

Review Article

**A REVIEW STUDY ON THE PREVALENCE OF HELICOBACTER PYLORI INFECTION IN LARYNGEAL CARCINOMA**

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**Abstract**

**Introduction:** Malignant tumors of the larynx make up 2 to 5 percent of cancers each year. Infections can cause about 15% of the world's cancers with great environmental variations. One of the cases that have been investigated for its etiologic role in laryngeal carcinoma is Helicobacter pylori infection.

**Object:** The aim of this review study is to investigate the available paper that evaluate association between Helicobacter pylori infection and laryngeal carcinoma.

**Material and method:** Extensive research was conducted on some medical and microbiology database of life sciences such as Pub Med, EMBASE, MEDLINE, LILACS database, global independent network of Cochrane. By referencing these databases, a comprehensive literature review was carried out through combining numerous recent studies in terms of laryngeal carcinoma, Helicobacter pylori infection, epidemiology and management in accordance with many related articles published from 2000 to 2020 which could cover this area of recommendations.

**Conclusions:** The Helicobacter pylori infection can affect the larynx cancer. Some studies investigated this relation. In this study we evaluated these studies. Different effect of Helicobacter pylori on larynx cancer was detected in these paper, some study showed strong effect of this infection in larynx cancer while another study reported any relation. So further studies needed to evaluate this relation although the Helicobacter pylori infection is main reason of many disease and its prevention and treatment is necessary.

**Keywords:** Helicobacter pylori, Laryngeal carcinoma, Infection, Cancer.

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**INTRODUCTION**

Malignant tumors of the larynx make up 2 to 5 percent of cancers each year[1]. Benign laryngeal tumors are not common except squamous papilloma cancer. Squamous cell carcinoma accounts for 98-95% of all laryngeal malignancies. Smoking and high alcohol consumption has a great impact on laryngeal cancer[2]. Exposure to organic amines and polycyclic carbohydrates empirically causes laryngeal tumor. Tobacco may be a predisposing factor, but it is not the main cause of disease. Some studies have shown that herpes papillomatosis can be a factor in this type of cancer. Some viruses may alter cellular immunity and cause malignancy. Chronic infections, radiation and air pollution are other factors[3, 4].

Infections can cause about 15% of the world's cancers with great environmental variations[5].prevalence of cancer due to infection are happen higher in less developed countries[6-8]. The International Agency for Research on Cancer (IARC) classified group 1 of the 11 infectious pathogens as a carcinogen agent[9]. And the four most important of them are high-risk human papillomavirus (HPV), Helicobacter pylori, hepatitis C virus (HCV) and hepatitis B virus (HBV) and they cause 90% of infection-dependent cancers[10].

One of the cases that have been investigated for its etiologic role in laryngeal carcinoma is Helicobacter pylori infection. Helicobacter pylorus is a type of gram-negative bacterium and one of the most common human infections worldwide that cause

chronic gastritis, gastric ulcer, duodenal ulcer, and gastric cancer [11-13].

The aim of this review study is to investigate the available paper that evaluate association between Helicobacter pylori infection and laryngeal carcinoma.

**MATERIAL AND METHOD**

Extensive research was conducted on some medical and microbiology database of life sciences such as Pub Med, EMBASE, MEDLINE, LILACS database, global independent network of Cochrane. By referencing these databases, a comprehensive literature review was carried out through combining numerous recent studies in terms of laryngeal carcinoma, Helicobacter pylori infection, epidemiology and management in accordance with many related articles published from 2000 to 2020 which could cover this area of recommendations.

**HELICOBACTER PYLORI**

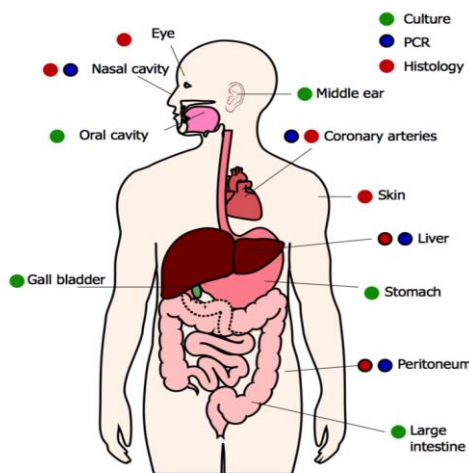
Helicobacter pylori was isolated from dogs for the first time in 1893. And in 1903, it was discovered in the human body[14]. Then for 30 years, the presence of gram-negative and microaerophilic vibrations in the stomach of patients with Peptic ulcers was reported from different parts of the world. The cell wall structure of Helicobacter pylori has a general map of gram-negative bacteria. The fatty acids contained in it are distinct from the Campylobacter design. The cell wall is formed by long-chain

fatty acids, including tetradecanoic and 19 cyclopropane. Fatty acids with lower amounts include hexadecanoic, octadecanoic, linoleic, octadecanoic and phospholipids with polycystic ovaries containing 79% phosphatidylethanolamine, 16% lysophosphatidylethanolamine, and 2% phosphatidylcholine[15, 16].

while the gastric mucosa can kill many types of bacteria but *H. pylori* are highly adapted to the gastric environment. these bacteria have special properties such as easy entry into the mucus, spatial orientation and swimming in the mucus, epithelial cells attachment and avoidance of immune response[15]. But presence of this bacteria do not limited to the gastric mucosa. Fig 1 shows the *H.pylori* detection in numerous site of body. As can be seen this bacteria can present in many site of body. Also the summarized of disease related to *H. pylori* are shown in table 1.

**Table 1: Extra gastric diseases and *H. pylori* infection[17]**

<b>Cardiovascular diseases</b>
Ischaemic heart disease
Noncardioembolic ischaemic stroke
Pre-eclampsia
Raynaud phenomenon
Migraine
Diabetes mellitus
The metabolic syndrome
Neurodegenerative diseases
Multiple sclerosis
Neuromyelitis optica
carcinoma



**Figure 1: Detection of Pylori infection in numerous site of body**

**EPIDEMIOLOGY OF HELICOBACTER PYLORI**

*H. pylori* infection is common worldwide. But it has various prevalence in countries[18]. The *H. pylori* infection prevalence is powerfully associate to socioeconomic[19]. In many developing countries the *Helicobacter pylori* prevalence is about 80 percent among middle-aged adults. This infection is entered through oral and it is largely transmitted in families in early childhood[20]. The transmission in industrialized countries accrue from

person to person with saliva, vomitus, water and feces predominates[21, 22]. Currently, there is no recorded about zoonotic transmission[23, 24]. In adults, the *H. pylori* infection is a chronic disease and improves with specific treatment. but in childhood spontaneous elimination of *H.pylori* probably may happen[25]. During recent decades the prevalence of *H. pylori* has decreased in industrialized countries[26].

**LARYNGEAL CANCER**

Defect in proliferation and cell death mechanisms cause cancer[27]. The disease is mainly caused by exposure to carcinogens by inhalation, eating, drinking and exposure to the workplace and the environment. Individual habits, such as smoking and diet, play a greater role in cancer than inherited genetic factors[28]. Cancer after cardiovascular disease is the second most common cause of death in developed countries and the third leading cause of death in less developed countries[29]. Laryngeal carcinoma is a neoplastic defect that occurs predominantly in smokers and squamous cell carcinoma is majority of them. This tumor may occur in various areas of the larynx including the supraglottic, such as aryepiglottic, false ropes, and ventricles, the gluteal area containing true vocal cords, anterior and posterior commissures, or the subglottic area below the vocal cords. The mild dysplasia seen in the larynx epithelium of some smokers may progress and lead to severe dysplasia and eventually in situ carcinoma, which is a prerequisite for the development of small invasive cancers and invasive squamous cell carcinoma[30]. Changes in the laryngeal epithelium in carcinoma occur in the form of white or red localized thickening, where irregularities are due to keratosis (increased superficial horny layers). Laryngeal carcinoma metastases occur during a long process of tumor growth and are usually confined to the surrounding tissues in the neck[31, 32].

**ASSOCIATION BETWEEN HELICOBACTER PYLORI INFECTION AND LARYNGEAL CARCINOMA**

The important thing in the beginning of the larynx lesion is reach of the contents of the stomach above the upper sphincter. Various studies have reported that the digestive contents reach even as much as hibernate[33]. Today, it is estimated that 10-40% of patients being examined by ear and throat specialists have gastroesophageal reflux disease[33, 34]. Symptoms of reflux include stomach-esophageal contents, heartburn, acid reflux and dysphagia, painful swallowing, and foreign body sensations[34]. Cherry first showed in 1968 that reflux was a major contributor to chronic voice violence and posterior laryngeal erythematic and swelling[33]. Reflux in the larynx can lead to a range of diseases from mild posterior laryngitis to Cancer[33, 34]. The association of *Helicobacter pylori* with reflux needs special attention because epidemiological evidence suggests that infection with *Helicobacter pylori* based on the bacterial replacement area in the stomach can even decrease GERD and esophagitis.

The relation between *helicobacter pylori* infection and laryngeal carcinoma has been investigated in many studies[35-38]. Some of studies reported on relation. In 2008 Naderpour et al examined the percent of *Helicobacter pylori* infection in the larynx cancer. They selected laryngeal cancer patients and benign laryngeal lesion patients as controls and no *Helicobacter pylori* infection was detected in each group[39]. In a case study the relationship between *Helicobacter pylori* and laryngeal carcinoma was estimated by real-time PCR analyze and the no significant relation was detected[40]. Kizilay et al investigated possible risk of *H. pylori* infection in Laryngeal Carcinoma and they did not detected relation between Laryngeal cancer and *H. pylori* infection[41].

but in another study the presence of *Helicobacter pylori* infection was observed[42]. In a study the association between *H. pylori* infection and larynx carcinoma was determined. IgG antibodies presence against antigens of *H. pylori* was estimated with ELISA technique and etiologic role for *H. pylori* infection on the progress of cancer cells was proved[43]. In a meta analyze study the possible link between *H. pylori* infection and laryngeal cancer risk was studied. 15 papers were analyzed and the five of them were selected as a control studies. Laryngeal cancer peril related to *H. pylori* infection was high compared to the controls[44]. Shi et al investigated the relation between *Helicobacter pylori* Infection and Laryngeal Squamous Cell Carcinoma and the *Helicobacter pylori* infection detected in tumor site[45]. In 2013 presence of *cagA* gene *Helicobacter pylori* in etiopathogenesis of starting and progress of larynx squamous cell carcinoma (LSCC) was evaluated and the *H. pylori* was observed in cancer larynx tissue [46]. In 2016 the *Helicobacter pylori ureA* gene and *cagA* gene-positive strains prevalence was evaluated in two group of patients with laryngeal squamous cell carcinoma (LSCC) and benign laryngeal polyps. The significant link between presence of *H. pylori* and LSCC as compared to benign laryngeal polyp was detected[47]. In 2019 presence of immunoglobulin (IgG) antibody was evaluated against *H. pylori* in blood of patients with laryngeal lesions and benign versus malignant lesions. Laryngeal lesions are related to the *H. Pylori* infection specially in laryngeal SCC [48] In 2018 the presence of *H. Pylori* in Stomach and laryngeal mucosal linings was estimated in laryngeal cancer patients. And *H. pylori* was detected in the cancer area, and its migrate from the stomach to the mouth and oral cavity to the stomach[49].

Also we investigated in the prevalence of *Helicobacter pylori* infection in laryngeal carcinoma in previous studies. In a case-control study we evaluated the possible effect of *Helicobacter pylori* on squamous cell carcinoma otolaryngology ward of an academic university. Two test groups including with and without cancer by about 65 patients in each group are assessed for detecting *Helicobacter pylori* infection. and we cannot show the *Helicobacter pylori* effect on laryngeal cancer[50].

In an amazing study Majidi et al was investigated the association between *H. pylori* infection and hypo pharyngeal squamous cell carcinoma by measuring the level of anti-*Helicobacter pylori* antibodies in serum. The control group showed a significant difference with *Helicobacter pylori* infection. This may be due to the protective effect of *Helicobacter pylori* against laryngeal and hypo pharyngeal malignancies[51].

## CONCLUSIONS

The relation between infection and cancer has been shown in last decade. *Helicobacter pylori* infection is one of the main causes in of gastric diseases that can also penetrate the upper limbs such as larynx. Therefore the *Helicobacter pylori* infection can affect the larynx cancer. Some studies investigated this relation. In this study we evaluated these studies. Different effect of *Helicobacter pylori* on larynx cancer was detected in these paper, some study showed strong effect of this infection in larynx cancer while another study reported any relation. So further studies needed to evaluate this relation although the *Helicobacter pylori* infection is main reason of many disease and its prevention and treatment is necessary.

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