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The association of Helicobacter pylori infection with the risk of anemia in children: systematic review and meta-analysis

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Abstract

Background Children are among the most vulnerable groups for Helicobacter *pylori (*H. *pylori)* infection, which was linked with an increased risk of anemia. H. *pylori* infection may cause the development of anemia through affecting the absorption of different micronutrients and increasing hepcidin production from hepatocytes. This study aimed to assess the effect of H. *pylori* infection on the occurrence of anemia in children.

Methodology Previously published articles were systematically searched on major databases including Science Direct, PubMed, Embase, Scopus, Cochrane Library, and Science Citation Index using search terms. The search results were imported into EndNote X9 to organize and remove duplicates. Then, relevant data was extracted and analyzed using STATA version 16.0. The pooled odds ratio (OR) was calculated to evaluate the associations of H. *pylori* infection with Anemia. Moreover, pooled standardized mean difference (SMD) of Hemoglobin (Hgb) and Serum ferritin (SF) levels between cases and controls were calculated for group comparisons.

Results A total of nine published articles were included in this study. The result showed that H. *pylori*-infected children had 2.68 times more risk of developing anemia compared to H. *pylori*-negative children (OR: 2.68:95% CI:1.44–4.99, $p=0.002$). Subgroup analyses based on study design showed an increased significant association between H. *pylori* infection and anemia among case-control studies (OR:3.792:95%CI;1.767, 8.142, $p=0.001$). Subgroup analyses based on the H. *pylori* detection method indicated an increased significant association between H. *pylori* infection and anemia when the stool antigen test method was used (OR:3.801;95%CI:1.090,13.250, $p=0.036$). Moreover, there was a significant decrement of Hgb and SF levels in the H. *pylori* positive group compared to the negative group with SMD of -0.54(95%CI: -0.65, -0.42, $p<0.001$) and − 0.49(95% CI: -0.91, -0.08, $p<0.020$), respectively.

Conclusions This study revealed that children with H. *pylori* infection are at a higher risk of developing anemia as compared to non-infected children. Moreover, the observed decrease in Hgb and SF levels in infected children suggests that H. pylori may contribute to the development of anemia. Future research need to focus on the mechanisms by which H. pylori infection contributes to anemia, as well as the potential benefits of targeted interventions in reducing both H. pylori prevalence and anemia rates in children.

Keywords Helicobacter *pylori*, H. *Pylori*, Anemia, Hemoglobin, Ferritin, Children, Meta-analysis

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Introduction

Helicobacter *pylori (*H.*pylori)* is a Gram-negative, spiral-shaped, microaerophilic pathogenic bacterium that causes inflammation of the stomach lining [1]. It plays a major role in chronic gastritis [2] and peptic ulcer disease [3]. H. *pylori* affects 44.3% of world's population with the range of 34.7% in developed countries to 50.8% in developing countries [4], which varies according to location and sanitation standards [5]. It is acquired during early childhood and remains asymptomatic in most infected individuals. The routes of transmission include person-to-person through oral–oral (kissing, mouth feeding) or fecal-oral route, consumption of contaminated water, and vertical transmission through breastfeeding [6].

H. *pylori* infection has been linked with the development of anemia in children [7]. Childhood anemia is a condition where a child has an insufficient hemoglobin (Hgb) level to provide adequate oxygen to the body tissues. World Health Organization (WHO) suggests Hgb cut-off values for diagnosing anemia at sea level as < 10.5 g/dL in children aged 6–23 months, < 11 g/dL in children aged 24–59 months, and < 11.5 g/dL in children aged 5–11 years [8]. It has been hypothesized that H. *pylori* infection can cause the development of different kinds of anemia including, iron deficiency anemia (IDA) [9], pernicious anemia [10], anemia of chronic disease (ACD) [11, 12].

Iron deficiency anemia is a type of anemia due to depressed levels of total body iron [13]. Serum ferritin (SF) level was confirmed to be a good marker of total body iron stores and IDA [14]. H.*pylori* infection might cause IDA through different mechanisms, including affecting dietary iron absorption [9], causing blood loss [15], influencing iron transporter molecules [16], and competing with the host [17]. Most dietary irons are in non-hemic ferric form, and an increased gastric acid level is needed to reduce into ferrous form for absorption [18]. However, chronic H. *pylori* infection frequently results in atrophic gastritis, which leads to reduced gastric acid secretion [17, 19], and ultimately results in impaired iron absorption [9]. In addition, H. *pylori* induces hemorrhagic gastritis and active bleeding peptic ulcers [15, 20] which results in blood loss and anemia [18]. Furthermore, H.*pylori* infection may influence the expression of iron transport regulators in the gastric mucosa [21] as some signals from H. *pylori* might influence the secretion of lactoferrin, an iron-binding glycoprotein, in the gastric mucosa [16]. Lastly, H. *pylori* may cause IDA through competing with the host in the gastric mucosa [16, 21]. The bacteria require continuous supplementation of nutrients for their growth [22]. As a result, it could compete with its host to uptake iron available in the microenvironment of the stomach lumen [17, 23].

H. *pylori* infection is implicated in pernicious anemia, which is characterized by low serum vitamin B12, important for red blood cell (RBC) production [10]. Gastric parietal cells are important to secrete intrinsic factors that aid vitamin B12 absorption by a mechanism of molecular mimicry [24]. The infection causes chronic gastritis that may proceed to atrophic gastritis and achlorhydria [25]. This could stimulate an autoimmune process against the gastric parietal cells which results in a reduced availability of intrinsic factors for vitamin B12 absorption and transport [25, 26] and then eventually progresses to vitamin B12 deficiency and pernicious anemia [24].

The proposed mechanism to explain H. *pylori*-associated ACD is increased hepcidin production from hepatocytes due to H. *pylori* residing in the gastric mucosa [21, 27]. Hepcidin acts as an acute-phase reactant in response to the inflammation produced in the gastric mucosa [11]. The production of hepcidin increases from hepatocytes in response to interleukin-6 production in H. *pylori* gastritis [21]. Hepcidin binds to and induces degradation of cell-surface ferroportin, the main cells capable of releasing iron into plasma, on macrophages and jejunal enterocytes. This inhibits iron release from macrophages and enterocytes which decreases iron transport across a membrane [28]. In general, several studies indicated an association between H. *pylori* infection and anemia in children. However, reports from different areas are not consistent and remain unclear [29]. Therefore, the current study was conducted to investigate the effect of H. *pylori* infection, if any, on the occurrence of anemia in children.

Methodology

Study design and protocol registration

A Preferred Reporting Items for Systematic Review and Meta-Analysis protocol (PRISMA) 2020 guideline was used to conduct this systematic review and meta-analysis. The protocol of the study has been registered in the Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42024535879. The study analyzed findings from published articles to investigate the effect of H. *pylori* infection on the occurrence of anemia among children globally.

Eligibility criteria

Studies that met the following criteria were included in this study.

Study design

All published observational studies with cohort, case-control, and cross-sectional study designs; that evaluated

the relationship between H. *pylori* infection and Anemia (any type of anemia) in children.

Study area

Studies that were conducted in any geographic region of the world.

Language and time restrictions

Studies that were written in the English language and published online in peer-reviewed journals up to November 10, 2023.

Study participants

Human studies that were carried out on children with H. *pylori* infection, regardless of gender.

Target data

Studies that presented data regarding the association between H. *pylori* infection and anemia among children were included.

On the other hand, the following studies were excluded after a thorough screening of the abstracts and the full texts.

* Studies with insufficient or ambiguous data for meta-analysis or difficult data to extract.
* Animal, non-human, and non-children studies.
* Studies with low methodological quality.
* Reviews, case reports, poster presentations, and letters to the editor.
* Articles published other than English language.
* Studies that did not enable to calculation of odds ratio (OR) from 2 by 2 tables.

Information sources and search strategy

Relevant articles for this systematic review and meta-analysis were identified through comprehensive electronic searching of major databases including Scopus, Embase, PubMed, Science Direct, Cochrane Library, and Science Citation Index. The following MeSH terms were used to search: Helicobacter pylori, H. *pylori*, iron deficiency, anemia, Hemoglobin, and Ferritin. During the literature search, the results were limited by study population, language, and availability of full text. Additional relevant studies were retrieved through reference probing of identified articles. This was done by two independent reviewers (MW and FG), with the involvement of the third reviewer (MA) in cases of disputes.

Study selection and quality assessment

The search results were imported into EndNote X9 (Thomson Reuters, Toronto, Canada) to organize and remove duplicate articles. The title/abstract of

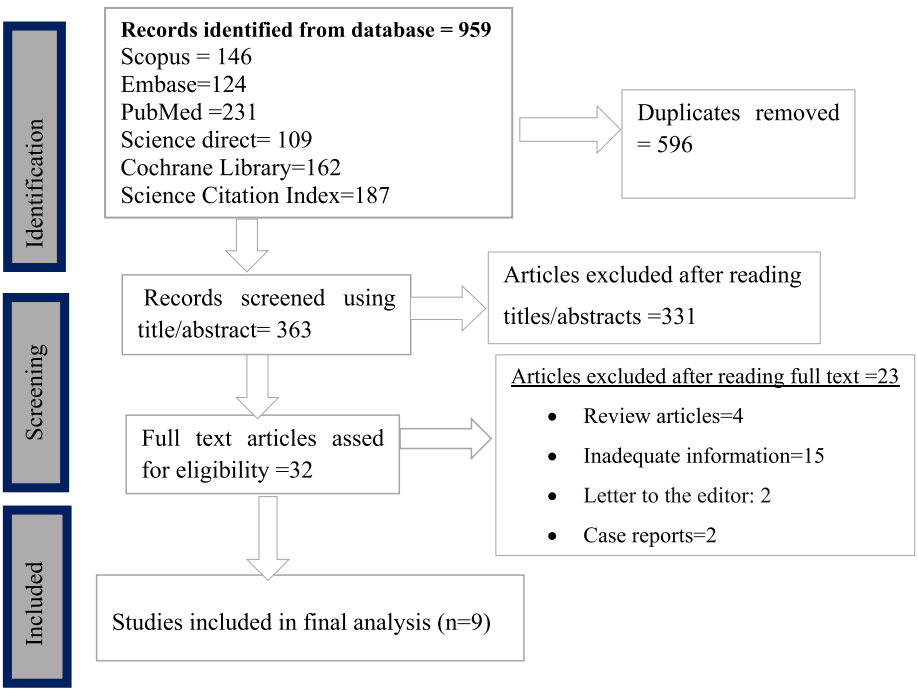

Fig. 1 PRISMA flow chart to describe the selection of included studies for the systematic review and meta-analysis on the association of H.pylori infection with the risk of anemia in children

Table 1 Study characteristics of included studies

Author/ year	Study design	Country	Details of outcome definition	Source population	H.pylori + ve		H.pylori –ve		Hgb level (g/dl)		SF level		H.pylori detection method	Type of Anemia
					Anemia	No anemia	Anemia	No anemia	H.pylori +ve	H. pylori -ve	H.pylori +ve	H. pylori -ve		
Choe et al., 2000 [7]	Prospective	S. Korea	IDA: SF < 12 ng/ml, transferrin saturation < 15% & Hgb < 120 g/l	School	10	53	22	290					ELISA	IDA
Baysoy et al., 2004 [3]	Cross-sectional	Turkey	IDA: SF < 12 g/L, serum iron < 50 g/dL & Hgb > 2SD below normal	Hospital	12	16	12	12					Histology	IDA
Süoglu et al., 2007 [30]	Case-control	Turkey	IDA: determined according to Dallman's criteria	Hospital	20	15	6	29	11.6 ± 1.7	12.2 ± 0.7	11.9 ± 8.4	42.1 ± 31.8	Histology	IDA
Muhsen et al., 2010 [33]	Prospective	Israel	Anemia: Hgb < 11.5 g/dL for children & <11.0 g/dL for infants	Community	17	93	4	69	12.4 ± 1.1	12.8 ± 0.9	36.1 ± 17.3	35.6 ± 19.6	ELISA	Anemia
Shak et al., 2011 [34]	Cross-sectional	Haiti	Anemia:<110 g/L(age 6 month to 5 years)	Community	3	1	36	9					Serology	Anemia
Taye et al., 2015 [35]	Prospective	Ethiopia	Anemia : Hgb: < 11.5 g/dL for children 5–11 years	Community	169	261	88	221					Stool antigen	Anemia
Elnemr et al., 2016 [31]	Case-control	Egypt	Anemia: SF < 12 ng/mL and Hgb < 11 18 g/dL	Hospital	18	10	32	40	10.2 ± 1.4	11.03 ± 1.08	29.05 ± 18.3	35.92 ± 21.5	Serology	Anemia
Mohammed et al., 2019 [36]	Case-control	Iraq	NA	Hospital	6	1	44	49					Stool antigen	IDA
Abdelaziz et al., 2021 [32]	Cross-sectional	Egypt	Anemia: Hb < 11.5 g/dL	Community	99	201	60	840	12.24 ± 1.11	12.66 ± 0.59	15.33 ± 8.8	20.51 ± 10.2	Stool antigen	Anemia

H. *pylori*: Helicobacter *pylori*, *Hgb* Hemoglobin, *SF* Serum ferritin, *IDA* Iron deficiency anemia, and *ELISA* Enzyme Linked Immunosorbent Assay

retrieved articles were screened for eligibility, and then the methodological quality of each article which was considered to appear pertinent for inclusion was evaluated in detail using the Newcastle Ottawa Scale (NOS) critical appraisal tool. The tool awards a score range of 0–9 points for 8 items under three categories (selection, comparability, and exposure or outcomes). Each done item within the selection and outcome categories has a maximum score of 1 point while a maximum of 2 points can be given for the item under comparability. A value of 0 was assigned for each item that is not clearly stated in the method part. To evaluate the quality of case-control studies, the tool awards a point score range of 0–4 for selection of the cases and controls, 0–2 for comparability of the cases and controls, and 0–3 for identification of the exposure. Likewise, cohort and cross-sectional studies are evaluated using three sections including, selection (0–4 points), comparability (0–2 points), and outcome (0–3 points). Studies with a total score of 0–3 points, 4–5 points, and 6–9 points are considered poor, fair, and high quality, respectively. Therefore, studies with an overall NOS score greater than 3 according to the number of done items in the three sections were included in the quantitative meta-analysis. The title/abstract screening and quality assessment were performed by two independent reviewers (MS and AT), and any disagreement was resolved through discussion and/or with the consultation of a third review author (FG).

Outcomes of interest

The main outcome of interest in this systematic review and meta-analysis was the associations of H. *pylori* infection with the occurrence of Anemia among children using OR as an effect measure. The secondary outcome was the comparison of Hgb and SF values between H. *pylori*-positive and H. *pylori*-negative children in the form of standardized mean difference (SMD).

Data extraction

Data including, first author name, study design, publication year, country, number of H. *pylori*-infected participants, number of non-infected participants, number of anemic participants, number of non-anemic participants, and H. *pylori* diagnostics method were extracted from

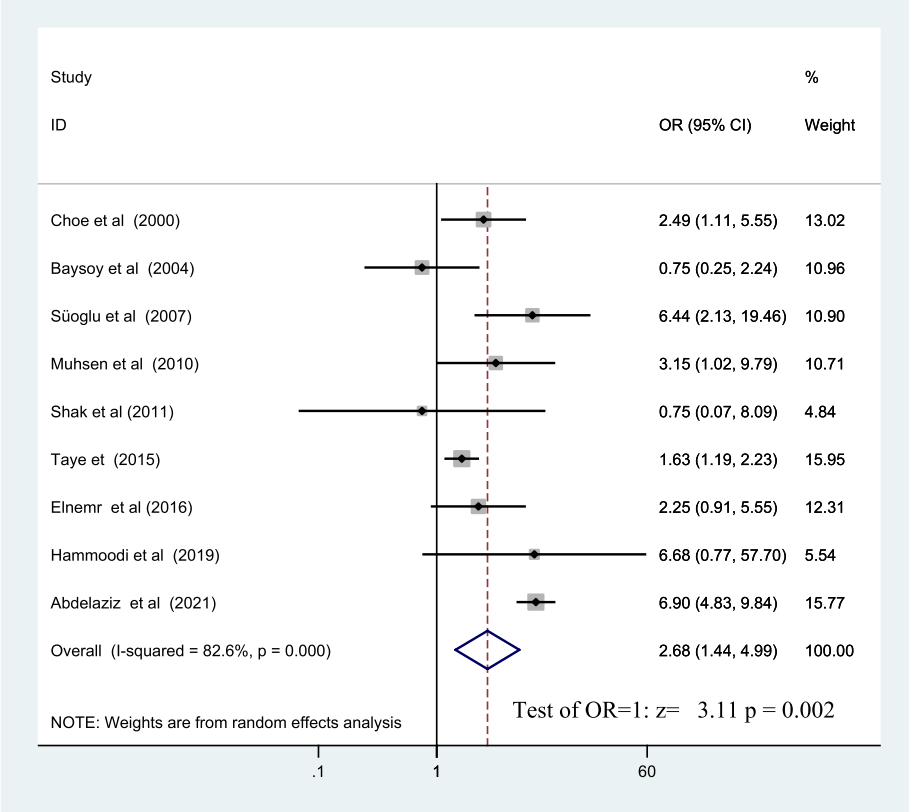

Fig. 2 Forest plot of included studies; pooled effect size (OR) estimates of H.pylori infection for the development of anemia in pediatric patients

the included studies using Microsoft excel format. Moreover, Hgb and SF levels between H. *pylori* infected and H. *pylori* negative children were extracted, if reported in the same study. Additionally, the specific type of anemia according to the individual study report was extracted (when available). Two independent reviewers (MS and MA) were responsible for data extraction, any disagreements were resolved through negotiation/involving a third reviewer (MW).

Statistical analysis

Relevant data were extracted using Microsoft Excel and analyzed using STATA version 16.0 (StataCorp Corporation, College Station, TX, USA). The analysis was performed by MW and FG together. Pooled OR with its 95% confidence interval (CI) was calculated to evaluate the associations of H. *pylori* infection with the occurrence of Anemia. Moreover, the pooled SMD analyses were used to compare Hgb and SF levels between the case and control groups. A random-effects model was employed to estimate the pooled effect size for all analyses. Subgroup analysis was conducted to explore the potential source of heterogeneity between the included studies. The logarithm of OR (log OR), and standard error (Se log OR) were calculated from the corresponding effect measure. All analyses with $p < 0.05$ were considered as statistically significant.

Results

Study selection

Initially, a total of 959 search results were identified from different databases including, Scopus (146), Embase (124), PubMed (231), Science Direct (109), Cochrane Library (162), and Science Citation Index (187). Of the total, 950 studies were excluded through duplicate identification (596), title/abstract screening (331), and after full-text reviewing (23). Finally, nine studies that satisfied the eligibility criteria were included in this meta-analysis. The flowchart represents the search and selection strategy for the study (Fig. 1).

Study characteristics

A total of 2,805 participants, including 942 H. *pylori*-infected and 1,863 H. *pylorii*-negative children from nine studies were included in the analysis. The sample size ranged from 7 to 430 in the H. *pylori*-infected group and 24 to 900 in the H. *pylori*-negative group. Regarding the study area, among the nine included studies in this review, two studies were conducted in Turkey [3, 30], two studies in Egypt [31, 32], and the remaining five studies were conducted in South Korea [7], Israel [33], Haiti [34], Ethiopia [35], and Iraq [36]. Based on the study design of the included studies, three were case-control, three were

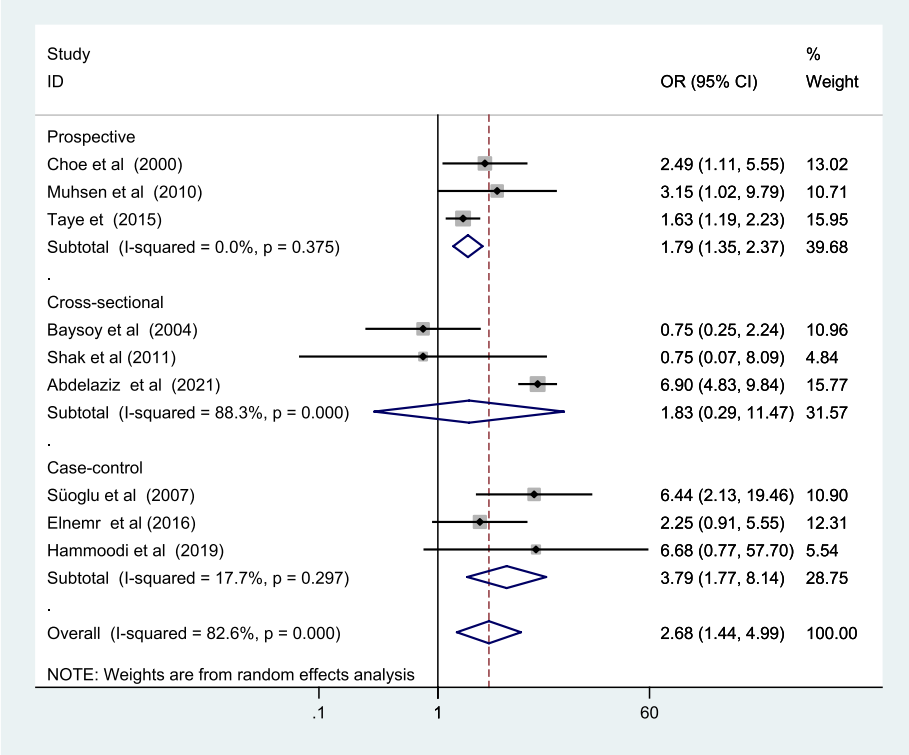

Fig. 3 Forest plot of included studies; sub-group analysis pooled effect size (OR) estimates of H.pylori infection for development of anemia among children stratified by study design

cross-sectional, and the remaining three had prospective study designs. Four of the included articles reported information related to Hgb and SF levels with mean ± SD for both case and control groups (Table 1).

The association between H. Pylori infection and the occurrence of anemia in children

A total of nine studies were included in this meta-analysis to assess the associations of H. *pylori* infection with the occurrence of Anemia in children by calculating the odds of participants with anemia in the H. *pylori*-infected group compared with the controls, using a random-effect model. The overall pooled OR showed that the risk of anemia occurrence among H. *pylori*-infected children was 2.68 times higher than among H. *pylori*-negative children (2.68:95% CI;1.44–4.99, $p=0.002$) (Fig. 2).

Subgroup analyses

A random effect model was applied because of the significant heterogeneity between studies ($I^2=82.6\%$). In our pursuit to identify sources of heterogeneity among the studies, we conducted subgroup analysis which involved categorizing studies based on study design and H. *pylori* detection method. Subgroup analysis by study design showed that there was a significant association between H. *pylori* infection, type of anemia, and occurrence of anemia in case-control and prospective studies with a pooled OR of 3.792 [95%CI;1.767,8.142, $p=0.001$] and 1.787[95%CI;1.346,2.371, $p<0.001$], respectively. However, there was no significant association in cross-sectional studies with a pooled OR of 1.828 [95% CI;0.291, 11.472, $p=0.520$] (Fig. 3).

A subgroup analysis by laboratory detection method of H. *pylori* infection showed that the pooled odds of H. *pylori* infection for the occurrence of anemia among children were significant when H. *pylori* was detected using ELISA [2.692:95%CI;1.399,5.18, $p=0.003$] and Stool antigen [3.801:95% CI;1.090, 13.250, $p=0.036$]. On the other hand, there was no significant association when H. *pylori* was detected using Histologic [2.196:95%CI; 0.267–18.078, $p=0.465$] and Serologic methods [1.960:95%CI; 0.843, 4.555, $p=0.118$] (Fig. 4). A subgroup analysis based on the type of anemia showed that there was a significant effect of H. *pylori* infection on the occurrence of anemia in children. The pooled OR of H. *pylori* infection for the development of Anemia was 2.663[95% CI:1.117–6.345, $p=0.027$] and the odds of IDA occurrence in children was 2.658 [95% CI:1.005–7.031, $p=0.049$] (Fig. 5).

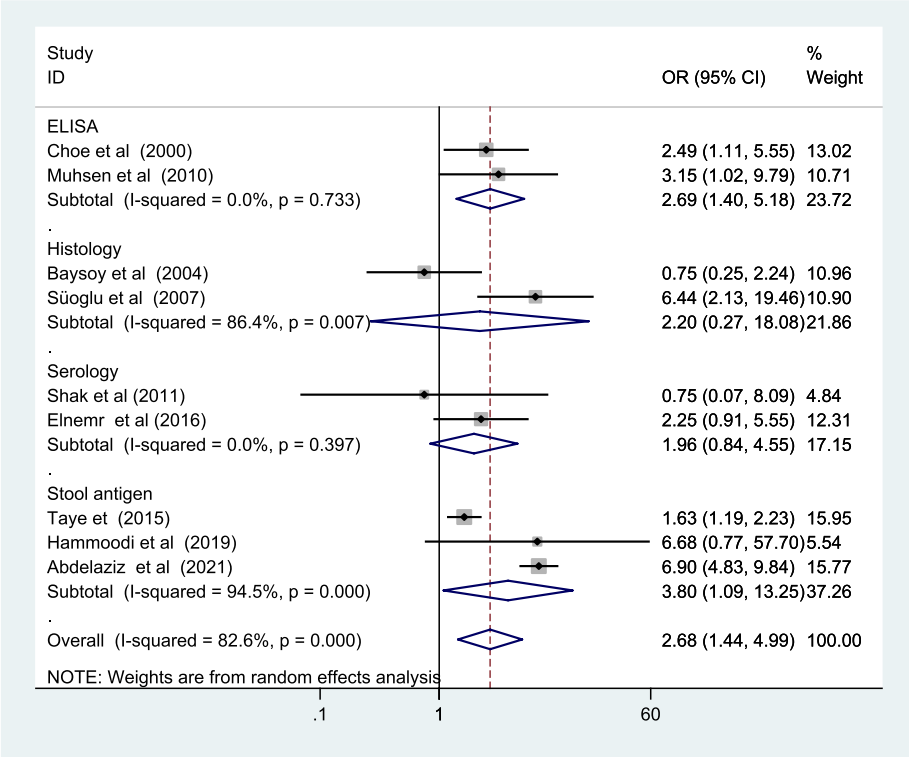

Fig. 4 Forest plot of included studies; sub-group analysis pooled effect size (OR) estimates of H. pylori infection for development of anemia among children stratified by H.pylori detection method

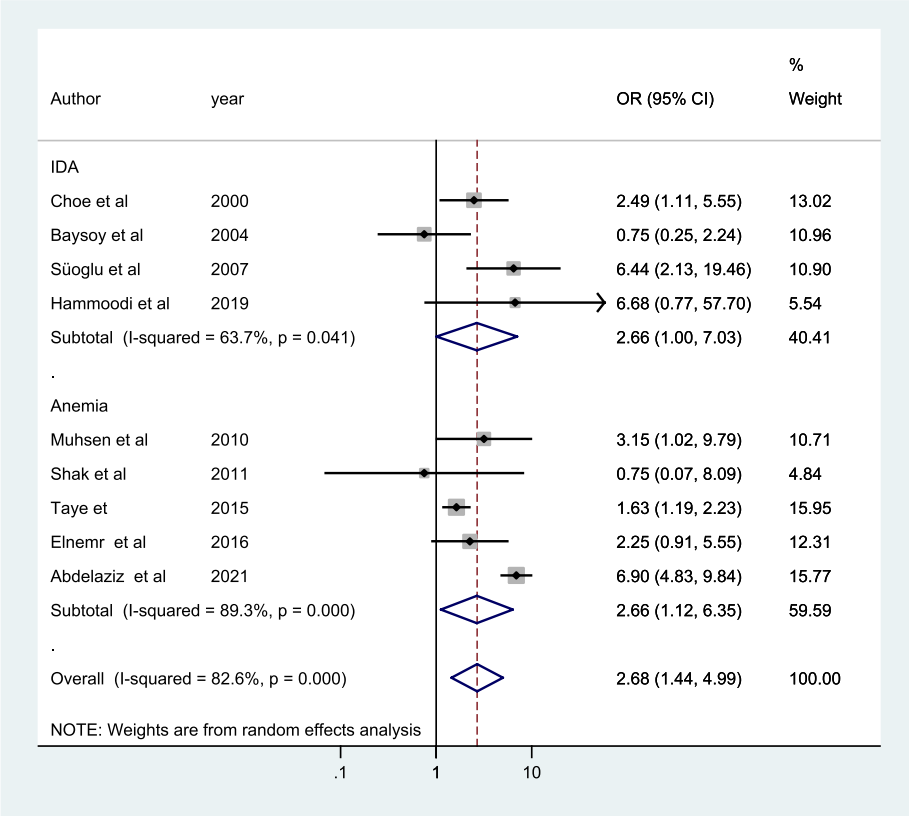

Fig. 5 Forest plot of included studies; sub-group analysis pooled effect size (OR) estimates of H. pylori infection for development of anemia among children stratified by type of anemia

Comparisons of hemoglobin and serum ferritin levels between H. *Pylori*-infected and H. *Pylori*-negative children

We performed a random-effect model for pooled SMD analysis of Hgb and SF levels between H. *pylori*-positive compared to H. *pylori*-negative groups in the included four studies. In the pooled analysis, a significant decrease in Hgb and SF levels was observed in the H. *pylori*-positive groups compared to H. *pylori*-negative children. The overall pooled SMD of Hgb between H. *pylori* positive and negative groups was −0.54[95% CI: −0.65, −0.42, $p < 0.001$] (Fig. 6). Similarly, the overall pooled SMD of SF between H. *pylori*-infected and control groups in children was −0.49[95% CI: −0.91, −0.08, $p < 0.020$] (Fig. 7).

Publication bias

The funnel plot was used to assess the presence of publication bias for the analysis of pooled OR estimates of H.pylori infection for the development of anemia in children.The graph appears a symmetrical funnel which indicates the absence of publication bias of included studies (Fig. 8).

Discussion

H. *pylori* infection is one of the most widespread chronic bacterial infections that causes chronic gastritis and severe gastroduodenal pathologies. This infection is usually transmitted in childhood and persists for life if untreated [5]. H. *pylori* infection has been linked with the occurrence of Anemia, which can be the result of nutritional, environmental, social, and infectious etiologies [34]. Several mechanisms have been proposed for the development of anemia in H. *pylori* infection. The most plausible mechanisms are malabsorption of iron [9] and vitamin B12 [10] which are important for RBC production and increased hepcidin production from hepatocytes due to H. *pylori* residing in the gastric mucosa [21, 27]. It was concluded that H. *pylori* is a highly suspected cause of IDA due to its iron-deficient state [31]. Children are more likely to develop IDA from H. *pylori* infection as they may have diminished iron stores due to dietary deficiency [37].

The current results from a meta-analysis of nine epidemiological studies revealed an association between H. *pylori* infection and Anemia (OR, 2.68:95% CI;1.44–4.99, $p = 0.002$). This finding could supported by a study

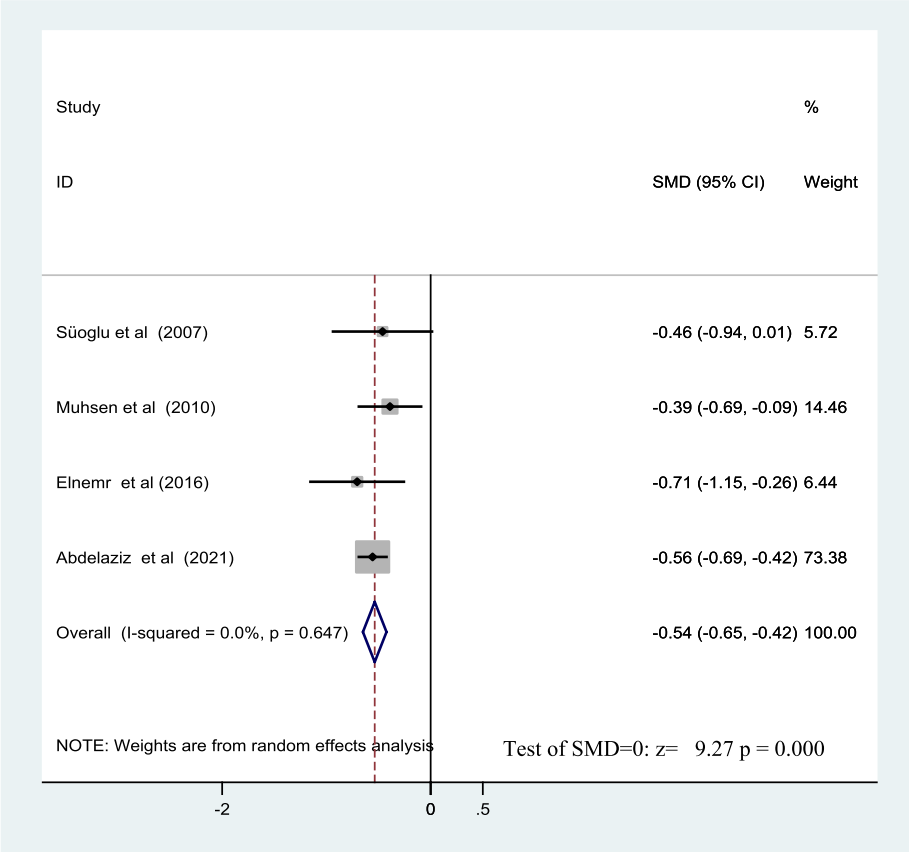

Fig. 6 A forest plot showing SMD of the Hemoglobin level between H.pylori positive and H.pylori negative control in pediatric patients

by Muhsen et al. (2010) that noted H. *pylori* eradication therapy would reduce the burden of anemia [33]. A meta-analysis by Qu et al., 2010 [38] which included all age groups and genders suggests an association between H. *pylori* infection and IDA with the pooled OR of 2.22 (95% CI:1.52–3.24, $P<0.0001$). They also revealed a significant association between H. *pylori* and IDA in children and adolescents from a subgroup analysis for different age groups. The pooled OR of children younger than 11 years was 4.76 (95% CI: 1.73–13.08) while the pooled OR in Adolescents was 2.85 (95% CI: 1.68–4.31). The results of the meta-analysis by Muhsen et al., 2008 [39] also revealed an increased risk for IDA; pooled OR 2.8 (95% CI: 1.9–4.2) among H. *pylori*-infected subjects. Furthermore, a meta-analysis by Azami et al., 2016 [40] found a statistically significant relationship between H. *pylori* and IDA in pregnant women with an estimated OR 1.82 (CI: 95%, 1.43–2.30). The possible reason for the observed minor difference in the strength of association could be the unmeasured confounding variable (e.g., socioeconomic status, bacterial load, location, or inherited disease) [34].

A subgroup analysis by laboratory detection method of H. *pylori* infection showed H. pylori infection has a significant role in the occurrence of anemia among pediatrics when H. pylori was detected using ELISA and Stool antigen methods. Whereas, there were no significant associations when H. pylori was detected using Histology and Serologic methods. Different diagnostic methods for H. *pylori* contribute to the variation of the pooled estimates because of their different sensitivities. The pooled OR value increased with the sensitivity of the diagnostic method [38]. A subgroup analysis based on the type of anemia indicated that there was a significant effect of H. *pylori* infection on the occurrence of IDA and anemia in children with the pooled OR of 2.658 [95%CI:1.005–7.031] and 2.663 [95%CI:1.117–6.345], respectively. Similarly, Hudak et al. on their meta-analysis study showed that there was an increased likelihood of IDA; pooled OR 1.72 [95% CI 1.23–2.42] and anemia; pooled OR 1.15 [95%CI 1.00–1.32] in H. pylori-infected individuals compared to uninfected persons [41].

The findings of this meta-analysis indicate a significant association between H. pylori infection and reduced

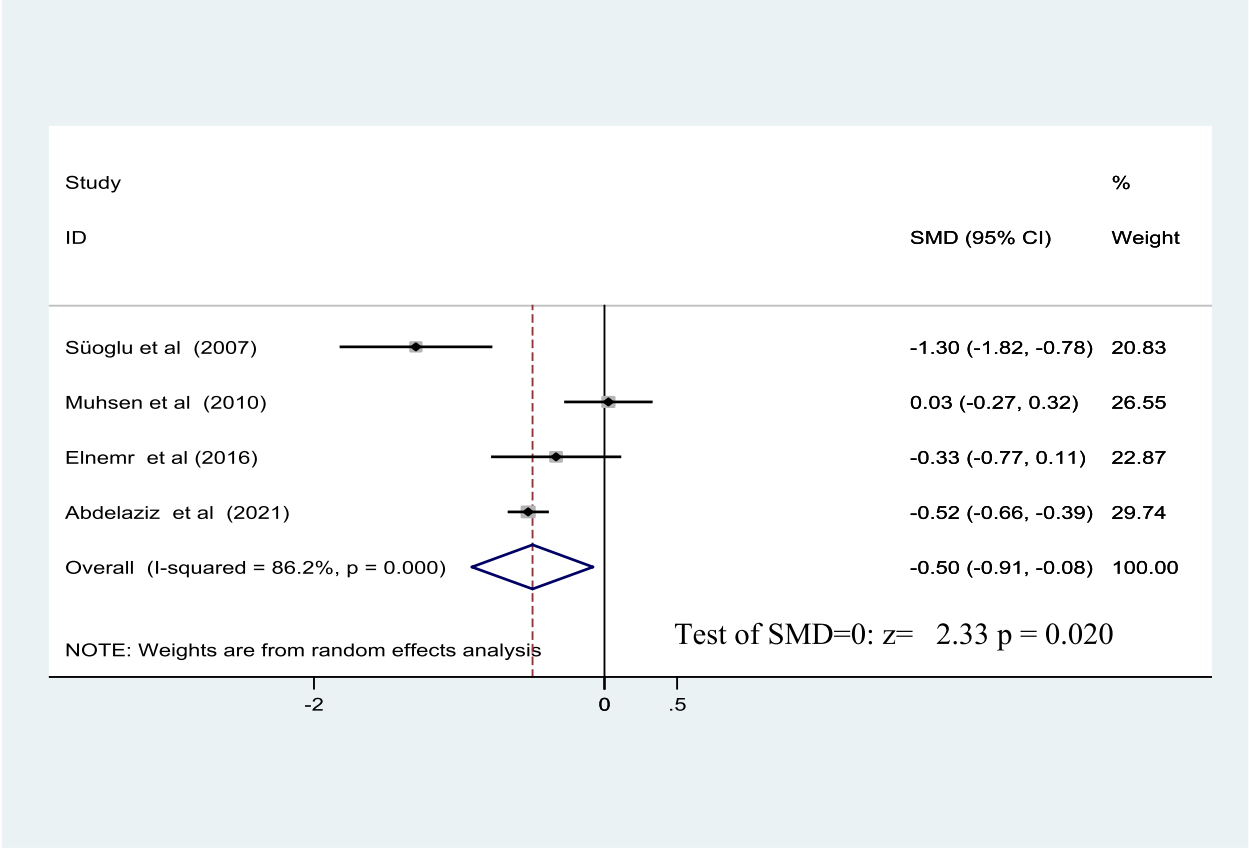

Fig. 7 A forest plot showing SMD of the serum ferritin level between H.pylori positive and H.pylori negative control among children

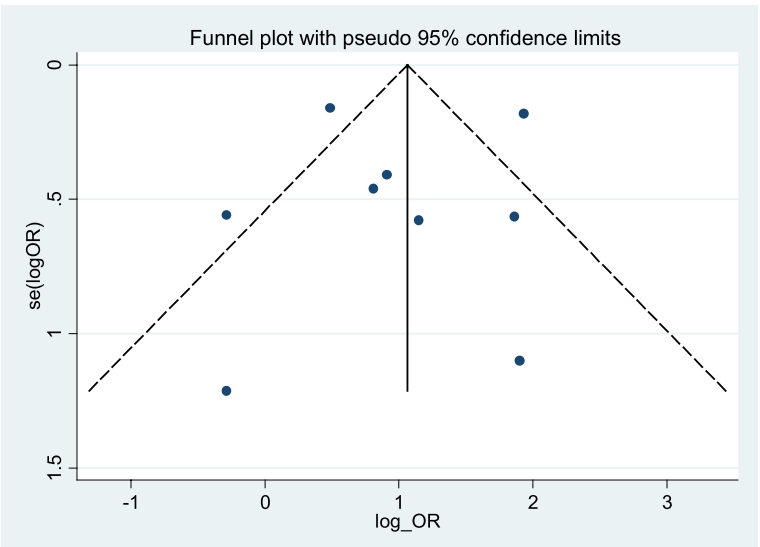

Fig. 8 Funnel plot of the included studies assessing publication bias for the pooled effect size (OR) estimates of H.pylori infection for the development of anemia in pediatric patients

levels of Hgb and SF. The overall pooled SMD of −0.54 [95% CI: −0.65, −0.42, $p < 0.001$] and −0.49 [95%CI: −0.91, −0.08, $p < 0.020$] for Hgb and SF, respectively. This highlights that individuals infected with H. pylori exhibit lower levels of these critical hematological parameters compared to their H. pylori-negative counterparts. Similar findings were reported by Azami et al., 2016 [40] that investigated the relationship of H. *pylori* with Hgb and SF levels among pregnant women and found H. *Pylori* significantly reduces these two variables ($P < 0.05$). These was also supported by previous reports that revealed a significantly higher response to iron therapy and a rise of Hgb after the eradication of H. *pylori* compared to their response before eradication [22, 42]. Furthermore, a meta-analysis by Hudak et al. showed an increased ferritin but not Hgb following anti-H. pylori eradication therapy plus iron therapy as compared with iron therapy alone [41]. The reduction in SF levels is indicative of depleted iron stores, which is consistent with the pathophysiology of H. pylori-related anemia [43].

Strengths and limitations of the study

In this review, a comprehensive search was done on different databases using different search strategies. The study included all relevant articles done around the globe. Furthermore, the review was done following the protocol of the PRISMA guideline and the NOS tool was used to appraise the methodological quality of the included studies. However, some limitations remain in this study. This study included articles that were published in English languages. Even though subgroup analysis was performed high heterogeneity was still observed. Most of the included studies are from developing county, which may influence the representativeness of the pooled estimate. Moreover, other iron-related tests are required for the confirmation of iron deficiency and different types of anemia.

Conclusions and recommendations

In conclusion, this study indicates that children with H. *pylori* infection are at a higher risk of developing anemia as compared to non-infected children. Moreover, the observed decrease in Hgb and SF levels in infected children suggests that H. pylori may contribute to the development of anemia through impaired iron absorption or chronic inflammation. These findings underscore the importance of screening for H. pylori in pediatric population, particularly in those presenting with symptoms of anemia. Early diagnosis and treatment of H. pylori infection could play a crucial role in preventing anemia and improving overall health outcomes in affected children. Moreover, parents are recommended to keep the hygiene of their children to prevent the diseases and adopt treatment measures based on clinician orders for children with H. *pylori* infection. Future research need to focus on the mechanisms by which H. pylori infection contributes to anemia, as well as the potential benefits of targeted interventions in reducing both H. pylori prevalence and anemia rates in children.

Abbreviations

ACD	Anemia of Chronic Disease
H. Pylori	Helicobacter Pylori
HGB	Hemoglobin
IDA	Iron Deficiency Anemia
NOS	Newcastle Ottawa Scale
OR	Odds Ratio
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol
PROSPERO	Prospective Register of Systematic Reviews
RBC	Red Blood Cell
SF	Serum Ferritin
SMD	Standardized Mean Difference
WHO	World Health Organization

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

MW conceived the concept for this systematic review and meta-analysis. MW, AT, MA, SM, MS and FG were involved in the data searching, data extracting, data analysis, and Manuscript writing. All authors reviewed and approved the final manuscript.

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Data availability

All relevant data supporting the findings are within the manuscript.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare no competing interests.

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