Association of hypertension with helicobacter pylori: A systematic review and meta-analysis

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Abstract

Background and aims

The number of hypertensive population rises year by year recently, and their age becomes more youthful. For a long time, hypertension has long been regarded as a multi-factorial disease. In addition to smoking, genetics, diet and other factors, helicobacter pylori (H. pylori) had been regarded as a potential risk factor for hypertension in recent years. However, most studies had certain limitations and their results were inconsistent. Thus, it is necessary for us to assess the impact of H. pylori on hypertension through meta-analysis.

Methods

We searched all published relevant literature through multiple databases by July 23, 2021. Pooled results were calculated under the random effect model. Heterogeneity was evaluated by the Q statistic and the I² statistic. The risk of bias was evaluated via ROBINS-I tool. Publication bias was evaluated by the Egger test and Begg funnel plot.

Results

6 eligible studies involving 11317 hypertensive patients and 12765 controls were selected from 20767 retrieval records. Our research confirmed that H. pylori significantly increased the probability of suffering from hypertension in the random effect model (OR: 1.34, 95% CI: 1.10–1.63, P = 0.002, I² = 74%). The same results were also found in both Asian population and developing country (OR: 1.28, 95%CI: 1.05–1.55, P = 0.003, I² = 78.5%).

Conclusions

Our results confirmed that H. pylori was a vital risk factor for hypertension. H. pylori-infected people were 13.4% higher risk for hypertension than uninfected individuals. In addition, it will be a new method to prevent and treat hypertension by eradicating H. pylori.

Trial registration

The registration number for systematic review in PROSPERO CRD42021279677.
Introduction

Hypertension is a common senile disease in modern society and is the underlying cause of many cardiovascular diseases such as acute coronary syndrome, aortic dissection, heart failure and aortic dissection. Hypertension remains a global health priority, as twenty-six percent of the population worldwide suffer from hypertension and the percentage is expected to reach twenty-nine percent in five years [1]. According to traditional views, hypertension is considered as a multi-factorial disease which is affected by age, gender, genetic background and living environment [2, 3]. Much of the recent evidence suggests that pathogen infection is a new and important risk factor for hypertension. Vahdat et al found that co-infection of multiple pathogens was significantly related to hypertension [4]. In addition, Mycobacterium tuberculosis infection elevated incidence of hypertension and patients with treated latent tuberculosis infection significantly reduced the risk of hypertension [5]. Several studies have reported that the chronic infection with cytomegalovirus [6], herpes simplex virus [7] and helicobacter pylori [8] was linked with hypertension.

Helicobacter pylori (H. pylori) is an acid-resistant gastric colonizing bacterium and the extremely high infection rate in the population makes it become the biggest hidden danger to human health. Since H. pylori was discovered in human stomach, it has long been thought to be only related to gastrointestinal diseases. Currently, many studies have found that H. pylori was etiologically linked to many extra-intestinal diseases, such as cardiovascular disease, diabetes, immune thrombocytopenic purpura and chronic urticaria [9]. H. pylori infection could establish lifelong inflammation [10], and persistent low-grade inflammation played an important part in accelerating the progression of hypertension [11]. In addition, high-salt conditions and Vitamin D (Vit D) metabolism close linked to H. pylori which may be an explanation alternative to hypertension caused by H. pylori infection [12, 13]. In a multi-center study, systolic blood pressure (SBP) and diastolic blood pressure(DBP) were significantly elevated in H. pylori positive adults compared with H. pylori negative adults [14]. A growing body of epidemiological data supported the view that H. pylori promoted the occurrence of hypertension [8, 15]. Xiong et al reported that H. pylori was still positively related to hypertension while adjusting for gender, age and family history of hypertension [15]. And beyond that, a 2020 study said that H. pylori eradication in hypertensive patients could decrease overall mortality and cardiovascular mortality in eastern Asian population [16]. However, Liu et al took a negative opinion on this view [17], and a study in Mongolian population also showed that H. pylori was entirely unrelated to hypertension [18]. At present, many relevant studies had contradictory results, so the purpose of this study was to explore the etiological correlation between H. pylori and hypertension, meanwhile, further to determine that whether H. pylori was a risk factor for hypertension through meta-analysis.

Materials and methods

We conducted the present review according to the set of items for PRISMA guidelines 2020 [19]. This study protocol has been registered with the PROSPERO(CRD42021279677).

Literature retrieval strategy

We obtain all published eligible literature from four major databases (PubMed, Cochrane Library, Excerpt Medica Database and Web of Science) by July 23, 2021. The following MeSH (Medical Subject Heading) terms and keywords were used for systematic literature search: (Blood Pressure or Hypertension or hypertensive or high blood pressure or raised blood pressure) and (Helicobacter pylori or Helicobacter or Helicobacter infection or H. pylori or HP). Language limited to English and the no time limit for publication data.
**Inclusion and exclusion criteria**

Two authors conducted literature screening respectively according to the inclusion and exclusion criteria. When there was great divarication in the literature screening process, the third author was required to give a decision.

Inclusion criteria were listed as follows: (1) Study was underwent with the clinical case-control study or cross-sectional study, (2) The exposure factor was *H. pylori* infection, (3) the outcome of interest was hypertension, (4) Complete research data was available to calculate odds ratios (ORs) and 95% confidence interval (CIs), (5) Study was carried out on human being.

Exclusion criteria were listed as follows: (1) Some article types including letter, case report, editorial, review and meeting abstract, (2) study participants with a history of helicobacter pylori eradication treatment.

The process of literature screening was showed in the Fig 1.

**Data extraction**

Two investigators separately obtained data from all included studies. When differences arose, the third investigator was required to give a decision. The extracted data contained the following: the name of the first author, the time of publication, country, race, detection method of *H. pylori*, study type, average age of hypertensive patients, human development index (HDI), the

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**Fig 1. Flow chart of literature screening.**

https://doi.org/10.1371/journal.pone.0268686.g001
number of case and control groups. When there was missing data in the article, our corresponding author would contact with the author to get the missing data. No automatic tool was used during the whole process.

**Quality score and evaluation of risk of bias**

We conducted an exhaustive quality evaluation for each included study according to the Newcastle–Ottawa Scale (NOS) [20]. The NOS describes research with three domains, including selection, comparability and exposure. The quality of included studies were graded from 0 to 9 by the scale and the study with NOS score 7 was perceived as a high quality study. The risk of bias in the included studies was evaluated via ROBINS-I tool (Risk Of Bias In Non-randomized Studies-of Interventions) [21]. The ROBINS-I tool consists of seven domains, including confounding, selection of participants, intervention, deviations from intended interventions, missing data, measurement of outcomes and selection of the reported result. The risk level of bias was divided into five grades: low risk, moderate risk, serious risk, critical risk and no information (NI). Two authors independently evaluated each article according to the NOS and ROBINS-I tool. A third author settle all disputes.

**Statistical analysis**

Pooled ORs and 95% CIs were calculated to evaluate the correlation between hypertension and *H. pylori*. Heterogeneity was evaluated by the Q statistic and the I$^2$ statistic. When the heterogeneity was significant (Q statistic: $P<0.1$ and I$^2$ statistic: $I^2>50\%$), the pooled ORs and 95% CIs were be calculated under the random effect model. The fixed-effect model was be applied to calculate when statistical results were not remarkable in the Q statistic ($P\geq 0.1$). Sensitivity analysis was conducted by eliminating a single study at a time to assess the change in pooled ORs and 95% CIs. Publication bias was evaluated by the Egger test and Begg funnel plot ($P<0.05$ indicated the result suffer from significant bias). The STATA software V12.0 was applied to statistical analysis in this review.

**Results**

**Screening results**

A total of 20767 literature were retrieved according to the retrieval strategy. 5560 articles are excluded due to the duplication and 15207 records were further screened by reviewing their titles and abstracts. Then 15197 unrelated studies were removed. Full-text review was conducted in the rest 10 articles and 4 articles were further eliminated, including one letter [22], one review [23] and two conference abstracts [24, 25]. Ultimately, a total of 6 eligible studies with 11317 hypertensive patients and 12765 controls were included in this meta-analysis.

**Major characteristics of included studies**

No missing data were found in all included studies and major characteristics of all included studies were showed on Table 1. According to the type of study design, three of these studies were cross-sectional studies and the others were case-control studies. Among these studies, one was came from England [8], one from India [26], three from China [15, 17, 27] and one from Italy [28]. The sample size for all studies ranged from 80 to 17100 and studies from China contributed to the largest sample size (98.4%). In three Chinese studies, the control group included volunteers with normal blood pressure from the community and non-hypertensive patients form hospital. However, three other studies from England, India and Italy did not describe the source of the control group. In the case group, the average age of hypertensive
patients was between 42.58 and 68.05 years old. Moreover, only two included studies matched the age and gender proportions between control group and hypertensive group. The major testing method of H. pylori included enzyme linked immunosorbent assay (ELISA), $^{13}$C urea breath test ($^{13}$C-UBT) and $^{14}$C urea breath test ($^{14}$C-UBT) in all studies. The quality score of included articles were range from 3 to 8 according to the NOS and over fifty per cent of included studies were judged to be high-quality study (S2 Table).

Risk of bias

Risk of bias in included studies were assessed via ROBINS-I tool (S3 Table). The majority of studies had controlled for one or more known confounding variables, such as age, gender, smoking and so on. However, none of included studies has fully considered all confounding factors. Thus, all studies presented a serious or moderate risk of bias in the confounding. Furthermore, one study had a moderate risk of bias in selection of participants. All studies had low risk of bias in intervention, deviations from intended interventions, missing data, measurement of outcomes and selection of the reported result.

Meta-analysis

The link of H. pylori infection with hypertension existed in three studies and their results with the ORs were range from 1.42 to 3.06. The meta-analysis of all included studies suggested that H. pylori infection could significantly increase the risk of hypertension in the random-effects model (OR: 1.34, 95% CI: 1.10–1.63, P = 0.002, $I^2 = 74\%$) (Fig 2). The potential influence of confounding factors on the pooled result were performed by subgroup analysis according to the ethnicity (Asian population, European population), study design (case-control study, cross-sectional study), detection methods of H. pylori (ELISA, $^{13}$C-UBT, $^{14}$C-UBT), study quality (low quality, high quality) and HDI (developed country, developing country). In subgroup analysis concerning on the study type, the pooled OR for case-control studies was 2.07 (95%CI: 1.12–3.81) without significant heterogeneity ($I^2 = 41.6\%$, P = 0.181), while the pooled OR for cross-sectional studies was 1.24 (95%CI: 1.03–1.48) with an evidence of heterogeneity ($I^2 = 81.3\%$, P = 0.005). By stratifying based on detection methods of H. pylori, a clear correlation between H. pylori and hypertension existed in the $^{13}$C-UBT subgroup without heterogeneity (OR: 1.41, 95% CI: 1.23–1.63, P = 0.709, $I^2 = 0\%$), yet no positive correlation was observed in ELISA subgroup (OR: 1.97, 95% CI: 0.99–3.91, P = 0.042, $I^2 = 68.5\%$). When subgroup analysis stratified by ethnicity and HDI, H. pylori could remarkably increase the risk of hypertension in both Asian population and

Table 1. Major characteristics of included studies.

| First author year | country | study design | No. case | No. control | race | HDI* | mean ageb | measure method | NOS score |
|-------------------|---------|--------------|----------|-------------|------|------|-----------|---------------|-----------|
| Lip 1996 England  | Case control | 124 | 38 | European population | developed country | 53.2 | ELISA | 3 |
| Kibria 2003 Italy | Case control | 72 | 70 | European population | developed country | 53 | $^{13}$C-UBT | 5 |
| Shankar 2012 India | Case control | 40 | 40 | Asian population | developing country | 46.71 | ELISA | 7 |
| Wan 2018 China Cross sectional | 955 | 4213 | Asian population | developing country | 42.58 | $^{13}$C-UBT | 7 |
| Xiong 2020 China Cross sectional | 9638 | 7462 | Asian population | developing country | 68.05 | $^{14}$C-UBT | 7 |
| Liu 2007 China Cross sectional | 488 | 942 | Asian population | developing country | 51.65 | ELISA | 8 |

ELISA, enzyme-linked immunosorbent assay.

$^{13}$C-UBT, $^{13}$C urea breath test.

$^{14}$C-UBT, $^{14}$C urea breath test. NOS, Newcastle–Ottawa Scale.

*HDI means human development index.

bmean age represents the average age of the case group.

https://doi.org/10.1371/journal.pone.0268686.t001
developing country (OR:1.28, 95%CI:1.05–1.55, P = 0.003, I² = 78.5%). However, no significant association was found in European population and developed country (OR:1.88, 95%CI:0.78–4.52, P = 0.099, I² = 63.3%). In subgroup analysis concerning on study quality, high quality studies yielded a significant pooled OR of 1.28 (95%CI:1.05–1.55, P = 0.003, I² = 78.5%). As the above results showed, detection methods of *H. pylori* and the study design may be the source of heterogeneity. The other variables could not significantly decreased the heterogeneity, suggesting that these variables could not explain the sources of heterogeneity.

**Sensitivity analysis and publication bias**

The sensitivity analysis was conducted to determine the stability of combined results by omitting one study each time. The results showed none of the studies influence the pooled result significantly, indicating that the pooled result was stable and reliable (S4 Table). Additionally, we detected the publication bias by two statistical methods (Egger test and Begg test) and neither method detected the publication bias (Egger test: p = 0.062, Begg test: p = 0.707) (Fig 3).

**Discussion**

The influence of *H. pylori* on the hypertension has been examined in a great number of published studies, yet with inconsistent results. It is the first time to investigated on the correlation
between *H. pylori* and hypertension through meta-analysis. This meta-analysis contain a larger sample size and applied rigorous statistical methods to get more reliable results. Combined results suggested that people with *H. pylori* infection had a 13.4% increased risk of hypertension. The positive relation with *H. pylori* and hypertension was also found in both Asian population and developing country. While, not seen to the similar result for European population and developed country. Compared with developed countries, the total infective rate of *H. pylori* was higher in developing countries. Especially, the most severely affected was Asian population [29, 30]. In addition, the high-salt eating habit of Asians could increase the colonization of *H. pylori* in the stomach [31]. The above reasons may explain the differences of pooled results between Asian population and European population. On the other hand, the economic environment might also potentially affect the pathogenesis of *H. pylori*. Compared with developing countries, a better health-care system in developed countries could timely reduce negative effects of *H. pylori*, including inflammatory reaction, toxins, dyslipidemia and so on. So as to further undermine the negative impacts of *H. pylori* in the development of hypertension.

The overall heterogeneity was high in this meta-analysis. We explored the source of heterogeneity by subgroup analysis. Notably, the heterogeneity was significantly reduced from 74% to 0% in the $^{13}$C-UBT subgroup and heterogeneity was still present in the ELISA subgroup. The above result indicated that the cause of heterogeneity may be explained by the difference in detection methods of *H. pylori*. The accuracy of serology experiments depends on the antigen used in ELISA kit. Thus, ELISA kits from different companies have different levels of diagnostic accuracy. In addition, the serologic detection could not precisely identify infection status. The $^{13}$C-UBT was recognized as a golden standard for detecting *H. pylori*. The $^{13}$C-UBT was superior to ELISA serology test in diagnosis of *H. pylori* infection because the level of *H. pylori* antibody is unpredictable [32, 33]. In addition, the heterogeneity also significantly decreased in the case-control studies subgroup (from 74% to 41.6%), however, there was still heterogeneity in the cross-sectional studies subgroup. On the one hand because the
level of evidence in case-control studies was superior to cross-sectional studies. On the other hand, cross-sectional studies often collected samples from a specified population, which may cause potential biases.

The connection between *H. pylori* and hypertension has been proposed, according to most of the world’s clinical evidences correlating inflammation and salt intake with variation in arterial blood pressure [34, 35]. Inflammation may promote hypertension by causing endothelial dysfunction and inducing oxidative stress. Migneco et al have suggested that *H. pylori* infection may lead to the activation of the inflammatory cytokines cascade with the release of vasoactive substances from the site of infection [36]. A variety of inflammatory cytokines, including IL-1beta, IL-2, IL-6 and TNF-alpha, increased significantly in individuals with *H. pylori* infection [37–40]. Those inflammatory cytokines could promote insulin resistance [41]. Then, insulin resistance may further increase the total peripheral vascular tension [42]. In addition, people with *H. pylori* may enhance the level of fibrinogen, a biomarker of vascular inflammation which could suppress the decrease of nitric acid (NO), in turn, would cause vasoconstriction and increasing the peripheral blood vessel tension [43].

Salt intake was known as a major causative factor in hypertension. Studies indicated that *H. pylori* was strongly linked to high salt intake [44]. Bevers et al have certified that high salt consumption was directly related to *H. pylori* infection [12]. Akita is the region with the highest intake of salt in the daily diet, as well as the region with the highest *H. pylori* infection rate in Japan, which suggested a direct link between *H. pylori* and high sodium consumption [45]. The gastric mucosa could be injury by high salt, which enhanced the ability of *H. pylori* to survive and colonize in stomach [46]. These evidences might suggest that high sodium consumption and *H. pylori* in coordination with each other could enhanced the development of hypertension.

*H. pylori* directly interfered with the Vit D metabolism could be an alternate explanation for cause-and-effect link between *H. pylori* and hypertension. It has been confirmed that Vit D could regulate the Renin-Angiotensin-Aldosterone System (RAAS), a major hormonal mechanisms in the regulation of blood pressure [47]. *H. pylori*-related gastritis might interfere with absorption of multiple microelement and *H. pylori*-positive subjects had lower Vit D levels [13, 48]. Shafrir et al also proved that individuals without *H. pylori* infection could efficiently absorb Vit D in their diet [49]. It could be inferred that *H. pylori* was able to promote the development of hypertension by its effects on vitamin D metabolism in vivo.

It is the fast growth period that the number and the formation of the elder in the world in the 21st century and hypertension seriously threaten the health of the elderly. Controlling risk factors for hypertension actively could reduced cardiovascular diseases and better utilization of medical resources. So, reducing people’s exposure to risk factors of hypertension is an effective way to prevent and treat hypertension. At present, the hypertension guideline did not list *H. pylori* as the predisposing factor for hypertension and the indication for *H. pylori* eradication did not include hypertension. However, new discoveries had upended traditional ideas and indicated the underlying connection between hypertension and *H. pylori*. For hypertensive patients infected with *H. pylori*, their SBP and DBP both dropped significantly after the eradicating therapy for *H. pylori* [28]. Another study also confirmed the result that the 24-hours average systolic pressure and 24-hours average diastolic pressure in hypertensive patients dropped by 8.78 per cent and 19.04 per cent respectively after eradicating the *H. pylori* [36]. Another interesting study revealed that most hypertensive patients with *H. pylori* infection get their blood pressure down to normal and quit their medications after *H. pylori* eradication treatment [50]. Due to the global *H. pylori* pandemic in recent decades, the therapy of *H. pylori* eradication might be an alternative method for treatment or prevention of hypertension.
Though we conducted this meta-analysis rigorously, yet there still existed some limitations. First, hypertension is identified as a multifactorial disease and could be affected by the individual genetic background. Most studies came from Asian countries and no relevant studies in African countries. Thus, the results of this meta-analysis may not be appropriate for other ethnic groups. Second, all studies presented a serious or moderate risk of bias in the confounding and most research were not adequately adjusted for confounding factors (smoking, the situation of drugs, age, gender, family history of hypertension), which may have influenced the reliability of the evidence. Third, this meta-analysis consisted of cross-sectional and case–control studies, so the selection bias was inevitable and we may not be able to deduce the causal relationship between hypertension and *H. pylori* although it was etiologically plausible.

Conclusions

This meta-analysis demonstrated that *H. pylori* could significantly increase the risk of hypertension, particularly among Asian population and developing country. Due to the widespread prevalence of *H. pylori* and the pathogenic behavior of *H. pylori* in hypertension, the *H. pylori* eradication may be an alternative method for treatment or prevention of hypertension. Moreover, additional high-quality research involving different regions and ethnicities is need to solve the key limitations in the meta-analysis.

Supporting information

S1 Table. PRISMA 2020 checklist. (DOCX)
S2 Table. Quality evaluation for each included study by the Newcastle–Ottawa Scale. (DOCX)
S3 Table. Evaluation of risk of bias for each included study by the ROBINS-I tool. (DOCX)
S4 Table. Sensitivity analysis. (DOCX)

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References

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet. 2005; 365(9455): 217–223. https://doi.org/10.1016/S0140-6736(05)17741-1 PMID: 15652604.

2. Buford TW. Hypertension and aging. Ageing Res Rev. 2016; 26: 96–111. https://doi.org/10.1016/j.arr.2016.01.007 PMID: 26835847.

3. Manuck SB, McCaffery JM. Gene-environment interaction. Annual review of psychology. 2014; 65: 41–70. https://doi.org/10.1146/annurev-psych-0123-115100 PMID: 24405358.

4. Vahdat K, Pourbehi MR, Ostovar A, Hadavand F, Bolkhei A, Assadi M, et al. Association of pathogen burden and hypertension: the Persian Gulf Healthy Heart Study. American journal of hypertension. 2013; 26(9): 1140–1147. https://doi.org/10.1093/ajh/hpt083 PMID: 23744497.

5. Mandieka E, Saleh D, Chokshi AK, Rivera AS, Feinstein MJ. Latent Tuberculosis Infection and Elevated Incidence of Hypertension. Journal of the American Heart Association. 2020; 9(24): e019144. https://doi.org/10.1161/JAHA.120.019144 PMID: 33263262.

6. Li C, Samaranake NR, Ong KL, Wong HK, Cheung BM. Is human cytomegalovirus infection associated with hypertension? The United States National Health and Nutrition Examination Survey 1999–2002. PloS one. 2012; 7(7): e39760. https://doi.org/10.1371/journal.pone.0039760 PMID: 22768311.

7. Sun Y, Pei W, Wu Y, Jing Z, Zhang J, Wang G. Herpes simplex virus type 2 infection is a risk factor for hypertension. Hypertension research: official journal of the Japanese Society of Hypertension. 2004; 27(8): 541–544. https://doi.org/10.1291/hypres.27.541 PMID: 15492472.

8. Lip GYH, Wisse R, Beever G. Association of Helicobacter pylori infection with coronary heart disease—Study shows association between H-pylori infection and hypertension. British Medical Journal. 1996; 312(7025): 250–251. https://doi.org/10.1136/bmj.312.7025.250b PMID: 8563608.

9. Kuo CH, Chen YH, Goh KL, Chang LL. Helicobacter pylori and Systemic Disease. Gastroenterology research and practice. 2014; 2014: 358494. https://doi.org/10.1155/2014/358494 PMID: 24772167.

10. Kalisperati P, Spanou E, Pateras IS, Korkolopoulou P, Varvarigou A, Karavoyikos I, et al. Inflammation, DNA Damage, Helicobacter pylori and Gastric Tumorigenesis. Frontiers in genetics. 2017; 8: 20. https://doi.org/10.3389/fgene.2017.00020 PMID: 28289428.

11. Ridker PM. Inflammation, atherosclerosis, and cardiovascular risk: an epidemiologic view. Blood coagulation & fibrinolysis: an international journal in haemostasis and thrombosis. 1999; 10 Suppl 1: S9–12. PMID: 10070810.

12. Beever G, Lip GY, Blann AD. Salt intake and Helicobacter pylori infection. J Hypertens. 2004; 22(8): 1475–1477. https://doi.org/10.1097/01.hjh.0000133736.77866.77 PMID: 15257168.

13. Franceschi F, Annalisa T, Teresa DR, Giovanna D, Ianiro G, Franco S, et al. Role of Helicobacter pylori infection on nutrition and metabolism. World journal of gastroenterology: WJG. 2014; 20(36): 12809–12817. https://doi.org/10.3748/wjg.v20.36.12809 PMID: 25278679.

14. Kopacova M, Koupil I, Seifert B, Fendrichova MS, Spirkova J, Vorisek V, et al. Blood pressure and stature in Helicobacter pylori positive and negative persons. World journal of gastroenterology: WJG. 2014; 20(19): 5625–5631. https://doi.org/10.3748/wjg.v20.i19.5625 PMID: 24914321.

15. Xiong XL, Chen J, He MA, Wu TC, Yang HD. Helicobacter pylori infection and the prevalence of hypertension in Chinese adults: The Dongfeng-Tongji cohort. Journal of Clinical Hypertension. 2020; 22(8): 1389–1395. https://doi.org/10.1111/jch.13928 PMID: 32687255.

16. Kim YI, Kim YA. Effect of Helicobacter pylori Treatment on Long-term Mortality in Patients with Hypertension. 2020; 14(1): 47–56. https://doi.org/10.5009/gnl18510 PMID: 30974928.

17. Liu L, Liu Y, Tong W, Ye H, Zhang X, Cao W, et al. Pathogen burden in essential hypertension. Circulation Journal. 2007; 71(11): 1761–1764. https://doi.org/10.1253/circj.71.1761 PMID: 17965498.

18. Tang H, Wang AL, Bai SL. Relationship between pathogenic infection and hypertension in Mongolian. Chinese Journal of Public Health. 2010; 26(3):295–296.

19. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ (Clinical research ed). 2021; 372: n71. https://doi.org/10.1136/bmj.n71 PMID: 33782057.

20. Wells GA, Shea B, O’Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Non-randomised Studies in Meta-analyses, http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. 2018.

21. Sterne JA, Hernán MA, Reeves BC, Savovíć J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ (Clinical research ed). 2016; 355: i4919. https://doi.org/10.1136/bmj.i4919 PMID: 27733354.
22. Gavrilaki E, Chatzidiymiou D, Chatzopoulou F, Gkaliagkousi E, Douma S. Pathogen burden and hypertension: more questions than answers. American journal of hypertension. 2013; 26(12): 1459. https://doi.org/10.1093/ajh/hpt184 PMID: 24113360.

23. Tang BW, Wang XM, Wu J. Progress in research on the relationship between Helicobacter pylori infection and cardiovascular diseases and its risk factors. Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine]. 2020; 54(3): 327–331. https://doi.org/10.3760/cma.j.issn.0253-9624.2020.03.016 PMID: 32187941.

24. Shahraki M, Eslami O. Association of helicobacter pylori infection with anthropometric indices and blood pressure among undergraduate students in southeast of Iran. Annals of Nutrition and Metabolism. 2017; 71: 490. https://doi.org/10.1159/000480486.

25. Harvey RF, Lane AJ, Murray LJ, Harvey IM, Egger M, Nair P, et al. Is there a relationship between Helicobacter infection and blood pressure? Evidence from the community-based Bristol Helicobacter Project. Gastroenterology. 2000; 118(4): A723–A723. https://doi.org/10.1016/s0016-5085(00)85023-4.

26. Shankar MSV, Kutty AVM, Annamalai N. Helicobacter pylori infection and hypertension: Is there an association? Biomedical Research-India. 2012; 23(4): 537–539.

27. Wan Z, Hu L, Hu M, Lei X, Huang Y, Lv Y. Helicobacter pylori infection and prevalence of high blood pressure among Chinese adults. Journal of human hypertension. 2018; 32(2): 158–164. https://doi.org/10.1038/s41371-017-0028-3 PMID: 29289960.

28. Kibria MG, Sultana N, Akther M, Begum H, Haque MA, Haque R, et al. Eradication of Helicobacter pylori infection improves blood pressure values in patients affected by hypertension. JGH Open. 2003; 8(6): 585–589. https://doi.10.1111/j.1523-5378.2003.00180.x PMID: 14632672.

29. Ahmad MM, Rahman M, Rumi AK, Islam S, Huq F, Chowdhury MF, et al. Prevalence of Helicobacter pylori in asymptomatic population—a pilot serological study in Bangladesh. J Epidemiol. 1997; 7(4): 251–254. https://doi.org/10.2188/jea.7.251 PMID: 9465552.

30. Fock KM, Ang TL. Epidemiology of Helicobacter pylori infection and gastric cancer in Asia. Journal of gastroenterology and hepatology. 2010; 25(3): 479–486. https://doi.org/10.1111/j.1440-1746.2009.00188.x PMID: 20370726.

31. Tsugane S, Tei Y, Takahashi T, Watanabe S, Sugano K. Salty food intake and risk of Helicobacter pylori infection. Japanese journal of cancer research: Gann. 1994; 85(5): 474–478. https://doi.org/10.1111/j.1349-7006.1994.tb02832.x PMID: 8014104.

32. Cutler AF, Prasad VM. Long-term follow-up of Helicobacter pylori serology after successful eradication. The American journal of gastroenterology. 1996; 91(1): 85–88 PMID: 8561150.

33. Pérez-Pérez GI, Cutler AF, Blaser MJ. Value of serology as a noninvasive method for evaluating the efficacy of treatment of Helicobacter pylori infection. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 1997; 25(5): 1038–1043. https://doi.org/10.1086/516089 PMID: 9402353.

34. Meneely GR, Dahl LK. Electrolytes in hypertension: the effects of sodium chloride. The evidence from animal and human studies. The Medical clinics of North America. 1961; 45: 271–283. https://doi.org/10.1016/s0025-7125(16)33891-3 PMID: 13769394.

35. Agita A, Alsagaff MT. Inflammation, Immunity, and Hypertension. Acta medica Indonesiana. 2017; 49 (2): 158–165 PMID: 28792351.

36. Micneco A, Ojetti V, Specchia L, Franceschi F, Candelli M, Mettimano M, et al. Eradication of Helicobacter pylori infection improves blood pressure values in patients affected by hypertension. Helicobacter. 2003; 8(6): 585–589. https://doi.org/10.1111/j.1523-5378.2003.00180.x PMID: 14632672.

37. Yamaoka Y, Kita M, Kodama T, Sawai N, Kashima K, Imanishi J. Induction of various cytokines and cytokine messenger RNA in gastric mucosa. Gastroenterology. 1996; 110(6): 1473–1477. https://doi.org/10.1053/gast.1996.110.pm10.1053/gast.1996.110.001053 PMID: 8964939.

38. Wellen KE, Hotamisligil GS. Inflammation, stress, and diabetes. The Journal of clinical investigation. 2005; 115(5): 1111–1119. https://doi.org/10.1172/JCI25102 PMID: 15864338.
42. Kotsis V, Stabouli S, Papakatsika S, Rizos Z, Parati G. Mechanisms of obesity-induced hypertension. Hypertension research: official journal of the Japanese Society of Hypertension. 2010; 33(5): 386–393. https://doi.org/10.1038/hr.2010.9 PMID: 20442753.

43. Longo-Mbenza B, Naenga JN, Mokondjimobe E, Gombet T, Assori IN, Ibara JR, et al. Helicobacter pylori infection is identified as a cardiovascular risk factor in Central Africans. Vascular health and risk management. 2012; 6: 455–461. https://doi.org/10.2147/VHRM.S28680 PMID: 22923995.

44. Zaidi SF. Helicobacter pylori associated Asian enigma: Does diet deserve distinction? World J Gastro-intest Oncol. 2016; 8(4): 341–350. https://doi.org/10.4251/wjgo.v8.i4.341 PMID: 27096029.

45. Dahl LK. Possible role of salt intake in the development of essential hypertension. 1960. Int J Epidemiol. 2005; 34(5):967–972; discussion 972–964, 975–968. https://doi.org/10.1093/ije/dyh317 PMID: 16143660.

46. Fox JG, Dangler CA, Taylor NS, King A, Koh TJ, Wang TC. High-salt diet induces gastric epithelial hyperplasia and parietal cell loss, and enhances Helicobacter pylori colonization in C57BL/6 mice. Cancer research. 1999; 59(19): 4823–4828 PMID: 10519391.

47. Jeong HY, Park KM, Lee MJ, Yang DH, Kim SH, Lee SY. Vitamin D and Hypertension. Electrolyte & blood pressure: E& BP. 2017; 15(1): 1–11. https://doi.org/10.5049/EBP.2017.15.1.1 PMID: 29042901.

48. Yang L, He X, Li L. Effect of vitamin D on Helicobacter pylori infection and eradication: A meta-analysis. 2019; 24(5): e12655. https://doi.org/10.1111/hel.12655 PMID: 31411799.

49. Shafrir A, Shauly-Aharonov M, Katz LH, Paltiel O, Pickman Y, Ackerman Z. The Association between Serum Vitamin D Levels and Helicobacter pylori Presence and Eradication. 2021; 13(1). https://doi.org/10.3390/nu13010278 PMID: 33478000.

50. Nasrat SA, Nasrat AM. An Alternative Approach for the Rising Challenge of Hypertensive Illness via Helicobacter pylori Eradication. Cardiol Res. 2015; 6(1): 221–225. https://doi.org/10.14740/cr382e PMID: 28197229.