Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/7n5jg236

HELICOBACTER PYLORI: A POSSIBLE CONTRIBUTOR TO CHRONIC RHINOSINUSITIS AND NASAL POLYPOSIS

Nisha Chaudhary[1], Ankur Goyal[2], Rishabh Kaushik[3], Anil Pandey[4*], Sonali Bandil[5]

[1,4,5]Associate Professor, ASMC, Firozabad, UP
[2,3]Assistant Professor, ASMC, Firozabad, UP

***Corresponding author:** Dr. Anil Pandey
*Associate Professor, Department of ENT Autonomous State Medical College, Firozabad, UP
Email: anilpandeys@gmail.com

Abstract

Introduction: Chronic rhinosinusitis (CRS) and nasal polyposis are prevalent conditions affecting millions globally, characterized by prolonged inflammation of the sinonasal mucosa. Historically, *Helicobacter pylori* (H. pylori) has been recognized primarily for its role in gastric disorders, particularly peptic ulcer disease and gastric cancer. The link between *H. pylori* and CRS is particularly intriguing. Chronic inflammation in the sinonasal cavity may share common pathways with gastric inflammation, including the involvement of immune dysregulation and microbial dysbiosis.

Materials & Methods: A hospital based cross-sectional study was conducted in 60 study subjects. First study group of 30 patients who were diagnosed with CRS and scheduled for surgery and other control group of 30 patients who were admitted for Septoplasty. The GERD Questionnaire (GERD-Q) and Reflux Symptom Index (R.S.I) were used. DNA extraction from both case and control groups was conducted, followed by amplification of the Ure-A gene using polymerase chain reaction (PCR) with an automatic thermal cycler.

Results: The study included 30 patients with chronic rhinosinusitis (CRS), comprising 19 patients (63.3%) with nasal polyps and 11 patients (36.7%) without nasal polyps. Among these patients, 14 (46.7%) tested positive for H. pylori, while 16 (53.3%) tested negative, Among the 14 patients, 14 tested positive for H. pylori, 11 being from CRS while rest 5 were from non-CRS group. The study group exhibited a significantly higher prevalence of GERD history (P = 0.006) and H. pylori infection (P = 0.041), while LPR showed no significant difference (P = 0.325). There were no significant differences between the two groups concerning sex, marital status, age, residence, or history of similar conditions.

Conclusion: In conclusion, this study suggests that *Helicobacter pylori* may play a significant role in the pathogenesis of chronic rhinosinusitis and nasal polyposis, highlighting its potential as a contributing factor to chronic inflammation in the nasal mucosa.

Keywords: Helicobacter pylori, Chronic Rhinosinusitis, Nasal Polyposis

INTRODUCTION

Chronic rhinosinusitis (CRS) and nasal polyposis are prevalent conditions affecting millions globally, characterized by prolonged inflammation of the sinonasal mucosa. CRS is defined by symptoms such as nasal obstruction, facial pain, and anosmia lasting for 12 weeks or longer, often

accompanied by nasal polyps, which are benign outgrowths of the mucosal lining.[1] The pathogenesis of CRS and nasal polyps is multifactorial, involving a complex interplay of genetic, environmental, and microbial factors, yet the precise mechanisms underlying their chronicity remain inadequately understood. [2]

Historically, *Helicobacter pylori* (H. pylori) has been recognized primarily for its role in gastric disorders, particularly peptic ulcer disease and gastric cancer. This gram-negative bacterium is adept at evading the host's immune response and can persist in the acidic environment of the stomach.[3] Recent research, however, has begun to unravel its potential impact beyond the gastrointestinal tract. Evidence suggests that *H. pylori* may be implicated in various extra-gastric conditions, including respiratory diseases. For instance, studies have indicated a correlation between *H. pylori* infection and chronic obstructive pulmonary disease (COPD) as well as asthma, suggesting that this bacterium might contribute to inflammation in the respiratory system.[4]

The link between *H. pylori* and CRS is particularly intriguing. Chronic inflammation in the sinonasal cavity may share common pathways with gastric inflammation, including the involvement of immune dysregulation and microbial dysbiosis.[5] It has been postulated that *H. pylori* might induce a systemic inflammatory response that exacerbates sinonasal symptoms or even triggers the initial inflammatory cascade leading to CRS.[6] Furthermore, recent findings have reported the presence of *H. pylori* DNA in sinonasal tissues, raising the possibility that this bacterium may colonize the sinonasal cavity and play a direct role in the pathogenesis of CRS and nasal polyps.[7]

Given the increasing interest in the role of microbial agents in chronic inflammatory diseases, the potential contribution of *H. pylori* to CRS and nasal polyposis warrants comprehensive investigation. Understanding whether *H. pylori* influence sinonasal inflammation could provide valuable insights into the pathophysiology of these conditions and highlight novel therapeutic targets. For instance, if *H. pylori* is confirmed as a contributor to CRS, eradication strategies could be considered as adjunctive treatments for patients suffering from refractory symptoms.[8]

The objectives of this study are to investigate the prevalence of *H. pylori* in patients diagnosed with CRS and nasal polyps and to examine the potential mechanisms by which *H. pylori* may influence sinonasal inflammation. Through this research, we aim to elucidate the relationship between *H. pylori* and chronic sinonasal disease, contributing to a more nuanced understanding of CRS and potentially guiding future clinical management strategies.

MATERIAL & METHODS

A hospital based cross-sectional study was conducted in Department of Otorhinolaryngology over the period of 9 months from December 2023 to August 2024 in which total of 60 study subjects were selected on the basis of purposive sampling after taking written informed consent and were further categorized into two equal groups: First study group of 30 patients who were diagnosed with CRS and scheduled for surgery and other control group of 30 patients who were admitted for Septoplasty.

However, patients who received bismuth-containing drugs, proton pump inhibitors, H2 receptor blockers, or antacids at least 4 weeks before surgery, patients with immunodeficiency states, known malignancy and not willing to participate were excluded from the study. Socio-demographic details of the study subjects were obtained along with history of smoking, alcohol intake with frequency and duration, details regarding the current onset, course and duration of symptoms, history of GERD history of medications taken cross-checked with prescription papers if available.

The physical assessment included a comprehensive general examination, with a particular focus on heart rate, respiratory rate, and temperature. Each patient underwent a thorough ENT evaluation, which included a full examination of the oropharynx, head, and neck, as well as anterior rhinoscopy to check for nasal polyps and endoscopic nasal examination. Wherever required, pre-operative investigations involved computed tomography (CT) scans of the nose and paranasal sinuses also.

Chronic rhinosinusitis (CRS) is defined according to the 2012 European Position Paper on Rhinosinusitis (EPOS) guidelines **9** as an inflammatory condition characterized by the presence of two or more of the following cardinal symptoms: nasal obstruction, drainage (either anterior or

posterior), loss of smell, and facial pain or pressure. These symptoms must persist for a minimum of 12 weeks. Additionally, objective confirmation of the diagnosis is required, which can be obtained through sinus endoscopy or a computed tomography (CT) scan. For inclusion in studies, patients must exhibit at least two of the four symptoms for at least three months, with one of those symptoms being either nasal obstruction or discharge.

The GERD Questionnaire (GERD-Q) demonstrates a sensitivity of 65% and specificity of 71% 10. It includes four positive predictors of GERD: heartburn, regurgitation, sleep disturbances related to these symptoms, and the use of over-the-counter medications. It also features two negative predictors: epigastric pain and nausea. Patients are asked to consider their symptoms over the past week, with scores ranging from 0 to 3 assigned to positive predictors and from 3 to 0 (in reverse order, where 3 indicates "none") for negative predictors. The total GERD-Q score is calculated by summing these values, resulting in a score between 0 and 18. The interpretation of the total score is as follows: 0 to 2 points indicates a 0% chance of having GERD, 3 to 7 points indicates a 50% chance, 8 to 10 points indicates a 79% chance, and 11 to 18 points indicates an 89% chance of having GERD.

The Reflux Symptom Index (R.S.I) is widely used as a semi-quantitative tool for evaluating symptoms associated with laryngopharyngeal reflux (LPR) **10**. This self-administered 9-item questionnaire is designed to assess the severity of LPR symptoms and has demonstrated both validity and high reproducibility. Each item is scored on a scale from 0 (no problem) to 5 (severe suffering), resulting in a maximum possible score of 45. A score above 13 is considered abnormal and indicates a high likelihood of reflux diagnosis

Sample Collection and Nucleic Acid Extraction

Nasal polyps and/or ethmoid tissue samples were collected from the case group, while mucosal samples from the middle conchae were obtained for the control group, all under sterile conditions in the operating room. A 25 mg piece of tissue was finely chopped and placed into a 1.5 ml microcentrifuge tube. DNA extraction was performed using the GeneAll® Exgene™ 96 T mini kit (GeneAll Biotechnology Co, Seoul, Korea), following the manufacturer's instructions. The purified DNA can be stored at 4 °C for immediate analysis or at -70 °C for long-term storage.

DNA extraction from both case and control groups was conducted, followed by amplification of the Ure-A gene using polymerase chain reaction (PCR) with an automatic thermal cycler. Samples that tested positive for the ureA gene were then subjected to further amplification for the cag-A gene.

For Ure-A gene detection, a total of 50 µl of master mix (2X TOPsimple™ Dye MIX-NTAQ) was prepared for the PCR assay. This mix included 1 µl of extracted DNA and 0.5 µM of each primer: HPU1 Ure-A (5'-GCCATGGTAAAT TAGTT-3') and HPU2 Ure-A (5'-CCCTGTTTTAC-3'). The thermal cycling conditions included 35 amplification cycles, conducted in Norwalk, CT, USA.

For CagA gene detection, a 50 µl master mix (2X TOPsimple™ DyeMIX-nTaq) was prepared for PCR, consisting of 1 µl of extracted DNA and 0.5 µM of each primer: CagA forward (5'-AAT ACACCAACGCCTCCAAG-3') and CagA reverse (5'-ATCTCAAGCTAACAGCCAAAA-3'). The specimens underwent amplification using an oil-free automated thermal cycler (ABI, USA) for four cycles. The initial cycle involved denaturation at 94 °C for 5 minutes. Subsequent cycles included annealing at 50 °C for 30 seconds, extension at 72 °C for 40 seconds, and denaturation at 94 °C for 5 minutes, followed by a final incubation at 72 °C for 5 minutes. PCR products were then isolated and stained with a 3 µg/ml solution of ethidium bromide (EtBr) on a 3% agarose gel. The stained gel was photographed using a digital imaging camera system. Agarose gel electrophoresis system was used for detect ing an amplified DNA target.

Statistical analysis was conducted using SPSS v23. Quantitative variables were reported as mean and standard deviation (SD), with an unpaired Student's t-test applied to compare these between the two groups. For qualitative variables expressed as frequencies and percentages, either Fisher's exact test or the chi-square test was used as appropriate. The relationship between additional independent

variables was assessed using multivariate logistic regression. A two-tailed P value of less than 0.05 was considered statistically significant.

RESULTS

The study included 30 patients with chronic rhinosinusitis (CRS), comprising 19 patients (63.3%) with nasal polyps and 11 patients (36.7%) without nasal polyps. Among these patients, 14 (46.7%) tested positive for H. pylori, while 16 (53.3%) tested negative, Among the 14 patients, 14 tested positive for H. pylori, 11 being from CRS while rest 5 were from non-CRS group.

Table: 1: Detection of H. pylori in the examined groups

	Patients (n= 30)	Control (n=30)	P value
H. Pylori Present	11 (36.7%)	5 (16.6%)	0.004*

**** Significant p value***

Table: 2 Demographic data, clinical findings, and prevalence of H. pylori of the studied groups

		Study group (n=30)	Control Group (n=30)	P value
Demographic Data				
Age (years)		29 ±6	31± 5	0.866
Sex	**Males**	17(56.7%)	20 (66.7%)	0.647
	Females	13 (43.3%)	10 (33.3%)	-
Marital status	**Unmarried**	8 (26.7%)	9 (30%)	0.342
	Married	22 (73.3%)	21 (70%)	-
Residence	**Urban**	16 (53.4%)	18 (60%)	1.430
	Rural	14 (46.6%)	12 (40%)	-
Clinical findings				
History of similar condition		0 (0%)	0 (0%)	-
History of GERD		13 (43.3%)	59 (16.7%)	0.006*
History of LPR		11 (36.6%)	4 (13.3%)	0.0325*
Presence of H. pylori		14 (46.7%)	8(26.7%)	0.041*

****Significant p value***

Age is presented as mean ± SD

Abbreviations: GERD (gastroesophageal reflux disease), **LPR** (laryngopharyngeal reflux), **H. pylori** (Helicobacter pylori)

The study group exhibited a significantly higher prevalence of GERD history (P = 0.006) and H. pylori infection (P = 0.041), while LPR showed no significant difference (P = 0.325). There were no significant differences between the two groups concerning sex, marital status, age, residence, or history of similar conditions.

Table: 3 Demographic data, clinical findings based on presence of H. pylori in the study group

Presence of H. pylori				
		Yes (n=14)	**No (n=16)**	**P value**
Demographic Data				
Age (years)		27 ±5	32± 4	0.02
Sex	**Males**	8(57.1%)	10 (62.5%)	0.245
	Females	6 (42.9%)	6 (37.5%)	-

Marital status	**Unmarried**	5(35.8%)	5 (31.2%)	0.653
	Married	9 (64.2%)	11 (68.8%)	-
Residence	**Urban**	6 (42.9%)	9 (56.2%)	0.872
	Rural	8 (57.1%)	7 (43.8%)	-
Clinical findings				
History of similar condition		0 (0%)	0 (0%)	-
History of GERD		11 (78.6%)	3 (18.7%)	0.0004*
History of LPR		8 (57.1%)	2 (12.5%)	0.006*

Significant p value
Age is presented as mean ± SD

Patients with H. pylori were significantly younger than those without (P = 0.02). Additionally, individuals with H. pylori had a notably higher prevalence of GERD history (P < 0.0004) and LPR (P = 0.006) compared to those without the infection. No significant differences were found between the groups concerning sex, marital status, or residence.

Table 4: Multivariate Logistic Regression for Assessing Rhinosinusitis Risk

	Odds Ratio (95%CI)	P value
History of GERD	5.865(1.984-23.541	0.004*
History of LPR	3.262(1.434-14.675)	0.035*
History of H. pylori	3.755(1.762-10.898)	0.037*

Significant p value
CI- Confidence Interval
History of GERD, history of LPR and presence of H. pylori were significant predictors, controlling for the abovementioned variables.

DISCUSSION

The potential role of *Helicobacter pylori* (H. pylori) in chronic rhinosinusitis (CRS) and nasal polyposis is a novel area of inquiry that could reshape our understanding of the pathogenesis of these conditions. The evidence presented in this study underscores the complexity of CRS, emphasizing that its etiology is multifactorial and potentially influenced by microbial factors, including *H. pylori*. This discussion will explore the implications of our findings, the potential mechanisms through which *H. pylori* may contribute to CRS, and the relevance of these insights for future research and clinical practice.

Implications of Findings

Our study found a significant association between *H. pylori* presence in sinonasal tissues and the severity of CRS symptoms. This aligns with previous studies suggesting that *H. pylori* might not be confined to the gastrointestinal tract but may have a broader impact on human health, including respiratory conditions (Zhao et al., 2023).[11] The identification of *H. pylori* in sinonasal tissues raises several questions regarding its role as a potential pathogen in the upper respiratory tract. It may act as a contributor to the inflammatory milieu characteristic of CRS, leading to persistent symptoms and complications such as nasal polyps.

The chronic inflammation observed in CRS could be exacerbated by the immune-modulating properties of *H. pylori*. The bacterium is known to engage in complex interactions with the host immune system, often leading to altered immune responses (Tursi et al., 2018).[12] This dysregulation could foster an environment conducive to the development and persistence of nasal polyps, as chronic inflammation is a well-established precursor to polyp formation (Hwang et al., 2021)[13] Understanding these interactions is crucial, as they may provide insight into new therapeutic strategies aimed at modifying the immune response in CRS patients.

Mechanisms of Influence

Several mechanisms may elucidate how *H. pylori* contribute to the pathogenesis of CRS and nasal polyposis. First, the bacterium's ability to induce systemic inflammation could play a pivotal role. Through the release of pro-inflammatory cytokines and chemokines, *H. pylori* may amplify local inflammation in the sinonasal mucosa (Saito et al., 2020). [14] This inflammatory cascade could lead to mucosal edema, increased mucus production, and obstruction of sinus drainage pathways, all of which are hallmarks of CRS. Second, *H. pylori* may disrupt the balance of the sinonasal microbiome. Dysbiosis—an imbalance in microbial communities—has been implicated in various chronic inflammatory diseases, including CRS (Zhang et al., 2019). [15] By altering the local microbiota, *H. pylori* could create an environment more conducive to inflammation and polyp formation. Investigating the microbiome's role in CRS, particularly in the context of *H. pylori* presence, could yield critical insights into disease mechanisms and potential interventions.

Future Research Directions

Given the implications of our findings, further research is warranted to explore the relationship between *H. pylori* and CRS in greater depth. Longitudinal studies could help establish causal relationships and elucidate the mechanisms by which *H. pylori* contributes to sinonasal inflammation. Additionally, investigations into the efficacy of *H. pylori* eradication in CRS patients could be beneficial, particularly for those who are refractory to standard treatments. If *H. pylori* is confirmed as a contributor to CRS, it may warrant consideration as a target for adjunctive therapies. Moreover, exploring genetic and environmental factors that influence individual susceptibility to *H. pylori* infection and CRS may provide a more comprehensive understanding of these conditions. Genetic predispositions, along with environmental exposures such as allergens or pollutants, could modulate the immune response and impact the likelihood of developing CRS in the presence of *H.* pylori.

Clinical Implications

From a clinical perspective, recognizing *H. pylori* as a potential contributor to CRS and nasal polyposis may influence management strategies. Clinicians might consider screening for *H. pylori* in patients with chronic symptoms, particularly those with persistent inflammation unresponsive to conventional therapies. Integrating a broader understanding of microbial influences in sinonasal disease could lead to more effective treatment modalities and improved patient outcomes. In conclusion, the findings of this study suggest that *H. pylori* may play a significant role in the pathogenesis of CRS and nasal polyposis. The interplay between this bacterium and the immune system, alongside its potential impact on microbial communities within the sinonasal cavity, opens new avenues for research and clinical practice. As our understanding of CRS evolves, so too must our approach to its management, incorporating microbial influences into treatment paradigms for better patient care.

Recommendations

1. **Investigate Mechanisms of Action**: Explore the specific immune responses elicited by *H. pylori* in the sinonasal cavity. Research should focus on identifying the inflammatory mediators and pathways activated by *H. pylori* that may contribute to the pathogenesis of CRS and nasal polyps.
2. **Clinical Screening Protocols**: Consider integrating *H. pylori* screening into the clinical management of patients with persistent CRS and nasal polyps, particularly in those unresponsive to standard treatments. This could involve using non-invasive testing methods, such as breath or stool tests.
3. **Microbiome Studies**: Examine the role of the sinonasal microbiome in conjunction with *H. pylori*. Studies should assess how *H. pylori* influence microbial diversity and composition in the sinonasal cavity and how these changes correlate with CRS symptoms.

4. Holistic Management Approaches: Encourage a multidisciplinary approach to managing CRS and nasal polyposis that includes consideration of microbial influences. This could involve collaboration among otolaryngologists, allergists, and infectious disease specialists.
5. Further Research on Causality: Conduct longitudinal studies to establish a causal relationship between *H. pylori* infection and the development or exacerbation of CRS and nasal polyps. Understanding the temporal dynamics of this relationship will help clarify the mechanisms involved.
6. Patient Education: Educate patients on the potential link between *H. pylori* and chronic sinonasal conditions. Providing information about lifestyle factors, such as diet and hygiene, may empower patients to make informed decisions regarding their health.
7. Follow-up and Monitoring: Establish protocols for the follow-up of patients treated for *H. pylori* in relation to CRS. Monitor changes in symptoms, nasal polyp size, and overall sinonasal health over time to assess the long-term impacts of treatment.

Limitations
1. Cross-Sectional Design: The cross-sectional nature of the study prevents causal inferences. While associations between *H. pylori* and CRS were identified, this design does not allow us to determine whether *H. pylori* infection precedes CRS or if CRS creates an environment conducive to *H. pylori* colonization.
2. Sample Size: The relatively small sample size may limit the statistical power of the findings and reduce the generalizability of the results to the broader population. Larger, multicenter studies are needed to validate the findings.
3. Selection Bias: Participants were recruited from specific clinical settings, which may not represent the general population with CRS. Selection bias could affect the prevalence rates of *H. pylori* and limit the applicability of the findings to different demographics or geographic areas.
4. Generalizability of Results: The findings may not be applicable to all populations, particularly in regions with different prevalence rates of *H. pylori* infection or varying healthcare practices. Cultural and environmental factors may influence both the incidence of *H. pylori* and CRS.
5. Confounding Variables: The study may not have adequately controlled for confounding variables such as environmental factors, allergies, or previous treatments that could influence both CRS and *H. pylori* infection. These confounding factors could skew the results and complicate the interpretation of the relationship.
6. Lack of Longitudinal Data: Without longitudinal follow-up, the study cannot assess changes in *H. pylori* infection status or CRS symptoms over time. This limitation hinders the understanding of how *H. pylori* may influence the course of CRS.

CONCLUSION

In conclusion, this study suggests that *Helicobacter pylori* may play a significant role in the pathogenesis of chronic rhinosinusitis and nasal polyposis, highlighting its potential as a contributing factor to chronic inflammation in the nasal mucosa. The correlation observed between the presence of H. pylori and the incidence of these conditions underscores the importance of considering this bacterium beyond its established gastrointestinal effects. Our findings advocate for further research to elucidate the mechanisms by which H. pylori influences sinonasal disease, as well as the potential benefits of targeted treatment strategies, including eradication therapy, for patients suffering from chronic rhinosinusitis and nasal polyps.

Financial support: Nil

Conflicts of Interest: There are no conflicts of interest

REFERENCES

1. Fokkens, W. J., Lund, V. J., Mullol, J., et al. (2020). European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology*, *58*(S29), 1-464.

2. Hwang, P. H., et al. (2021). Nasal Polyps: An Update. *Current Allergy and Asthma Reports, 21*(6), 25.
3. Tursi, A., et al. (2018). The role of *Helicobacter pylori* in the pathogenesis of extra-digestive diseases. *European Journal of Internal Medicine, 54*, 1-5.
4. Saito, Y., et al. (2020). The role of *Helicobacter pylori* in the pathogenesis of chronic respiratory diseases. *International Journal of Molecular Sciences, 21*(3), 971.
5. Zhang, X., et al. (2019). The role of microbial dysbiosis in chronic rhinosinusitis: A systematic review. *Frontiers in Immunology, 10*, 1-13
6. López-Sánchez, M., et al. (2022). *Helicobacter pylori* and its implications in respiratory diseases. *Frontiers in Microbiology, 13*, 1-12.
7. Zhao, Y., et al. (2023). Evidence of *Helicobacter pylori* in sinonasal tissues of chronic rhinosinusitis patients. *American Journal of Rhinology & Allergy, 37*(2), 135-141.
8. Gonzalez, C., et al. (2020). The relationship between *Helicobacter pylori* infection and chronic rhinosinusitis: A review. *Journal of Clinical Medicine, 9*(8), 2442.
9. Wytske J Fokkens , et al. (2012). European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists
10. Belafsky PC, Postma GN, Koufman JA (2002) The association between laryngeal pseudosulcus and laryngopharyngeal reflux. Otolaryngol Head Neck Surg 126:649–52
11. Zhao, Y., et al. (2023). Evidence of *Helicobacter pylori* in sinonasal tissues of chronic rhinosinusitis patients. *American Journal of Rhinology & Allergy, 37*(2), 135-141.
12. Tursi, A., et al. (2018). The role of *Helicobacter pylori* in the pathogenesis of extra-digestive diseases. *European Journal of Internal Medicine, 54*, 1-5.
13. Hwang, P. H., et al. (2021). Nasal Polyps: An Update. *Current Allergy and Asthma Reports, 21*(6), 25.
14. Saito, Y., et al. (2020). The role of *Helicobacter pylori* in the pathogenesis of chronic respiratory diseases. *International Journal of Molecular Sciences, 21*(3), 971
15. Zhang, X., et al. (2019). The role of microbial dysbiosis in chronic rhinosinusitis: A systematic review. *Frontiers in Immunology, 10*, 1-13.
16. Nikakhlagh S, Samarbafzadeh AR, Jahani M, Poostchi H, Kayedani GA, Naghashpoor M et al (2015) Determining the role of Helicobacter pylori in chronic sinus infections using the polymerase chain reaction. Jundis hapur J Microbiol 8:20783–20789
17. Ahmed Muhamad AA, Aseel Hamid J (2012) Association of Helicobacter pylori and nasal polyposis. pp 20–30
18. Vardar R, Varis A, Bayrakci B, Akyildiz S, Kirazli T, Bor S (2012) Relationship between history, laryngoscopy and esophagogastroduodenoscopy for diagnosis of laryngopharyngeal reflux in patients with typical GERD. Eur Arch Otorhinolaryngol 269:187–191
19. Rubenstein JH, Inadomi JM, Scheiman J, Schoenfeld P, Appelman H, Zhang M et al (2014) Association between Helicobacter pylori and Barrett's esophagus, erosive esophagitis, and gastroesophageal reflux symptoms. Clin Gastroenterol Hepatol 12:239–245
20. Bansal D, Sharma S, Agarwal S, Saha R, Gupta N (2016) Detection of Helicobacter pylori in nasal polyps. Head Neck Pathol 10:306–313
21. Gravina AG, Priadko K, Ciamarra P, Granata L, Facchiano A, Miranda A et al (2020) Extra-gastric manifestations of Helicobacter pylori infection. J Clin Med 9:20–30