

PREVALENCE OF RENAL FUNCTION DEFECTS AMONG COPD PATIENTS ATTENDING A RESPIRATORY DISEASE HOSPITAL IN SOUTH INDIA

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Received : 29/10/2022
Received in revised form : 30/11/2022
Accepted : 13/12/2022

Keywords:

Diabetes, Renal dysfunction, Hypertension, Urine protein, Creatinine.

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DOI: 10.47009/jamp.2023.5.1.61

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (1); 295-299



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Abstract

Background: COPD is a multisystem disorder with inflammation leading to high mortality. The extent of the inflammation directly correlates with the severity of the disease. Various comorbidities like DM, hypertension and coronary artery disease are associated with COPD. Renal dysfunctions related to COPD are mostly understudied. The aim is to study the prevalence of renal function defects in COPD patients. **Materials and Methods:** One-year cross-sectional study was conducted at Govt Thiruvotteeswarar Hospital of Thoracic Medicine, Chennai. One hundred forty-six patients were included after informed written consent. Spirometry was done for all study patients. Spirometry was done and the severity of obstruction was graded using GOLD guidelines. In addition, RFT and creatinine clearance/eGFR using the Cockcroft Gault formula were done. All the data were analysed. **Result:** Among the 146 patients, 110 (75%) were males, and 36 (25%) were females. Most patients were 51-60 years [54 (36.2%)]. 78 (53%) had COPD for >10 years and 68 (47%) with <10 years duration. Patients with normal creatinine were 136 (93%), and those with >1.2 mg/dl were 10 (7%). Patients with renal function defects were 83.6%. 13 (9%) were diabetic 11 (9%) were hypertensive. There was a significant association between renal defects, COPD duration, and the severity of obstruction ($p < 0.005$). There was no significant association between renal defects in COPD patients with hypertension and diabetes mellitus ($p > 0.005$) and COPD without hypertension or diabetes. **Conclusion:** The duration of COPD and the severity of obstruction were statistically associated with Renal dysfunction in COPD.

INTRODUCTION

COPD is characterised by persistent respiratory symptoms and airway and alveolar abnormalities usually caused by significant exposure to noxious particles or gases. The main risk factor for COPD is tobacco smoking, but other environmental exposures, such as biomass fuel exposure and air pollution, may contribute.^[1]

The chronic airflow limitation characteristic of COPD is caused by a mixture of small airway disease (e.g., obstructive bronchiolitis) and parenchymal destruction (emphysema). These changes do not always occur together but evolve simultaneously over time.^[2] The airflow limitation is usually measured by spirometry as this is the most widely available and reproducible lung function test. It is important to recognise that chronic respiratory

symptoms may precede the development of airflow limitation and may be associated with acute respiratory events.^[3]

COPD is a leading cause of morbidity and mortality worldwide that induces an economic and social burden that is both substantial and increasing. COPD results from long-term exposure to harmful gases and particles and various host factors, including genetics, airway hyper-responsiveness, and poor lung growth during childhood.^[4] The risk of developing Chronic Obstructive Pulmonary Syndrome (COPD) is proportional to the number of cigarettes or bidis smoked daily. Risk also increases with the duration of smoking. People working in the rubber, plastic, and leather industries are at increased risk of COPD.^[5]

In developing countries like India, outdoor air pollution has also been implicated as a cause of COPD and various respiratory diseases. It is due to

the pollutants from industries and motor vehicles causing pathological changes in the lung and airways. Exposure to biomass fuel is an important source of indoor air pollution contributing to COPD.^[6] COPD is a multisystem disorder with inflammation at its peak leading to high mortality. Smoking is a common risk factor for many other comorbidities, including coronary heart disease, heart failure, and lung cancer. The probable mechanisms involved in the pathogenesis may include persistent hypercapnia and chronic hypoxia that drives the development of renal dysfunction.^[7] An increase in inflammatory mediators in COPD has been thought to result from the interaction between the large airways, small airways, and the alveolar wall. The role of the spillover hypothesis has been further emphasised by observing the association between inflammatory mediators and pulmonary tissue-derived proteins.^[8] Pulmonary hypertension developing secondary to COPD is involved in the progression of kidney disease. Coronary artery disease associated with vascular dysfunction may lead to the development of chronic kidney disease. In addition, the inflammatory mediators released to contribute to various other comorbidities, such as coronary artery disease, heart failure, and lung cancer.⁹ Renal dysfunctions associated with COPD are mostly under-studied.

Aim

To study the prevalence of Renal Function defects in COPD patients.

MATERIALS AND METHODS

For one year, a cross-sectional study was conducted at Govt Thiruvoteeswarar Hospital of Thoracic Medicine, Chennai. One hundred forty-six patients were included, and informed consent was obtained.

Inclusion Criteria

Patients already diagnosed with COPD / newly diagnosed with COPD as per GOLD guidelines.

Exclusion Criteria

COPD patients who were known CKD patients, patients not willing to participate in the study, and patients on long-term nephrotoxic drug therapy.

The data of each patient was collected on a proforma, which included the name, age, gender,

and anthropometry. In addition, detailed clinical history was collected, which included presenting illness, smoking and alcohol history, comorbid illness, previous treatment details, and drug intake. Chest X-ray, RBS, B.urea, S. creatinine and blood pressure data were collected and compiled in the proforma.

A pulmonary function test was done for all patients who were enrolled. The test was performed following the criteria set by the American Thoracic Society using Easy one Spirometer. The procedure was explained to all the patients before the test. All participants were kept in a sitting posture for the procedure. All participants were instructed and demonstrated to hold their heads slightly elevated, position the mouthpiece and close the lips, inhale completely and rapidly, and then exhale maximally until no more air can be expelled. Any recent history of smoking, illness, or medications was enquired about, and the height and weight of the patient were recorded. The severity of obstruction was graded as per GOLD guidelines. Using the Cockcroft-Gault formula, creatinine clearance /GFR was calculated. Value >90ml/min was considered normal, whereas value < 90ml/min was taken as the presence of renal function defects per KDIGO guidelines of CKD stages. Urine protein was measured by the dipstick method.

Statistical analysis was done using Microsoft Excel and SPSS. Pearson correlation is used to assess the strength of correlation between variables. The Chi-square test was performed between two groups, and its statistical significance was calculated.

RESULTS

Most patients were male, 110 (75%), while 36 (25%) were females. In the age group most patients were in the age group of 51-60 years [54 (36.2%)], followed by 61-70 years [46 (31.9%)], and 41-50 years [25 (17%)]. Maximum patients had COPD for >10 years of duration [78 (53%)] while those with <10 years duration was 68 (47%). No of patients with creatinine levels of 0.6-1.2 mg/dl was 136 (93%), and >1.2 mg/dl was 10 (7%). Patients with diabetes were 13 (9%), and without diabetes were 133 (91%). Patients with hypertension were 11 (9%), and without hypertension were 135 (92%) [Table 1].

Table 1: Demographic data

		Frequency (%)
Gender	Male	110 (75%)
	Female	36 (25%)
Age group	41-50	25 (17%)
	51-60	54 (36.2%)
	61-70	46 (31.9%)
	71-80	14 (9.9%)
	>80	7 (5%)
Duration of illness	<10 years	68 (47%)
	>10 years	78 (53%)
Creatinine level	0.6-1.2 mg/dl	136 (93%)

	>1.2 mg/dl	10 (7%)
Diabetes mellitus	Yes	13 (9%)
	No	133 (91%)
Hypertension	Yes	11 (8%)
	No	135 (92%)

Table 2: Distribution of patient's characteristics

		Frequency (%)
PFT degree of obstruction	Mild	7 (54.6%)
	Moderate	32 (21.3%)
	Severe	37 (24.1%)
eGFR	>91	24 (17%)
	60-89	51 (34.8%)
	30-59	63 (42.6%)
	15-30	8 (5.7%)
eGFR ml/min	>90	24 (17%)
	<90	122 (83%)

In PFT, most patients were affected severely; 37 (24.1%) and 32 (21.3%) patients had moderate severity of obstruction and 77(54.6%) had mild COPD. COPD patients with GFR values of 30-59 were 63 (42.6%), value of 60-89 were 51 (34.8%), and values of 15-30 was 8(22.6%). 122 (83.6%) patients were in <90eGFR ml/min, and 24 (16.4%) patients were in >90eGFR ml/min [Table 2].

Table 3: Comparison of the case with eGFR values and duration and severity of COPD

		Case with eGFR values				P-value
		>91	60-89	30-59	15-30	
Duration of illness	<10 years	21	31	16	0	<0.005
	>10 years	3	20	47	8	
Severity of obstruction	Mild	24	33	20	0	<0.005
	Moderate	0	14	17	1	
	Severe	0	4	26	7	

In the comparison of duration of illness with eGFR values, only 21(30.8%) patients had normal eGFR, while 47 (69.1%) had renal function defects in patients with < 10 years of illness(n=68). In those with more than ten years duration of COPD(n=78), only 3 (3.84%) had normal eGFR value, whereas 75 (96.1%) had renal function defects. There was a significant association between the duration of illness and the presence of renal function defects (p=<0.005).

Based on KDIGO guidelines 2012, CKD stages based on creatinine clearance were made among the study population, which showed (24)17% in stage 1 (normal), (51) 34.8% in stage 2 CKD, (63) 42.6% in stage 3 CKD and (8) 5.7% in stage 4 CKD. In mild COPD patients, 53(68.8%) out of 77 had renal function defects(eGFR<90ml/min), while all 32 with moderate COPD and all 37 with severe COPD had renal function defects. There was a significant correlation between the severity of obstruction and the presence of renal function defects (p=<0.005). [Table 3]

Table 4: Comparison of the variables with eGFR/CCml/min.

		eGFR/ CCml/min		P-value
		<90	>90	
Duration of illness	<10 years	21	47	<0.005
	>10 years	3	75	
Severity of obstruction	Mild	53	24	<0.05
	Moderate	32	0	
	Severe	37	0	
Hypertension	Present	10	1	>0.05
	Absent	113	22	
Diabetes mellitus	Present	12	1	>0.05
	Absent	111	22	

In COPD patients with hypertension(n=11), ten patients had renal function defects, whereas in COPD without hypertension(n=135), 113 had renal function defects. In COPD with DM(n=13), 12 had renal function defects, whereas, for those without DM(n=133), 111 had renal function defects. There was no significant correlation between the presence of DM and hypertension and the presence of renal function defects(p=>0.05) [Table 4].

DISCUSSION

In the present study, the prevalence of renal dysfunction was 83%. Among them, the prevalence of overt renal failure(GFR <60 ml/min and S.creatinine>1.2 mg/dl) was 7%, and the prevalence of concealed renal failure was (GFR<60/ml/min but S.creatinine <1.2mg/dl) 34.9%. Various studies had

been done in India to estimate the prevalence of renal dysfunction among the general population.

Singh AK et al.¹⁰ found that the prevalence of CKD with eGFR < 60 was approximately 6%. Singh NP et al.^[11] found that the prevalence of renal failure (eGFR < 60) was 6% among the urban population and 4.2% among the semi-urban population. In a study by Tiwari et al.^[12] the prevalence was 4%. Hence comparing it with other Indian studies showed that the prevalence of renal dysfunction was four times higher among COPD when compared with the general population.

Elmahallawy et al.^[13] reported an increased incidence of 46% of renal dysfunction. Among them, the prevalence of overt renal failure was 20%, and concealed renal failure was 26%. Lattanzio et al.^[14] reported an incidence of 43% of renal dysfunction. Among them, the prevalence of overt renal failure was 22.2%, and concealed renal failure was 20.8%. Yoshizawa et al.^[15] found that 31% of the study population developed renal dysfunction. Sharanya et al.^[16] reported an incidence of 37% of renal dysfunction among COPD patients. Gjerde et al.^[17] found a prevalence of 9.6% in Female COPD patients and 5.1% in male COPD patients.

In our study, the prevalence of renal dysfunction was high among COPD patients, where the mean age under study was > 60. When the duration of COPD was taken as a criterion, as the duration increased, the percentage of patients falling into overt renal failure (eGFR < 60ml/min) increased. It was 61.5 % in the group with a duration of >10 years compared to 38.5 % with a duration of < 10 years.

In our study population, Diabetes and Hypertension were not significantly associated with the development of renal dysfunction. In our study Prevalence of Renal dysfunction among diabetes and hypertension was 92%, and 91% taken eGFR > 90 being normal. But the prevalence of renal function defects in COPD patients who did not have diabetes or hypertension was also high. The prevalence was higher when compared with the general population. But the population in our study group was very low for the results to be significant and comparable. In a study done by Prasannakumar et al.^[18] in Haryana the prevalence of renal dysfunction (eGFR < 60) in diabetes mellitus was 16.9%. In a study done by Crews et al.^[19] in the United States the prevalence of renal dysfunction (eGFR < 60) in hypertension was 19.6%. Elmahallawy et al.^[13] found that the presence of comorbidities like Diabetes and Hypertension was significantly associated with the development of Concealed renal dysfunction.

In our study, Urine proteins using the dipstick method to detect proteinuria/macro albuminuria were negative in all patients, indicating no significant association between COPD and proteinuria in our study population.

Shayo et al.^[20] reported 25/104 (24%) patients had albuminuria, and 16/104 (15.4%) patients had CVD.

Albumin-creatinine ratio (ACR) was then calculated to determine the level of albuminuria and expressed it as mg/mmol. ACR < 2 mg/mmol for males and < 2.8 mg/mmol for females was normal. ACR ≥ 2.5–29.9 mg/mmol for males and ≥ 3.5–29.9 mg/mmol for females was defined as albuminuria, and ACR ≥ 30 mg/mmol for both males and females was defined as macroalbuminuria/proteinuria. Abnormal urine albumin (Albuminuria and

Proteinuria) was present in all patients with CVD. In the subset of 46 COPD patients assessed for severity, 60.9% (95% CIs 46.1–73.9) had moderate COPD, and 30.4% (95% CIs, 17.9–49.0) had severe COPD. Albuminuria was significantly associated with COPD severity.

CONCLUSION

We concluded that significant risk factors associated with the development of renal dysfunction in COPD patients were age > 60 years, long duration of illness, and severe grade of airway obstruction in spirometry. Even though Diabetes and Hypertension were associated with the development of Renal dysfunction, their prevalence in our study population was very low to make a significant association. In addition, urine proteins/macroalbuminuria did not make any correlation with COPD, severity, or duration of COPD in our study.

Limitations of our study

Since this was a hospital-based single-centre cross-sectional study, the study's results may not be extrapolated to the general population. Hence further studies need to be done on the general population. Controls were not included in the study. Glomerular Filtration Rate (GFR) was not measured directly. However, the Cockcroft gault equation can be used as a reliable surrogate for measured GFR in the healthy elderly and the diseased population.

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