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Review Paper

Investigating the Association Between Smoking and Death in Patients With COVID-19 in Iran: A Meta-analysis Study

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ABSTRACT

Background: With reducing the immune function of the pulmonary, smoking is considered a risk factor for contracting other infections with more severe outcomes. The present study investigates a meta-analysis of the association between smoking and the progression of COVID-19 infection in Iran.

Materials and Methods: The online databases of PubMed/MEDLINE and Web of Science were searched on August 23, 2022, with the following terms: ("COVID-19" OR "SARS-CoV-2" OR "Coronavirus"), AND ("smoking" OR "smoker*"), AND ("Iran"). In this review, we included the studies with molecular-confirmed cases of COVID-19 and the outcome of death. The Mantel-Hensel meta-analysis method with random effects was used to investigate the relationship in the data.

Results: We identified 8 papers with a total of 9199 COVID-19 patients, of whom 1861(20.2%) had the outcome of death, and 1105(12%) had a history of smoking. A total of 274 patients with a history of smoking (24.7%) were dead. The meta-analysis showed a significant association between smoking and death related to COVID-19 (odds ratio=1.22, 95% confidence interval [1.03-1.44], P=0.001). Therefore, the probability of death in COVID-19 patients with a history of smoking is about 22% higher than other people.

Conclusion: Smoking is a risk factor for the progression of COVID-19, with smokers having higher odds of COVID-19 progression than non-smokers.

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Introduction

COVID-19 rapidly spread worldwide after the World Health Organization (WHO) declared it a global pandemic in March 2020 [1]. According to WHO reports Iran experienced a significant increase in COVID-19 cases [2, 3]. The first confirmed case in Iran was reported on February 20, 2020. By August 26, 2022, confirmed cases had reached 7 516 596 with 143 550 fatalities. The Coronavirus enters the respiratory epithelial cells through the angiotensin-converting enzyme 2 (ACE2) receptor [4]. Compared to non-smokers, the high concentration of ACE2 enzyme in smokers can have irreparable effects on the body's immune system by inducing a cytokine storm, causing the absorption of numerous viruses and overstimulating the immune system [5, 6]. Additionally, a higher concentration of the ACE2-enzyme receptor in smokers' bodies, compared to non-smokers, leads to a faster Coronavirus entry into the lung cells [5, 6]. Therefore, this virus destroys various body organs, particularly the respiratory system. It is expected to be concerned about individuals with underlying respiratory diseases as their lung capacity, including smokers, is reduced [7]. Furthermore, smokers are more likely to contract influenza than non-smokers [8, 9]. In addition, smokers' fingers can carry millions of viruses due to increased contact with hands, nose, and eyes. As a result, the transmission of the Coronavirus is accelerated [10]. The current study explores the meta-analysis of the association between smoking and mortality resulting from COVID-19 infection in Iran.

Materials and Methods

This study was based on the preferred reporting items for systematic reviews and meta-analysis checklists. We conducted a systematic search of the PubMed/MEDLINE and Web of Science databases from the beginning of 2020 to August 23, 2022, using the following search terms: ("Smoker*" OR "smoking"), AND ("COVID-19" OR "SARS-CoV-2" OR "Coronavirus"), AND ("Iran"). This study included molecular-confirmed cases of COVID-19 with a smoking history and a specific outcome in terms of mortality (both smokers and non-smokers). The required information was extracted from the selected studies, and the abstracts were independently evaluated by two authors (PD and ES). A meta-analysis was conducted, estimating the odds ratio (OR) with 95% confidence interval (CI) for molecularly confirmed COVID-19 patients with a history of smoking and the death outcomes of all patients (both smokers and nonsmokers) in a case study. The analysis was discussed and completed. Statistical analysis was performed using the R software, version 4.2.2, utilizing the meta package and the Mantel-Haenszel meta-analysis method. The investigation of publication bias was carried out using a funnel plot and the Egger regression. The heterogeneity of the model was determined using the I^2 index, and outlier studies were identified using the Galbraith diagram.

Results

In the initial search, a total of 112 articles were identified. After removing duplicate articles (n=23), the titles and abstracts of the remaining 89 articles were evaluated. From this evaluation, 81 articles were excluded due to not meeting the inclusion criteria. Finally, 8 retrospective articles were included in the study, consisting of 9199 COVID-19 patients and a total of 1861(20.2%) outcomes [11-18]. The search strategy is illustrated in Figure 1. Among the patients included in the study, 1105 (12%) individuals were either smokers or had a history of smoking. The mortality rate among this group was calculated at 274(24.7%). Based on the results of the meta-analysis, a significant relationship between smoking and mortality in COVID-19 patients was observed (OR=1.22, 95% CI, 1.03%-1.44%). Therefore, the odds of death in COVID-19 patients with a smoking history were approximately 22% higher compared to individuals without such a history (Figure 2).

According to studies from various communities, the lack of a specific time interval, and differing outcomes (seven studies on death and one study on death or hospitalization in the intensive care unit), this study considers using a model with random effects. Furthermore, considering the I^2 index (43%) and the high heterogeneity of the studies, the model with random effects is considered appropriate for this study. Additionally, the Galbraith diagram (Figure 3) indicates the presence of studies with outlier data among the overall studies. Furthermore, there was no evidence for publication bias in the funnel plot (Figure 4), as indicated by the Egger test (t=0.34, df=5, P=0.751). Also, the stability assessment of the results from the sensitivity analysis (Figure 5) shows that the OR value can vary between 1.07 and 1022 with the deletion of each study. Therefore, considering that the OR value is greater than 1, the probability of disease progression will be higher in individuals with a history of smoking.

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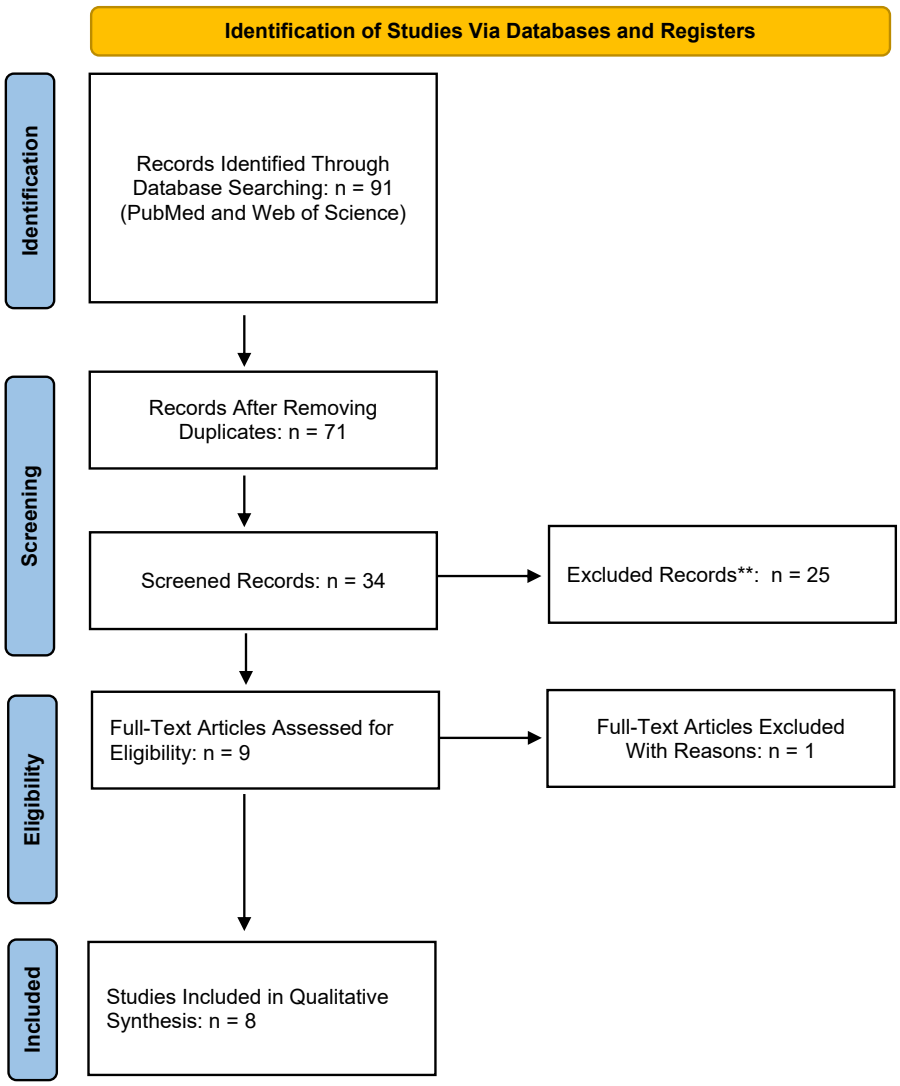

Figure 1. Prisma chart for search strategy

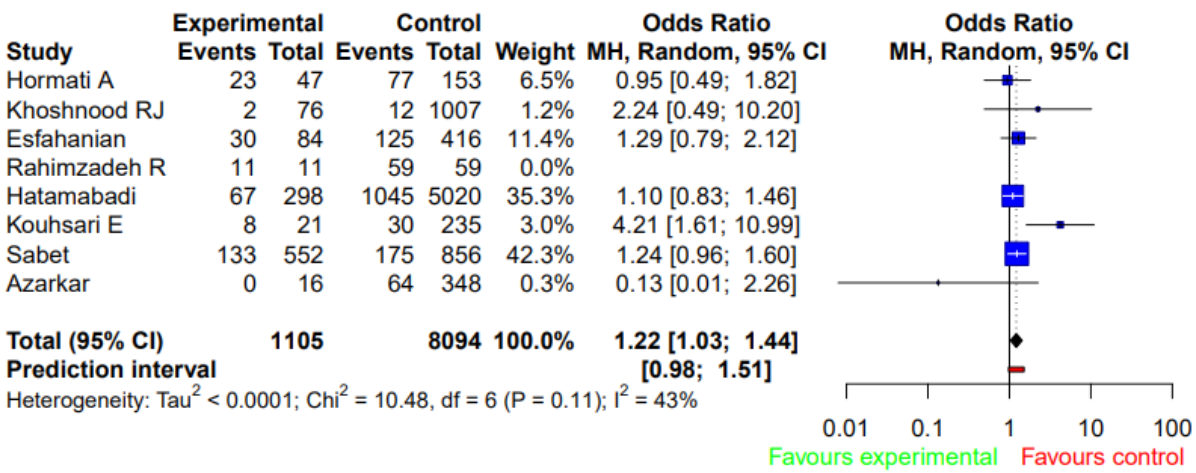

Figure 2. Association between smoking and COVID-19 mortality rate

CI: Confidence interval; OR: Odds ratio.

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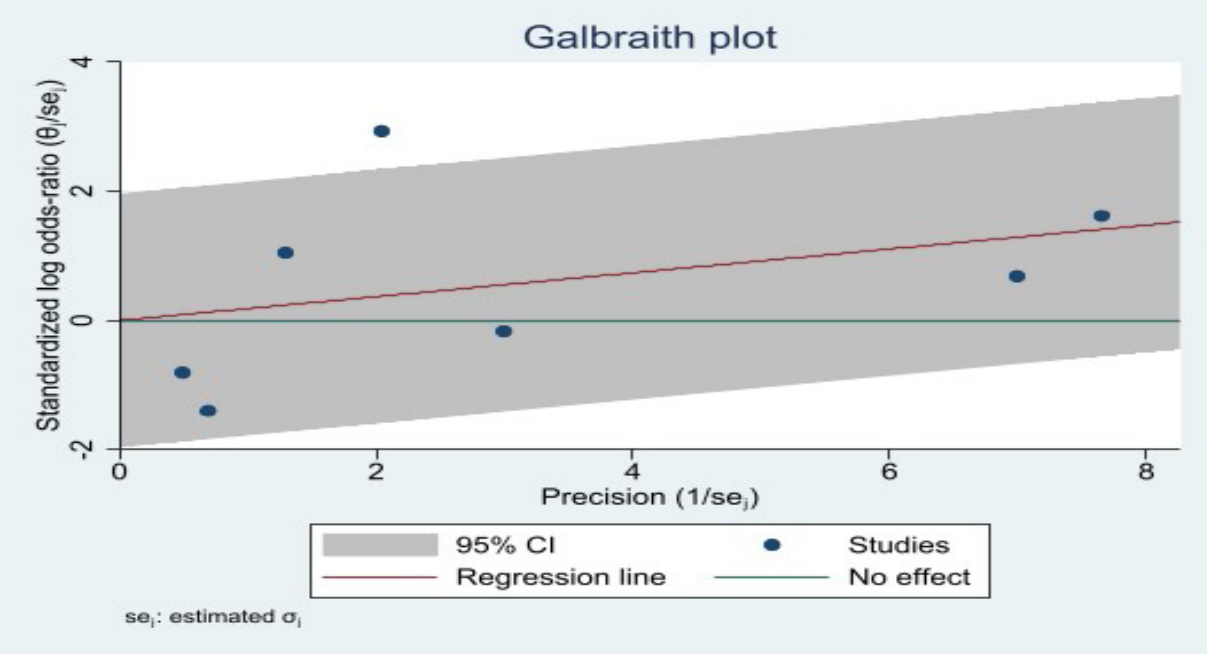

Figure 3. Galbraith diagram to assess the dispersion of studies and identify outlier data

Discussion

The induction of ACE2 receptors on the surface of parenchymal lung cells due to nicotine leads to increased entrance and proliferation of Coronavirus, leading to destructive effects [19-21]. Additionally, lead, another toxic compound in cigarette smoke, enhances immune response, including lymphocytes T Helper 2 (Th2). The induction of inflammatory cytokine production, particularly tumor necrosis factor (TNF-α) and interferon-gamma (IF-γ), because of Th2, leads to inflammation and stimulation of the immune system [22, 23]. The cytokine storm caused by the synergistic effects of nicotine and lead can destroy parenchymal lung cells [4, 24]. Smoking is a risk factor for the development of COVID-19. This finding was consistent with the study conducted by Patanavanich et al., which showed that smokers have a higher risk of severe COVID-19 (1.91 times) compared

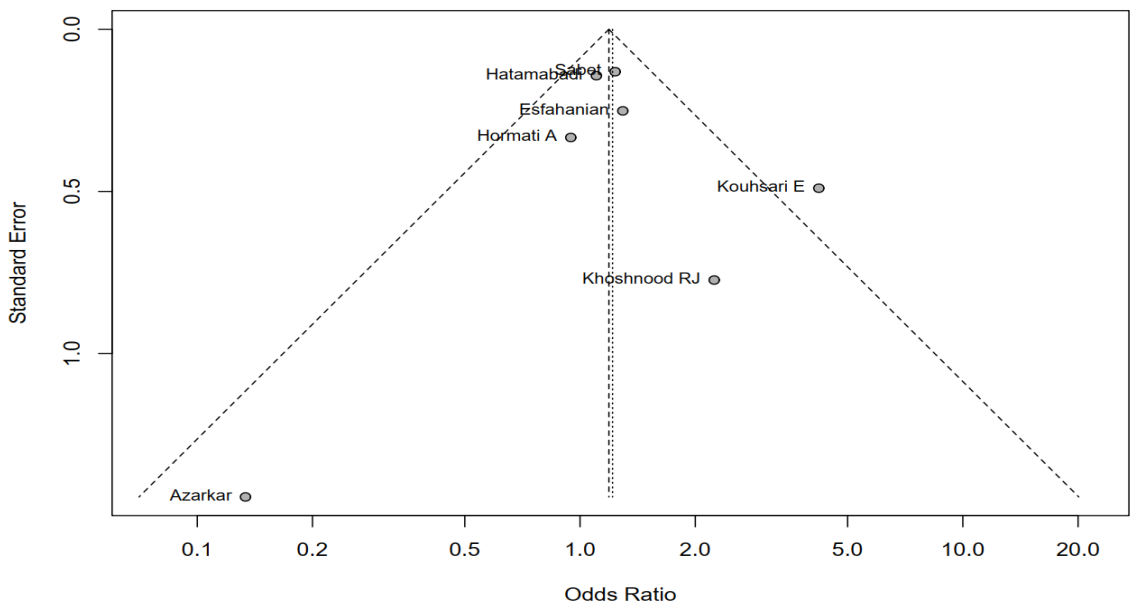

Figure 4. Funnel plot to check publication bias

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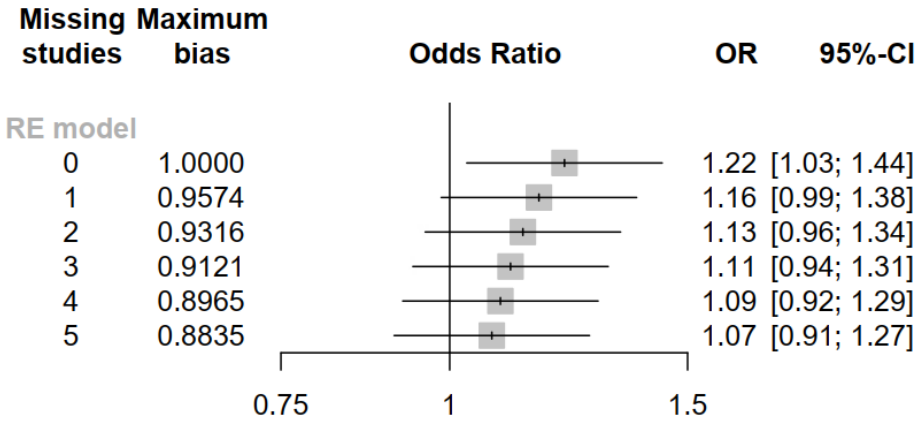

Figure 5. Sensitivity analysis for importance assessment

to non-smokers [25]. However, a meta-analysis review conducted by Lippi et al. on five studies using a non-standard method for calculating meta-analysis showed no association between smoking and the development of COVID-19 [26]. The probable explanation for the low prevalence of smoking in COVID-19 patients is that smoking evaluation during the COVID-19 pandemic has been lower than before.

Conclusion

This review study showed that the chances of contracting COVID-19 or its harmful effects are higher in smokers than in non-smokers. Therefore, it is necessary to provide predictive and warning solutions to quit smoking and incentives and economic support to communities from governments or non-governmental organizations to quit smoking and reduce deaths caused by COVID-19.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by Hormozgan University of Medical Sciences (Code: IR.HUMS.REC.1402.083).

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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