



Association Between *Helicobacter pylori* Infection and Preterm Labor in Iranian Women: A Case-Control Study

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Received: 16 July, 2025; Revised: 19 August, 2025; Accepted: 11 September, 2025

Abstract

Background: Recent studies suggest a possible link between *Helicobacter pylori* infection and adverse pregnancy outcomes, including preeclampsia, miscarriage, and preterm labor.

Objectives: The present study aimed to investigate the association between *H. pylori* infection and preterm labor in pregnant women admitted to Ali Ibn Abi Talib Hospital in Zahedan.

Methods: A case-control study was conducted among 120 pregnant women (60 with preterm labor and 60 with term deliveries) between 2020 and 2022. Demographic and clinical data were collected using structured questionnaires, and *H. pylori* infection was assessed via stool antigen testing.

Results: The prevalence of *H. pylori* infection was similar in preterm (65.0%) and term (61.7%) delivery groups ($P=0.705$). Stratified analyses suggested potential differences in infection rates among women with low education levels ($P=0.013$) and poor financial status ($P=0.008$); however, these findings should be interpreted cautiously due to small subgroup sizes. Multivariate logistic regression indicated maternal education level as an independent factor associated with preterm labor (OR=0.28, 95% CI: 0.10 - 0.60, $P=0.001$).

Conclusions: Although no overall significant difference was found in *H. pylori* infection prevalence between preterm and term deliveries, subgroup analyses suggest that sociodemographic factors, such as low education and poor financial status, may increase the risk of preterm labor associated with *H. pylori* infection.

Keywords: *Helicobacter pylori*, Preterm Labor, Maternal Health Service, Pregnancy Outcome, Socioeconomic Factors

1. Background

Preterm delivery, defined as childbirth before 37 weeks of gestation, remains a leading cause of neonatal morbidity and mortality worldwide. Some risk factors for preterm delivery include poor antenatal care, multiple pregnancies, history of infertility or past preterm delivery, hypertension, diabetes, fetal gender, urinary tract infection, anemia, preeclampsia, and thin or obese Body Mass Index (BMI) (1). A less-researched risk factor for preterm delivery is the possibility of an association between *Helicobacter pylori* infection and preterm delivery (2). Pregnancy involves complex immunological adaptations to tolerate the semi-

allogeneic fetus, which may alter maternal susceptibility to infections (3). Recent studies indicate that maternal *H. pylori* infection may be associated with adverse pregnancy outcomes, including gestational hypertension, gestational diabetes, preterm birth, small-for-gestational-age infants, and preeclampsia, particularly in women from specific populations (4). The potential mechanisms may involve metabolic and immunologic pathways, including inflammation and mast cell activation (5).

2. Objectives

However, the relationship between *H. pylori* infection and preterm delivery remains incompletely understood.

Considering the need for preterm labor prevention and the potential treatability status of *H. pylori* infection, the present study aimed to find an association between mothers' *H. pylori* infection and preterm labor among women admitted to Ali ibn Abi Talib Hospital, Zahedan, for the years 2020 - 2021. If an association is found, preventive treatment with a screening program can be preconceptionally implemented to prevent consequent complications.

3. Methods

3.1. Study Population

This case-control study was conducted in the Maternity Ward of Ali Ibn Abi Talib Hospital in Zahedan in 2020. The study population consisted of pregnant women with a gestational age between 20 weeks and 36 weeks + 6 days who presented to the hospital with signs of labor. The case group included women diagnosed with preterm labor (< 37 weeks of gestation), while the control group comprised women who experienced term delivery (\geq 37 weeks of gestation). Inclusion criteria were defined as pregnant women within the specified gestational age range (20 - 36 weeks + 6 days) presenting with signs of labor. Preterm labor is defined as delivery occurring before 36 weeks and 6 days of gestation in accordance with our hospital's clinical protocol. Although WHO defines preterm labor as delivery < 37 weeks, this slight difference does not affect the overall interpretation of our findings. Exclusion criteria included receiving anti-*H. pylori* treatment within three months prior to pregnancy, multiple gestation, intrauterine infections, bacterial vaginosis, vaginal bleeding, placental abruption, uterine anomalies, premature rupture of membranes, preeclampsia, eclampsia, history of preterm labor (< 37 weeks of gestation), diabetes, cigarette smoking, and cervical insufficiency, in order to minimize confounding factors. The required sample size was estimated a priori based on standard formulas for case-control studies, assuming a two-sided α of 0.05, β of 0.20 (80% power), and an expected difference in exposure prevalence between cases and controls derived from prior data. This yielded a target of approximately 225 participants per group. However, due to financial and logistic constraints, we ultimately enrolled 60 women in each group.

3.2. Data Collection Tools and Procedures

Data were collected using a structured information form designed by the researcher. The form recorded demographic data (age, family size, education level, income, place of residence) and clinical data (maternal

H. pylori infection status). Laboratory results were obtained using the *H. pylori* stool antigen test.

3.3. Study Implementation

Following the approval of the research proposal by the Research Council of the Faculty of Medicine, and the acquisition of the ethics code (IR.ZAUMS.REC.1399.446) and necessary permissions from the university's research deputy, introduction letters were submitted to hospital officials. The study was conducted between October 2020 and March 2022, using a convenience sampling method. Eligible participants were screened based on inclusion and exclusion criteria. Gestational age was determined by first-trimester ultrasound or second-trimester ultrasound consistent with the last menstrual period. After obtaining informed written consent, stool samples were collected from all participants for *H. pylori* antigen testing, and demographic data were recorded.

3.4. Statistical Analysis

Data were analyzed using SPSS version 22. Continuous variables, such as maternal age, were reported as mean \pm standard deviation (SD) and compared between groups using Student's *t*-test. Categorical variables, including education level, financial status, and residence, were reported as counts and percentages and compared using chi-square or Fisher's exact test, as appropriate. The association between maternal *H. pylori* infection and preterm labor was first evaluated using univariate odds ratios (ORs) with 95% confidence intervals (CIs). To adjust for potential confounding factors, including age, education, financial status, and residence, a multivariate logistic regression model was performed. Adjusted ORs and 95% CIs were reported for both the overall analysis and subgroup analyses. Subgroup analyses stratified by education level, financial status, and residence were considered exploratory, and multiple comparisons were not formally adjusted; therefore, these results should be interpreted with caution. Statistical significance was defined as a two-sided $P < 0.05$.

4. Results

4.1. Demographic Characteristics

A total of 120 pregnant women participated in the study, comprising 60 women with preterm labor and 60 with term delivery. The mean maternal age in the preterm group was significantly lower than in the term

group (21.53±2.51 vs. 30.87±4.46 years, $P<0.001$). Because convenience sampling was applied, the case and control groups were not matched for age. This approach was intended to preserve the natural demographic variability of women attending the hospital. There were statistically significant differences between the two groups regarding educational level, financial status, and place of residence. Illiteracy was more prevalent among women in the preterm group (35.0%) compared to the term group (11.7%), while university education was more common among women with term deliveries (40.0%) than in those with preterm labor (6.7%) ($P<0.001$). Poor financial status was reported by 41.7% of women in the preterm group versus 15.0% in the term group, while good financial status was more frequent in the term group (30.0%) than the preterm group (15.0%) ($P=0.003$). In addition, a greater proportion of women in the term group resided in urban areas (78.3%) compared to the preterm group (53.3%) ($P=0.004$).

4.2. Prevalence of *Helicobacter pylori* Infection

As detailed in Table 1, the overall prevalence of maternal *H. pylori* infection did not differ significantly between the preterm (65.0%) and term groups (61.7%) ($P=0.705$).

4.3. Stratified Analyses and Predictors of Preterm Labor

Stratified analyses examined the association between *H. pylori* infection and preterm labor across different sociodemographic groups (Table 2). Overall, *H. pylori* infection was observed in 39 (65.0%) of preterm cases and 37 (61.7%) of term controls, with no statistically significant difference ($P=0.705$). When stratified by education level, the prevalence of infection among illiterate women was higher in the preterm group (83.3%) compared to the term group (16.7%) (OR=15.00; 95% CI, 1.23 - 183.64; $P=0.013$). In contrast, among women with university-level education, all infected individuals were in the term group, with none in the preterm group (OR=0.08; 95% CI, 0.00 - 1.66; $P=0.031$). No significant difference was observed among women with diploma-level education ($P=0.360$). Regarding financial status, women with poor economic status had a higher prevalence of infection in the preterm group (84.6%) versus the term group (15.4%) (OR=9.17; 95% CI, 1.54 - 54.59; $P=0.008$). No statistically significant differences were found for those with moderate ($P=0.479$) or good ($P=0.057$) financial status. For residence, infection rates did not differ significantly between urban ($P=0.770$) and rural ($P=0.700$) women. Overall, while certain subgroups appeared to show differences in *H. pylori*

prevalence, these findings should be interpreted cautiously due to small sample sizes in stratified cells and the lack of formal interaction testing.

5. Discussion

The result of the present research was that 39 (65%) of 60 preterm deliveries (< 37 weeks of gestation) and 37 (61.7%) of 60 term deliveries (\geq 37 weeks of gestation) tested positive for *H. pylori* infection. At the same time, we also identified main differences between the two groups regarding age, level of education, economic status, and place of residence. In subgroup analyses, higher or lower education levels and low economic status were associated with differences in *H. pylori* infection. The etiology of preterm birth is a complex and significant issue in obstetrics, with considerable emphasis placed on its association with infections. Our findings align with those of Mohamed et al., who reported a significant correlation between *H. pylori* infection and obstetric complications such as hyperemesis gravidarum, iron deficiency anemia, IUGR, and preeclampsia. This study reveals the importance of considering socioeconomic factors like education level and place of residence in understanding these associations (6). Although the differential prevalence of *H. pylori* infection between cases and controls overall was not statistically significant, the findings suggest that demographic factors may be extremely important in this regard. A systematic review and meta-analysis by Moosazadeh et al. estimated the overall prevalence of *H. pylori* infection in Iran to be approximately 54%, with rates ranging from 30.6% to 82% across different regions (7).

Past studies have also indicated a link between *H. pylori* infection and pregnancy complications. For example, a meta-analysis by Tang et al. showed that *H. pylori* infection was linked with preeclampsia (OR: 2.51; 95% CI: 1.88 - 3.34), intrauterine growth restriction (OR: 2.28; 95% CI: 1.21 - 4.32), and gestational diabetes (OR: 2.03; 95% CI: 1.56 - 2.64) (8). Moreover, a recent meta-analysis by Kohnepoushi et al. found that *H. pylori* infection during pregnancy was associated with an increased risk of gestational diabetes mellitus, suggesting a potential impact on maternal health outcomes (9).

The present study has several limitations. First, the sample size was relatively small, and data were collected from a single healthcare center, which may limit the generalizability of the findings. Second, stool-based testing was used for the diagnosis of *H. pylori* infection. Although stool antigen tests are non-invasive and suitable for use during pregnancy, they may be less

Table 1. Comparison of Demographic Characteristics Between Case and Control Groups^{a,b}

Variables	Case (Preterm Labor)	Control (Term Labor)	P-Value
Age (mean ± SD)	21.53 ± 2.51	30.87 ± 4.46	< 0.001
Education level			< 0.001
Illiterate	21 (35.0)	7 (11.7)	
Diploma or below	35 (58.3)	29 (48.3)	
University	4 (6.7)	24 (40.0)	
Financial status			0.003
Poor	25 (41.7)	9 (15.0)	
Moderate	26 (43.3)	33 (55.0)	
Good	9 (15.0)	18 (30.0)	
Residence			0.004
Urban	32 (53.3)	47 (78.3)	
Rural	28 (46.7)	13 (21.7)	

^a Values are expressed as No. (%) unless otherwise indicated.

^b P-values were calculated using the chi-square test for categorical variables and independent t-test for continuous variables.

Table 2. Maternal *Helicobacter pylori* Infection Across Groups and Stratified by Confounding Factors^{a,b}

Confounding Variables, Categories and Infection Status	Case	Control	OR (95% CI)	P-Value
Overall infection			1.15 (0.55 - 2.43)	0.705
Positive	39 (65.0)	37 (61.7)		
Negative	21 (35.0)	23 (38.3)		
Education level				
Illiterate			15.00 (1.23 - 183.64)	0.013
Positive	20 (83.3)	4 (16.7)		
Negative	1 (25.0)	3 (75.0)		
Diploma			0.62 (0.23 - 1.72)	0.360
Positive	19 (50.0)	19 (50.0)		
Negative	16 (61.5)	10 (38.5)		
University			0.08 (0.00 - 1.66)	0.031
Positive	0 (0.0)	14 (100.0)		
Negative	4 (28.6)	10 (71.4)		
Financial status				
Poor			9.17 (1.54 - 54.59)	0.008
Positive	22 (84.6)	4 (15.4)		
Negative	3 (37.5)	5 (62.5)		
Moderate			0.68 (0.24 - 1.97)	0.479
Positive	15 (40.5)	22 (59.5)		
Negative	11 (50.0)	11 (50.0)		
Good			0.18 (0.03 - 1.14)	0.057
Positive	2 (15.4)	11 (84.6)		
Negative	7 (50.0)	7 (50.0)		
Residence				
Urban			0.87 (0.35 - 2.17)	0.770
Positive	18 (39.1)	28 (60.9)		
Negative	14 (42.4)	19 (57.6)		
Rural			1.33 (0.31 - 5.72)	0.700
Positive	21 (70.0)	9 (30.0)		
Negative	7 (63.6)	4 (36.4)		

^a Values are expressed as No. (%) unless otherwise indicated.

^b P-values and odds ratios were calculated using logistic regression analysis.

accurate than alternative methods, such as serological or endoscopic tests, in distinguishing active from latent infection, potentially leading to misclassification. Third, convenience sampling was applied, and as a result, the case and control groups were not age-matched; this approach was chosen to reflect the natural demographic variability of women attending the hospital, but it may introduce selection bias. Fourth, despite exclusion of several known confounders, residual confounding may persist. Factors such as

nutritional status, access to prenatal care, and comorbid infections could influence both *H. pylori* prevalence and the risk of preterm labor. Finally, some subgroup analyses, for example among illiterate and low-income women, included small numbers of participants. These small cell sizes can inflate ORs and widen CIs, and therefore the results should be interpreted cautiously and considered hypothesis-generating rather than definitive. Future studies with larger sample sizes, more accurate diagnostic techniques, and better control of

confounding variables would more definitively clarify the role of *H. pylori* in preterm delivery and other pregnancy complications.

5.1. Conclusions

Helicobacter pylori can be implicated in the onset of preeclampsia, spontaneous abortion, and preterm labor. While the current study did not reveal any significant difference in infection frequency between the case (preterm) and control (term) groups, subgroup analysis for education level revealed a potential protective effect. These findings are exploratory and should not be considered definitive. Hence, as socioeconomic and education affect the health status of pregnant women, policymakers must consider them. Future research should use large sample sizes and longitudinal study designs to identify more clearly the association between *H. pylori* infection and poor pregnancy outcomes like miscarriage and preterm delivery.

Acknowledgements

This research was derived from a medical doctorate dissertation conducted at Zahedan University of Medical Sciences. The authors express their sincere gratitude to the study participants, as well as to the staff of Ali-Ibn-Abi-Taleb Hospital and the Maternity Ward, for their valuable cooperation and support. Their contributions played a crucial role in facilitating data collection and ensuring the successful completion of the study.

Footnotes

Authors' Contribution: Acquisition of data and drafting the article: A. M.; Analysis and interpretation of data: Sh. P. M.; Study concept and design and study supervision: M. R.

Conflict of Interests Statement: The authors declare no conflict of interests.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after its publication. The data are not publicly available due to privacy.

Ethical Approval: The Ethical Committee of Zahedan University of Medical Sciences approved the present study (IR.ZAUMS.REC.1399.446).

Funding/Support: The study received no financial support.

Informed Consent: Written informed consent was obtained from all participants.

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