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### Cigarette smoking and *H. pylori* infection: A meta-analysis of literature

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#### ABSTRACT

The present study was designed to determine the association of the smoking with *H. pylori* infection by conducting a meta analysis of literature. A comprehensive in depth search was conducted on following search engines: Pubmed, EMBASE, Google Scholar, Medscape, Plosone and Scopus. The following terms were used as keywords in the database search: “*Helicobacter pylori*”, “Smoking”, “association”, “cohort”, “case control”, “observational”, “cross sectional” till June 2011. Only reports fulfilling the following inclusion criteria were included in the meta-analysis. In the study conducted by Ahmad et al., 2006, the odds ratio was found out to be 1.371(0.760-2.471). The z value and p value were computed to be equal to 1.048 and 0.295 respectively. In the study conducted by Brenner et al., 2007, the odds ratio was found out to be 1.236(0.706-2.164). The z value and p value were computed to be equal to 0.743 and 0.458 respectively. In the study conducted by Karima et al., 2006, the odds ratio was found out to be 1.5(0.659-3.413). The z value and p value were computed to be equal to -0.967 and 0.334 respectively. In the study conducted by Modena et al., 2007, the odds ratio was found out to be 0.846(0.355-2.015). The z value and p value were computed to be equal to -0.378 and 0.705 respectively. In the study conducted by Maoyeddi et al., 2002, the odds ratio was found out to be 10.932(6.508-18.363). The z value and p value were computed to be equal to 9.038 and 0.07 respectively. In the study conducted by Nurgalieva et al., 2004, the odds ratio was found out to be 1.5(0.659-3.413). The z value and p value were computed to be equal to -0.378 and 0.705 respectively. In the study conducted by Pillay et al., 2007, the odds ratio was found out to be 6.768(4.398-10.415). The z value and p value were computed to be equal to 8.695 and 0.06 respectively. In the study conducted by Khan et al., 2007, the odds ratio was found out to be 1.236(0.706-2.164). The z value and p value were computed to be equal to 0.743 and 0.458 respectively. In the study conducted by Zhang et al., 2009, the odds ratio was found out to be 1.217(0.455-3.260). The z value and p value were computed to be equal to -0.391 and 0.696 respectively. Smoking has emerged as a major risk factor in modulating the susceptibility of an individual suffering with ulcers to *H. pylori* infection. Hence, a cue needs to be taken from the investigation and significant steps taken for its cessation to halt the progression of *H. pylori* infection. Findings from this meta-analysis suggest that there is a close relationship between cigarette smoking and *H. pylori* infection.

**Keywords:** smoking, *H. pylori*, meta analysis.

**Abbreviations:** OR Odds ratio, CI Confidence interval, *H. pylori Helicobacter pylori*.

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## INTRODUCTION

*Helicobacter pylori* is a panmictic, gram negative, helical bacteria which affects more than half the population of world [1]. It is responsible for the transformation of an ulcer into MALT lymphoma [2]. There are various risk factors that play a pivotal role in the transmission of the bacteria in the population and enhancing the susceptibility of an individual to the infection [3]. These include smoking and NSAID use [4]. It has been investigated by many authors that smoking plays an indispensable part in the enhancement of the risk of an individual to infection of *Helicobacter pylori* [5,6]. A recent meta analysis has shown the inverse correlation of alcohol consumption with *H. pylori* infection [7]. Smoking has also been implicated to enhance the virulent infection in individuals by increasing the expression of the virulent genes like *cag A*, *E* and *T* [4-6]. *Helicobacter pylori* exists in both asymptomatic subjects and those demonstrating the clinical symptoms of acid peptic disease. In both the classes of individuals, the risk of virulent infection is escalated by smoking [5].

The underlying reason has been investigated and interplay of cellular biomarkers in the *H. pylori* and host gastric and oral cavity have been proven for such a transformation. However, the various studies dedicated to derive a relation between *H. pylori* infection and smoking have been performed in various countries over a period of time [8,9]. It is worth considering that this relation has not been statistically evaluated and proven.

The objective of the present investigation was to elucidate the underlying relation between smoking and *H. pylori* by applying statistical comparison of the outcomes of the previously reported studies.

## MATERIAL AND METHODS

Search strategy, selection criteria, and inclusion criteria and data abstraction:

A comprehensive in depth search was conducted on following search engines: Pubmed, EMBASE, Google Scholar, Medscape, Plosone and Scopus. The following terms were used as keywords in the database search: "*Helicobacter pylori*", "Smoking", "association", "cohort", "case control", "observational" and "cross sectional" till June 2011. Only reports fulfilling the following inclusion criteria were included in the meta-analysis (figure 1).

- 1.The inclusion studies that contained the minimum information necessary to estimate the odds ratio associated with tobacco smoking and a corresponding measure of uncertainty (ie, 95% confidence interval [CI], z value, and p value of the significance of the estimate).
  - 2.Case-control and cohort studies, published as original articles.
  - 3.Articles were reviewed and data extracted and cross-checked independently by 3 investigators (Any disagreement was resolved by common consensus among the 3 reviewers).
- Initial screening yielded 1030 articles. They were screened and thereafter 975 studies were excluded due to non compliance with the inclusion criteria. Out of these 75 case control and cohort studies were identified. Thereafter 64 studies were excluded due to insufficient data for statistical analysis. Finally, 11 studies were selected for Meta analysis [10-18].

**1.Data synthesis and analysis:**

Data was analyzed using Comprehensive Meta analysis software and odds ratio, 95% confidence interval, z value and p value were calculated for each study. The entire data was plotted and represented in the form of Forest plot depicting the odds ratio with 95% confidence interval of odds ratio. Odds ratios (OR) and 95% confidence intervals (95% CI) was calculated for the association between smoking and *H. pylori* infection. ORs and 95% CIs were calculated for each individual study. Random-effects model (DerSimonian-Laird method) was employed to calculate summary ORs and 95% CIs.

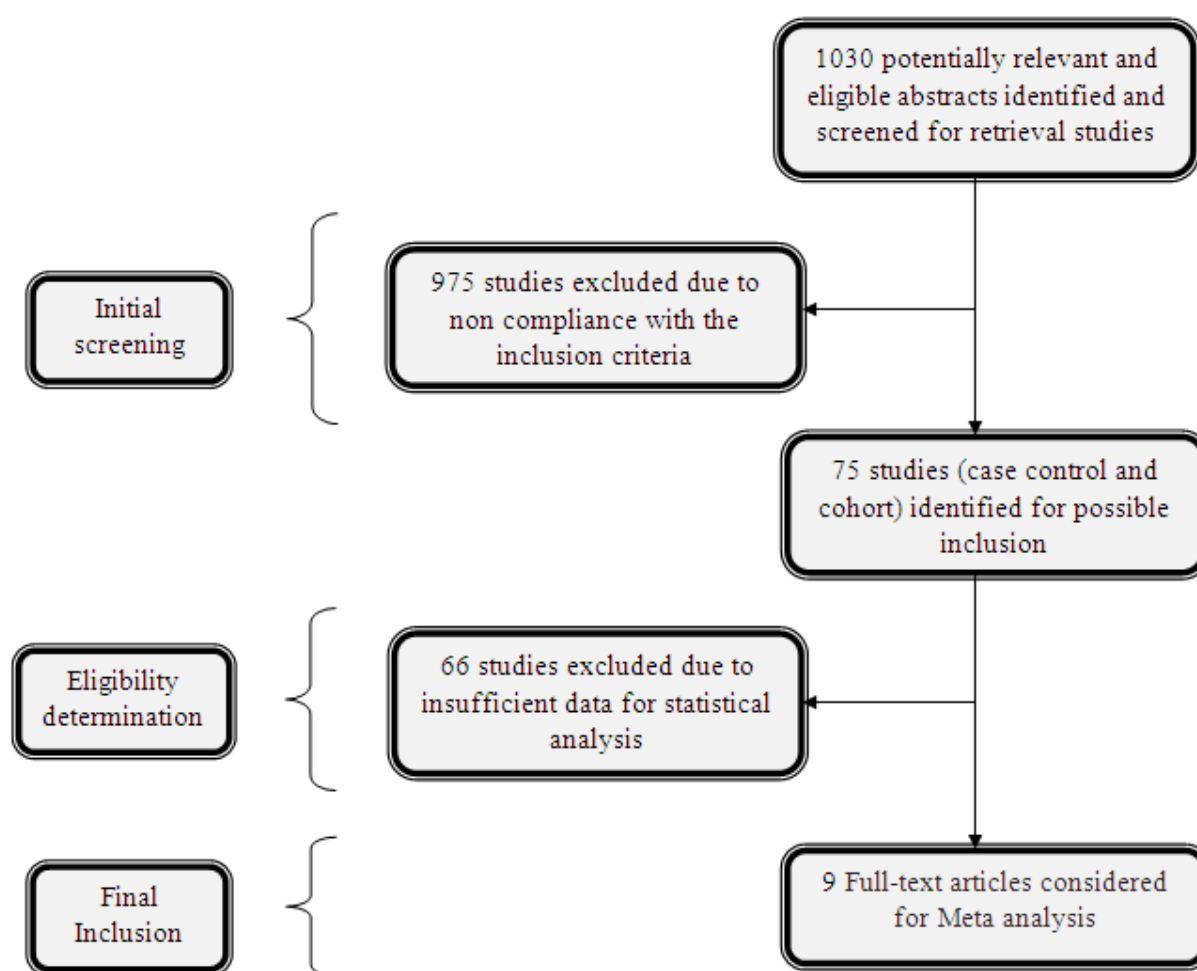


Fig 1. Flow chart depicting the process of selection of studies for inclusion in Meta-analysis

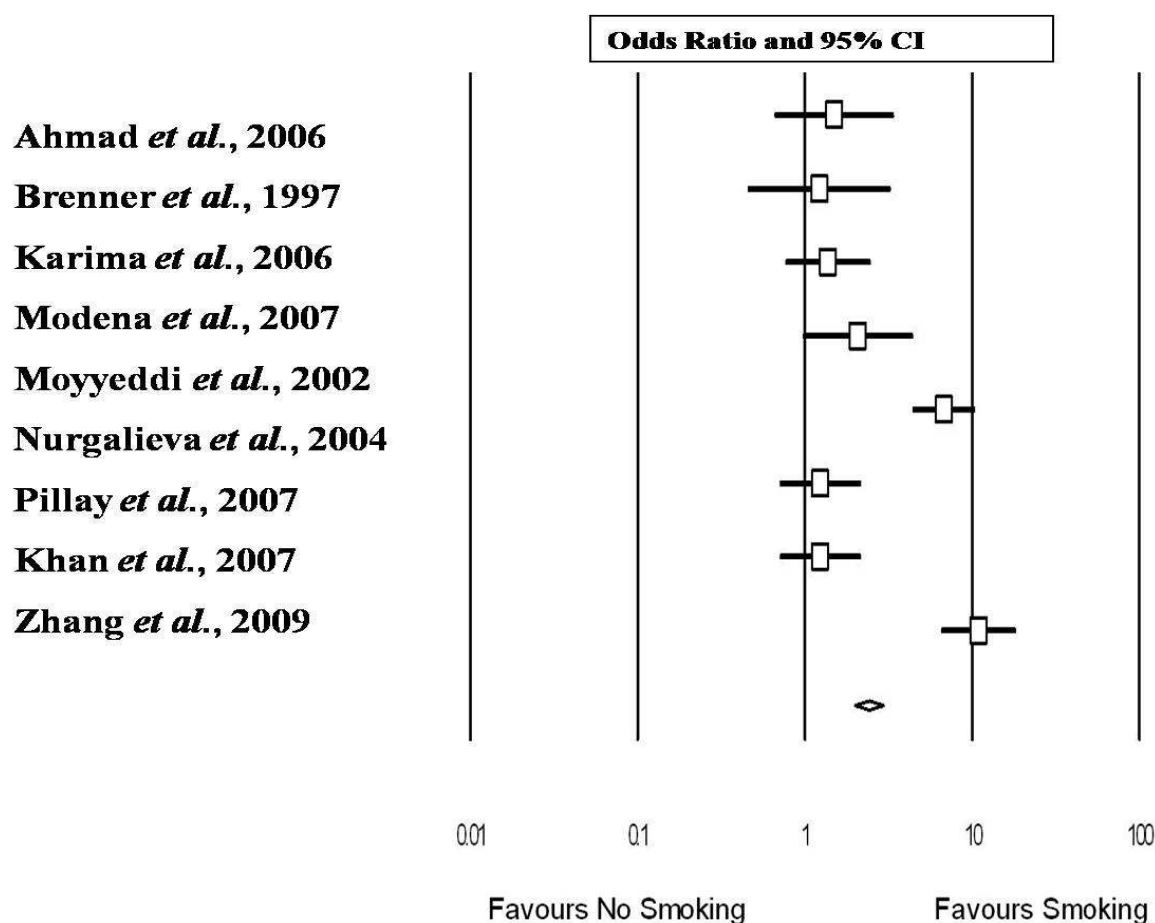


Fig 2. A forest plot depicting the meta analysis of the association of smoking with the prevalence of *H. pylori* infection. It shows odds ratio, 95% CI (confidence interval).

## RESULTS

The figure 2 depicts the forest plot representing the OR and 95% CI. In the study conducted by Ahmad *et al.*, 2006, the odds ratio was found out to be 1.371 (0.760-2.471). The z value and p value were computed to be equal to 1.048 and 0.295 respectively. In the study conducted by Brenner *et al.*, 2007, the odds ratio was found out to be 1.236 (0.706-2.164). The z value and p value were computed to be equal to 0.743 and 0.458 respectively.

In the study conducted by Karima *et al.*, 2006, the odds ratio was found out to be 1.5 (0.659-3.413). The z value and p value were computed to be equal to -0.967 and 0.334 respectively. In the study conducted by Modena *et al.*, 2007, the odds ratio was found out to be 0.846 (0.355-2.015). The z value and p value were computed to be equal to -0.378 and 0.705 respectively.

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In the study conducted by Nurgalieva *et al.*, 2004, the odds ratio was found out to be 1.5 (0.659-3.413). The z value and p value were computed to be equal to -0.378 and 0.705 respectively. In the study conducted by Pillay *et al.*, 2007, the odds ratio was found out to be 6.768 (4.398-10.415). The z value and p value were computed to be equal to 8.695 and 0.06 respectively.

In the study conducted by Khan *et al.*, 2007, the odds ratio was found out to be 1.236 (0.706-2.164). The z value and p value were computed to be equal to 0.743 and 0.458 respectively. In the study conducted by Zhang *et al.*, 2009, the odds ratio was found out to be 1.217 (0.455-3.260). The z value and p value were computed to be equal to -0.391 and 0.696 respectively.

The combined value of odds ratio and 95% CI was 1.597 (0.197-3.977). The  $I^2$  value was 16.77%. The diamond represents the combined value. The line projecting upwards from 1 depicts the null value (figure 2).

## DISCUSSION

*Helicobacter pylori* (*H. pylori*) infection is synonymous with a broad spectrum of gastro duodenal pathologies which span across asymptomatic gastritis to gastric malignancy. *H. pylori* is a gram-negative, panmictic, curved or spiral, flagellated bacteria thriving in microaerophilic conditions that can be existing in the mucus layer, in the gastric epithelium, in the oral cavity and in the gastric pits. It exists in VBNC (viable but non culturable form) in water and food articles. It is transmitted via a plethora of factors like drinking water and food [21, 22].

*Helicobacter pylori* prevalence and virulence is influenced by an array of factors. These include contaminated water, smoking, NSAID use, spicy food, ethnicity etc. [5-7, 21-23]. These factors orchestrate the expression of *Helicobacter pylori*'s virulent genes and in turn modulate its pathogenic competency. Smoking is a social stigma that is fast growing into an epidemic. *H. pylori* in non virulent state are present in the oral and the gastric milieu in acid peptic disease patients and asymptomatic subjects. Previous studies suggest that *H. pylori* is spread across a considerable asymptomatic population pool which spans across boundaries of social, geographical, age and other allied demographic facets [4].

In such a scenario, generation of statistical evidence underlying the association of smoking and risk of *H. pylori* becomes increasingly important. In the present investigation various studies were shortlisted which satisfied the inclusion criteria. The meta analysis suggests that the individuals exposed to smoking have a distinct risk of *H. pylori* infection as the infection favors smoking in the forest plot. It has been studied that the prevalence of virulent *H. pylori* in smokers in India is significantly higher than the subjects who are not exposed to cigarette smoke. It has been elucidated in molecular studies that smoking causes the expression of cag A, E and T genes in the gastric milieu. These genes are the needle and syringe mechanism of *H. pylori* and play a pivotal role in the transformation of an ulcerated gastric lining into a malignant tumor. The present study provides statistical credence to the dictum smoking is a predominant risk factor stimulating virulence of *H. pylori*. The studies conducted by Pillay *et al.*, Moyyeddi *et al.*, discernibly indicate the role of smoking in increasing the risk of *H. pylori* infection. Other studies exhibit a similar trend. The literature and the meta analysis suggest that *H. pylori* infection is precipitated due to smoking habit in subjects.

In the study conducted by Ahmad *et al.*, 2006, it was evident that smoking played a detrimental role in the pathological manifestation of ulcers infected with *H. pylori*. In the investigation of Brenner *et al.*, 1997, a similar trend was evident where smoking had a malefic effect on the ulcer pathogenesis. The study of Karima *et al.*, elucidated the role of smoking in the aggravation of the *H. pylori* induced gastric maladies. The investigation by Modena *et al.*, 2007, re iterated the pathobiological role of smoking in aggravation of *H. pylori* infected ulcers. Moyyeddi *et al.*, 2002 demonstrated indispensable role of smoking in the culmination of the complex gastropathies and its association with *H. pylori* infection. The study conducted by Nurgalieva *et al.*, 2004 exhibited similar findings. Recent investigations by Pillay *et al.*, 2007 and Zhang *et al.*, 2009, demonstrated the close association of smoking induced aggravation of *H. pylori* infection. These studies have contributed to the development of evidence to provide credence to the evidence that *H. pylori* infection favors smoking. A similar trend was discernable after the meta analysis [11-18].

Smoking has emerged as a major risk factor in modulating the susceptibility of an individual suffering with ulcers to *H. pylori* infection. Hence, a cue needs to be taken from the investigation and significant steps taken for its cessation to halt the progression of *H. pylori* infection.

### CONCLUSION

Findings from this meta-analysis suggest that there is a close relationship between cigarette smoking and *H. pylori* infection.

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