

# Meta-Analysis on Relation Between Helicobacter Infection and Primary Liver Carcinoma

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**Abstract:** The Helicobacter infection was caused many diseases, and found in the liver tissue of primary liver cancer patients. Liver cancer was seriously dangerous of healthy, it confirmed that the correlation between liver cancer and multiple viruses, such as HBV and HCV, even include helicobacter. In this study, we explored the association between helicobacter and primary liver carcinoma. by searching relevant literature with database. The separated case-control studies on relationship between helicobacter infection and primary liver carcinoma were analyzed by Meta-analysis with Revman 5.0. 9 studies were included in the final analysis. Overall the prevalence of helicobacter infection was 52.53% (166 of 316) in case group vs 9.96% (23 of 231) in control group, and the summary odds ratio for the association of helicobacter infection with the risk for primary liver carcinoma (using the fixed-effects model, which accounted for the homogeneity across the 9 studies) was determined to be odds ratio 14.19 (95% CI, 7.92~15.14). Sensitivity analysis showed the results were no publication bias.the funnel plot was approximately standard symmetric, Failure safety number (Nfs) analysis: Calculate Nfs at P=0.05 level, Nfs 0.05=( $\sum Z/1.64$ )<sup>2</sup>-K=369.395, the large Nfs value also indicated that there was no publication bias in the study. So the Meta-analysis demonstrated there was a positive association between helicobacter infection and the risk of primary liver carcinoma.

**Keywords:** Helicobacter, Primary Liver Cancer, Meta Analysis

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## 1. Introduction

The major diseases of Liver cancer was seriously endanger human health, and the main pathogenic factors include viral infections such as HBV and HCV [1]. In recent years, there have been reported that the causes of liver cancer include Helicobacter pylori infection. The presence of Helicobacter pylori has been found in the liver tissue of primary liver cancer patients, and animal experiments have also confirmed that Helicobacter pylori infection can cause chronic hepatitis and liver cancer [2, 3]. However, there was unclear conclusion on the epidemiological research of Helicobacter pylori infection and liver cancer both domestically and internationally. Therefore, this article intends to use the method of meta-analysis to comprehensively and quantitatively analyze 9 publicly reported literature on the relationship between

Helicobacter pylori infection and liver cancer at home and abroad, in order to clarify whether there was a correlation between Helicobacter pylori infection and the occurrence of liver cancer and provide epidemiological basis for the prevention and control of liver cancer.

## 2. Data and Methods

### 2.1. Data Sources

CNKI, Wanfang Database, Pubmed and other databases were searched from January 2004 to December 2013. The Chinese keywords were liver cancer, Helicobacter pylori, and case-control study, while the English search terms were primary liver cancer, helicobacter, and case-control study. In addition, simultaneously review all retrieved paper references to collect relevant clinical studies as much as possible.

## 2.2. Inclusion and Exclusion Criteria

### 2.2.1. Inclusion Criteria

- 1) Research results designed as case-control studies, including the entire text and complete data;
- 2) Involve the relationship between Helicobacter pylori and liver cancer, and provide the number of cases and control groups, as well as the infection rate of Helicobacter pylori;
- 3) Liver cancer patients are diagnosed through pathology;
- 4) Helicobacter pylori infection is judged by at least one diagnostic method.

### 2.2.2. Exclusion Criteria

- 1) Literature with only abstracts but lacking full text literature and incomplete data that cannot be utilized;
- 2) Repeated publications;
- 3) Literature without control group and review literature.

## 2.3. Statistical

Statistical analysis was conducted with Revman 5.0 software, the continuous measurement data using standardized mean

difference (SMD) as the analysis statistic. Count data was analyzed using odds ratio (OR) as the statistical measure, and heterogeneity tests between studies were conducted using  $\chi^2$ . When there was no heterogeneity in the research results, a fixed effect model (FEM) was selected, and when there was heterogeneity, a random effect model (REM) is selected. The evaluation indicators are rate difference (RD) and its 95% confidence interval (CI), and forest plot and funnel plot were performed.

## 3. Results

### 3.1. Basic Information of Included Literature

9 studies were included according to the above criteria, by conducting a detailed search of the data and reviewing the retrieved references, the total of 316 liver cancer patients and 231 control cases. Each study provided detailed information on the patient's condition characteristics, examination methods, and evaluation indicators. The characteristics of each study included in the meta-analysis are shown in Table 1.

Table 1. Basic characteristics of included studies.

study	OG	CG	items	conclusion
CHENYan-ling2007 [4]	liver Ca	normal	16SrRNA	relation
CHEN REN2010 [5]	liver Ca	normal	Hp、16SrRNA	relation
JiLi Yang2013 [6]	liver Ca	normal	16SrRNA	relation
Lining 2006 [7]	liver Ca	normal	16SrRNA-mRNA	relation
M Rocha2011 [8]	liver Ca	normal	16SrRNA	relation
Rinaldo Pellicano [9]	liver Ca	normal	16SrRNA	relation
Shi-Ying Xuan2006 [10]	liver Ca	normal	16SrRNA	relation
Y Huang2004 [11]	liver Ca	normal	16SrRNA	relation
ZHANGShi-qiang2004 [12]	liver Ca	normal	HP-DNA	relation

(OG: observation group; liver Ca: liver cancer; CG: Control group)

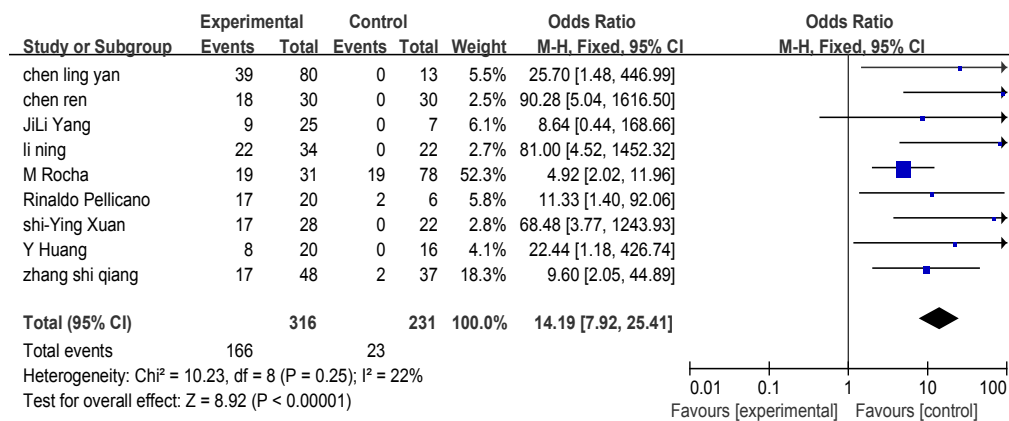


Figure 1. Analysis of forest.

### 3.2. Analysis of the Impact of Helicobacter Pylori Infection on the Occurrence of Liver Cancer

Heterogeneity tests were conducted on the 9 randomized controlled studies included, and the results showed no heterogeneity ( $\chi^2=10.23$ ,  $P=0.25$ ), therefore a fixed effects model was used for meta-analysis. The infection rate of Helicobacter

pylori in the observation group of liver cancer cases was 52.53%, while the infection rate of Helicobacter pylori in the control group was 9.96%(OR=14.19,95%CI: 7.92~25.41). This indicates that the infection rate of Helicobacter pylori in the observation group is significantly higher than that in the control group, indicating that Helicobacter pylori infection can significantly increase the incidence of liver cancer. The forest map evaluated is detailed in Figure 1.

3.3. Analysis of Publication Bias

The funnel plot uses the OR value of the effect size as the horizontal axis, and the standard error of the OR value of the log is the vertical axis as the scatter plot. As shown in Figure 2, The funnel plot is approximately standard symmetric, indicating that there is no publication bias. Failure safety number (Nfs) analysis: Calculate Nfs at P=0.05 level,  $Nfs\ 0.05=(\sum Z/1.64)^2-K=369.395$ , the z-values for each study are summarized in Table 2). The large Nfs value also indicates that there is no publication bias in the study.

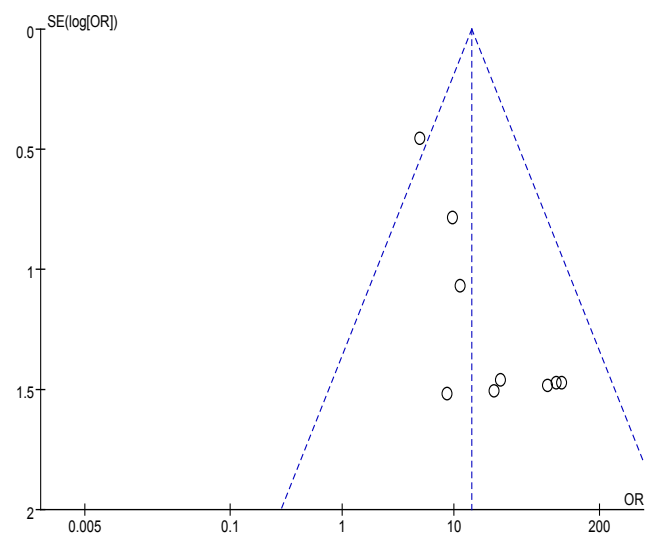


Figure 2. Analysis of bias.

Table 2. Analysis of Nfs:  $Nfs0.05=(\sum Z/1.64)^2-K=369.395$ .

a	b	c	d	$\chi^2$	Z
17	2	31	35	10.84259	3.292808
22	0	12	22	23.44637	4.842145
39	0	41	13	10.91458	3.303723
17	2	3	4	6.2621554	2.5024299
8	0	12	16	8.228571	2.868549
17	0	11	22	20.238095	4.498677
18	0	12	30	25.71429	5.070926
19	19	12	59	13.323894	3.650191
9	0	16	7	3.506087	1.872455

4. Discussion

Meta analysis was a research process that quantitatively combines and comprehensively evaluates multiple independent studies with the same research objectives. This study conducted a meta-analysis on the data of 9 selected studies, and the results showed that the Helicobacter pylori infection rate in the observation group of liver cancer cases was 52.53%, while the control group had a Helicobacter pylori infection rate of only 9.96%, with significant differences. The statistical combined OR was 14.19, with a 95% CI of 7.92-25.41, indicating a correlation between Helicobacter pylori infection and liver cancer. Helicobacter pylori infection is an important factor in inducing liver cancer. This is consistent with the research by Pandey et al. [2] indicating that

Helicobacter species play a positive role in increasing the risk of liver and gallbladder cancer.

The data analysis of this study showed no heterogeneity, and funnel plots and safety factors were used to test and evaluate publication bias during the analysis process, effectively ruling out the possibility of publication bias. Supporting Helicobacter pylori infection is an important factor in the occurrence of liver cancer.

Meta analysis was susceptible to bias and confounding factors. There may be a problem with this article: bacterial culture is used as a detection standard for Helicobacter pylori, but existing methods and methods have not been able to culture Helicobacter pylori from human liver tissue. Therefore, most current studies on Helicobacter pylori detection use PCR amplification of 16s rDNA, but some studies have shown that Helicobacter pylori 16s rRNA is positive in liver tissue and serological testing is negative [13]. Therefore, the existence of false positives is not excluded from the research results of various literature, which directly determines the conclusion of the relationship between Helicobacter pylori infection and liver cancer. Secondly, each study controls for confounding factors. The selection of study subjects based on different inclusion criteria, age distribution, and the setting of the control group (patients with liver cirrhosis, chronic viral hepatitis, and external liver damage) may all affect the results of the study.

5. Conclusion

In summary, our studies provide evidence that there was a positive relationship between helicobacter infection and the risk of primary liver carcinoma, helicobacter was one of the important factors for induced liver cancer.

Conflicts of Interest

The authors declare no conflicts of interest.

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