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RESEARCH ARTICLE

# *Helicobacter pylori* infection is associated with anemia, weight loss or both conditions among Bulgarian children

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**ABSTRACT**

Some studies suggested an association between *Helicobacter pylori* infection and iron-deficiency anemia, however, the link between weight loss and the infection in childhood remains non-established. In a retrospective cohort study, we compared *H. pylori* positivity rates of Bulgarian children without or with anemia (47 children in each group) or weight loss (45 children in each group) and both conditions (17 children in each group). *H. pylori* infection was associated with the presence of anemia (in 76.6% of the anemic vs. 21.3% of the non-anemic patients, $P < 0.0001$) and weight loss (in 82.2% of the patients vs. 17.8% of the control children, $P < 0.0001$). All 17 patients with both conditions were *H. pylori* positive. Relative risk of anemia, weight loss and both conditions was 3.6 (95% CI, 2.0–6.4), 4.6 (95% CI, 2.4–8.8) and 5.7 (95% CI, 2.0–15.8), respectively, in the children with *H. pylori* infection. In conclusion, *H. pylori* infection was significantly associated with iron-deficiency anemia or/and weight loss in Bulgarian pediatric patients. Therefore, diagnostics and treatment of the infection as well as a proper control of the eradication success can be beneficial and thus, can be recommended for children with those conditions.

**KEYWORDS**

*Helicobacter pylori*, infection, children, anemia, weight loss

## INTRODUCTION

In 1993, Bruel et al. [1] reported a case of 11-year old patient with severe anemia, *Helicobacter pylori* gastritis and upper gastrointestinal bleeding and suggested that the infection and anemia were linked. Other authors also detected an association between *H. pylori* infection and iron-deficiency anemia [2–4]. Anemia was refractory to iron treatment, whereas patients recovered after both iron therapy and eradication of *H. pylori* infection [5–7]. Both *H. pylori* infection and anemia, in particular iron-deficiency anemia, are predominant in populations with low socio-economic status [8]. However, results of some studies did not show any association between *H. pylori* status and iron deficiency anemia [9].

In Maastricht V/Florence Consensus Report, the need of gastro-duodenoscopy of patients with anemia has been stressed [10]. However, unlike the probable link of *H. pylori* infection to the iron-deficiency anemia, the association between weight loss/obesity and the infection in childhood remains unclear [11]. Therefore, the aim of the present study was to assess a possible association between *H. pylori* status and the presence of anemia or weight loss, or both conditions in Bulgarian pediatric patients.

## MATERIAL AND METHODS

We carried out a retrospective cohort study on *H. pylori* positivity rates with 47 children with anemia 45 children with weight loss and 17 children and both conditions and compared the

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results with groups of children with the same number in each group and similar characteristics (Table 1).

Anemia was documented by laboratory tests such as hemoglobin (Hb) level <120 g/L (<12 g/dL), hematocrit (<40%), erythrocytes, Mean Corpuscular Volume, MCV and Mean Corpuscular Hemoglobin, MCH). Presence of weight loss (≥2 BMI-for-age percentiles) during the last year most often occurred during the last 3–5 months. Ten boys and seven girls had both anemia and weight loss.

Two gastric biopsy specimens were taken from each patient and were used for direct Gram staining with carbol fuchsine, a rapid urease test with 10% urea and culture on both non-selective and selective media as described in our prior publications [12, 13]. Positivity of either culture or two of the three diagnostic tests was considered as *H. pylori* positive status. Written informed consent was taken from the children' parents. The study was approved by the Ethics Committee of the Medical University of Sofia, Sofia, Bulgaria.

Statistical analysis. $\chi^2$ with Fisher's exact test was used to compare the groups. Odd ratios and relative risks were calculated as well (https://www.medcalc.org/calc/odds_ratio.php; https://www.medcalc.org/calc/relative_risk.php).

## RESULTS

We found that the children who had anemia were significantly more often *H. pylori* positive (76.6%, 36/47 children) compared with those without anemia (21.3%, 10/47, $P < 0.0001$), (Table 1). Children who had weight loss were much more frequently *H. pylori* positive (82.2%, 37/45) compared with the other patients (17.8%, 8/45, $P < 0.0001$).

All 17 children with both anemia and weight loss were *H. pylori* positive vs. only 17.7% (3/17, $P < 0.0001$) in the control group. The calculated relative risk of anemia was 3.6 (95% CI, 2.0–6.4), that of weight loss was 4.6 (95% CI, 2.4–8.8) and that of both conditions was 5.7 (95% CI, 2.0–15.8) in the *H. pylori* positive children compared with those in the control groups (Table 2).

## DISCUSSION

*H. pylori* gastritis is a common, although not the only reason for anemia refractory to treatment, mostly in adolescence [5]. The high incidence of *H. pylori* infection in patients with anemia suggests that the bacteria may be involved in the pathogenesis of the condition trough different mechanisms such as *H. pylori* competition with the host for available iron, *H. pylori* proteins for iron transport or storage, diminished iron absorption owing to hypochlorhydria and bleeding erosions or microerosions [4].

Decreased iron absorption has been linked to the increased pH of gastric juice and transient hypochlorhydria in the early phase of infection and atrophic changes in the stomach later in life [14]. Moreover, *H. pylori* virulence factors were related to the acquisition of iron by bacteria. CagA (cytotoxin-associated gene A) protein and VacA (vacuolating cytotoxin A) are conjointly involved in bacterial iron acquisition through the cholotransferin and in enhanced colonization of gastric cells, NapA (neutrophil-activating protein A) can increase bacterial Fe ion uptake and SabA (sialic acid–binding adhesin) can be of importance as well [2, 4, 15]. In our previous study, we detected a high frequency (>85%) of virulent (*vacA* s1 and *cagA* positive) *H. pylori* strains in symptomatic Bulgarian patients [16].

*Table 1. H. pylori* positivity in Bulgarian pediatric patients according to the presence or absence of anemia, weight loss or both conditions

| Children groups | Boys | Girls | Aged 1–8 years | Aged 8–18 years | Total | No. of *H. pylori* positive | % of *H. pylori* positive | *P* value |
|---|---|---|---|---|---|---|---|---|
| With anemia | 25 | 22 | 16 | 31 | 47 | 36 | 76.6 | 0.0001 |
| Without anemia | 19 | 28 | 12 | 35 | 47 | 10 | 21.3 | |
| With weight loss | 19 | 26 | 7 | 38 | 45 | 37 | 82.2 | 0.0001 |
| Without weight loss | 15 | 30 | 10 | 35 | 45 | 8 | 17.8 | |
| With both anemia and weight loss | 10 | 7 | 5 | 12 | 17 | 17 | 100.0 | 0.0001 |
| Without both anemia and weight loss | 8 | 9 | 4 | 13 | 17 | 3 | 17.7 | |

*Table 2.* Risk factors for anemia and weight loss among *H. pylori* positive children

| Outcome variable | Exposure (independent) variable | OR | 95% CI for OR | | Z statistic | *P* value | RR | 95% CI for RR | | Z statistic | *P* value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Lower | Upper | | | | Lower | Upper | | |
| Anemia | *H. pylori* | 12.1 | 4.6 | 32.0 | 5.0 | <0.0001 | 3.6 | 2.0 | 6.4 | 4.4 | <0.0001 |
| Weight loss | *H. pylori* | 21.4 | 7.3 | 63.0 | 5.6 | <0.0001 | 4.6 | 2.4 | 8.8 | 4.7 | <0.0001 |
| Both anemia and weight loss | *H. pylori* | 175.0 | 8.4 | 3,645 | 3.3 | 0.0009 | 5.7 | 2.0 | 15.8 | 3.3 | 0.0009 |

OR – odd ratio (https://www.medcalc.org/calc/odds_ratio.php); RR-relative risk (https://www.medcalc.org/calc/relative_risk.php).
95% CI – 95% confidence interval.

Unlike the anemia, weight loss association with *H. pylori* positivity remains unclear. The weight loss was found to be neither an indication for gastroduodenoscopy in the USA [17], nor as a risk factor for *H. pylori* infection in China [18].

An important result of our study was the significant association of *H. pylori* infection with weight loss. This result indirectly corresponds to that of Choi et al. [11], who found that, although there was no difference in *H. pylori* positivity rates between obese and non-obese Korean children, a significant gain of weight was observed two months after *H. pylori* eradication of the treated children. Some authors have suggested an association between *H. pylori* infection and gastric or serum concentrations of appetite-regulating peptides such as leptin, ghrelin and obestatin, however, more studies are required to evaluate the association [11, 19, 20]. Nevertheless, Talley et al. [21] have reported the presence of dyspepsia, involving reduced or lost appetite in 65% of the infected children vs. only 15% in those with *H. pylori* negative status. The results of our study show that both anemia and weight loss, alone and in combination with each other, are much more common in *H. pylori* positive children than in the noninfected pediatric patients.

## CONCLUSION

In conclusion, *H. pylori* infection was closely linked to iron-deficiency anemia and weight loss in Bulgarian children. The infected pediatric patients were at much higher risk of anemia and weight loss compared with *H. pylori* negative children. The results imply that in children with anemia and weight loss, the diagnosis of infection and the proper control of eradication success are of utmost importance.

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