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An ecological analysis on seroprevalence of *Helicobacter pylori* IgG among Iranian general population

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Abstract

Introduction: *Helicobacter pylori* is associated with pathogenesis of various gastrointestinal diseases. Prevalence of this infection is different with high heterogeneity around the world. To investigate seroprevalence of *H. pylori* IgG among Iranian general population during 2008-2017 as a 10-year epidemiological interval using previously published documents. This is an ecological study based on the related data previously published documents in English and Persian.

Materials and Methods: Data were collected through the international databases Google Scholar, PubMed and Web of Science, as well as the local Persian databases Magiran, SID and Irandoc. Excel 2013 and STATA 14 were used to analyze the data. After an exact search 14 populations from 10 studies, 10 cities and 9 provinces were used. The total number of samples was 10470.

Results: The funnel plot showed that 5 populations had significantly lower prevalence than the average, seven populations had significantly higher prevalence than the average, and two populations were inside the funnel. The weightless average was 63.8%. The forest plot showed that the pooled prevalence of *H. pylori* in Iran is significantly more than 50%. The contour plot and ecological map are also shown.

Conclusion: The pooled prevalence of *H. pylori* IgG seropositivity in Iran during recent 10 years was 63.8% (weightless average) which was significantly higher than 50%. Khorramabad and Babol had the lowest prevalence (43%) whereas Izeh had the highest prevalence (76%) followed by Neyshabur.

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Introduction

Helicobacter pylori is a bacterium very adaptive to stomach which has already been known for a long-time. This is why the argument of its being a normal flora has been raised since 1998 (1). Being carcinogen, peptic ulcer disease and its negative impact on the normal flora are the concerns about this bacteria (2). In 2016 it was said that lactobacilli in mother's milk can reduce the proliferation capacity of this bacteria in the stomach (3).

Helicobacter pylori is the most prevalent cause of gastroduodenal diseases. In 2004, a triplet treatment was recommended in *Gut* journal which was composed of two antibiotics clarithromycin and amoxicillin along with a proton pump inhibitor. Nevertheless some of these treatments had failed mainly due to the antibiotic resistance to the antibiotics particularly clarithromycin. Thus metronidazole had been suggested to which there was less resistance. Effect of triplet treatments on the *H. pylori* eradication in many studies has been reported in a range of 66% to 95% (4). Bago

Core tip

This is an ecological study on seroprevalence of *Helicobacter pylori* IgG among Iranian general population during 2008-2017 as a 10-year epidemiological interval. The total number of samples was 10470. Five populations had significantly lower prevalence than the average, and seven populations had significantly higher prevalence than the average. The pooled prevalence of *H. pylori* IgG seropositivity in Iran during recent 10 years was 63.8% (weightless average). Khorramabad and Babol had the lowest prevalence (43%) whereas Izeh had the highest prevalence (76%) followed by Neyshabur.

et al studied the effect of ranitidine and omeprazole on *H. pylori* eradication. Their study showed that ranitidine accompanied by clarithromycin and metronidazole or amoxicillin is more effective than omeprazole with those same antibiotics (5). De Francesco et al published a systematic review on resistance to *H. pylori* antibiotic. *H. pylori* antibiotic resistance in different countries from 2006 to 2009 was 17.2% for clarithromycin, 26.7% for metronidazole, 11.2% for amoxicillin, 16.2% for ofloxacin, 5.6% for tetracycline, 1.4% for rifabutin, and 9.6% for multiple resistance. Additionally the antibiotic resistance in women was significantly higher (6). Hwang et al studied 222 participants and found that antibiotic resistance in South Korea had increased from 2007 to 2009. The rate of eradication for strains sensitive to clarithromycin and strains resistant to it were 95% and 67% respectively. In contrast, this rate was 100% for people resistant to amoxicillin which shows that resistance to amoxicillin induces fewer problems compared to the resistance to metronidazole and clarithromycin (7). An et al compared antibiotic resistance in two (2009-2010) and (2011-2012) intervals in Korea found that resistance to clarithromycin and multiple resistance were increasing (8). Bago et al evaluated 332 patients' feces samples and found a 65% antibiotic resistance to clarithromycin (9). Recently Thung et al found antibiotic resistance to *H. pylori* is a universal warning. They emphasized the difference of antibiotic resistance in different parts of the world (10).

According to the importance mentioned, it is necessary to have updated ecological information. In this study we aimed to investigate seroprevalence of *H. pylori* IgG among Iranian general population during 2008-2017 as a 10-year epidemiological interval using previously published documents.

Materials and Methods

Study design

This is an ecological study based on the related data previously published documents in English and Persian. The eligibility criteria for selection of documents were having Iranian samples, sampling during 2008-2017, serological evaluation of *H. pylori*, having adult or mixed of adult and children samples, and the samples should be from general population or referral individuals.

Data source

Data were collected through the international databases Google Scholar, PubMed and Web of Science, as well as the local Persian databases Magiran, SID and Irandoc.

Statistical analysis

Excel 2013 (Microsoft, US) and STATA 14 (StataCorp LLC, US) were used to analyze data. The confidence interval (CI) of each prevalence was calculated through the Cochran formula [$n = z^2 P (1-P) / d^2$] in which n is sample size, d is CI, P is reference prevalence, and z =1.96 considered for significance at 0.05 (95% CI). The standard error (SE) of each study was calculated through 95% CI/1.96.

Funnel plot was used to compare the studies with reference prevalence. The reference prevalence of this plot was calculated through weightless average of the studies' prevalence. The funnel is the very 95% CI area insides of the reference prevalence. Hence being inside the funnel area shows that the mentioned study is not significantly different from references prevalence. Forest plot was used to compare CI of the studies with 50% as another reference prevalence. The pooled result was based on similar weight (n=747 individuals). Weighted average was not used because of high heterogeneity and publication bias. Contour plot and dendrogram were used for additional analysis.

Results

After an exact search 14 populations from 10 studies, 10 cities and 9 provinces were used (11-20). The total number of samples was 10470 (Table 1). The funnel plot showed that 5 populations had significantly lower prevalence than the average, seven populations had significantly higher prevalence than the average, and 2 populations were inside the funnel. The weightless average was 63.8% (Figure 1). The forest plot showed that the pooled prevalence of *H. pylori* in Iran is significantly more than 50% (Figure 2). The contour plot and ecological map are also shown (Figures 3 and 4). The dendrogram shows that at first level, the populations fall into two categories (group with lower prevalence and group with higher prevalence). The group with lower prevalence is the very 5 studies at the left side of the funnel plot. In addition the group with higher prevalence in turn falls into two categories (Figure 5).

Discussion

Summary of evidence

For the pooled prevalence of *H. pylori* in Iran, there were

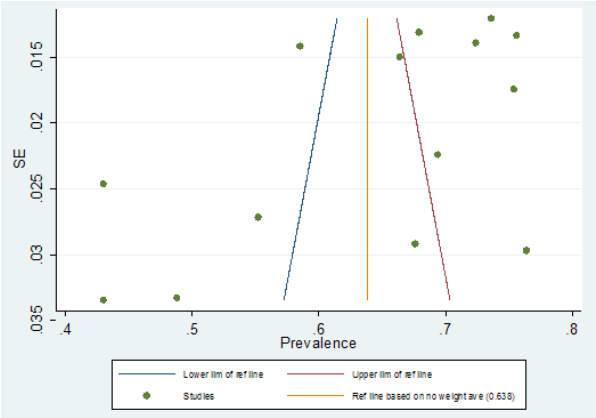

Figure 1. This funnel plot shows that only two studies were in the estimated 95% CI. The studies on the right side of the upper limit have significantly higher prevalence than the average; the studies on the left side of the lower limit have significantly lower prevalence than the average (at $P<0.05$). The CI is calculated based on the reference prevalences 63.8% which is weightless average of the studies' prevalences.

Table 1. Summary of the studies

First author	City	Province	Publication time	Sampling time	Prevalence (%)	Sample size	Reference society of samples	Ref
Ghasemi-Kebria	Gorgan [a]	Golestan	2009	2008	0.664	1028	General population	(14)
Halakou	Izeh	Khouzestan	2011	2008	0.764	263	General population	(16)
Sheikhian	Khorramabad	Lorestan	2011	2008	0.430	381	General population	(18)
Gholizadeh	Gachsaran	Buyerahmad	2012	2011	0.676	272	General population	(15)
Fani	Arak	Markazi	2014	2011	0.585	1150	General population	(13)
Abdi	Varamin	Tehran	2014	2012	0.552	314	General population	(11)
Taghinejad	Salmas	Azarbaijan	2016	2013	0.694	461	Suspected/requested [b]	(19)
Ashrafmodarres	Ahvaz [c]	Khouzestan	2017	2015	0.488	209	General population	(12)
Zamani	Babol	Mazandaran	2017	2015	0.430	207	General population	(20)
Salehi 1	Neyshabur	Khorasan	2017	2010	0.736	1583	General population	(17)
Salehi 2	Neyshabur	Khorasan	2017	2011	0.679	1348	General population	(17)
Salehi 3	Neyshabur	Khorasan	2017	2012	0.724	1195	General population	(17)
Salehi 4	Neyshabur	Khorasan	2017	2013	0.756	1297	General population	(17)
Salehi 5	Neyshabur	Khorasan	2017	2014	0.754	762	General population	(17)

[a] This studies consists of all cities of Golestan province. Gorgan is its center. [b] In this study the patients imported had clinical suspect. [c] The imported patients were from the control group of this case-control study.

two meta-analyses. The first one was a meta-analysis done by Sayehmiri et al showed a pooled prevalence of 50.7% (random effect) (21). The second one was a meta-analysis done by Moosazadeh et al showed a pooled prevalence of 62% in adults and 42% in children (fixed effect). Our study investigated newer populations in a 10-year period with an ecological approach; hence we excluded many of the studies existed in that two meta-analyses (22). Another meta-analysis showed that 45.9% of Iranian pregnant women had this infection (23). As we previously investigated in Khorramabad, prevalence of this infection was higher in children those who had parents with lower income (24). Among the ecological studies, Lin et al reported *H. pylori* seropositivity 54.7% in Taiwan (25). In another ecological study, Lender et al found a correlation between *H. pylori* seropositivity and obesity rate (26). Among the international meta-analyses Hooi et al investigated data of 62 countries. They found that African countries had the highest pooled prevalence. The prevalence in Iran was reported as 50%-69% (27). As well in an updated meta-analysis it was reported that *H. pylori* infection can increase the likelihood of iron deficiency anemia (28).

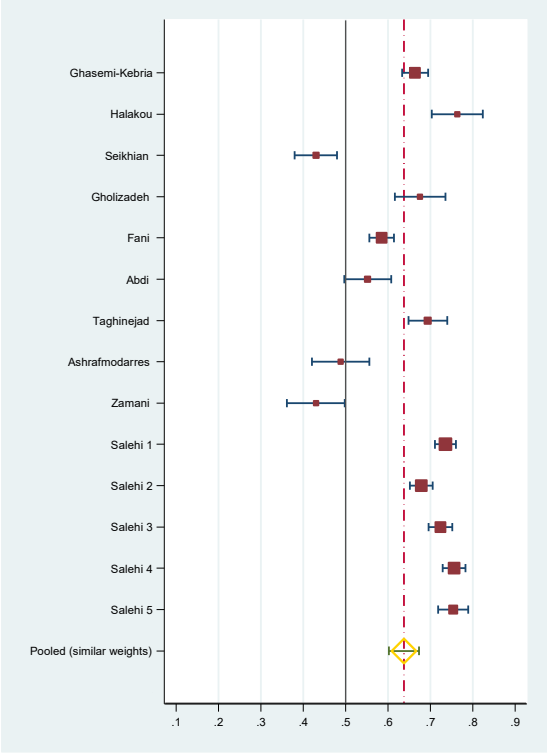

Figure 2. This forest plot shows the prevalence and 95% CI error bar of each study. The CI is calculated based on reference prevalence 50%. The pooled plot which is calculated based on mean sample size (747 individuals) shows that this 63.8% prevalence is significantly higher than 50% (at $P<0.05$).

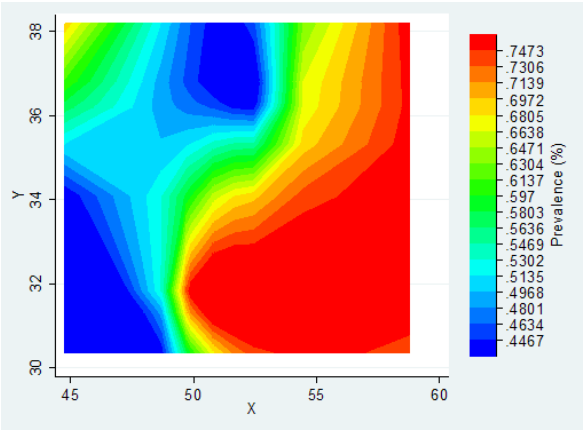

Figure 3. This contour plot shows estimated prevalence based on geographical coordinate.

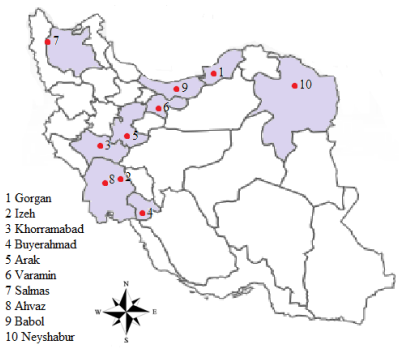

Figure 4. The coordinate of the investigated cities and provinces. The wight colored provinces are not investigated during 2008-2017.

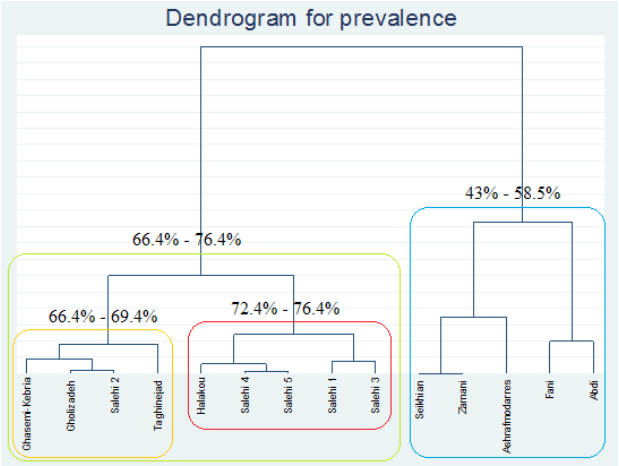

Figure 5. The studies are grouped based on prevalence using dendrogram.

Limitations

During the recent 10 years, only 9 out of 31 provinces of Iran was investigated for *H. pylori* prevalence. The studies of the other provinces were old. Many of recent studies are not descriptive. Because of policies of indexed journals, most of such studies are found in non-indexed local language journals. To resolve this limitation we used Persian language databases. Another limitation was the high heterogeneity of the studies. For example Izeh and Ahvaz are in the same province, but they had different results (you find it in our contour plot). Another limitation was sample selection bias in individual studies. One of them had said that their samples were from the patients those who were clinically suspected with higher pretest probability; but we think that some other studies had also pretest probability bias.

Conclusion

The pooled prevalence of *H. pylori* IgG seropositivity in Iran during recent 10 years was 63.8% (weightless average) which was significantly higher than 50%. Khorramabad and Babol had the lowest prevalence (43%) whereas Izeh had the highest prevalence (76%) followed by Neyshabur. Descriptive studies should be repeated every 4-10 years in all cities and be published in scientific local journals.

Authors' contribution

AH, RS and SAYA searched the literature and gathered the data. SAYA prepared the primary draft. KA completed the paper. KA and SAYA finalized the manuscript. All authors read and signed the final manuscript.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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