24.7%) subjects have iron deficiency anemia. There were no significant association between iron state with age, gender, or place of residence. And no significant correlation between different blood parameter (RBC count, hemoglobin concentration, MCV, serum ferritin), in patients with iron deficiency anemia with or without H. pylori infection.

Conclusion

The prevalence of iron deficiency anemia is higher among individual with positive stool antigen test for H. pylori infection compare to those with negative infection, but the result need to be reproduce in multicenter study on larger population sample.

Keys words: Iron deficiency anemia, Serum ferritin, H. pylori infection

I. INTRODUCTION

Iron deficiency is the most common nutritional deficiency in the world (Johnson-Wimbley & Graham, 2011; Milman, Rosenstock, Andersen, Jørgensen, & Bonnevie, 1998; Organization, 2001). The resulting iron deficiency anemia (IDA) is the most common form of anemia worldwide (DeLoughery, 2017; DeMaeyer & Adiels-Tegman, 1985; Short & Domagalski, 2013). The prevalence of IDA is different with different geographic area (Organization, 2001), race (Barton et al., 2020), age groups (Philip et al., 2020), gender and in women is different in pre-menopause form that of post-menopause.

There are many causes of iron deficiency, generally etiology fall into three main causes: decrease intake of iron or dietary, impaired iron absorption, and iron loss from any cause. In certain cases of IDA, there are other factors

could cause or accentuate the problem, one of them is infection with *Helicobacter pylori* (Hershko, Lahad, & Kereth, 2005). The implication of *H. pylori* in the etiology of iron deficiency anemia been an area of interest in last two decades, with several study found a significant associations between *H. pylori* infection and iron deficiency, especially refractory type (Fraser, Scragg, Schaaf, Metcalf, & Grant, 2010; Gheibi, Farrokh-Eslamlou, Noroozi, & Pakniyat, 2015; Milman et al., 1998). And more over some studies found improvement of iron state and store after eradication of *H. pylori* (Hershko & Camaschella, 2014; Huang et al., 2010). The association between *H. pylori* infection and iron deficiency been an area of interest since awhile. There are several propose mechanisms by which *H. pylori* can cause iron deficiency include: gastrointestinal blood loss from acute gastritis (Rockey & Cello, 1993), autoimmune gastritis (Hershko & Camaschella, 2014), gastric cancer (Wong et al., 2004) and iron use by the organism itself (Realdi, Dore, & Fastame, 1999).

The aim of this study, is to provide an idea about the prevalence of iron deficiency anemia in patients with active *H. pylori* infection illustrated by positive stool antigen test for *H. pylori* and compared it to a matched control group with negative *H. pylori* infection.

II. METHOD AND MATERIALS

Study design: A cross-sectional observational study was performed on 447 individuals who attended the consultation clinic at Al-Sadr Teaching Hospital, Misan-Southern Iraq, from January to December 2019, for different digestive complaints. The study enrolled 290 women and 157 men. Figure 1 illustrated the study design and final enrollment. The demographic characteristics for each individual were documented.

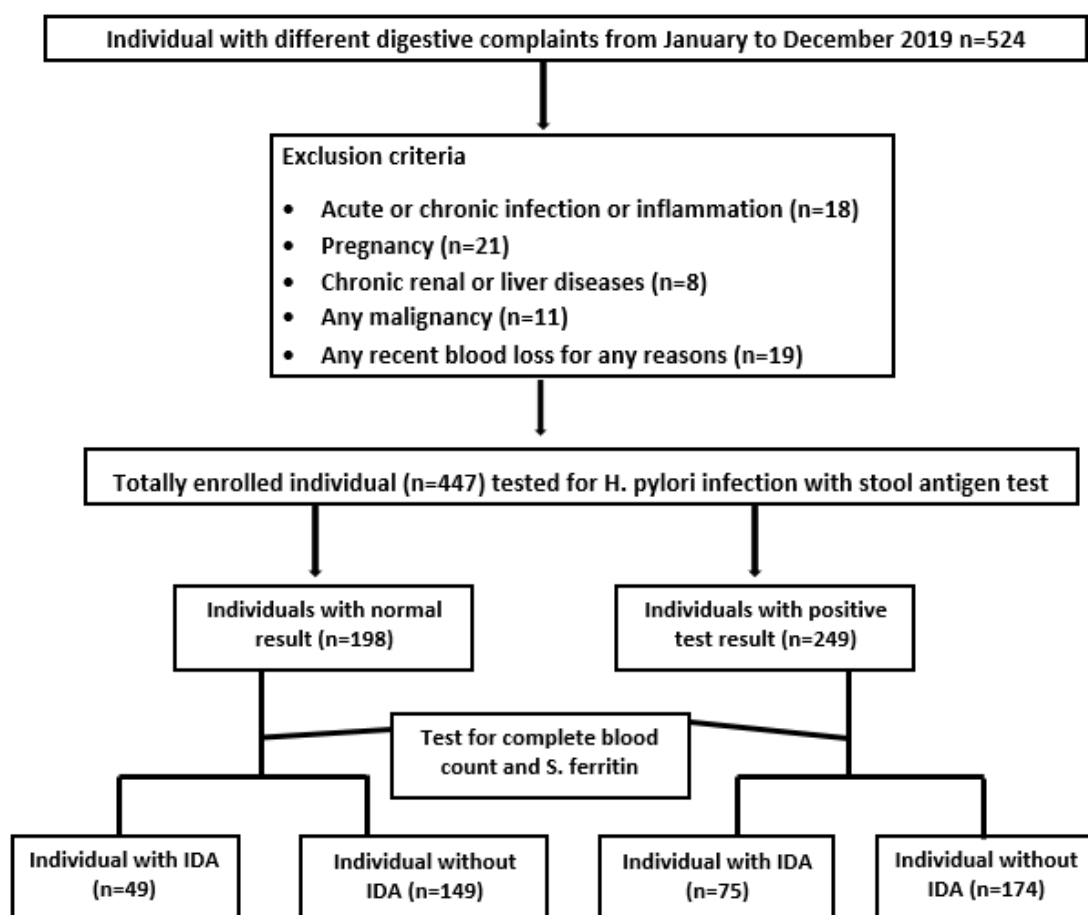


Figure 1: Flow chart of the study

Laboratory Evaluation: For *Helicobacter pylori* infection, we used a plain tube with stool sample. The samples were processed for *Helicobacter pylori* antigen using qualitative rapid antigen test based immunoassay cassette.

Three milliliters of venous blood were drawn into an EDTA tube for complete blood count, and the sample was processed by (SYSMEX XT-2000i, Japan, S.N. 67101).

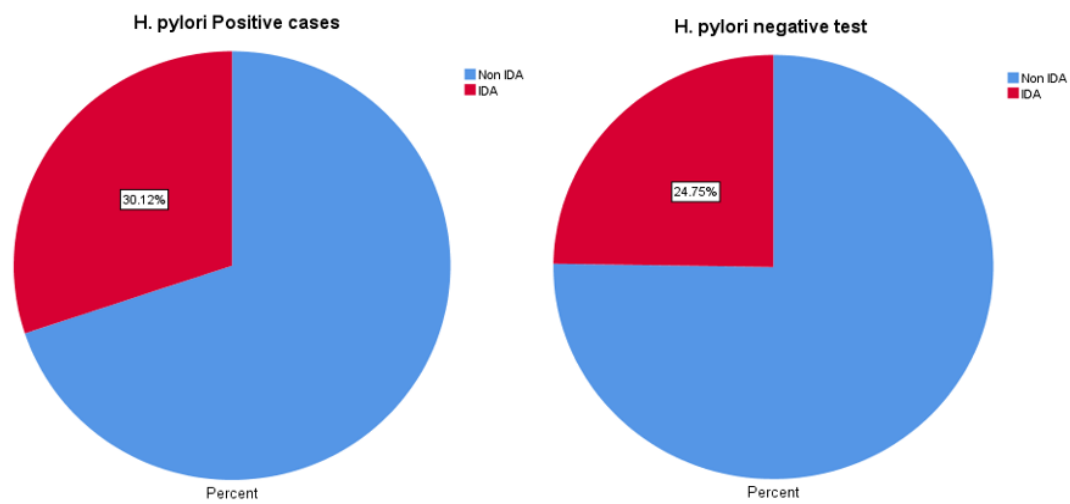
One milliliter of venous blood was drawn into a gel tube for assessing serum ferritin level, and the sample analyzed using (HITACHI/cobas e411, Japan, S.N. 1085-25).

Anemia was defined as hemoglobin <13 g/dl for men and <12 g/dl for women according to WHO criteria (Organization, 2001). Serum ferritin <20 ng/ml for men and <10 ng/ml for women define IDA (Jameson JL, 2015).

Ethical Approval: The Research and Ethics Committee of Misan College of Medicine approved the study protocol. All enrolled individuals signed informed written consent.

Statistical Analysis: Data were entered and matched via Microsoft Access and Excel and then analyzed on IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY). The study used univariate and multivariate analysis with the mean ± standard deviation or frequency (%) for data expression. The study considered a p<0.05 to be statistically significant. Association of baseline variable with Helicobacter pylori serology was assessed using multivariable logistic regression analysis.

III. RESULTS



Out of the 447 subjects included in our study, there are 290 women, and 157 men. The average age of the participant is 36 (±16) years. Subjects with positive tests for H. pylori were 249 (55.7%) of them 75 (30.1%) subject have iron deficiency anemia. Of the control group (subject with negative tests for H. pylori n=198), 49 (24.7%) subjects have iron deficiency anemia (Figure 2).

Figure 2: percentage of iron deficiency anemia in H. pylori positive and negative patient (IDA – iron deficiency anemia)

The enrolled individuals' age, gender and place of living had no significant association with between the two groups. And although the prevalence of IDA is higher in subjects with positive test for H. pylori, the relationship was statistically non-significant (table 1).

Further analysis of IDA in subjects with positive test for H. pylori show significant association to gender, with IDA being higher in women (table 2).

There were no significant relationship between H. pylori infection and different RBC parameters (number, MCV, Hb, serum ferritin) in patients with diagnosis of iron deficiency anemia (table 3).

Table 1. Relationship between Helicobacter pylori infection and demographical characteristics in individuals with iron deficiency anemia.

Variables	IDA	p-value
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		H. Pylori + (n=75)	H. pylori - (n=49)	
Age (mean ± standard deviation) years		35.2 ± 13	31.3 ± 16	0.140
Prevalence of IDA	Total n (%)	75 (30.1)	49 (24.7)	0.208
Gender n (%)	Women (n=96)	59 (61.4)	37 (38.5)	0.688
	Men (n=28)	16 (57.1)	12 (42.8)	
Residence n (%)	Urban (n=92)	57 (61.9)	35 (38)	0.57
	Rural (n=32)	18 (56.2)	14 (43.7)	

Abbreviation: IDA - iron deficiency anemia,

Table 2. Relationship between iron deficiency anemia and demographical characteristics in individuals with Helicobacter pylori infection.

Variables	H pylori Positive stool Ag test		p-value	
	IDA (n=75)	Non IDA (n=174)		
Age (mean ± standard deviation) years	35.2 ± 12	36.9 ± 15	0.41	
Gender n (%)	Women (n=165)	59 (35.7)	106 (64.2)	0.006**
	Men (n=84)	16 (19)	68 (80.9)	
Residence n (%)	Urban (n=176)	57 (32.3)	119 (67.6)	0.228
	Rural (n=73)	18 (24.6)	55 (75.3)	

Abbreviation: IDA – Iron deficiency anemia

Table 3. Relationship between Helicobacter pylori infection and RBC count, MCV, hemoglobin and serum ferritin, in patients with confirmed iron deficiency anemia diagnosis.

Variables mean ± standard deviation	Patients with Iron deficiency anemia			p-value	
	H. pylori +ve	H. pylori -ve	Total		
Red Blood Cell Count (in millions) mean ± SD	4.7 ± .63	4.8 ± .68	4.7 ± .65	.378	
Mean Corpuscular volume (fL) mean ± SD	74.9 ± 6.6	73.5 ± 6.4	74.3 ± 6.5	.254	
			10.5 ± 1.6		
Hemoglobin (g/dL) mean ± SD	Total	H. pylori +ve	10.1 ± 1.4	.615	
			H. pylori -ve		10.2 ± 1.3
			Total		10.1 ± 1.4
Ferritin (ng/mL) mean ± SD	Total	H. pylori +ve	12 ± 1.7	.774	
			H. pylori -ve		11.9 ± 2.3
			Total		12 ± 1.7
Ferritin (ng/mL) mean ± SD	Women	H. pylori +ve	37.5 ± 30	.388	
			H. pylori -ve		7 ± 1.7
Ferritin (ng/mL) mean ± SD	Men	H. pylori +ve	12.6 ± 4	.506	
			H. pylori -ve		12 ± 3.7

IV. DISCUSSION

Iron deficiency anemia is the most common type of anemia world-wide (DeLoughery, 2017; DeMaeyer & Adiels-Tegman, 1985; Short & Domagalski, 2013) with prevalence different according to several factors (geographical, racial, gender, and age). The prevalence of IDA is more than 24% over the world according to the WHO(Organization, 2005) and it was 30.2% among non-pregnant, 12.7% among adult men. In this study, the overall prevalence of IDA in a sample of 447 Iraqi patients was 27.7%. Among females, the percentage was 33.1% and 17.8% among male’s patients, which are nearly similar to previous figures provided by the WHO(Organization, 2005).

The prevalence of IDA in patients with positive stool antigen test for H. pylori was 30.1% which was high when compared with the prevalence of IDA in patient without H. pylori infection (24.5%), but the difference was statistically non-significant. There are several studies that show significant associations between H. pylori infection and iron deficiency and iron deficiency anemia (Fraser et al., 2010; Milman et al., 1998; Khitam Muhsen et al., 2009). The implication of H. pylori in the causation of iron deficiency anemia can be pointed to, by the fact that eradication of H. pylori in patients with refractory iron deficiency anemia will result in improvement of the condition in the majority of cases as shown by many studies (Gheibi et al., 2015; Hershko & Camaschella, 2014; Huang et al., 2010).

There are several possible mechanisms by which *H. pylori* can cause or participate in causing iron deficiency. Chronic gastritis affecting more 65% of the world population, and considered the most common type of chronic infection known to date (Marshall, 1988; Marshall, Armstrong, McGeachie, & Glancy, 1985). This type of gastritis responsible for 15% to 20% of the lifetime risk for peptic ulcers, and more than two thirds of gastric adenocarcinoma and the majority of primary gastric lymphomas (Odze RD, 2009). And all of these conditions associated with iron deficiency anemia. *H. pylori* also implicated in the pathogenesis of autoimmune atrophic gastritis with resultant of achlorhydria and iron deficiency (Smyk et al., 2014). Lastly, there are possible cause of iron deficiency result from iron use by the organism itself for their growth (Realdi et al., 1999).

In patients with positive test for *H. pylori*, there seems to be a significant correlation between iron deficiency anemia and gender (table 2), being more in female, which is logic as female in general are more liable to develop iron deficiency anemia due to several physiological causes like menses and pregnancies. But comparison of the iron state between females of positive *H. pylori* tests and those with negative test (table 1) show no significant associations, which support our explanation.

By comparing patients with iron deficiency anemia of positive *H. pylori* to those with negative test, there were no significant difference regarding RBC count, MCV, hemoglobin level, and serum ferritin between the two groups. There are several studies found a significant association between serum ferritin level and *H. pylori* infections being lower among patient with evidence of *H. pylori* infection (Fraser et al., 2010; Milman et al., 1998; Khitam Muhsen et al., 2009; K. Muhsen & Cohen, 2008).

The main limitation of this study is small sample size due to limited resources. It is a single center study as this is the only teaching hospital with gastrointestinal unit. Lack of more sensitive method of diagnosing *H. pylori* infection like urea breathe test.

In conclusion, the prevalence of iron deficiency anemia is higher among individual with positive stool antigen test for *H. pylori* infection compare to those with negative test for *H. pylori* infection, but the result need to be reproduce in multicenter study on larger population sample.

Conflict of interests: The author declare that he has no conflict of interest.

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REFERENCES

- Barton, J. C., Wiener, H. H., Acton, R. T., Adams, P. C., Eckfeldt, J. H., Gordeuk, V. R., . . . Reboussin, D. M. (2020). Prevalence of iron deficiency in 62,685 women of seven race/ethnicity groups: The HEIRS Study. *PLoS One*, 15(4), e0232125. doi:10.1371/journal.pone.0232125
- DeLoughery, T. G. (2017). Iron Deficiency Anemia. *Med Clin North Am*, 101(2), 319-332. doi:10.1016/j.mcna.2016.09.004
- DeMaeyer, E., & Adiels-Tegman, M. (1985). The prevalence of anaemia in the world. *World Health Stat Q*, 38(3), 302-316.
- Fraser, A. G., Scragg, R., Schaaf, D., Metcalf, P., & Grant, C. C. (2010). Helicobacter pylori infection and iron deficiency in teenage females in New Zealand. *N Z Med J*, 123(1313), 38-45.
- Gheibi, S., Farrokh-Eslamlou, H. R., Noroozi, M., & Pakniyat, A. (2015). Refractory iron deficiency anemia and Helicobacter Pylori Infection in pediatrics: A review. *Iran J Ped Hematol Oncol*, 5(1), 50-64.
- Hershko, C., & Camaschella, C. (2014). How I treat unexplained refractory iron deficiency anemia. *Blood*, 123(3), 326-333. doi:10.1182/blood-2013-10-512624
- Hershko, C., Lahad, A., & Kereth, D. (2005). Gastropathic sideropenia. *Best Pract Res Clin Haematol*, 18(2), 363-380. doi:10.1016/j.beha.2004.10.002
- Huang, X., Qu, X., Yan, W., Huang, Y., Cai, M., Hu, B., . . . Xiong, P. (2010). Iron deficiency anaemia can be improved after eradication of Helicobacter pylori. *Postgrad Med J*, 86(1015), 272-278. doi:10.1136/pgmj.2009.089987
- Jameson JL, K. D., Fauci AS, Hauser SL, Longo DL, Loscalzo J. (2015). Harrison's Principles of Internal Medicine (19 ed.). New York: McGraw Hill Education.
- Johnson-Wimbley, T. D., & Graham, D. Y. (2011). Diagnosis and management of iron deficiency anemia in the 21st century. *Therap Adv Gastroenterol*, 4(3), 177-184. doi:10.1177/1756283x11398736
- Marshall, B. J. (1988). The Campylobacter pylori story. *Scand J Gastroenterol Suppl*, 146, 58-66. doi:10.3109/00365528809099131
- Marshall, B. J., Armstrong, J. A., McGeachie, D. B., & Glancy, R. J. (1985). Attempt to fulfil Koch's postulates for pyloric Campylobacter. *Med J Aust*, 142(8), 436-439. doi:10.5694/j.1326-5377.1985.tb113443.x
- Milman, N., Rosenstock, S., Andersen, L., Jørgensen, T., & Bonnevie, O. (1998). Serum ferritin, hemoglobin, and Helicobacter pylori infection: a seroepidemiologic survey comprising 2794 Danish adults. *Gastroenterology*, 115(2), 268-274. doi:10.1016/s0016-5085(98)70192-1
- Muhsen, K., Barak, M., Shifnadel, L., Nir, A., Bassal, R., & Cohen, D. (2009). Helicobacter pylori Infection Is Associated With Low Serum Ferritin Levels in Israeli Arab Children—A Seroepidemiologic Study. *Gastroenterology*, 136(2), 262-264. doi:10.1097/MPG.0b013e31818f0a0d
- Muhsen, K., & Cohen, D. (2008). Helicobacter pylori infection and iron stores: a systematic review and meta-analysis. *Helicobacter*, 13(5), 323-340. doi:10.1111/j.1523-5378.2008.00617.x
- Odze RD, G. J. (2009). Inflammatory disorders of the stomach. In: *Surgical Pathology of the GI Tract, Liver, Biliary Tract, and Pancreas*. Philadelphia.
- Organization, W. H. (2001). Iron Deficiency Anaemia: Assessment, Prevention, and Control: A Guide for Programme Managers. Geneva, Switzerland: World Health Organization.

18. Organization, W. H. (2005). Worldwide prevalence of anaemia 1993–2005 : WHO global database on anaemia. Geneva, Switzerland.
19. Philip, K. E. J., Sadaka, A. S., Polkey, M. I., Hopkinson, N. S., Steptoe, A., & Fancourt, D. (2020). The prevalence and associated mortality of non-anaemic iron deficiency in older adults: a 14 years observational cohort study. *Br J Haematol*, 189(3), 566-572. doi:10.1111/bjh.16409
20. Realdi, G., Dore, M. P., & Fastame, L. (1999). Extradigestive manifestations of *Helicobacter pylori* infection: fact and fiction. *Dig Dis Sci*, 44(2), 229-236. doi:10.1023/a:1026677728175
21. Rockey, D. C., & Cello, J. P. (1993). Evaluation of the gastrointestinal tract in patients with iron-deficiency anemia. *N Engl J Med*, 329(23), 1691-1695. doi:10.1056/nejm199312023292303
22. Short, M. W., & Domagalski, J. E. (2013). Iron deficiency anemia: evaluation and management. *Am Fam Physician*, 87(2), 98-104.
23. Smyk, D. S., Koutsoumpas, A. L., Mytilinaiou, M. G., Rigopoulou, E. I., Sakkas, L. I., & Bogdanos, D. P. (2014). *Helicobacter pylori* and autoimmune disease: cause or bystander. *World J Gastroenterol*, 20(3), 613-629. doi:10.3748/wjg.v20.i3.613
24. Wong, B. C., Lam, S. K., Wong, W. M., Chen, J. S., Zheng, T. T., Feng, R. E., . . . Chen, J. S. (2004). *Helicobacter pylori* eradication to prevent gastric cancer in a high-risk region of China: a randomized controlled trial. *Jama*, 291(2), 187-194. doi:10.1001/jama.291.2.187