

Original article

Serum creatine in COPD: A Case Control Study from SMBT Medical College, Igatpuri, Maharashtra

Dr. Srinath Taklikar¹, Dr. Manoj Chitale², Dr. Ashutosh Gupta³, Dr. Anant A. Takalkar⁴

^{1,3}Junior resident, ²Professor and HOD, Department of Medicine, SMBT Medical College, Igatpuri, Maharashtra

⁴Professor, Department of Community Medicine, MIMSR Medical College, Latur, Maharashtra

Corresponding author: Dr. Anant A. Takalkar

Abstract

Introduction: Chronic renal failure (CRF) rises in prevalence with age and is frequently associated with chronic diseases such as congestive heart failure and diabetes mellitus. When present as a comorbidity, CRF carries negative prognostic implications and impacts the therapeutic strategy.⁶ It is unknown to which extent COPD is associated with CRF and the relationship between renal failure and COPD is largely undescribed.

Objective: To study the role of serum creatine in COPD and non-COPD patients

Methodology: The present case control study was conducted at Department of Medicine, SMBT Medical College, Igatpuri involving 50 cases and 50 controls visiting to Medicine department OPD as well as inpatients admitted in the same department of SMBT Medical College, Igatpuri during the study period from January 2023 to October 2023.

Results: We included 50 cases and 50 controls in our study. Majority of the cases i.e. 64% and controls i.e. 62% were from 61-70 years age group. Equal number of males (64%) and females (36%) were included in our study. Abnormal levels of serum creatine were seen in 24% of cases and 6% of controls. This difference in the proportion of cases and controls was found to be statistically significant ($p < 0.05$). It means number of cases with abnormal serum creatine were significantly higher compared to controls.

Conclusion: In our study, abnormal levels of serum creatine were seen in 24% of cases and 6% of controls. This difference in the proportion of cases and controls was found to be statistically significant ($p < 0.05$). Our study findings strongly support the association of increased prevalence of CKD in patients with COPD.

Key words: COPD, CKD, serum creatine

Introduction:

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disorder characterized by irreversible airway obstruction. According to WHO estimates, COPD is poised to become the third leading cause of death, and the fifth leading contributor to overall morbidity burden by the year 2020.¹

The 1995 European Respiratory Society (ERS) consensus statement defined COPD as "a disorder characterized by reduced maximum expiratory flow and slow emptying of the lungs; features which do not change markedly over several months. Most of the airflow limitation is slowly progressive and irreversible. The airflow limitation is due to varying combinations of airways disease and emphysema; the relative contribution of the two processes is difficult to define in vivo". Unfortunately, there is no agreed labelling of the airways disease component that is mainly an inflammatory process.²

The prevalence of COPD in India is estimated to be 3.49% based on nationwide prevalence study conducted by ICMR.³ But since these prevalence studies were conducted based on respiratory symptoms questionnaire and spirometry was not done to define irreversible airway obstruction it is estimated that the actual prevalence and disease burden may be higher. Apart from the mortality, COPD causes loss of productivity, huge increases in health expenditure and decreased quality of life.⁴

Chronic renal failure (CRF) rises in prevalence with age and is frequently associated with chronic diseases such as congestive heart failure and diabetes mellitus. When present as a comorbidity, CRF carries negative prognostic implications and impacts the therapeutic strategy.⁶ It is unknown to which extent COPD is associated with CRF and the relationship between renal failure and COPD is largely undescribed. A proportion of patients with COPD has a reduced muscular mass, and thus, serum creatinine might be falsely low as the result of decreased creatine release. Also, CRF may be associated with normal serum creatinine concentration, a condition known as unrecognized or concealed CRF. It is diagnosed by glomerular filtration rate (GFR) < 60 mL/min/1.73 m².⁷

Objective: To study the role of serum creatine in COPD and non-COPD patients

Materials and Methods:

Study setting:

The present study was conducted at Department of Medicine, SMBT Medical College

Study population:

Both male and female patients with COPD as cases and without COPD as controls visiting to Medicine department OPD as well as inpatients admitted in the same department of SMBT Medical College, Igatpuri

Study period: January 2023 to October 2023

Study design: Case Control study

Sample size: We included 50 cases and 50 controls in our study.

Sampling technique: Simple random sampling technique

Inclusion criteria:

- Age above 40 years
- Diagnosed as having COPD on the basis of spirometry/clinical features
- Both OP and IP patients visiting to Medicine and Pulmonology department
- Those who are willing to participate in the study after consent

Exclusion criteria:

- **Age below 40 years**
- Patients with COPD who have other comorbid illness which are likely to cause renal failure are excluded.
- These comorbid illnesses include,
 - Diabetes mellitus
 - Known renal disease such as renal stones, polycystic kidney disease etc.
 - Coronary artery disease.
 - Cardiac failure.
 - Cirrhosis.
 - Ingestion of nephrotoxic drugs.
- Those who are not willing to participate in the study after consent

Selection of control population:

Control population included age and sex matched persons without COPD and other illness known to affect renal function which are listed above. For each COPD patient one control patient was selected.

Methods of data collection:

Information will be collected through a pre-tested and structured proforma for each patient. Qualifying patients will be undergoing detailed history, clinical examination and laboratory investigations

Definition and classification of CKD:⁸

The Kidney Disease: Improving Global Outcomes (KDIGO) defines CKD as abnormalities of kidney structure or function, present for >3 months, with implications for health.

CKD is either kidney damage or decreased glomerular filtration rate <60 ml/min/1.73m² for >3 months. Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

Criteria for CKD by KDIGO 2012 (Either of the Following Present for >3 Months)⁸

- 1. Markers of kidney damage (one or more)**
 - Albuminuria (albumin excretion rate [AER] ≥30 mg/24 hours; albumin to- creatinine ratio [ACR] ≥30 mg/g [≥3 mg/mmol])
 - Urine sediment abnormalities
 - Electrolyte and other abnormalities due to tubular disorders
 - Abnormalities detected by histology
 - Structural abnormalities detected by imaging
 - History of kidney transplantation
- 2. Decreased GFR <60 ml/min/1.73 m² (GFR categories G3a–G5)**

Statistical analysis and methods-

Data was collected by using a structure proforma. Data thus was entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms

of percentages and proportions. Quantitative data was expressed in terms of Mean and Standard deviation. Association between two qualitative variables was seen by using Chi square/ Fischer's exact test. Comparison of mean and SD between two groups will be done by using unpaired t test to assess whether the mean difference between groups is significant or not. Descriptive statistics of each variable was presented in terms of Mean, standard deviation, standard error of mean. A p value of <0.05 was considered as statistically significant whereas a p value <0.001 was considered as highly significant.

Results

Table 1: Distribution according to age group

		Cases		Controls	
		Frequency	Percent	Frequency	Percent
Age group in years	50-60	14	28.0	15	30.0
	61-70	32	64.0	31	62.0
	71-80	4	8.0	4	8.0
	Total	50	100.0	50	100.0

We included 50 cases and 50 controls in our study. Majority of the cases i.e. 64% and controls i.e. 62% were from 61-70 years age group

Table 2: Distribution according to gender

		Cases		Controls	
		Frequency	Percent	Frequency	Percent
Gender	Male	32	64.0	32	64.0
	Female	18	36.0	18	36.0
	Total	50	100.0	50	100.0

Equal number of males (64%) and females (36%) were included in our study

Table 3: Prevalence of CKD stages in cases and controls

		Cases		Controls	
		Frequency	Percent	Frequency	Percent
CKD STAGE	1	6	12.0	31	62.0
	2	16	32.0	7	14.0
	3a	20	40.0	9	18.0
	3b	3	6.0	3	6.0
	4	3	6.0	0	0.0
	5	2	4.0	0	0.0
	Total	50	100.0	50	100.0

Chi square test-26.81, p-0.00001 (<0.001), Highly significant

Majority of the cases i.e. 46% were from CKD stage 3 compared to 24% of controls. This difference in the proportion of cases and controls was found to be statistically significant (p<0.001). It means number of cases with CKD severity were significantly higher compared to controls

Table 4: Distribution according to abnormal serum creatine in cases and controls

		Cases		Controls	
		Frequency	Percent	Frequency	Percent
Serum Creatine	Normal	38	76.0	47	94.0
	Abnormal	12	24.0	3	6.0
	Total	50	100.0	50	100.0

Chi square test-6.35, p-0.011(<0.05), Significant

Abnormal levels of serum creatine were seen in 24% of cases and 6% of controls. This difference in the proportion of cases and controls was found to be statistically significant (p<0.05). It means number of cases with abnormal serum creatine were significantly higher compared to controls.

Discussion:

Age and gender

We included 50 cases and 50 controls in our study. Majority of the cases i.e. 64% and controls i.e. 62% were from 61-70 years age group. Mean age of cases was 64.72 ± 5.33 years and that of controls was 64.58 ± 5.36 years. The difference in the mean age was found to be statistically not significant ($p > 0.05$)

Equal number of males (64%) and females (36%) were included in our study.

Trudzinski FC et al⁹ reported in his study that the majority of all patients (60.6%) were male, and the mean \pm SD age was 65.0 ± 8.4 years.

Baha A et al¹⁰ carried out record-based study in which files of 320 patients with COPD and reported that Ninety (80.4%) of the patients were male and 23 (19.6%) were female.

Elmahallawy II et al¹¹ conducted a study that included 300 COPD patients aged 65.28 ± 6.32 years, 148 of them (49.3%) were females and the rest were males and 300 control age and gender matched patients with diseases other than COPD; aged 64.70 ± 7.12 years, 138 of them (46%) were males and the rest were females. Our findings are consistent with the findings of above-mentioned authors

CKD stage in cases and controls

Majority of the cases i.e. 46% were from CKD stage 3 compared to 24% of controls. This difference in the proportion of cases and controls was found to be statistically significant ($p < 0.001$). It means number of cases with CKD severity were significantly higher compared to controls

Trudzinski FC et al⁹ reported in his study that among the 161 patients with CKD, 114 (70.8%) were category 3A, 43 (26.7%) were category 3B, and 4 (2.5%) were category 4.

Elmahallawy II et al¹¹ reported that according to the GOLD classification; 18% ($n = 54$) of them had moderate COPD (stage II), 10% ($n = 30$) had severe COPD (stage III) and 72% ($n = 216$) had very severe COPD (stage IV). Our findings are consistent with the findings of above-mentioned authors.

Prevalence of renal failure in cases and controls

In our study, abnormal levels of serum creatine were seen in 24% of cases and 6% of controls. This difference in the proportion of cases and controls was found to be statistically significant ($p < 0.05$). It means number of cases with abnormal serum creatine were significantly higher compared to controls

There are several studies focusing on the prevalence of CKD in patients with COPD, conducted in a range of populations.¹²⁻¹⁸ Most of these studies are single centre study with a small sample size One recent meta-analysis by Gaddam and colleagues showed an increased prevalence of CKD in patients with COPD even after adjustment for co-variates including age, gender, BMI and smoking status, thus suggesting an independent association of CKD with COPD.¹⁹

Baha A et al¹⁰ reported the prevalence of ARF in their study as 17.7% which is closely matching with our study findings.

Conclusion

- In our study, abnormal levels of serum creatine were seen in 24% of cases and 6% of controls. This difference in the proportion of cases and controls was found to be statistically significant ($p < 0.05$).
- Our study findings strongly support the association of increased prevalence of CKD in patients with COPD.

References

1. Burney P, Jarvis D and Perez-Padilla R. The global burden of chronic respiratory disease in adults. *Int J Tuberc Lung Dis* 2015; 19: 10-20.
2. Siafakas NM, Vermeire P, Pride NB, et al. Optimal assessment and management of chronic obstructive pulmonary disease (COPD). *Eur Respir J* 1995; 8: 1398–1420.
3. Epidemiology of COPD. Available from: <http://www.who.int/respiratory/copd/burden/en/> Accessed 7 July 2019.
4. Inker LA, Astor BC, Fox CH, Isakova T, Lash JP, Peralta CA, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. *Am J Kidney Dis*. 2014;63(5):713–35.
5. Saran R, Robinson B, Abbott KC, Agodoa LY, Albertus P, Ayanian J, et al. US renal data system 2016 annual data report: epidemiology of kidney disease in the United States. *Am J Kidney Dis*. 2017;69(3 Suppl 1): A7–8.
6. J. Joseph, M. Koka, W.S. Aronow, Prevalence of moderate and severe renal insufficiency in older persons with hypertension, diabetes mellitus, coronary artery disease, peripheral arterial disease, ischemic stroke, or congestive heart failure in an academic nursing home, *J.Am.Med.Dir.Assoc.*9(4) (2008) 257–259.
7. R.A. Incalzi, L. Fusco, M. De Rosa, et al, Co-morbidity contributes to predict mortality of patients with chronic obstructive pulmonary disease, *Eur. Respir.J.*10(1997)27942800.
8. Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco AL, De Jong PE, et al. Kidney disease: Improving Global Outcomes (KDIGO) CKD work group: KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3(1):5–14.
9. Trudzinski FC, Alqudrah M, Omlor A, Zewinger S, Fliser D, Speer T, Seiler F, Biertz F, Koch A, Vogelmeier C, Welte T. Consequences of chronic kidney disease in chronic obstructive pulmonary disease. *Respiratory research*. 2019 Dec;20(1):151.
10. Baha A, Ogan N, Akpınar EE, Ateş C, Gülhan M. The Course of Renal Functions in COPD. Two Stipitation: Exacerbation and Stable Period. *Eurasian Journal of Pulmonology*. 2019 Jan 1;21(1):63.
11. Elmahallawy II, Qora MA. Prevalence of chronic renal failure in COPD patients. *Egyptian Journal of Chest Diseases and Tuberculosis*. 2013 Apr 1;62(2):221-7.
12. Yoshizawa T, Okada K, Furuichi S, Ishiguro T, Yoshizawa A, Akahoshi T, et al. Prevalence of chronic kidney diseases in patients with chronic obstructive pulmonary disease:

- assessment based on glomerular filtration rate estimated from creatinine and cystatin C levels. *Int J Chron Obstruct Pulmon Dis.* 2015; 10:1283–9.
13. Chen CY, Liao KM. Chronic obstructive pulmonary disease is associated with risk of chronic kidney disease: a Nationwide case-cohort study. *Sci Rep.* 2016; 6:25855.
 14. Gjerde B, Bakke PS, Ueland T, Hardie JA, Eagan TM. The prevalence of undiagnosed renal failure in a cohort of COPD patients in western Norway. *Respir Med.* 2012;106(3):361–6.
 15. Incalzi RA, Corsonello A, Pedone C, Battaglia S, Paglino G, Bellia V, et al. Chronic renal failure: a neglected comorbidity of COPD. *Chest.* 2010;137(4):831–7.
 16. Mapel DW, Marton JP. Prevalence of renal and hepatobiliary disease, laboratory abnormalities, and potentially toxic medication exposures among persons with COPD. *Int J Chron Obstruct Pulmon Dis.* 2013; 8:127–34.
 17. Schnell K, Weiss CO, Lee T, Krishnan JA, Leff B, Wolff JL, et al. The prevalence of clinically-relevant comorbid conditions in patients with physiciandiagnosed COPD: a cross-sectional study using data from NHANES 1999- 2008. *BMC Pulm Med.* 2012; 12:26.
 18. Baty F, Putora PM, Isenring B, Blum T, Brutsche M. Comorbidities and burden of COPD: a population-based case-control study. *PLoS One.* 2013;8(5): e63285.