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Correlation of Smoking Habit and COVID-19 infection

Assist prof. Dr. Abbas F. Hlaihel, Assist prof Dheyaa Khalf Al-Omer

University of Th-Qar, College of medicine, Iraq

Abstract

Background

Covid-19 is an acute infection caused by novel corona virus called SARS-Cov2 and is consider a major global health disaster causing millions of infected and dead people all over the world

The age ,gender and smoking habit is well recognized risk factors for many diseases including respiratory disease

Their relation to COVID -10 infection is still controversy a though there is a lot of studies that try to clarify theses relatinship

Aim of Study

Study of correlation of smoking habit with COVID-19 infection in Thi-Qar province in the south of Iraq and evaluate sex and age in studied group

Patients and Methods

Retrospective analytic study of smoking habit in of 325 patients with COVID -19 in thi-Qar province in different centers of isolation prove by PCR testing and or CT findings consist with diagnosis of COVID-19.The control group include 329 healthy persons with PCR negative

Result and Discussion

In our study two third of patients with COVID-19 are men [66.5%] this difference can explain by small number of size and social factors that limited the movement of female in community. In our study two third of severe COVID-19 are men [81:41] this go with most of studies that showed that the outcomes of illness were worse for men than women. In our study the mean age of COVID-19 patients in 46 which little pit less than mean age reported at early months COVID pandemic but later the mean start to dropping reaching in USA 34

In our study mean age of patients with severe COVID-19 is 53.2439 while for moderate one is 49.0256 and for mild COVID-19 patients is 36.8871 with highly significant P value 0.000. Active smoking seen in 81 [24,6] of control group while seen only in 43 [13.2 %] in patients with covid-19 with highly significant value P value 0.0001

In this study most of cases of severe COVID are non smokers 84 and 26 are x-smoker while only 13 are active smoking with highly significant difference P value 0.000. A lotof studies revealed an unexpected low number of current smokers among subjects tested for SARS-CoV-2 infections[1]. The prevalence of current smokers suffering from symptomatic COVID-19 was frequently significantly lower than in the general population. Current smokers were at reduced risk of being tested positive compared to former smokers and never smokers, which might have been caused by different testing frequencies, but were at higher risk for severe symptomatic COVID-19[1]. This low prevalence of current smokers among COVID-19 patients led to the hypothesis that smoking/ nicotine uptake might have a preventive effect.

Conclusion

The COVID -19 is more infect men than women and infected men are more severe than infected women. The mean age is 46 which show dropping in comparison to early report that show mean age is 49. the low prevalence of active smoking in COVID-19 and there inverse relationship to severity of COVID-19.

key words: COVID-19.smoking .SARS-Cov2.age.gender

Introduction

COVID-19 epidemic is the major global health disaster today and the supreme challenge to the universe. It is caused by new corona virus called SARS-Cov2 and it extremely transmissible causing million of infected and dead individuals [1.]

Data collected from many countries around the world suggest that men and women are equally likely to acquire COVID-19, global study confirms men at higher risk for COVID-19 complications, death. Men and women have a nearly equivalent risk of COVID-19 infection, but men are about 40 percent more likely to die [2]

At global level for each 10 cases in women there is 11 cases ,for each 10 women admitted to hospital there is 12 male admitted to hospital m for each 10 women admitted to ICU there is 19 men admitted and for each ten confirmed death due to COVID -19 in women there is 14 death in men [3]

Age is a major factor in determining the risk of severe illness outcomes. SARS-Cov2 infect all age group and many studies showed that the meaning age of infected person decreasing compared to the early stages of the COVID-19 pandemic and this decrease my reaching to more than 5 year reaching in some states in USA to 35 years old. [4]

The risk for severe illness with COVID-19 increases with age, with older adults at highest risk.

The greatest risk for severe illness from COVID-19 is among those aged 85 or older. Older adults are at greater risk of requiring hospitalization or dying if they are diagnosed with COVID-19. in the USA 8 of 10 deaths due to COVID-19 have been noted in adult aged 65 and more [5]

Ageing is associated with certain changes in pulmonary physiology, pathology and function, during the period of lung infection. In addition to presence of co-morbid illness and poly pharmacy [6]

The adverse effects of smoking are well-recognized. smoking causes 8 million deaths every year related to cardiovascular diseases, lung disorders, cancers, diabetes, and hypertension. Smoking tobacco is also a well-known risk factor for severe disease and death from many respiratory infections [7,8 9,10,11]

The role of smoking and risk of COVID -19 is still not clear

Most of data published so far reported that COVID-19 patients show a very low prevalence of smokers, with no significant association between current smoking and severe disease in COVID-19 patients [12]

The new study, report up regulation of pulmonary ACE2 (angiotensin-converting enzyme 2) gene expression in ever-smokers compared with nonsmokers in several transcriptomic data sets of lung samples from healthy never- and ever-smokers and patients with chronic obstructive pulmonary disease. Also, they report an increase in ACE2-producing goblet cells in ever-smoker versus never-smoker lungs. These findings have putatively important implications for patients with COVID-19 because ACE2 has been shown to be the receptor used by SARS-CoV-2 to enter the host cells and yet seem in contrast with the consolidated epidemiological data worldwide indicating a low prevalence of active smokers among patients with COVID-19. Cigarette smoke induces epigenetic modifications of the bronchial epithelium, leading to mucous (goblet) cell metaplasia. As goblet cells are a major source of ACE2 in the lung, this could, in part, justify the increased levels of ACE2 found by Cai and colleagues in lungs of smokers. However, goblet cells are also the main source of mucous, which provides an essential first host barrier to inhaled pathogens that can prevent pathogen invasion and subsequent infection.

Additional factors could play a role in the interaction between active smoking and SARS-CoV-2.

First, naturally occurring structural changes in the ACE2 allelic variants can interfere with the intermolecular interactions of such variants with SARS-CoV-2 spike protein [4.] It is conceivable that, upon cigarette smoke (or nicotine?) stimulation, some ACE2 allelic variants that inhibit the SARS-CoV-2 binding may undergo positive selection.

Second, nicotine interacts with many components of the RAS (renin–angiotensin system) in multiple organ systems. In the ACE/AT-II (angiotensin II)/AT_1R (angiotensin$_1$ receptor) arm, nicotine increases the expression and/or activity of renin, ACE, and AT_1R, whereas, in the compensatory ACE2/angiotensin (1–7) arm, nicotine down regulates the expression and/or activity of ACE2 and AT_2R [5.] How these findings fit with the ones from Cai and colleagues is worth investigation. Interestingly, activation of nicotinic receptors can lead to enhanced protease activation that may cleave and activate the spike protein of SARS-CoV for membrane fusion [5.] This effect may counterbalance the increase in ACE2 levels observed in the lungs of smokers by Cai and colleagues.

Third, ACE2 knockout mice exposed to cigarette smoke exhibit increased pulmonary inflammation with activation of metalloproteinases [6] that could, in part, contribute to the inactivation or modification of ACE2 in the lungs of the smokers.

Last, though it is possible that cigarette smoke increases the ACE2 expression by the bronchial epithelium, thus facilitating the entry of SARS-CoV-2, this does not necessarily translate into a higher risk for developing COVID-19 pneumonia.

Aim of Study

TO evaluate the correlation of smoking habit with COVID-19 infection in Thi-Qar province in the south of Iraq and evaluate sex and age in studied group

Patients and Methods

Retrospective analytic study of 325 patients with COVID -19 in thiqar province in different

centers of isolation hospital prove by PCR testing and or CT findings consist with diagnosis of COVID-19

Age . sex and smoking habit and severity are recorded

The control group include 329 healthy persons with PCR negative and age , sex and smoking habit are also recorded,

Ethical consent are taken from patients and control group orally

Data analysis was done by statistical package for social science (SPSS) version 22 for percentage and frequencies. Fisher extract test were used for study association, Correlation between variables was analyzed using Pearson equation, P value of less than 0.05 was considered statistically significant

Results

Table (1) Sex Distribution of Patients with COVID-19

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	109	33.5	33.5	33.5
	male	216	66.5	66.5	100.0
Total		325	100.0	100.0	

Table (2) Sex Distribution among Control Group

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	FEMALE	97	29.5	29.5	29.5
	MALE	232	70.5	70.5	100.0
Total		329	100.0	100.0	

Table (3) Sex Correlation between Control and Covid-19 Patients

			Sample			X^2
			Control	cases	Total	P
Gender	Female	Count	97	109	206	1.246[a]
		% within	47.1%	52.9%	100.0	

		gender			%	
	Male	Count	232	216	448	.264
		% within gender	51.8%	48.2%	100.0 %	
Total		Count	329	325	654	
		% within gender	50.3%	49.7%	100.0 %	

In this study 216 [66.5%] of patients with COVID-19 are male and 109 [33.5] are female as seen in Table 1while 232 [70.5%] of control group are male and 97 [29.5%] are female as seen in Table 2 with no significant difference P value 1.246 as seen in table 3

Table (4) Distribution of Smoking Habit According to Sex

Sex	Active smoker	X-smoker	Non-smoker	total
Male	39 [16.9%]	30 [14.8%]	147 [68.3%]	216
Female	3 [2.7%]	10 [9.4]	96[87.9%]	109

In this study thirty nine male are active smoker 16.9% while 147 [are non smoker [68.3%] and 30 are X-smoker [14.8%] while only three female are active smokers [2.7%] and 96 are non smoker[87.9%][and ten are x-smokers as seen in Table 4

Table (5) Distribution of Severity of COVID-19 According to Sex

Sex	Mild	Moderate	Severe	Total
Male	77	57	82	216
Female	48	20	41	109

In this study eighty one patients with severe COVID-19 are male while only forty one are female while 57 male are moderate while 20 female are moderate as seen in Table 5.

Table (6) Mean Age of Control and COVID-19 Patients

Group Statistics							
	VAR00001	**N**	**M.**	**Std. Dev.**	**M. Diff.**	**T**	**Sig. (2tailed)**
age	Contrll	329	34.1368	15.49084			
	Cases	325	45.9908	14.45160	-11.85399	-10.116-	.000
					-11.85399	-10.120-	.000

In this study mean age of patient with COVID-19 is 45.99 [11.853 year older] than the mean age of control group 34.136 years with high significant P value 0.000 as seen in table 6

Table (7) Mean Age of Patients with COVID-19 and Severity of the Ddisease

Mean Age of Cases					
Severity	**Mean**	**N**	**Std. Deviation**	**F**	**Sig.**
Mild	36.8871	124	10.12379	56.015	.000
Moderate	49.0256	78	13.12376		
Severe	53.2439	123	14.12261		
Total	45.9908	325	14.45160		

In this study mean age of patients with severe COVID-19 is 53.2439 while for moderate one is 49.0256 and for mild COVID-19 patients is 36.8871 with highly significant P value 0.000 as seen in the table 7

Table (8) Distribution of Severity among Patients with COVID-19

		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	mild	124	38.2	38.2	38.2
	Moderate	78	24.0	24.0	62.2
	severe	123	37.8	37.8	100.0

	Total	325	100.0	100.0	

In this study 123 [37.8%] of COVID-19 patient are severe while 202[66.2%] are mild to moderate in severity as seen in the table 8

Table (9) Smoking habit Distribution among Control Group

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	non smoker	248	75.4	75.4	75.4
	smoker	81	24.6	24.6	100.0
	Total	329	100.0	100.0	

Table (10) Smoking Habit Distribution in Patients with COVID-19

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	active	43	13.2	13.2	13.2
	non	236	72.6	72.6	85.8
	X	46	14.2	14.2	100.0
	Total	325	100.0	100.0	

In this study active smoking are seen in 81 [24.6%] in the control group and non –smoking are seen in 248 [75.4%] as seen in Table 9 while active smoking just seen in 43 [13.2%] of patients with COVID-19 while non-smoking and x-smoking are seen in 282[86.8%] as seen in Table 10

Table (11) Smoking Relation between COVID-19 and Control Group

			c. Smoking				X^2
			Active	non	X	Total	P
Control		No	81	248	0	329	696.581[a]
		%	24.6%	75.4%	0.0%	100.0%	
COVID-19 according to severity	Mild	No	22	98	4	124	
		%	17.7%	79.0%	3.2%	100.0%	0.0001
	moderate	No	8	54	16	78	

		%	10.3%	69.2%	20.5%	100.0%	
	severe	No	13	84	26	123	
		%	10.6%	68.3%	21.1%	100.0%	
Total		No	43	236	46	654	
		%	6.6%	36.1%	7.0%	100.0%	

Active smoking seen in 81 [24,6] of control group while seen only in 43 [16.6 %] in patients with covid-19 with highly significant value P value 0.0001 as seen in Tale 11

Table [12] Smoking Habit and Severity of COVID-19 Infection

			Severity				
			Mild	**Mode Rate**	**Severe**	**Total**	
Smoking	Active	No	22	8	13	43	
		%	51.2%	18.6%	30.2%	100.0%	21.160[a]
	Non	No	98	54	84	236	.000
		%	41.5%	22.9%	35.6%	100.0%	
	X	No	4	16	26	46	
		%	8.7%	34.8%	56.5%	100.0%	
Total		No	124	78	123	325	
		%	38.2%	24.0%	37.8%	100.0%	

In this study most of cases of severe COVID are non smokers 84 and 26 are x-smoker while only 13 are active smoking as seen in Tale 12 with highly significant difference P value 0.000as seen in table 12

Discussion

Man studiesall over the world showed that men and women are equally likely to acquire COVID-19, but men have a great risk of severe illness and death.[14]

In our study [66.5%] of patients with COVID-19 are men and [33.5] are women as while [70.5%] of control group are men and [29.5%] are women as seen with no significant difference P value 1.246

this difference can explain by small number of size and social factors that limited the movement of female in community

In this study 81 patients with severe COVID-19 are male while only 41 are female while 57 male are moderate while 20 female are moderate this go with most of studies that showed that the outcomes of illness were worse for men than women

I, men with COVID-19 are more likely to admittedto intensive care and they area high risk of death [14]

Many studies observed higher risk of mortality amongst males compared to females. Eight of them found male sex isassociated with increased risk of mortality from COVID-19. JustOne study found no significant association between male sex and mortality .

Sex-disaggregated COVID-19 mortality studies recogized a male patients with co morbidities as being at an increased risk of mortality worldwide. Further studiesrevealed differences in immune responsethat canexplained by sex hormones, angiotensin-converting enzyme 2 (ACE2) expression, and health behaviours as wellas other contributing factors to increased risk of mortality from COVID-19 among males. [15]

In our study thirty nine male are active smoker 16.9% while 147 [are non-smoker [68.3%] and 30 are X-smoker [14.8%] while only three female are active smokers [2.7%] and 96 are non-smoker[87.9%][and ten are x-smokers

The observations that smoking is more frequent among men than women, and that smokers are at higher risk of severe COVID-19 than non-smokers, are suggestive but not decisive[14.]

The ourstudy showed that mean age of patient with COVID-19 is 45.99 [11.8 year older] than the mean age of control group 34.136 years with high significant P value 0.000

COVID-19 can effect all anyage but the risk increase withincreased ageand median age is 49 but in late studied the

Median age is dropping specially in united state reaching in certain states to 35 [4,15]

In this study mean age of patients with severe COVID-19 is 53.2439 while for moderate one is 49.0256 and for mild COVID-19 patients is 36.8871 with highly significant P value 0.000

Studies have shown that age alone is therisk factor for severe disease, and generally this is the same with other coronaviruses and influenza viruses that affect the elderly."

He US Centres for Disease Control and Prevention has said that eight in 10 covid-19 related deaths reported in the country have been among people aged 65 years or over. Meanwhile, in the UK just being 70 years old or over puts someone into the medium risk covid-19 group[16]

In this study active smoking are seen in 81 [24.6%] in the control group and non –smoking are seen in 248 [75.4%] as seen in Table 9 while active smoking just seen in 43 [13.2%] of patients with COVID-19 while non-smoking and x-smoking are seen in 282[86.8%] as seen in Table 10 so in this study number of active smoker is less in COVID 19 patients in comparison to control group

Active smoking seen in 81 [24,6] of control group while seen only in 43 [16.6 %] in patients with covid-19 with highly significant value P value 0.0001 as seen in Table 11.

A lot ofstudies revealed an unexpected low number of current smokers among subjects tested for SARS-CoV-2 infections[1]. The prevalence of current smokers suffering from symptomatic COVID-19 was frequently significantly lower than in the general population. Current smokers were at reduced risk of being tested positive compared to former smokers and never smokers, which might have been caused by different testing frequencies, but were at higher risk for severe symptomatic COVID-19[1]. This low prevalence of current smokers among COVID-19 patients [17,18,19]

Other studies found an increased expression of ACE-2 in smokers, the entrance gate of the coronavirus into human cells [20,21]

Most of data for smoking and comorbidities (hypertension, diabetes mellitus, and chronic obstructive pulmonary disease) reported in 25 studies, and covid-19 which partially recognized a potentially beneficial effect of smoking/nicotine intake [22]

smoking cause down regulation of the expression of angiotens in converting enzyme 2 (ACE-2) as well as an inhibitory effect on the production of pro-inflammatory cytokines were identified as potential effects of exposure to nicotine [23].

In our study most of cases of severe COVID are non smokers 84 and 26 are x-smoker while only 13 are active smoking as seen in Tale 12 with highly significant difference P value 0.000

Five previousstudies have reported results that compatable with ourstudy ,showing no significant difference between patients with and without a smoking history in terms of COVID-19 severity [24,25,26,27,28]. In addition, a meta-analysis performed by Lippi et al. failed to find a relationship between active smoking and severe COVID-19 on Chinese patients, and another meta-analysis indicates that active smoking is not a predisposing factor for hospitalization

The present meta-analysis contained 16 studies and revealed that those with a history of smoking and active smokers had significantly increased risk for severe COVID-19(29). Previous studies have reported a similar result [30,31,32.]

Studydone by Vardavas and Nikitara, showed that smoking was associated with disease progression and adverse outcomes in COVID-19; In new studiespublished in the same time period, Lippi and Henry demonstrated no significant association between active smoking and COVID-19 severity .. A large study of the

general population of the UK showed that smoking was significantly associated with increased COVID-19 mortality after age and sex adjustment (OR 1.25 (1.12 to 1.40)) but the same study after adjustment for multiple additional covariates, the same study found that smoking was associated with a reduced risk for COVID-19 mortality (OR 0.88 (0.79 to 0.99)). This protective association remained consistent after several individual adjustments to the model [33-39]

Conclusions

- The covid-19 is more infect men than women and infected men are more severe than infected women
- The mean age is 46 which show dropping in comparison to early report that show mean age is 49
- The low prevalence of active smoking in COVID-19 and there inverse relationship to severity of COVID-19

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