

## **Tobacco and COVID-19: A Systematic Review for Public Health Implications**

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### **Abstract**

**Introduction:** Tobacco users are at higher risk for respiratory infections and estimated to be at increased risk for Covid-19 as well. Despite that and during the COVID-19 pandemic, there are conflicting data regarding clinical outcomes for smokers with Covid-19 and the susceptibility to infection compared with non-smokers. This systematic review assessed, highlighted, and discussed the possible biases and gap of the current knowledge from the available peer-reviewed literature that showed the association between smoking and level of COVID-19 severity. This will help to increase the level of awareness among the general population and health providers by addressing the importance of evidence-based medical practice, and the impact of compliance with the principles of risk communication in combating the myths and misinformation that sourced from researches with poor-quality through the commercial media.

**Methods:** The study aimed to assess the association between using Tobacco and COVID-19 outcomes that include the severity of symptoms or signs, the need for hospitalization, the Intensive Care Unit, and intubation. The searching was between December 2019 and September 2020, through Google Scholar, MEDLINE, EMBASE, Cochrane Library, and WHO Global Database to identify clinical studies suitable for inclusion and exclusion criteria. The registration number of the present study on PROSPERO is (CRD42020216062).

**Results:** The 15 selected studies are recording 14 867 hospitalized patients of COVID-19, and 3088 (20.7%) of them were reported with smoking history (Former and current smoker) and 11779 (79.3%) never smokers or unspecific smokers (not reported as smoker nor never smoker in the relevant study). The prevalence of current smoking in patients with severe or critical COVID-19 was 14.5%, while severe COVID 19 in nonsmokers was 65.5%. Patients with whatever smoking history are at risk to severe COVID-19 and bad in-hospital outcomes.

**Conclusions:** Claims that smoking is protective in COVID-19 can be risky to public health and should be addressed with high caution by the medical field and the general population, the researchers and the media have a responsibility about communicating the preliminary results that may have a non-evidence-based approach, inducing bad behaviors, and covered by commercial agendas from

**Keywords:** Tobacco Users; Smokers; COVID 19; Public Health; Risk Communication

### Abbreviations

HCW: Health Care Workers; MOH: Ministry of Health; COVID 19: Coronavirus Disease 2019; WHO: World Health Organization (WHO); CDC: Center for Diseases Control and Prevention

### Introduction

Coronavirus disease 2019 (COVID-19) is a newly emergent of viral respiratory tract infection caused by a coronavirus, SARS-CoV-2, that had recognized in Wuhan, China, since December 2019 [1]. In March 2020, the World Health Organization (WHO) declared the COVID-19 outbreak as pandemic health condition and international public health crisis. Therefore, all countries were required to take action in detecting infection and preventing spread [2]. As of 13 September 2020, the WHO reported 916,955 deaths caused by COVID-19 [3].

According to WHO, the number of recovered COVID-19 cases reached up to 80% of confirmed cases without needing special treatment and approximately one out of every 6 people who contract COVID-19 will become very sick and develop breathing difficulties [1,2]. Furthermore, updated researches [4-6] indicated that older people, and those with comorbid medical conditions like metabolic syndrome, heart and lung problems, renal diseases, or cancer, are at greater risk of developing serious illness of COVID 19. However, COVID-19 is a new disease with clearly limited information regarding risk factors of severity condition, and anyone can catch COVID-19 and become seriously ill.

Using the tobacco products is an epidemic preventable risk factor and one of the high prevalent public health problem, causing death for more than 8 million people every year around the world [7]. All types of tobacco are harmful without safe level of exposure [8]. Moreover, there is consensus about the nicotine contained in tobacco that considered very addictive and risk factor for respiratory and cardiovascular diseases [9,10]. Moreover, many researches highlighted the association between the tobacco and different types or subtypes of cancer [11,12], and different debilitating health conditions.

Smoking has adverse effects on lung in structure and functional aspects, thus impairing lung defenses against infection [13-15]. Therefore, Tobacco users are at higher risk for respiratory infections and assumed to be at increased risk for Covid-19 as well. Despite that and during COVID-19 pandemic, there are conflicting data regarding clinical outcomes for smokers with Covid-19 and the susceptibility to infection compared with non-smokers. Different articles indicate that SARS-Cov-2 infection rate is lower among smokers and lower in compared with the general population [16]. Recently, some mechanistic studies carried out to assess the association between nicotine and the main receptor used by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to enter the host mucosa and lead to active infection. Some of these studies assume that the increased susceptibility to infection might be attributed to the upregulation (increased gene expression) of the angiotensin converting enzyme 2 (ACE2) receptor [17,18]. On other hand, a French study suggests that smoking might have a protective effect against SARS-CoV-2 infection, through interaction with the acetylcholine receptor [19,20].

A review released by the World Health Organization that addressed the conflicting results of the available updated studies, and the gap of knowledge between smoking and the risk of SARS-CoV-2 infection and related disease severity, emphasizing the need for well-organized updated studies to assess the association between smoking and COVID-19 [20].

This systematic review will assess, highlight and discuss the possible biases and gap of the current knowledge from the available peer-reviewed literature that showed the association between smoking and level of COVID-19 severity. This will help to increase the level of awareness among the general population and health providers by addressing the importance of evidence-based medical practice, and the impact of compliance with the principles of risk communication in combating the myths and misinformation that sourced from researches with poor-quality through the commercial media.

## Materials and Methods

### Primary objectives

To assess the association between using of Tobacco and COVID-19 outcomes that include the severity of symptoms or signs, the need for hospitalization, Intensive Care Unit and intubation.

### Secondary objectives

Review the recommendations that delivered from scientific sources of updated information in order to prevent delivering the false information.

The present systematic review recorded and registered in the International Prospective Register of Systematic Reviews (<https://www.crd.york.ac.uk/Prospero>; registration number: CRD42020216062).

### Study search strategy

The electronic search for articles and papers by using Keywords and phrases provide the foundation for searching, and derived from the review objectives ['smoking' OR 'tobacco' OR 'risk factors' OR 'smoker\*'] AND ['COVID-19' OR 'COVID 19' OR 'novel coronavirus' OR 'sars cov-2' OR 'sars cov 2'].

The searching was through Google Scholar, MEDLINE, EMBASE, Cochrane Library, and WHO Global Database to identify clinical studies that meet with inclusion and exclusion criteria.

### Inclusion and exclusion criteria

Types of participants were patients with COVID-19 who are user or former user of any tobacco products. Types of outcome measures were any indication of severity: hospitalization- ICU admission or severe symptoms of COVID-19.

Inclusion criteria were as follows: (i) English language studies that examined COVID-19 patients; (ii) Quantitative studies (cross-sectional, prospective, or retrospective studies); (iii) studies that compared between smokers with mild and severe COVID-19; (iv) studies comparing smokers between survivors and non-survivors of COVID-19; and (v) studies comparing smokers who developed COVID-19 and indicated for intensive-care unit (ICU) and smoker who were on non-ICU treatment. Exclusion criteria were as follows: (i) Un published studies or lacking a full text (unavailable or not yet published, (ii) studies of non-English-language, (iii) editorial letters, (iv) reviews, (v) case reports or series.

### Data extraction

As an initial database search, a researcher (Hani Saad) reviewed the study titles and abstracts. There were two groups (14 researchers, seven for each) and two independent researchers from each group who assessed the full text of these articles for filtration whether they met study inclusion criteria or not. Any conflicts were discussed and resolved by a third investigator.

Data from each included study extracted and managed based on data extraction tool that had the following information (Authors, Study period/publication year, study setting, Study design, sample size, No. of current smokers and former smoker/never smoker and unspcific).

**Assessment of methodological quality**

The research incorporated a process of critical appraisal to assess the quality of the methodology of each study and to identify the possibility of bias in its design, conduct and analysis. However, two researchers evaluated the selected articles by using scale of study quality and risk of bias named the Newcastle- Ottawa scale (NOS)<sup>(21)</sup> This scale evaluates three aspects of each study: (i) selection (0 to 4 points), (ii) comparability (0 to 2 points), and (iii) detection of the outcome of interest (0 to 3 points). According to the collected total score, the study quality was categorized as follows: 0-3 points (poor), 4-6 points (fair), and 7- 9 points (Good).

**Data synthesis**

The reviewers synthesized the extracted data from included studies in line with the methods used for data collection and the included study designs. The data presented in narrative and tabular summary approach.

**Study plan and ethical consideration**

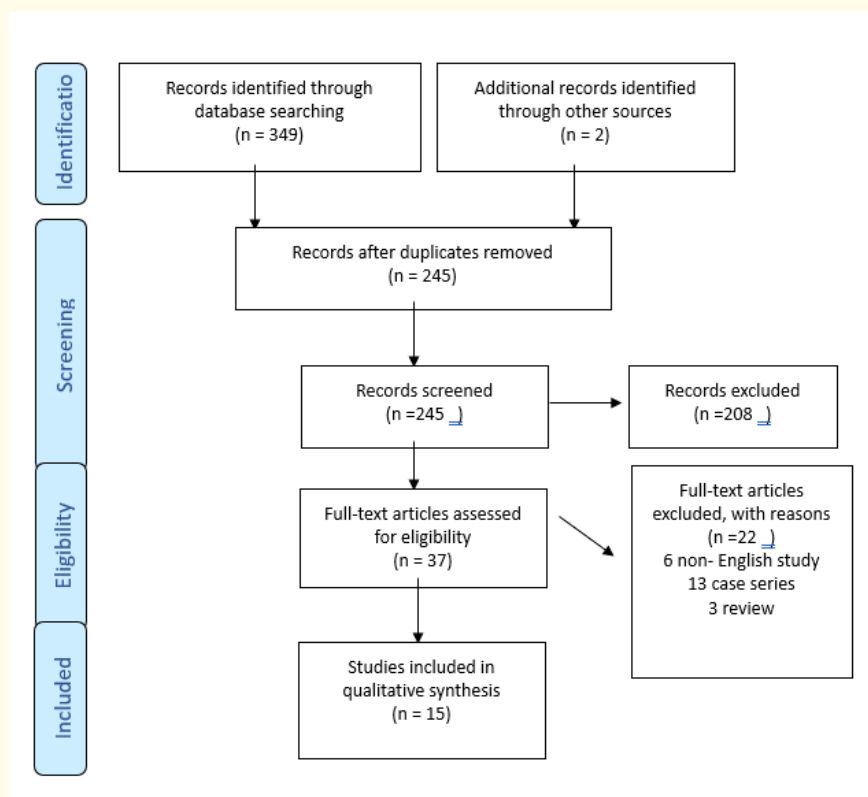
This research study recruited research studies who fulfill the criteria during the period from 2019 until the end of October 2020. Data collection started after getting permission from the ethical and scientific committee of King Abdullah International Medical Research Center Ethics and Scientific Committee. The authors or the reviewers of this research followed the pre- designed protocol in terms of data extraction and data synthesis from high quality research and they got training courses in critical appraisal.

**Results and Discussion**

**Results**

The initial search yielded 351 papers. The screening of their titles and abstract ruled out 106 duplicated articles and 245 articles remained. However, 37 articles met the inclusion criteria after evaluation of 245 articles for eligibility and appropriateness. A 22 of 37 studies met the exclusion criteria after reviewing the full texts. Finally, 15 studies had met all the inclusion criteria and included in the present study.

The relevant PRISMA study flow chart is shown in figure 1. A quality assessment of the selected articles are available in table 1.



**Figure 1:** Flow Diagram of Study Selection Procedures.

	Study setting	Study design	No. of centers	Study period	n	No. of current smokers and former smoker/ never smoker and unspecified	Study quality
Alharthy, <i>et al.</i> [22]	Saudi Arabia	Retrospective Cohort	1	March-May 2020	352	174 / 352	Good
Ziyad Almalki, <i>et al.</i> [23]	Saudi Arabia	Retrospective cross section	1	March-May 2020	458	64 / 458	Poor
Zhou, <i>et al.</i> [24]	China	Cohort	2	Dec-Jan 2020	191	11/180	Good
Azar, <i>et al.</i> [25]	United States	Cohort	24	Jan-Apr 2020	1052	200/852	Fair
Bhargava, <i>et al.</i> [26]	United States	Cohort	1	Mar-Apr 2020	197	11 / 186	Good
Guan, <i>et al.</i> [27]	China	Cohort	552	Dec-Jan 2020	1099	137 / 948	Poor
Hur, <i>et al.</i> [28]	United States	Cohort	10	Mar-Apr 2020	486	16/ 470	Good
Klang, <i>et al.</i> [29]	United States	Cohort	5	March-May 2020	3406	793 / 2613	Good
Kuderer, <i>et al.</i> [30]	United States, Canada, and Spain.	Cohort	3	March-May 2020	928	369/559	Fair
Liu, <i>et al.</i> [31]	China	Cohort	3	Dec-Jan 2020	78	5/73	Good
Petrilli, <i>et al.</i> [32]	United States	Cohort	4	March-May 2020	5279	1190/ 4089	Good
Shi, <i>et al.</i> [33]	China	Cohort	1	Feb 2020	487	40 / 447	Good
Toussie, <i>et al.</i> [34]	United States	Cohort	1	Mar-Apr 2020	338	51 / 287	Fair
Yu, <i>et al.</i> [35]	China	Cohort	24	Jan-Mar 2020	421	13 / 408	Good
Yu, <i>et al.</i> [36]	China	cross section	2	Jan-Feb 2020	95	8 / 87	Good

**Table 1:** Characteristics of Included Studies.

### Features of the included studies

The 15 included studies represented 14 867 hospitalized COVID-19 patients, and 3088 (20.7%) of them were reported with smoking history (Former and current smoker) and 11779 (79.3%) never smokers or unspecified smokers (not reported as smoker nor never smoker in the relevant study). Among the severe or critical patients, patients with history of smoking ranged from 5.2 to 72.1% (average: 25.5%). While 15 studies provided current smoker information and nine provided only historical smoking information. All of the included studies were retrospective. There were ten multicenter studies and five single-center studies.

The half of studies investigated a Chinese population, with the United States contributing seven studies and two studies carried out in Saudi Arabia. Overall, study quality was good in ten studies, fair in three and poor in two. A summary of the studies included in the present study is available in table 1.

**History of smoking and covid-19 severity**

Nine studies only provided the historical smoking information. Table 2 shows (11.8%) as the prevalence of patients with history of smoking among mild to moderate (non-severe) COVID-19 patients while among severe and critical cases was (24.9%). This clearly demonstrates a significant relationship between patients with history of smoking and severity of COVID-19.

Authors	Non Severe COVID-19 With History of Smoking			Severe COVID-19 With History of Smoking		
	Event	Total	%	Event	Total	%
Zhou., <i>et al.</i> [24]	6	137	4	5	54	9
Azar., <i>et al.</i> [25]	63	256	24.6	28	110	25.5
Guan., <i>et al.</i> [27]	12	913	1.3	9	172	5.2
Hur., <i>et al.</i> [28]	108	348	31	55	138	39.9
Kuderer., <i>et al.</i> [30]	27	326	8.3	235	326	72.1
Liu., <i>et al.</i> [31]	2	67	3	3	11	27
Petrilli., <i>et al.</i> [32]	337	2538	13.3	565	2741	20.6
Shi <i>et al.</i> [33]	34	438	7.8	6	49	12
Toussie., <i>et al.</i> [34]	27	202	13	24	136	18
Total	616	5225	11.8	930	3737	24.9

**Table 2:** The Relationship Between History of Smoking and the Severity of COVID-19.

**Smoking status and covid-19 severity**

Current smoking prevalence in patients with severe or critical COVID-19 was 14.5%, while severe COVID 19 in nonsmokers was 65.5% (Table 3). This may attributed to the presence of other risk factors in non-smokers severs COVID 19 patients.

Authors	Current Smokers with Severe COVID-19			Nonsmokers with Severe COVID-19		
	Event	Total	%	Event	Total	%
Alharthy., <i>et al.</i> [22]	109	239	45.6	130	239	54.4
Ziyad Almaliki., <i>et al.</i> [23]	8	27	29.6	19	27	70.4
Zhou., <i>et al.</i> [24]	6	137	4	5	54	9
Azar., <i>et al.</i> [25]	6	110	5.5	66	110	60
Bhargava., <i>et al.</i> [26]	6	74	8.3	68	74	91
Guan., <i>et al.</i> [27]	29	172	16.9	134	172	77.9
Hur., <i>et al.</i> [28]	55	138	39.9	83	138	60
Klang., <i>et al.</i> [29]	492	2270	21.7	1778	2270	78.3
Kuderer., <i>et al.</i> [30]	16	43	37	201	469	43
Liu., <i>et al.</i> [31]	3	11	3.4	8	11	72.7
Petrilli., <i>et al.</i> [32]	147	2741	5.1	1590	2741	58
Shi., <i>et al.</i> [33]	6	49	12	43	49	88
Toussie., <i>et al.</i> [34]	24	136	18	82	136	60
Yu., <i>et al.</i> [35]	0	64	0	64	64	100
Yu., <i>et al.</i> [36]	5	73	13	68	73	93
Total	912	6284	14.5	4339	6627	65.5

**Table 3:** The Relationship Between Smoking Status and the Severe COVID-19.

## Discussion

It is well recognized that using of tobacco is associated with mortality and morbidity among several respiratory infections. However, the claims that stated the protective characteristics of nicotine against severe symptoms and complications of COVID 19 were supported by underreporting the active smokers among patients with COVID-19 of results from recent studies of. The present systematic review identified 15 studies from the available peer-reviewed literature that showed the association between smoking and level of COVID-19 severity.

Overall, there are low degree of heterogeneity between studies investigating a history of smoking and medium to high degree of heterogeneity among the studies evaluating the effects of current smoking. Regarding the COVID 19 patients with a smoking history, there is an increased risk of presentation to hospital with severe, as well as severe or critical, COVID-19 and subsequent increased risk of mortality. Moreover, these patients were more likely to have disease progression and need mechanical ventilation. This finding is similar with the results of meta-analysis study included 47 studies with a total of 32,849 hospitalized COVID-19 patients and concluded that a history of smoking was associated with severe COVID-19 (RR: 1.31; CI: 1.12 - 1.54;  $p = 0.001$ ), severe or critical COVID-19 (RR: 1.35; CI: 1.19 - 1.53;  $p < 0.0001$ ), in-hospital mortality (RR: 1.26; CI: 1.20–1.32;  $p < 0.0001$ ), progression of COVID-19 (RR: 2.18; CI: 1.06 - 4.49;  $p = 0.035$ ), and need for mechanical ventilation (RR:1.20; CI: 1.01–1.42;  $p=0.043$ ) [37].

A paradoxical finding of the present study is the prevalence of current smoking, the present study revealed that severe or critical COVID-19 patients who were active smokers was lower than severe COVID 19 in nonsmokers. Majority of the studies revealed the low prevalence of active smokers among hospitalized patients with COVID-19 [22-36]. Another meta-analysis study of 13 studies with a total of 5960 patients showed that the prevalence of smokers among hospitalized COVID-19 patients in China was 6.5% (95% CI 4.9% to 8.2%) which is considered less than the prevalence of active smokers in the general population of China (26.6%) [38,39]. The way of expression and declaring this outcome was unscientific from media; they concluded that smoking and/or nicotine might be protective against COVID-19 while patients with COVID 19 who actively smoking were not associated with a significantly increased risk of severity compared with nonsmokers. However, and upon reviewing the included studies in the present systematic review, the majority of studies were not statistically adjust the effect of smoking for baseline covariates like demographic factors or other risk factors of COVID 19 and thus make this comparison is not appropriate between the prevalence of smoking in hospitalized COVID-19 patients with overall population estimates.

Lastly, the current study set a secondary objective of reviewing the recommendations that delivered from recognized sources of updated information. The authors of the present study agreed to review three website resources as follows: World Health Organization (WHO), Center for diseases control and prevention (CDC) and Saudi Ministry of Health (MOH).

- WHO recommends that tobacco users to stop using tobacco and activate the evidence based interventions to quit include hot lines, mobile text-messaging cessation support programs, nicotine replacement therapies and cognitive behavioral therapy [20].
- CDC is considering the current smokers or former cigarette smokers are increasing their risk of severe illness from COVID-19 and CDC always advise the public “If you currently smoke, quit. If you used to smoke, do not start again. If you’ve never smoked, don’t start.” [40].
- Saudi MOH has warned about the bad health effects of smoking on the individual and public, indicating that the smokers are included with the most vulnerable groups to have the complications of (COVID-19) [41].

## Conclusion

Patients with any smoking history are at risk to have severe COVID-19 and bad in-hospital outcomes. Public decision-makers responsible to provide the therapies, preventative, and supportive strategies to reduce morbidity and mortality and they must ensure that public health practices are adherent to the principles of the WHO Framework Convention on Tobacco Control. Claims that smoking is protective in COVID-19 can be risky to public health and should be addressed with high caution by the medical field and the general population, the researchers and the media have a responsibility about communicating the preliminary results that may have a non-evidence-based approach, inducing bad behaviors, and covered by commercial agendas from Tobacco companies.

## Conflict of Interest

There is no Financial Interest or any Conflict of Interest Exists.

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