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Prevalence of Helicobacter Pylori in Iranian Children: A Systematic Review and Meta-Analysis Study

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Abstract

Background: The prevalence of Helicobacter pylori infection is reported variously in different studies in Iran. These study aimed to determine the prevalence of Helicobacter pylori infection in children in Iran.

Materials and Methods: In this systematic review and meta-analysis, we searched Medline, Scopus, EMBASE, Web of Science, and Google scholar systematically from Jan 1990 to up to December 2020. "Helicobacter pylori", "Child", "H. pylori", "Campylobacter pylori" and "Iran" were used for search. All English-language articles associated with the prevalence of H. pylori performed in Iran were evaluated, and after passing the qualification assessment (Newcastle –Ottawa Quality Assessment Scale), these were entered into the analysis. The prevalence of H. pylori in children at a 95% confidence interval was estimated using a random-effect model.

***Results*:** The search initially identified a total of 778 publications, and finally, 43 studies involving 16,939 children were included. The pooled prevalence of H. pylori infection in Iranian children is estimated as 43% (I_2=98.1, p=0.001). Based on the diagnostic methods, the pooled prevalence in the group with stool antigen evaluation was 44% (I2=99%, p=0.001), the pooled prevalence in the serology evaluation group was 40% (I2=96%, p=0.001), in the biopsy group, 50%, in Rapid urease test/ urea breath test 40%, and in combined diagnostic tests group 56% (I2=84.5%, p=0.001), and in the not determined group the pooled estimate was 26%. The heterogeneity between groups was significant (p<0.001).

***Conclusion*:** The pooled prevalence of H. pylori infection in children in Iran is estimated as 43%, which has been higher than the global prevalence. Also, a higher prevalence rate was reported in studies in which the diagnostic test was a biopsy.

Key Words: Children, Helicobacter pylori, Iran, Prevalence.

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1- INTRODUCTION

Helicobacter pylori (H.pylori) is a Gram-negative, microaerophilic, and spiral-shaped bacterium with various infectious rates in different countries, with a higher infection rate in developing countries (1, 2). The infection, which plays a role in gastric-related diseases such as gastric cancer, could occur during childhood or adolescence (3, 4). Previous studies reported the infection prevalence as 23.1% and 32.5% in Canada and the USA and higher than 70% in Vietnam, Albania (5-8). Socioeconomic status is an important factor for developing the infection (9). Other factors include age, ethnicity, and geographic location (10). A previously done systematic review and meta-analysis by Zamani et al. (2018) reported the worldwide prevalence of H.pylori in children as 32.6% (11). Knowing the prevalence rate will help to consider the infection in children. The prevalence rate of infection in children in Iran differs between studies that were conducted in different provinces. Therefore, we aimed to do this systematic review and meta-analysis to determine the pooled prevalence of Helicobacter pylori infection in Iran children.

2- MATERIALS AND METHODS

2-1. Method

In this systematic review and meta-analysis study, the components such as "Helicobacter pylori", "H. pylori", "Campylobacter pylori", "Child", and "Iran" were used for search. These Synonyms were founded with Medical Subject Headings (Mesh). These topics were combined using the Boolean operators AND/OR. The Searching was conducted in online databases searched Medline/PubMed, Scopus, EMBASE, Web of Science, and Google scholar search engine from Jan 1990 to up to December 2020.

2-2. Search Selection

Two independent researchers independently evaluated the articles (title and abstract). The eligibility criteria were studies reporting on Iranian children aged < 18 years who had an existing diagnosis of H. pylori infection by either: 1) positive serum antigen, 2) positive stool antigen, 3) positive biopsy/endoscopy, 4) rapid urease test (RUT), and urea breath test (UBT). Also, all studies (observational, case-control, cohort) were published from Jan 1990 up to December 2020 via the English language. We excluded studies with non-original studies such as editorials, viewpoints review articles or commentaries, and studies with a sample size < 10 patients diagnosed with H. pylori infection. Additionally, studies that had no clear data regarding the prevalence of H.pylori infection in children were also excluded. All discrepancies were adjudicated by a third-person specialist in epidemiology (third author). All English-language articles associated with the prevalence of H.pylori performed in Iran were evaluated, and after passing the qualification assessment, they were entered into the analysis.

2-3. Data extraction

At first, the studies were screened according to inclusions criteria after reading their titles and abstracts. The articles' selection approach is visible in the PRISMA diagram (**Figure.1**). We extracted data regarding the total number of participants, first author, publication year, mean age, female/male ratio, type of cognition test, number of patients with any positive test results such as serum/stool/ rapid urease test/ urea breath test ***(*Table.1***). The information of the final articles was entered into a researcher-made checklist. Two researchers did data extraction, and in case of disagreement, it was resolved by a third person specialist in epidemiology (third author).

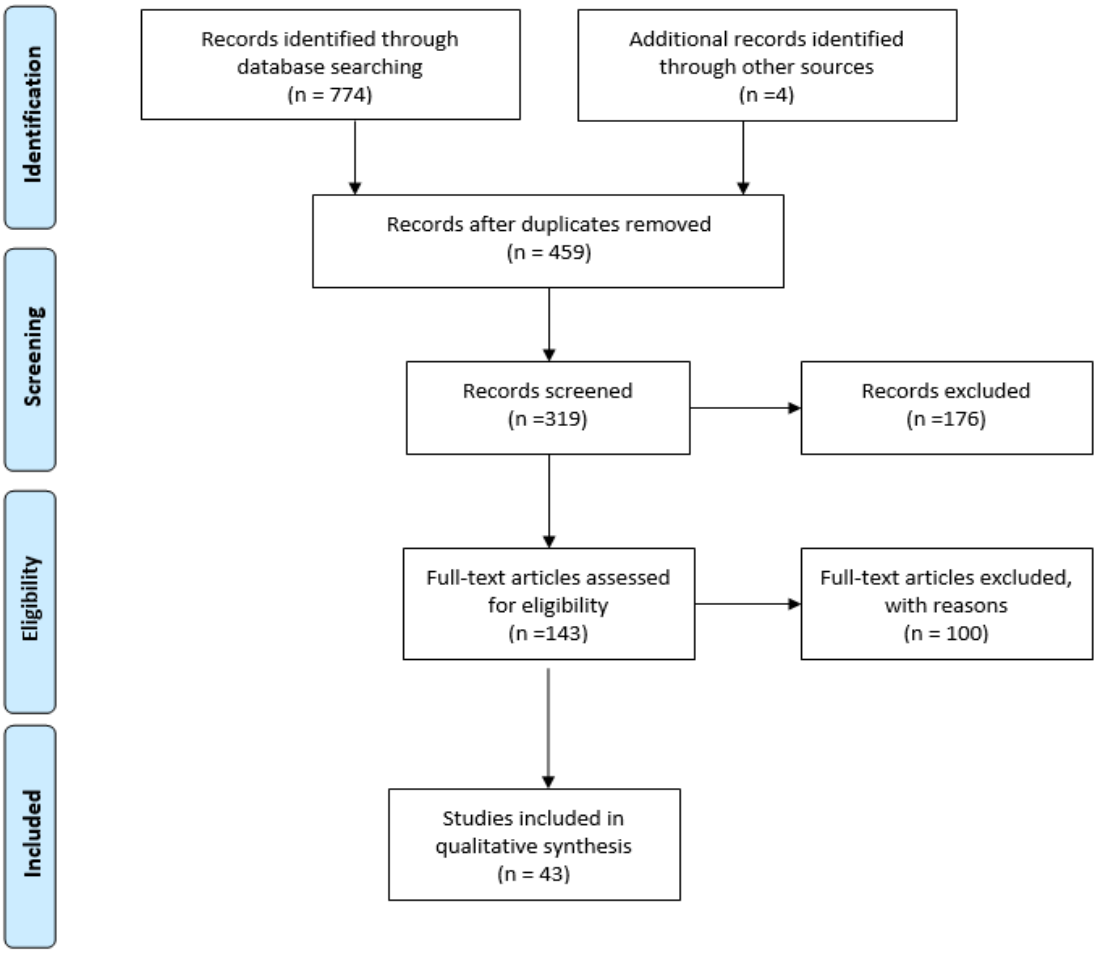

Fig.1: PRISMA flowchart of present study.

2-4. Risk of bias assessment

We evaluated the risk of potential bias by the Newcastle –Ottawa Quality Assessment Scale (12). Each item on the scale is scored from one point. Each study's maximum is 9, with less than 5 points being identified as representing a high risk of bias.

2-5. Statistical analysis

In this study, for each sample of the study, the prevalence of H.pylori was examined as the number of children with a positive test divided by the number of total assessed children. The pooled prevalence of H.pylori in children with nephrotic syndrome (NS) at a 95% confidence interval (CI) was estimated using a random-effect model. The I2 statistic was used to assess the heterogeneity of estimates. All statistical analyses were performed using STATA (Version 14.0; Stata Corp LP, College Station, TX, USA). Statistical tests were significant if P-value was < 0.05.

3- RESULTS

The search procedure initially identified 778 publications, and four extra articles identified through manual review of the bibliographies of the studies were included. After duplicates and non-relevant studies were removed, the full texts of articles were reviewed in depth. Finally, 43 studies (1, 2, 8, 13-52) involving 16939 children were eligible for inclusion in the meta-analysis (**Figure.2**).

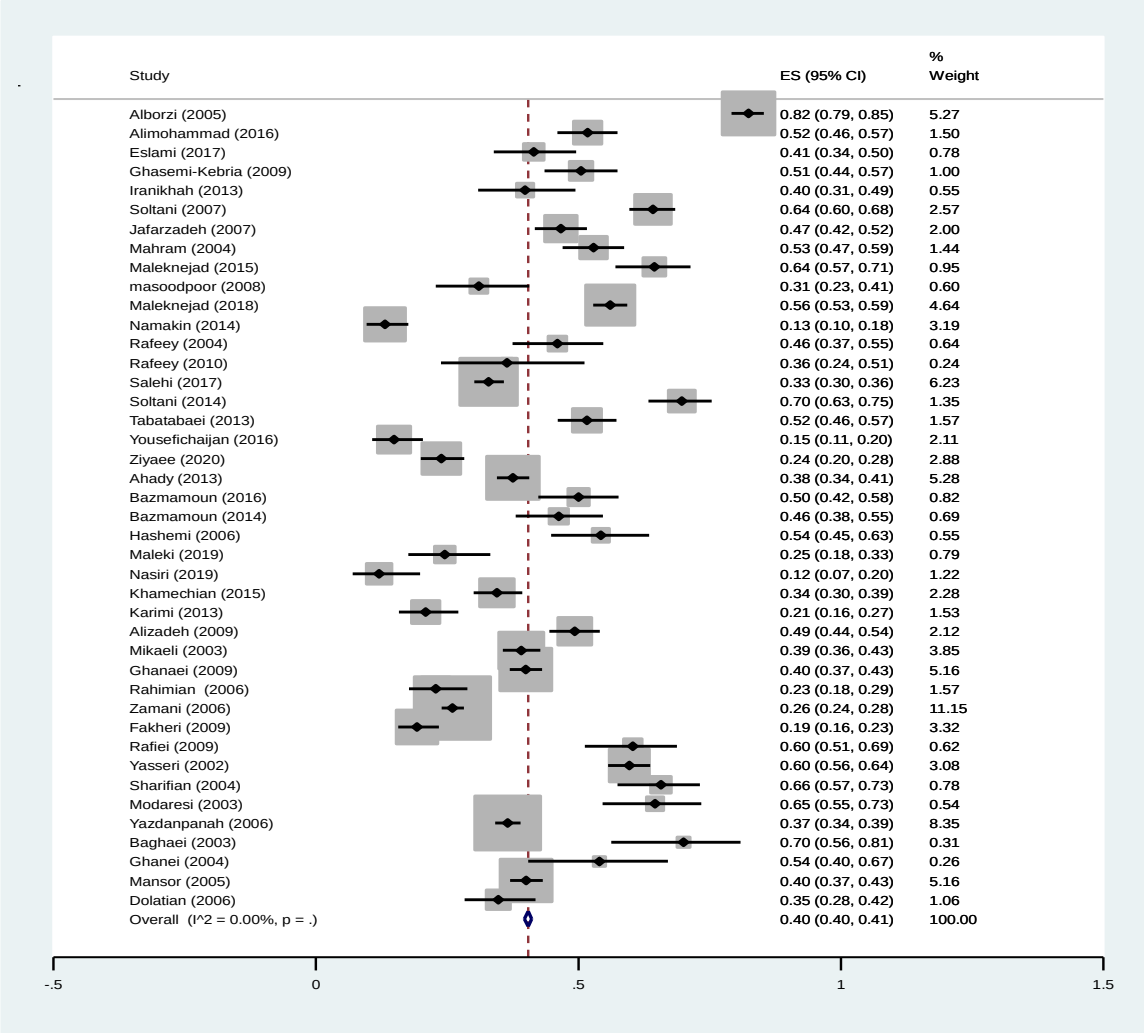

Fig.2: The pooled prevalence of H. pylori infection in Iranian children (1990-2020).

The main characteristics of the studies are presented in **Table.1** *(Please see at the end of paper)*. The pooled prevalence of H. pylori infection in Iranian children was estimated as 43% (I_2=98.1, p=0.001) (**Figure.2**). These studies used positive Serum antigen, Positive Stool antigen, positive biopsy/endoscopy, RUT, or UBT to detect H. pylori. In one classification, analysis was carried out based on the diagnostic methods. The pooled prevalence in the group with stool antigen evaluation was 44% (I2=99%, p=0.001), the pooled prevalence in the serology evaluation group was 40% (I2=96%, p=0.001), in biopsy group 50%, in RUT/UBT 40% and in combined diagnostic tests group 56% (I2=84.5%, p=0.001), and in the not determined group the pooled estimate was 26%. The heterogeneity between groups was significant (p<0.001) (**Figure. 3**).

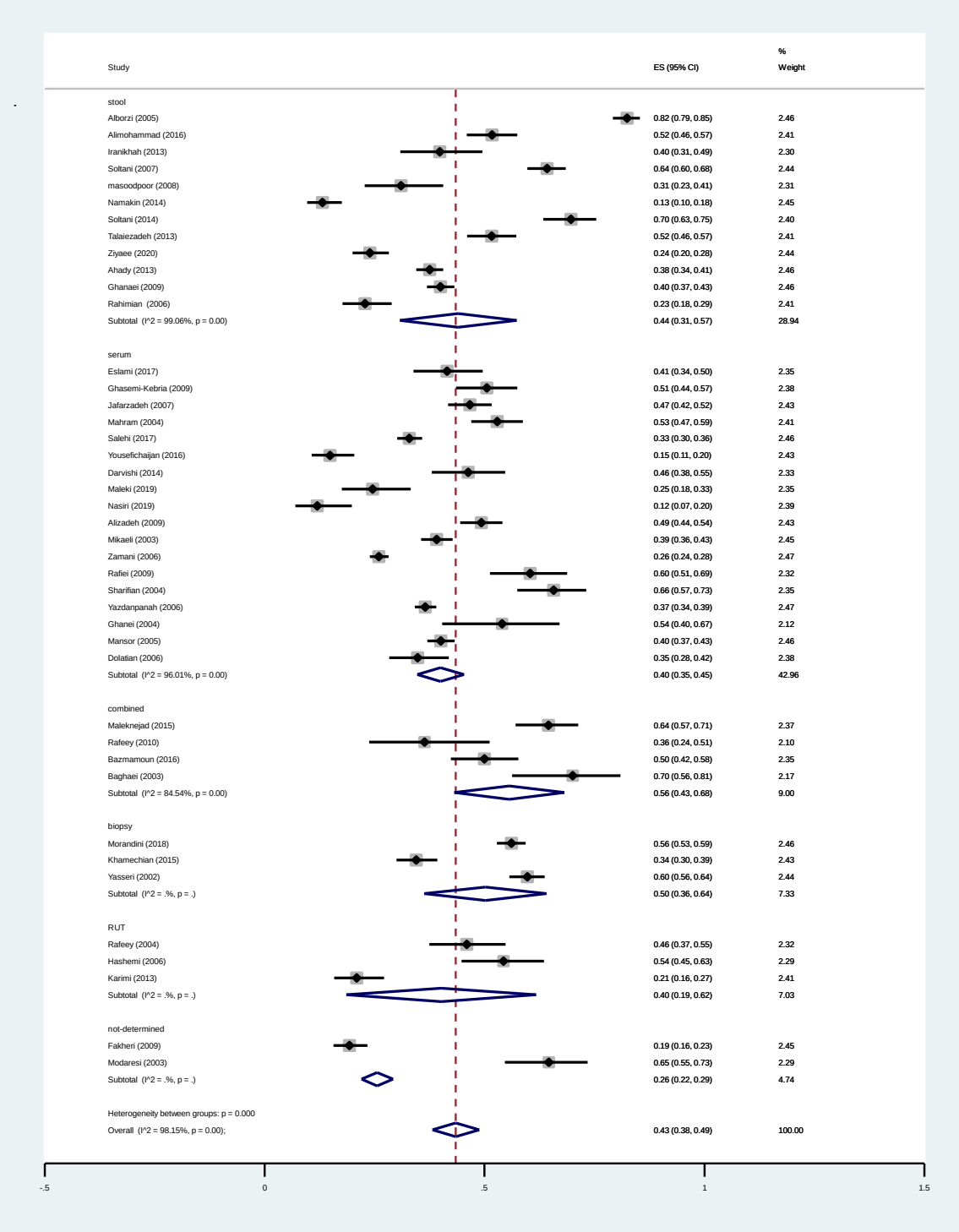

Fig.3: The pooled prevalence of H.pylori infection diagnostic tests Iranian children (1990-2020).

4- DISCUSSION

The present study was performed to estimate the prevalence of H. pylori in Iranian children via a systematic review and meta-analysis. The pooled prevalence estimate is found as 40%, while the crude prevalence ranged between 12-82% in different studies (3-8). In Zamani et al.'s study (11), the prevalence of H. pylori in children of the world was 32.6 %. In a previous systematic review and meta-

analysis, the pooled prevalence of H. pylori in Iranian children was reported as 42%, while the highest and the lowest prevalence rates were attributed to Tehran (74%) and Mazandaran (19.2%) (53). They found that the most sensitive diagnostic test is ELISA. The highest rate was reported by Alborzi et al. (2), who conducted their study in Shiraz city (a city in the South of Iran). The difference between existing studies could be due to various inclusion criteria, different applied diagnostic tests, and cut-off points. It should be noted that access to clean water, socioeconomic status, and family size differs significantly between different provinces in Iran. Helicobacter pylori is a Gram-negative, microaerophilic bacteria that could colonize in gastric mucosa in childhood and can be asymptomatic during a lifetime if treatment is not administered (54) which is more prevalent in adults than children with heterogeneous prevalence among nations (55).

Near 85% of helicobacter pylori are asymptomatic, and there is no exact relationship between symptoms and infection and symptoms such as continuous vomiting, bleeding of the gastrointestinal (GI) system, and iron deficiency without a specific cause. Therefore, malnutrition could be based on infection-related complications. The person-to-person transmission rate is high (oral-oral or oral-fecal routes), and mothers play an important role (56). Contaminated water could be another source, as well as milk, meat, and vegetables (57). Maternal infection is considered to be associated with the children's infection more than paternal infection, while paternal age and occupation were important factors for infection transmission (53). The family size also matters (58). Azevedo et al. reported socioeconomic status as an important factor for developing H.pylori infection (59). The diagnosis could be made by both invasive and non-invasive methods. The gold standard of diagnosis is a gastric biopsy. Most parents do not let their children undergo endoscopy and biopsy as it is an invasive test. As the results show, the most common administered diagnostic test was serology followed by stool antigen test. It is recommended to use serological tests as screening tests and confirm the results by other diagnostic tests. The sensitivity of serological tests is determined between 63%, and 86% in children (60-63). Stool antigen test is a non-invasive, cost-effective test, and its sensitivity is not different for various age groups nor patients with acute bleeding (64, 65). It can be used for both clinical and epidemiological studies. The urea breath test is another non-invasive test with high sensitivity and specificity (66). Rapid urease test (RUT) is another non-invasive test while its basis breaks down the urea to carbon dioxide and ammonia by the bacterium. The accuracy depends on the number of biopsy samples, the density of bacteria, and medication use such as antibiotics, proton pump inhibitor (PPI), and bismuth (66). A biopsy is invasive, and unlike in adults, gastric ulcers are rare in children. So, biopsy specimens are hardly available.

4-1. Study Limitations

We can mention the limitations of this study: 1. all studies did not use the same diagnostic test, 2. the inclusion and exclusion criteria were different, and 3. The prevalence was not adjusted based on sex, age groups, and other confounders in included studies.

5- CONCLUSIONS

The pooled prevalence of H. pylori infection in children in Iran is estimated as 43%, which has been higher than the global prevalence. Also, a higher prevalence rate was reported in studies in which the diagnostic test was a biopsy.

6- CONFLICT OF INTEREST: None.

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Table-1: General characteristics of included studies.

First Author, Year, (Reference)	Number of Cases/ Control	Average age, year, cases/ control	F/M ratio, cases/ control	Positive serum antigen. cases/ control	Positive RUT or UBT, cases/control	Positive Stool antigen, cases/ control	Positive biopsy/endoscopy, cases/ control	NOS score (12)
Alborzi, (2005), (2)	592	6.9	0.92	NA	NA	488	NA	7
Alimohammad, (2016), (52)	*145 /145	8.75/8.8	1.04/ 1.1	NA	NA	85/ 65	NA	8
Eslami, (2017), (1)	147	<20	NA	61	NA	NA	NA	7
Ghasemi Kebria, (2009), (49)	194	8.37/ NA	1.17/ NA	98	NA	NA/ NA	NA	7
Iranikhah, (2013), (9)	103	8.32/ NA	0.83/ NA	NA	NA	41/ NA	NA	6
Soltani, (2007), (13)	458	5.6±5.4/ NA	0.98	NA	NA	294/ NA	NA	7
Jafarzadeh, (2007), (14)	386	9.5 ± 3.9	1.06	180	NA	NA	NA	9
Mahram, (2004), (15)	278	7-9	NA	147	NA	NA	NA	8
.Maleknejad, (2015), (16)	169	7.30 ± 3.12	1.03	32	36	41	NA	8
Masood poor, (2008), (17)	*40 /60	12.7/12.7	NA/ NA	NA	NA/ NA	16/15	NA	9
Morandini, (2018), (18)	888	<30	NA	NA	NA	NA	498	7
Namakin, (2014), (19)	282	10.5 (9-12 Y)	2.09	NA	NA	13.1	NA	8
Rafeey, (2004), (20)	124	8.2	NA	NA	57	NA	NA	8
Rafeey (2010).(21)	44	7.77±3.51 months	1	NA	8	NA	8	7

Salehi, (2017).(25)	155/912	0-10 /10-20	NA/ NA	33/318	NA/ NA	NA/ NA	NA/ NA	8
Soltan (2014), (22)	**91 /130	36.17 /38.39 months	0.78/1.11	NA	NA/ NA	61/31	NA/ NA	9
Tabatabaei, (2020), (22)	469	2-24 m/ NA	NA	NA	NA	184	NA	7
Talaiezadeh, (2013), (24)	160/194	0-10/10-20	NA/ NA	NA	NA/ NA	53/104	NA/ NA	8
Yousefichaijan, (2016), (26)	***104 /104	7.23/6.5	2.05/1.6	13/18	NA/ NA	NA/ NA	NA/ NA	7
Ziyaee, (2020), (27)	80 128 92 109	1-28 days 6 months- 3 year 10 year 15 year	total: 0.94	NA	NA/ NA	20 28 18 31	NA/ NA	7
Ahady, (2013), (28)	960	2-12	1	NA	NA	360/ NA	NA	8
Bazmamoun, (2016), (29)	****80 /80	9.48/9.25	1.5/1.58	48/32	NA/ NA	48/32	NA/ NA	7
Darvishi, (2014), (30)	*****64/70	62.8/61.3 months	1.13/1.05	52/10	NA/ NA	NA/ NA	NA/ NA	9
Hashemi, (2006), (31)	105	<20/ NA	NA	NA	57	NA	NA	7
Maleki, (2019), (32)	114	15-25	NA	28	NA	NA	NA	7
Nasiri, (2019), (33)	***50 /50	8.12/8.19	0.19/0.61	8/4	NA/ NA	NA/ NA	NA/ NA	8
Khamechian, (2015), (34)	***36/364	11.23/10.72	1.25/1.07	NA	NA/ NA	NA/ NA	8/130	7
Karimi, (2013), (35)	**98/98	8.64/8.43	0.72/0.63	NA	18/23	NA/ NA	NA/ NA	8
Alizadeh, (2009), (36)	61/351	6-10/11-20	1.03/0.96	28/175	NA/ NA	NA/ NA	NA/ NA	8
Mikaeli, (2003), (37)	711	6-20	NA	278	NA	NA	NA	8

Mr-Ghanaei, (2009), (38)	961	7-11	1.02	NA	NA	384	NA	9
Rahimian, (2006), (39)	215	6	NA	NA	NA	49	NA	7
Zamani, (2006), (40)	1665	9.18	NA	433	NA	NA	NA	7
Fakheri, (2000), (41)	400	7-18	NA	Diagnostic method is undetermined: 77				8
Rafiei, (2009), (42)	116	3.21	NA	70	NA	NA	NA	8
Yasseri, (2002), (43)	576	8.8	NA	NA	NA	NA	344	8
Sharifian, (2004), (44)	137	2.2	NA	90	NA	NA	NA	8
Modaresi, (2003), (50)	96	0.03/ NA	NA	Diagnostic method is undetermined :62				8
Yazdanpanah, (2006), (45)	1503	14.91	NA	549	NA	NA	NA	8
Baghaei, (2010), (46)	50	11.67	NA	35	35	NA	35	8
Mr Ghnaei, (2004), (47)	50	11.3/	NA	27	NA	NA	NA	8
Ghanei, (2007), (51)	961	7-11 y	NA	385	NA	NA	NA	8
Dolatian, (2006), (48)	187	4.77	NA	65	NA	NA	NA	8

Positive Serum anti; No of patients with positive Serum antigen; No of patients with positive RUT (Rapid urease test) or UBT (Urea breathe test): positive RUT or UBT; Positive Stool anti: No of patients with positive Stool antigen; Positive biopsy/end: No of patients with positive biopsy/endoscopy; *: Children with recurrent abdominal pain/: Children without recurrent abdominal pain; **: Children without breastfed infants/ Children with breastfed infants; ***: Children with asthma / Children without asthma; ****: Children diabetic / Children non-diabetic; *****: Children with IDA/ Children non-anemic; F/M: Female/ Male; NOS: Newcastle Ottawa Scale.