Original Article

ISSN: 1735-0344 *Tanaffos 2023; 22(4): 426-432*

TANAFFOS

Mutual Effects of Coincident Chronic Renal Failure and Chronic Obstructive Pulmonary Disease

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Received: 8 January 2023
Accepted: 18 September 2023

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Background: The current study tried to assess the effects of CKD on the severity and outcome of COPD in a population of patients who referred to our tertiary center in Tehran through a 3-year time section.

Materials and Methods: Through a retrospective cross-sectional design, the current study tried to assess the effects of chronic kidney disease (CKD) on the health situation and some spirometric and para-clinical parameters as well as their outcomes in patients who had been hospitalized for COPD. The participants had already COPD and we separate them into two groups with or without CKD.

Results: Regarding the outcome of hospitalizations, 94% of the COPD and 77.9% of the COPD+CKD group were discharged in good health condition while 6% and 22.1% deceased, respectively. This shows significantly higher death rate in the latter group and the findings obtained the odds ratio of 4.5 for CKD to raise this rate.

Conclusion: The current study could suggest an absolute relationship between CKD and COPD in terms of respiratory and blood parameters as well as the mutual effects of the diseases on the outcome of each.

Keywords: Chronic Obstructive Pulmonary Disease; Chronic kidney disease; Spirometry

INTRODUCTION

Chronic kidney disease (CKD) with 13% prevalence in American adult population is a crucial public health concern which is chiefly resulted by cardiovascular conditions in diabetes mellitus, blood hypertension or obesity (1-3). This may also be affected by chronic obstructive pulmonary disease (COPD) as a risk factor for cardiovascular problems (4-6). COPD is a huge health problem over the world as the third prevalent cause of death (7) which is related to not only pulmonary, but also a systemic inflammation affecting on cardiovascular system, especially in kidneys as researchers figured out before (8-12). Patients with coincident COPD and CKD may have common risk factors such as diabetes mellitus and hypertension mainly due to inflammatory response in the body (13-15). COPD cases are usually at risk of atherosclerosis which may, in turn, affect renal vessels resulting in CKD (16) although there are just a handful of works to evaluate the relationship between COPD and CKD (17-19).

The current study tried to assess the effects of CKD on the severity and outcome of COPD in a population of patients who referred to our tertiary center in Tehran through a 3-year time section.

MATERIALS AND METHODS

Subject and Sampling

Through a retrospective cross-sectional design, the current study tried to assess the effects of chronic kidney disease (CKD) on the health situation and some spirometry and para-clinical parameters as well as their outcomes in patients who had been hospitalized for COPD. The participants had already COPD and we separate them into two groups with or without CKD.

The sampling was simple and the sample size was computed 32 participants for each group regarding the following formula:

$$n = \frac{(p_0 q_0)\{z_{1-\frac{\alpha}{2}} + z_{1-\beta}\left(\sqrt{\frac{p_1 q_1}{p_0 q_0}}\right)\}^2}{(p_1 - p_0)^2}$$

$$= \frac{(0.23 \times 0.77)\{1.96 + 0.842(\sqrt{\frac{(0.05 \times 0.95)}{(0.23 \times 0.77)}})\}^2}{(0.05 - 0.23)^2} \cong 32$$

The prevalence of CKD in COPD patients was estimated 23% and the prevalence in the population was estimated 4.7% (IR=470.9).The power of the study was estimated 80% in the significance rate of 0.05.

Method of Research

The Patients who had been hospitalized in Masih Daneshvari hospital in Tehran who had COPD with or without CKD enrolled the study from 2016 to 2019 considering the following inclusion and exclusion criteria.

Inclusion Criteria:

- COPD diagnosis based on the GOLD global guideline
- FEV1<30% of the predicted value
- Age > 18 years
- Patients' consent to attend the research

Exclusion Criteria:

- Lung transplantation cases
- Kidney transplantation cases
- Current COPD exacerbation or history of exacerbation among recent couple of months
- Willing to quit in every phase of the study

The participants' records were studied for demographics and every coincident diseases such as hypertension, diabetes mellitus, other cardiopulmonary diseases, neurologic diseases, chronic renal failure, etc. The exacerbation history in recent three years was checked as well. GFR was computed using Cockcroft Gault formula and the patients with GFR less than 60 ml/min/1.73MT[2] was considered as renal failure (12). For the final accepted participants, laboratory findings including serum creation, CRP and venous blood gas analysis (VBG) were recorded.

Statistics

Descriptive aspects of the study were reported as percentage, mean and standard deviation after evaluating the normalization of the distributions by the Kolmogorov Smirnov test. To assess the mean of differences between the groups, student t-test was used for quantitative variables while Chi-square-test and Fisher's exact test for qualitative ones.

The entire analysis was done by SPSS 25.0 defining the confidence interval of 95% and the significance of 0.05 to get 80% power of study.

Ethics

There was no intervention throughout the current study. Also, there was no charge for the attendance the current research and all the private information were safely kept by the principal investigators. The participants had given their consents to attend any research works when hospitalized in our center if they wished.

RESULTS

From 2016 to 2019, two groups of participants were enrolled the study including 84 with COPD alone and 68 with both COPD and CKD. There was no difference between the groups regarding age and sex as can be seen in tables 1. Although the groups were statistically similar in the case of COPD exacerbations, they showed different hospital stay durations (P<0.001) as the means show 1.5 times more hospitalization time in the group of participants who had both COPD and CKD (Table1).

Spirometry showed significantly higher FEV1 in COPD group (P<0.001). In terms of venous blood gas analysis (VBG), the COPD group had higher values of blood PH (P<0.001) but PCO_2 was similar in both groups as reported

in Table 2. Thanks to the PH, this would be truly expected that the COPD group had significantly higher venous bicarbonate (HCO3).

On the contrary, the means of blood urea, creatinine and CRP were higher in the COPD+CKD group with a pronounced significance (P value<0.001). Table 2 and Figures 1and 2 summarize the findings in this regard.

Regarding the outcome of hospitalizations, 94% of the COPD and 77.9% of the COPD+CKD group were discharged in good health condition while 6% and 22.1% deceased, respectively (P value=0.003). This shows significantly higher death rate in the latter group and the findings obtained the odds ratio of 4.5 for CKD to raise this rate (Table3).

Table 1. Demographics and hospitalization aspects of the participants of both groups

	Group								
	COPD (n=84)				CKD+COPD (n=68)				
	Mean	SD	Median	IQR	Mean	SD	Median	IQR	P-Value
Duration	8.25	7.37	7.00	6.00	12.41	9.13	10.00	9.00	<0.001**
Age	70.79	11.57	70.00	16.50	73.00	11.03	74.00	17.00	0.235*
Count Of Admission	2.62	2.93	2.00	2.00	2.53	2.33	2.00	2.00	0.942**

**Based on T-test*

***Mann-Whitney U*

Table 2. Some blood parameters and spirometry FEV1 results considering the groups

	Group								
	COPD (n=84)				CKD+COPD (n=68)				
	Mean	SD	Median	IQR	Mean	SD	Median	IQR	P-Value
PH	7.34	0.08	7.34	0.15	7.23	0.10	7.24	0.16	<0.001*
PCO2	49.60	11.47	48.00	15.50	53.47	13.38	52.65	18.70	0.065**
HCO3	25.16	2.90	25.00	3.20	20.96	3.35	20.90	4.15	<0.001**
urea	47.69	18.86	42.50	27.00	77.91	42.98	69.50	39.50	<0.001**
Cr	1.16	0.36	1.10	0.45	2.85	1.32	2.55	1.30	<0.001**
CRP	32.46	14.23	27.50	23.00	51.88	18.20	50.00	23.00	<0.001**
FEV1	39.60	10.42	39.00	19.00	28.74	9.54	28.00	14.00	<0.001**

*Based on T-test

**Mann-Whitney U

Table 3. The outcome in the both groups regarding sex and coincidence of the diseases

			Group		Total	p-value*	OR(95% CI)
			COPD	CKD+COPD			
Condition	**Good Health**	Count	79	53	132	0.003	4.5(1.53,13.04)
		% within Group	94.0%	77.9%	86.8%		
	Deceased	Count	5	15	20		
		% within Group	6.0%	22.1%	13.2%		
Total		Count	84	68	152		
		% within Group	100.0%	100.0%	100.0%		
Gender	**Female**	Count	24	24	48	0.375	1(0.98 , 1.04)
		% within Group	28.6%	35.3%	31.6%		
	Male	Count	60	44	104		
		% within Group	71.4%	64.7%	68.4%		
Total		Count	84	68	152		
		% within Group	100.0%	100.0%	100.0%		

**Based on chi-square*

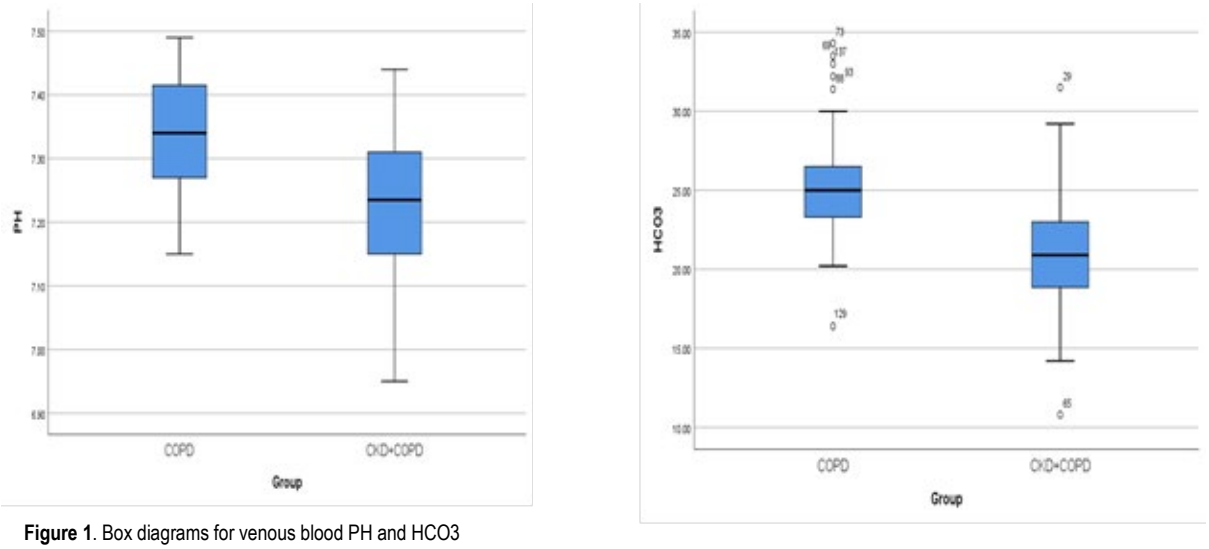

Figure 1. Box diagrams for venous blood PH and HCO3

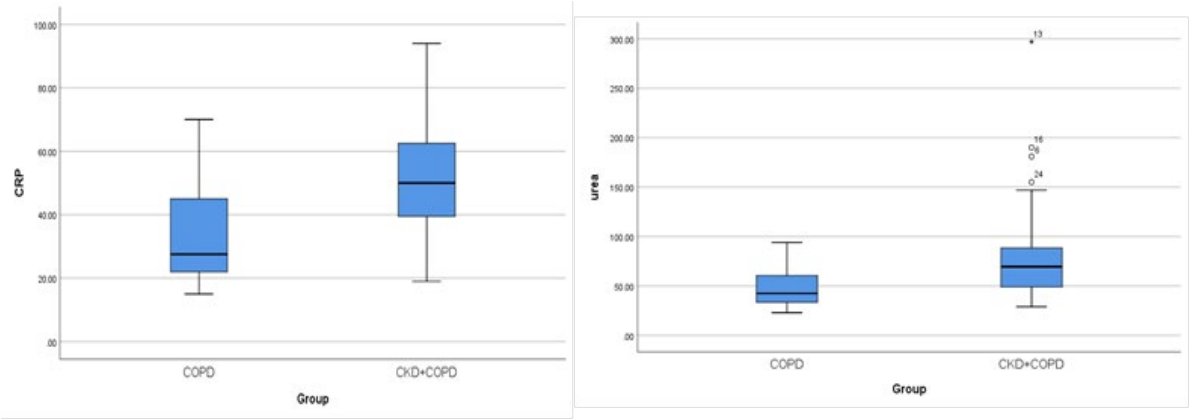

Figure 2. Box diagrams for venous blood CRP and Urea

DISCUSSION

The current research is a retrospective cross-sectional analytic study to assess the effect of coincident chronic kidney disease on the severity and outcome of chronic obstructive pulmonary disease among the hospitalized patients referred to Masih Daneshvari hospital in Tehran, Iran. The study, in the early aspects found longer hospitalization stay in COPD+CKD group although the frequency of COPD exacerbations was similar when compared with the group of COPD alone. In next steps, the blood acidity was higher in COPD+CKD group which may be resulted by lower HCO_3 and higher PCO_2 in VBG. However, the COPD + CKD group showed significantly higher level of blood urea, creatinine and CRP. Through a similar study, Yoshizawa et al. figured out higher serum creatinine in COPD+CKD patients against patients with only COPD to finally conclude that CKD is a coincident disease often occurs in COPD cases (20). Disregarding the main cause of CKD in the patients, we similar to Chen and Liao conclude that COPD is in a relationship with CKD since the named researcher describe a 1.6 higher rate of CKD in COPD cases in comparison to non-COPD patients through a long term follow up (21). They had added COPD as a risk factor for CKD which had included hypertension, hyperlipidemia and diabetes mellitus before. In terms of respiratory testing, spirometry showed significantly lower FEV1 in COPD + CKD group. Furthermore, when the outcome of disease was focused, death rate was around 3.7 times more in COPD+CKD group in comparison to the other (22.1% *vs* 6%) to define

the odds ratio of 4.5 in this matter. A study by Navaneethan et al. in 2016 showed 41% contribution for COPD in Death risk of CKD patients disregarding the cause of CKD working on 56,960 CKD patients to conclude that COPD may be a crucial risk factor for Death between patients with CKD and defined fourfold increased risk for respiratory related death which is comparable with our study (18).

Later in 2018, Lai et al. published a work to show that COPD may increase the risk of death among CKD patients which is completely against our study that proves higher death rate in patients with COPD who had coincident CKD (22). Now we may suggest a correlation between death and coincident CKD and COPD and it seems to need more investigations to know the relationship details more. Lai et al. (22) figures out a direct association between COPD/CKD combination death and advanced age as well as male sex.

Our findings are also on the way with a report by Trudzinski et al. which focused on age, sex, BMI, FEV1 and cardiovascular diseases to find an independent link between eGFR and the British Medical Research Council dyspnea scale, St. George's Respiratory Questionnaire results, six-minute walk test (6MWT) and timed up and go to reveal CKD impact on patient-centered outcomes and mortality in COPD (19).

Gembillo et al. explained how CKD may affect on respiratory tract by changing fluid hemostasis, acid-base balance, and vascular tone alteration. They believe that hemodynamic disturbances could result in ventilation control, pulmonary congestion, capillary stress failure and pulmonary vascular disease. This usually causes vascular stiffness, neurohormonal activation, tissue hypoxia such as pulmonary hypertension (PH) and COPD (23). Microalbuminuria (MAB) is a common consequence of CKD which affect endothelial permeability of all the cells in different organs in the body like what happens in lungs too. Oelsner et al. evaluated 6 population-based cohort studies on totally 11,911 participants including 51% non-smokers to finally show absolute association between MAB and increased COPD incidence/exacerbations disregarding smoking habits, diabetes and hypertension (24). This endorses Yoon et al. who found that MAB was correlated with both restrictive and obstructive patterns in respiratory tract (25).

On the other hand, many studies believe that fluid retention in CKD in combination with acid-base and electrolyte imbalance could cause chronic hypoxia and upper and lower respiratory tract edema pushing to parenchymal lung damage like what happen in COPD and also sleep apnea due to nocturnal hypoxia (26-31).

To sum up, the current study could suggest an absolute relationship between CKD and COPD in terms of respiratory and blood parameters as well as the mutual effects of the diseases on the outcome of each. So, we advise more studies, especially considering cellular and molecular aspects to know how the named common medical conditions may interact with each other.

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