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The Study of Biomarkers in Smokers Infected with Covid-19 in Basra, Iraq

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ABSTRACT

Background: The COVID-19 pandemic has heightened awareness of infectious illnesses and their links to host variables and underlying disorders.
Objectives: In this review, we look at current research on a possible link between smoking and COVID-19 and study the biomarker changes in patients.
Material and Methods: A case-control study included 45 smoker's patients with COVID-19 and 50 healthy subjects as a control group who visited Al-Basra Teaching Hospital and Allmwanei Hospital in Al-Basra province between October 2021 and February 2022. The age average for the study population was (25-80) years. Serum and blood levels of human CBC, ESR, CRP, Ferritin, D-Dimer, IL 6, Albumin, FBS, HbA1c, Troponin, Cholesterol, Triglyceride, HDL, LDL, VLDL, Creatinine, Urea, Uric acid and GFR were measured.
Results: The results show all biomarkers tend to have high sensitivity and specificity for smoker COVID patients based on the ROC curve analysis: Lymphocyte, CRP, Ferritin, D-Dimer, IL 6, Albumin, FBS, HDL, Creatinine, Urea, and GFR. These biomarkers might be helpful in determining the kind and severity of COVID-19 in smokers. Although the data is limited to a total number of patients.
Conclusion: Studying patient alterations and vital signs led to the conclusion that smoking and COVID-19 are related. It was also verified that all vital indicators had strong sensitivity and specificity for smoking COVID patients.

ARTICLE DETAILS

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1. INTRODUCTION

Coronavirus or SARS-CoV-2 a novel virus discovered in December 2019 Wuhan, China, which belongs to the genus beta-coronavirus and subgenus Sarbecovirus (1), it is a global pandemic spurred on by the coronavirus-transmitted infectious illness COVID-19 (2)(3). Particularly in older people, COVID-19 predominantly affects lung epithelial cells, leading to viral pneumonia and acute respiratory distress syndrome (ARDS). As a result, mortality is increased among senior individuals and those who have at least one comorbid condition (4). COVID-19, however, has been linked to more severe progression in COPD patients (5). Clinical signs of the 2019 coronavirus illness (COVID-19), which can vary from minor respiratory symptoms to severe pneumonia and is sometimes deadly, are exacerbated by cytokine release syndrome (CRS) or cytokine storm (6). It is important to keep in consideration that eight million people die from smoking each year in the world (7), in spite of any potential interactions with COVID-19, quitting smoking should be a top focus (8). Smoking may affect symptoms in a manner similar to how it influences the etiopathogenesis of COPD, And the main cause of death from COVID-19 is acute respiratory distress syndrome (ARDS) (9), which develops as a result of an exacerbated inflammatory response that releases pro-inflammatory cytokines such as interleukins (IL) and tumour necrosis factor-alpha (10). Comorbidities of various types are risk factors for severe coronavirus illness 2019 (COVID-19), Smoking's influence on COVID-19 severity has already been documented in many meta-analyses that were restricted by small sample numbers and inadequate methodology (11). Included were studies that reported the smoking status of hospitalized patients with varying degrees of illness severity and/or at least one clinical outcome of interest (disease progression, intensive care unit admission, requirement for mechanical ventilation, and death) (12). Patients with a history of smoking are more likely to develop severe COVID-19 and have poorer in-hospital outcomes (13).

This study aims to provide information and a database about verifying the relationship between risk factors and investigates biomarkers change and correlation coefficients in smokers infected with covid-19 patients in

Basra, Iraq, specifically in the General Allmwanei Hospital and Basra Teaching Hospital.

2. MATERIALS AND METHODS

2.1. Samples Collection

Participants in this study were 45 Smoker patients and 50 healthy subjects as a control group who visited Al-Basra Teaching Hospital and Allmwanei Hospital in AL Basra province between November 2021 and May 2022. The Age average for the study population was (25-80) years. Hospital specialists examined all patients in this study. The practical study portion was completed at Southern Technical University/ Basra's Department of Medical Laboratory Technology.

The blood samples were drawn with more than 5 ml of blood from both (patients and controls), and then about 1.8 ml of the blood was put into anticoagulant tubes containing sodium citrate. The sample was then separated by centrifugation at 3000 rpm for 15 minutes, and the plasma was then isolated and stored at a low temperature (-20 °C) until it was needed for analysis. ESR test tubes and EDTA-containing anticoagulant tubes are also available. Each patient's plasma and serum were divided among Eppendorf tubes and frozen Until the required number is completed and the laboratory examination begins. Too many individuals were excluded because they did not meet the inclusion criteria, such as patients with other diseases, such as hypertension, and all patients with hormonal imbalances, also, investigated verify the patient's information, age, gender, height, weight, vaccination or not, and the severity of the injury.

2.2. Statistical Analysis

Statistical analyses were performed in a statistical package for social sciences (SPSS) version 22. Means and SD were used for data representation, P-values ($P \leq 0.05$) are significant.

3. RESULTS

Table 1. Study groups and Basic characteristics of the participants according to gender and severity

Study Groups/ Age (year)	Groups number			Complication as a total number	
	Gender		Total number	Severity	
	Male	Female		Moderate	Severe
Control (not infected) Age = (30-80)	27	23	50	-------	-------
Smoker, age = (25-80)	45	-------	45	23	22

Table 2. Statistical (ANOVA) analysis of biomarkers as a total, number of COVID Smoker patients compared to the control group.

Biomarkers		Groups (Male ONLY)		*P*- value
		Control = 27	Smoker covid patients = 45	Control Vs Smoker covid patients
		Mean± SD	Mean± SD	
CBC	WBCs	7.29±3.55	9.55±5.43	0.999
	Lymp.	2.59±0.45	0.96±0.65	0.0001
	Plat	279.19±91.29	243.11±117.49	0.999
	Hb	13.29±1.45	11.67±2.72	0.073
ESR		12.04±6.24	57.22±32.69	0.0001
CRP		5.66±1.92	117.14±83.33	0.0001

Ferr	**100.50±82.25**	**701.45±563.12**	0.0001	
D-Dimer	**263.19±98.18**	**2722.77±3691.43**	0.001	
IL 6	**6.25±3.06**	**29.11±9.70**	0.0001	
Albumin	**3.76±0.75**	**2.88±0.57**	0.0001	
FBS	**97.70±8.77**	**157.27±46.87**	0.006	
HbA1c	**4.65±0.91**	**5.60±0.57**	0.009	
Troponin	**0.019±0.007**	**0.037±0.061**	0.999	
Cholesterol	**123.63±34.11**	**124.93±47.88**	0.999	
Tg	**128.27±49.21**	**122.54±68.51**	0.999	
HDL	**63.20 ± 10.94**	**30.11±12.41**	0.0001	
LDL	**60.70±35.15**	**75.04±41.10**	0.999	
VLDL	**21.22±5.37**	**22.70±11.19**	0.999	
Creatinine	**0.795±0.068**	**1.44±1.46**	0.169	
Urea	**25.93±4.67**	**72.65±57.99**	0.004	
Uric acid	**4.04±1.49**	**5.60±2.62**	0.293	
GFR	**109.15±10.89**	**76.04±30.87**	0.0001	

Table 3. Receiver-operating characteristic (ROC) curve analysis of biomarkers for smoker COVID patients as a total number.

Biomarker		**Area under the curve**	***P*- value (AUC =0.5)**	**Sensitivity %**	**Specificity %**	**PPV**	**NPV**
CBC	**WBCs**	0.585	0.152	27	94	80	59
	Lymp	0.953	0.0001	56	100	100	71
	Plat	0.619	0.046	20	96	82	57
	Hb	0.588	0.140	44	74	61	60
ESR		0.935	0.0001	87	86	85	88
CRP		1.000	0.0001	100	100	100	100
Ferr		0.950	0.0001	78	96	95	83
D-Dimer		0.932	0.0001	87	100	100	89
IL 6		0.999	0.0001	100	84	85	100
Albumin		0.858	0.0001	82	68	70	81
FBS		0.964	0.0001	69	100	100	78
HbA1c		0.775	0.0001	100	100	47	53
Troponin		0.564	0.283	9	100	100	55
Cholesterol		0.447	0.371	9	90	44	52
Tg		0.423	0.199	27	64	40	49
HDL		0.968	0.0001	98	8	49	80
LDL		0.538	0.529	20	78	45	52
VLDL		0.451	0.412	20	94	75	57
Creatinine		0.820	0.0001	27	100	100	60

Urea	0.896	0.0001	93	60	68	91
Uric acid	0.683	0.002	33	88	71	59
GFR	0.845	0.0001	78	82	80	80

Table 4. Nonparametric Spearman's statistical correlation coefficient for biomarkers in smoker covid patients

	Bio-markers	ESR	CRP	Ferr	D-Dimer	IL6	Albumin	FBS	HbA1c	Trop	Chol	Tg	HDL	LDL	VLDL	Creat	Urea	Uric acid	GFR
r value	**WBCs**	0.156	0.357	-0.111	0.277	-0.180	-0.124	-0.001	0.183	0.146	-0.091	0.009	0.117	-0.167	0.154	0.241	0.211	-0.002	-0.223
***P*value**		0.306	0.016	0.470	0.065	0.237	0.418	0.997	0.229	0.337	0.553	0.954	0.444	0.273	0.311	0.112	0.163	0.987	0.141
r value	**Lymp**	-0.209	-0.143	0.282	-0.105	0.387	0.047	-0.212	0.104	0.069	0.117	0.094	0.326	0.028	0.084	-0.087	-0.106	-0.050	0.141
***P*value**		0.169	0.349	0.061	0.491	0.009	0.758	0.162	0.496	0.654	0.443	0.537	0.029	0.857	0.583	0.568	0.488	0.744	0.357
r value	**plat**	0.389	0.346	-0.058	-0.137	0.235	-0.025	0.174	-0.036	0.060	0.261	0.072	0.133	0.185	0.184	0.013	0.005	0.074	-0.079
***P*value**		0.008	0.020	0.704	0.371	0.120	0.870	0.254	0.816	0.697	0.083	0.638	0.382	0.223	0.227	0.931	0.973	0.631	0.605
r value	**Hb**	-0.1	-0.3	0.0	0.0	-0.2	0.044	0.097	0.198	-0.0	0.294	0.018	0.218	0.332	-0.0	0.0	-0.1	-0.1	0.136
P value		0.249	0.035	0.590	0.918	0.074	0.773	0.526	0.193	0.565	0.050	0.905	0.150	0.026	0.969	0.599	0.467	0.507	0.373
r value	**ESR**	1.000	0.426	0.237	0.154	-0.021	0.273	0.206	0.111	-0.013	0.360	0.304	0.175	0.244	0.325	0.219	0.391	0.346	-0.287
***P*value**			0.004	0.117	0.313	0.892	0.069	0.174	0.467	0.933	0.015	0.043	0.251	0.106	0.029	0.149	0.008	0.020	0.056
r value	**CRP**	0.426	1.000	0.228	0.134	0.127	-0.112	-0.124	-0.134	-0.086	-0.127	0.246	-0.245	-0.142	0.177	0.364	0.587	0.304	-0.410
***P*value**		0.004		0.132	0.379	0.407	0.466	0.418	0.380	0.573	0.407	0.104	0.105	0.351	0.244	0.014	0.000	0.042	0.005
r value	**Ferr**	0.237	0.228	1.000	0.462	0.016	-0.322	0.100	-0.047	0.021	0.054	0.520	-0.336	0.099	0.317	0.441	0.581	0.231	-0.417
***P*value**		0.117	0.132		0.001	0.917	0.031	0.514	0.758	0.892	0.727	0.000	0.024	0.519	0.034	0.002	0.000	0.126	0.004
r value	**D-Dimer**	0.154	0.134	0.462	1.000	0.015	-0.335	0.143	-0.014	0.410	-0.008	0.143	-0.236	0.117	0.114	0.344	0.506	0.188	-0.403
***P*value**		0.313	0.379	0.001		0.923	0.025	0.349	0.928	0.005	0.957	0.350	0.119	0.445	0.455	0.021	0.000	0.216	0.006

r value	IL 6	-0.021	0.127	0.016	0.015	1.000	-0.178	-0.101	-0.447	0.009	-0.025	0.053	-0.208	-0.026	0.033	0.298	0.047	0.159	-0.296
*P*value		0.892	0.407	0.917	0.923		0.243	0.511	0.002	0.951	0.868	0.728	0.170	0.863	0.832	0.047	0.760	0.296	0.049
r value	Albumin	0.273	-0.112	-0.322	-0.335	-0.178	1.000	0.017	0.106	-0.222	0.407	0.024	0.410	0.348	0.101	-0.156	-0.159	0.026	0.203
*P*value		0.069	0.466	0.031	0.025	0.243		0.911	0.487	0.143	0.006	0.874	0.005	0.019	0.509	0.307	0.298	0.867	0.181
r value	FBS	0.206	-0.124	0.100	0.143	-0.101	0.017	1.000	0.291	0.163	0.044	-0.184	-0.006	0.103	0.304	0.070	0.029	0.024	0.021
*P*value		0.174	0.418	0.514	0.349	0.511	0.911		0.052	0.286	0.776	0.226	0.968	0.500	0.043	0.648	0.850	0.875	0.893
r value	HbA1c	0.111	-0.134	-0.047	-0.014	-0.447	0.106	0.291	1.000	-0.123	-0.022	-0.199	0.135	0.027	-0.141	-0.388	-0.159	-0.215	0.354
*P*value		0.467	0.380	0.758	0.928	0.002	0.487	0.052		0.423	0.884	0.190	0.376	0.863	0.355	0.008	0.298	0.156	0.017
r value	Trop	-0.013	-0.086	0.021	0.410	0.009	-0.222	0.163	-0.123	1.000	0.062	0.112	-0.104	0.137	0.247	0.109	0.224	0.175	-0.148
*P*value		0.933	0.573	0.892	0.005	0.951	0.143	0.286	0.423		0.687	0.464	0.497	0.371	0.101	0.475	0.140	0.249	0.333
r value	Chol	0.360	-0.127	0.054	-0.008	-0.025	0.407	0.044	-0.022	0.062	1.000	0.532	0.321	0.894	0.523	0.052	0.161	0.238	-0.024
*P*value		0.015	0.407	0.727	0.957	0.868	0.006	0.776	0.884	0.687		0.000	0.032	0.000	0.000	0.732	0.291	0.115	0.874
r value	Tg	0.304	0.246	0.520	0.143	0.053	0.024	-0.184	-0.199	0.112	0.532	1.000	-0.104	0.406	0.816	0.405	0.541	0.357	-0.318
*P*value		0.043	0.104	0.000	0.350	0.728	0.874	0.226	0.190	0.464	0.000		0.495	0.006	0.000	0.006	0.000	0.016	0.033
r value	HDL	0.175	-0.245	-0.336	-0.236	-0.208	0.410	-0.006	-0.135	-0.104	-0.321	-0.104	1.000	0.055	0.096	-0.128	-0.194	0.025	0.086
*P*value		0.251	0.105	0.024	0.119	0.170	0.005	0.968	0.376	0.497	0.032	0.495		0.721	0.532	0.403	0.201	0.873	0.573
r value	LDL	0.244	-0.142	0.099	0.117	-0.026	0.348	0.103	0.027	0.137	0.894	0.406	0.055	1.000	0.365	0.039	0.139	0.162	0.001
*P*value		0.106	0.351	0.519	0.445	0.863	0.019	0.500	0.863	0.371	0.000	0.006	0.721		0.014	0.800	0.361	0.289	0.996
r value	VLDL	0.325	0.177	0.317	0.114	0.033	0.101	-0.304	-0.141	0.247	0.523	0.816	0.096	0.365	1.000	0.468	0.540	0.386	-0.391
*P*value		0.029	0.244	0.034	0.455	0.832	0.509	0.043	0.355	0.101	0.000	0.000	0.532	0.014		0.001	0.000	0.009	0.008
r value	Creat	0.219	0.364	0.441	0.344	0.298	-0.156	-0.070	-0.388	0.109	0.052	0.405	-0.128	0.039	0.468	1.000	0.692	0.621	-0.945

***P*value**		0.149	0.014	0.002	0.021	0.047	0.307	0.648	0.008	0.475	0.732	0.006	0.403	0.800	0.001		0.000	0.000	0.000
r value	**Urea**	0.391	0.587	0.581	0.506	0.047	-0.159	-0.029	-0.159	0.224	0.161	0.541	-0.194	0.139	0.540	0.692	1.000	0.570	-0.696
***P*value**		0.008	0.000	0.000	0.000	0.760	0.298	0.850	0.298	0.140	0.291	0.000	0.201	0.361	0.000	0.000		0.000	0.000
r value	**Uric acid**	0.346	0.304	0.231	0.188	0.159	-0.026	0.024	-0.215	0.175	0.238	0.357	0.025	0.162	0.386	0.621	0.570	1.000	-0.642
***P*value**		0.020	0.042	0.126	0.216	0.296	0.867	0.875	0.156	0.249	0.115	0.016	0.873	0.289	0.009	0.000	0.000		0.000
r value	**GFR**	-0.287	-0.410	-0.417	-0.403	-0.296	0.203	0.021	0.354	-0.148	-0.024	-0.318	0.086	0.001	-0.391	-0.945	-0.696	-0.642	1.000
***P*value**		0.056	0.005	0.004	0.006	0.049	0.181	0.893	0.017	0.333	0.874	0.033	0.573	0.996	0.008	0.000	0.000	0.000	

4. DISCUSSION

In this study, the age ranges it effects of COVID span from 15 to 87 years old, and people of all these ages are susceptible to the disease. Smoking has been linked to higher infection rates and risk in people over the age of 18 (14). Cardiovascular and pulmonary disorders are brought on by nicotine's disruption of the renin-angiotensin system's (RAS) balance and increased expression of the ANG-I/ANG-II/ANG II receptor axis (15).

In this study, we discovered that lower albumin levels on admission can predict COVID-19 prognosis independently of other known indications such as lymphocyte count or comorbidities, this finding is consistent with a previous study that found hypoalbuminemia, or a drop in albumin levels, to be connected with the severity of ARDS 23 or acute kidney injury (16). Albumin is produced in the liver and has a serum half-life of about 21 days. In a previous study 12 and the current investigation, hypoalbuminemia was detected more frequently in severe COVID-19 cases than in mild cases, indicating that hypoalbuminemia was less likely to be caused by decreased albumin synthesis in severe COVID-19 (17)(18).

Much research has shown that if COVID-19 is present, the risk is likely to be lower than if the person does not smoke (19). The reduced risk could be explained by a significantly greater WBC count in smokers compared to healthy patients and those with other comorbidities validated by this study. When compared to healthy patients, the WBC count was significantly greater in smokers and lower in diabetics. Furthermore, while there was a non-significant higher blood level of hemoglobin in smokers when compared to healthy and diabetic patients, the range of HG in smokers was narrow when compared to healthy and diabetic patients, indicating that most smokers have a high level of HG. Also, smokers and current smokers had greater serum ferritin levels. According to correlation analysis, ferritin levels had a positive link with age and amount of smoking (pack-years) (20). Serum ferritin concentrations, on the other hand, did not correlate with lung function indicators, because ferritin may be actively secreted at the site of infection, it is likely that ferritin can perform tasks other than its traditional job as an iron storage protein (21).

Table (2) about the statistical distribution (COVID smoker patients) compared to the control group. This table shows that the significance of the control group is; All vital signs among (healthy complete control and smoker COVID patients) are significant ($P < 0.05$) for all vital signs of smoker COVID patients except there is no significance ($P > 0.05$) among vital signs of (white blood cells, platelets, hemoglobin, troponin, Cholesterol, TG, LDL and VLDL creatinine, uric acid). Cholinergic agonist nicotine also inhibits inflammatory cytokines. The pathophysiology of COVID-19 is thought to be related to an imbalance in the cholinergic system of nicotine caused by the interaction of SARS-CoV-2 with the nAChR (22). It is anticipated that smokers with COVID-19 will have a greater rate of smoking. Studies, however, indicate that the number of smokers hospitalized for SARS-CoV-2 infection is lower than anticipated (23). Benovitz and his associates 8 investigated how nicotine affected COVID-19. Evidence concerning nicotine's impact on airway cells shows that it causes quick and sustained increases in the expression of the ACE2 gene and protein, which increases vulnerability to SARS-CoV-2 (24).

Table (3) Following biomarkers tend to have high sensitivity and specificity for smoker COVID patients based on the ROC curve analysis: Lymphocyte, CRP, Ferritin, D-Dimer, IL 6, Albumin, FBS, HDL, Creatinine, Urea, and GFR. These biomarkers might be helpful in determining the kind and severity of COVID-19 in smokers. Although the data is limited to a total number of patients, it is significant to emphasize that caution should be used when interpreting these results because additional research may be required to support these conclusions.

Table (4): Nonparametric Spearman's statistical correlation coefficient for biomarkers in smoker COVID patients, in smoking COVID patients, there are differing degrees of association between various biomarkers. With p-values ranging from 0.000 to 0.997, Spearman's coefficient is between -0.417 and 0.587. Remember that correlation does not imply causation; therefore, additional research would be necessary to identify any causative relationships between these biomarkers.

5. CONCLUSION

In this research, we look at the current possible link between smoking and COVID-19 and study the biomarker changes in patients, and it was concluded that results showed the results show all biomarkers tend to have high sensitivity and specificity for smoker COVID patients. These biomarkers might be helpful in determining the kind and severity of COVID-19 in smokers. Although the data is limited to a total number of patients.

Author contributions

Contributors: Ahmed Jihad Abdulkadhim was responsible for material preparation, data collection and writing the draft, Dr. Nidhal Yousif Mohammed and Dr. Murtadha Allawi Jebur contributed to designing the study, analysing the collected data, and writing the manuscript. Both authors read and approved the final manuscript.

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