



EVALUATION OF THE FREQUENCY OF HELICOBACTER PYLORI IN THE GALLBLADDER SAMPLE OF IRANIAN PATIENT WHO UNDERWENT CHOLECYCTECTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Conflicts of Interest: Nil

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ABSTRACT

Introduction: The colonization by *Helicobacter pylori* is associated with various diseases in the upper gastrointestinal tract such as gastritis, peptic ulcers, gastric cancer and gastric lymphoma. Therefore the aim of this study was Evaluation of the frequency of *Helicobacter pylori* in the gallbladder sample of Iranian patient who underwent cholecystectomy.

Methods: The methods used in this systematic review were based on the Checklist (PRISMA) Guidelines. The searches were conducted by two independent researchers and the aim was to find the relevant studies published from 1/1/2000 to 30/5/2019.

Results: A total of 257 patients and a total of 4 studies from 3 provinces that met the inclusion criteria were evaluated. According to the random effect model, the total frequency of *Helicobacter pylori* in 257 patients was 26% (21%-31% at a 95% confidence interval, $I^2 = 91.1\%$).

Conclusions: Bacteria that lie in the gallbladder epithelium and bile ducts will be able to be a powerful source for causing gallbladder diseases. Surgeons should therefore not only consider the treatment of diseases and infections of the gallbladder, but they should also pay attention to the treatment of infected bile, which is rich in various bacteria.

Key words: cholecystectomy, *Helicobacter pylori*, cholecystitis

INTRODUCTION

Helicobacter pylori is a motile, curved or spiral Gram-negative bacterium that has been isolated from the human stomach throughout the world (1). The colonization by *Helicobacter pylori* is associated with various diseases in the upper gastrointestinal tract such as gastritis, peptic ulcers, gastric cancer and gastric lymphoma (2). The main repository of this microorganism seems to be human (3). Although the exact way of transmission of *Helicobacter pylori* is still controversial, it is thought that this organism is transmitted from one person to another through fecal-oral, oral-oral, or vomiting (5). *Helicobacter pylori* infection is present all over the world, but it should be noted that the prevalence of this infection not only varies across countries, but it can also be different in different regions of a country (6). The prevalence of *Helicobacter pylori* infection in developing countries is generally higher than that in developed countries. Epidemiological studies in different communities and different geographical areas are necessary in order to establish a proper policy for the prevention and control of this bacterial infection (7). It also plays an important role in gastric diseases such as gastric adenocarcinoma. *Helicobacter pylori* is able to survive and grow in

the acidic environment of the stomach (8). Warren and Marshall were the first to discover and identify *Helicobacter pylori* and confirmed the association between the presence of this bacterium in human gastric mucosa and gastric cancer (9). *Helicobacter pylori* infection has been seen in 95% of patients with duodenal ulcer and in 80% of patients with gastric ulcer. People with this bacterium are at least four times more likely than other people to be exposed to digestive wounds (10). There are significant differences in the prevalence of this infection in different geographical areas. Since infections, including *Helicobacter pylori* infection, play an important role in the development of the chronic inflammation of the gastric mucosa and provide the conditions for the incidence of peptic ulcer and gastric adenocarcinoma, recent studies have suggested a link between this bacterium and gallbladder cancer (11).

Methods

Inclusion criteria (eligibility criteria):

The methods used in this systematic review were based on the Checklist (PRISMA) Guidelines. In this research, cross-sectional, case-control, and cohort studies were included and case studies, letters to

editors, case reports, clinical trials, study protocols, systematic reviews were excluded.

Participants: All studies of the frequency of helicobacter pylori in the gallbladder sample of Iranian patient who underwent cholecystectomy.

Findings: The main purpose of this study was to determine the frequency of helicobacter pylori in the gallbladder sample of Iranian patient who underwent cholecystectomy and the findings were reported.

Sampling Methods and Sample Size: All observational studies were included in the systematic review regardless of their design. The minimum sample size was 25 patients or more.

Search Strategy

The searches were conducted by two independent researchers and the aim was to find the relevant studies published from 1/1/2000 to 30/5/2019. The researchers searched for published studies in the English language in MEDLINE via PubMed, EMBASE via Ovid, the Cochrane Library and Trip database. For studies published in other languages, National Database (Magiran and SID, KoreaMed and LILACS), and for unpublished studies, OpenGrey (www.opengrey.eu/), World Health Organization Clinical Trials Registry (who.int/ictrp), and ongoing studies were searched. To ensure that the studies are adequate, the reference lists of the retrieved studies were also searched and studied. Systematic review articles were searched using MeSH and open terms in accordance with publication standards. After the MEDLINE strategy was finalized, the results were compared to search for other databases, as well as PROSPERO was searched for recent or ongoing systematic reviews. The keywords used in the search strategy are: cholecystectomy, Helicobacter pylori, cholecystitis Study Selection and Data Extraction

The two researchers independently analyzed the titles and abstracts of the articles according to eligibility criteria. After excluding additional studies, the full text of each study was evaluated on the basis of eligibility criteria and the information about the authors was collected as needed. The general information (the first author, province in which the study was conducted and year of publication), study information (the sampling technique, diagnostic criteria, data collection method, research conditions, the sample size, and risk of bias) and output scale (frequency of helicobacter pylori in the gallbladder sample) were collected.

Quality Assessment

The extended scale of Hoy et al. was used to evaluate the quality of method and the risk of bias in each observational study. This 10-item scale assesses the quality of studies according to their external validity (items 1 to 4 evaluate the target population, sampling frame, and minimum selection bias) and internal validity (items 5 to 9 evaluate the data collection, problem statement, research scale and data collection tool, while item 10 evaluates the data analysis bias). The risk of bias was measured by two researchers independently and disagreements were resolved by consensus.

Data Collection

All eligible studies were included in the data collection after a systematic review and the data were integrated using the cumulative chart. The random effect model was evaluated based on the overall prevalence of the disease among the participants. The heterogeneity of the initial studies was assessed using the I^2 test. In addition, subgroups were analyzed to determine the heterogeneity by participants' male to female, year of publication, and Province. Finally, a meta-analysis was performed using STATA14 statistical software.

Study Selection

A total of 511 articles were extracted through preliminary searches in various databases. Of the 511 essential studies identified by the analysis of titles and abstracts, 484 ones were eliminated because of irrelevant titles. Of the 27 existing studies, 23 ones were excluded. Of the remaining studies, 4 met the study inclusion criteria. (Fig. 1)

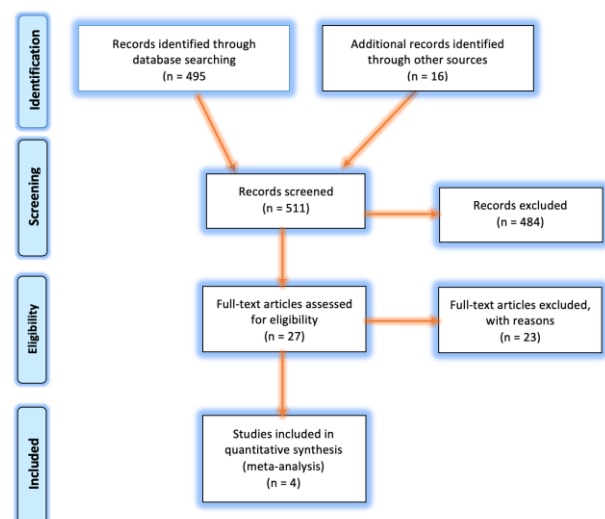


Figure 1: PRISMA flow diagram

Research Properties

A total of 257 patients and a total of 4 studies from 3 provinces that met the inclusion criteria were evaluated. Of the studies were retrospective.

studies were from Tehran, Isfahan and Kerman. In most studies the risk of bias was low. Data were originally collected from medical records. The hospital was the main study site. (Table 1)

Table 1: characteristics of the included studies

Author	Publication year	Province	Number of patients	Prevalence	Male to female	Mean of age
Safaei 15	2011	Isfahan	52	15%	-----	-----
Lashkarizade 16	2015	kerman	100	23%	62/38	48.63±16.46
Kheirmand 17	2016	Isfahan	70	25.7%	11/59	44.16±15.15
Nezam 18	2013	Tehran	35	68.2%	9/26	44.74±9.86

The meta-analysis of the frequency of helicobacter pylori in the gallbladder sample of Iranian patient who underwent cholecystectomy:

According to the random effect model, the total frequency of helicobacter pylori in 257 patients was 26% (21%-31% at a 95% confidence interval, $I^2 = 91.1\%$). (Fig. 2)

Subgroup Analysis

Meta Regression Results

The results of meta-regression between participants' publication year and the frequency of helicobacter pylori in the gallbladder sample of Iranian patient who underwent cholecystectomy:

The regression of the study was evaluated by the relationship between the frequency of helicobacter pylori in the gallbladder sample of Iranian patient who underwent cholecystectomy and participants' publication year and the total rate of helicobacter pylori. There was no significant linear trend in the univariate meta-regression to explain the effect size of participants' publication year. (Fig. 3)

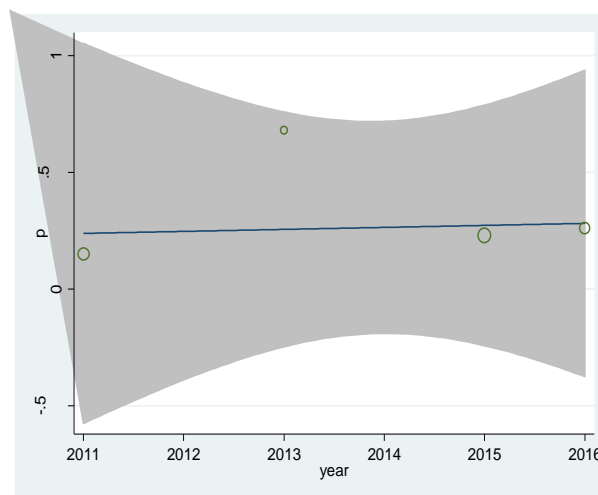


Figure 3: Meta-regression between publication year of study and frequency of helicobacter pylori in the gallbladder sample of Iranian patient who underwent cholecystectomy

Discussion:

According to the random effect model, the total frequency of helicobacter pylori in 257 patients was 26% (21%-31% at a 95% confidence interval, $I^2 = 91.1\%$). Epidemiological factors that may be associated with Helicobacter pylori infection need to be identified for each population. In particular, identifying those risk factors that are modifiable can lead to useful and effective measures (12). It is urease, catalase and oxidase positive and uses glucose as the sole source of the phosphorylation at the substrate level. It also derives energy from the breakdown of serine, renin, aspartate and proline (13). Infection with this bacterium, as a disease, is a major cause of chronic gastric cancer. In addition, it is the cause of chronic atrophic gastritis of the intestine. It is 50% prevalent in developing countries (14). According to population-based studies, it has been shown that the prevalence of Helicobacter pylori in Iran is high. The prevalence of this bacterium depends on age, race, health and lifestyle in developed or developing countries (15). In developing countries, infection rates are higher

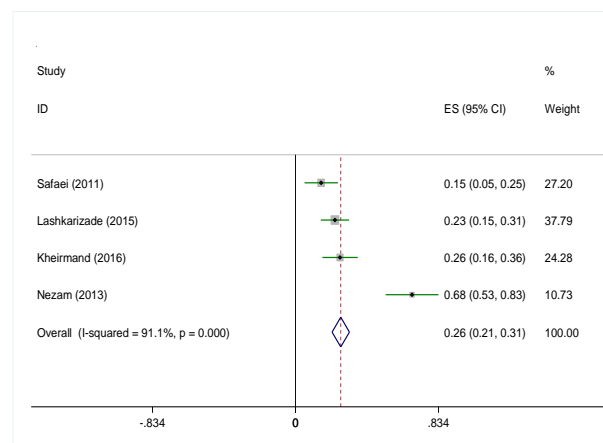


Figure 2: frequency of helicobacter pylori in the gallbladder sample of Iranian patient who underwent cholecystectomy and its 95% interval for the studied cases according to the year the study was conducted based on the model of the random effects model.

in childhood, and infection rates vary in populations of different races. More than 80% of people infected with *Helicobacter pylori* show no symptoms (16). It is known to be the major cause of gastric ulcer and duodenal ulcers, and if not treated, can lead to adenocarcinoma and MALT lymphoma. Scientists have found that the infection of this bacterium is directly linked to the incidence of gastric cancer. Gastric adenocarcinoma is the second leading cause of cancer-related deaths, and many people die each year because of a malignant cancer (17). The bacterium is transmitted from person to person orally and fecally through water, food, saliva, and so on. This gastric infection is associated with many diseases, including cardiovascular disease, ITP, iron deficiency anemia, chronic sinusitis-asthma, and liver disease (18). Bacteria that lie in the gallbladder epithelium and bile ducts will be able to be a powerful source for causing gallbladder diseases. Surgeons should therefore not only consider the treatment of diseases and infections of the gallbladder, but they should also pay attention to the treatment of infected bile, which is rich in various bacteria.

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