www.directivepublications.org

Journal of
Respiratory Medicine and Research

ISSN 2831-3240

Research Article

Early Detection Of Renal Injury In Elderly Patients With Chronic Obstructive Pulmonary Disease.

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Abstract

Background: One prevalent complication of COPD is renal damage. Our objective is to examine the function of cystatin C and β2 microglobulin as indicators for detecting early kidney damage among older individuals with stable COPD and during exacerbations.
Methods: Prospective comparative cross-sectional study recruited 135 COPD cases, classified as 86 COPD cases with acute exacerbation (AECOPD) admitted to the respiratory department in Sohag University Hospital and 49 patients with stable COPD during the period from September 2023 to March 2024. Serum level of creatinine, cystatin C and B2 microglobulin were measured on admission.
Results: The mean age of the 85 male cases was 68.2ł4.51 years. Compared to stable COPD, AECOPD cases had considerably higher mean serum levels of β2 microglobulin and cystatin C (P value = 0.001 for both). A significant positive correlation was identified between β2 micro-globulin and cystatin C (r= 0.539 and P value <0.001) and PaCO2 (r= 0.137 and P value <0.001) while a significant negative correlation with PaO2 (r= -0.785 and P value <0.001) in AECOPD. As regard cystatin C, there was significant positive correlation with β2 micro-globulin (r= 0.539 and P value <0.001) and PaCO2 (r= 0.003 and P value <0.001) while a significant negative correlation with PaO2 (r= -0.161and P-value = 0.045) in AECOPD.
Conclusion: Elderly individuals with AECOPD frequently experience acute kidney injury, which is positively correlated with the severity of hypoxemia and hypercapnia. Cys-C and β2-MG can be used as sensitive indicators to detect renal impairment early in older adults with AECOPD.

Keywords : *COPD, Acute kidney injury, Cystatin C, B2 microglobulin and biomarkers.*

BACKGROUND

Chronic Obstructive Pulmonary Disease (COPD) Is Marked By Persistent Airway Inflammation, Systemic Effects Or Comorbidities, And Poor Reversibility Of Airflow Obstruction[1–3] With 3.5 Million Fatalities From COPD In 2021—Nearly 5% Of All Deaths—It Ranks As The Fourth Most Common Cause Of Mortality Worldwide.[4]

Numerous Comorbid Diseases, Such As Diabetes Mellitus (DM), Heart Failure (HF), Ischemic Heart Disease, And Chronic Kidney Disease (CKD), Prevail In The Cases With COPD And Are Associated With Greater Mortality Rates And Morbidity Costs. [5] Numerous Investigations Have Suggested A Possible Connection Between Renal Insufficiency And COPD[6] Furthermore, Hypoxemia, Carbon Dioxide Retention, Prolonged Ischemia, And Inflammation Can All Contribute To Or Exacerbate Kidney Injury During A COPD Exacerbation. Acute Kidney Injury (AKI) Is Therefore Rather Common In Cases Who Are Hospitalized As A Result Of Exacerbations Of COPD. Thus, It Is Essential To Detect And Treat Renal Damage In COPD Patients As Soon As Possible.[7]

Deterioration In Health Status Is A Result Of COPD Exacerbation (AECOPD), One Of The Main Causes Of Disease And Death.[8, 9]

Significant Gas Trapping, Higher Mucus Formation, And Intensified Airway Inflammation Are Generally Associated With AECOPD. The Main Manifestation Of An Exacerbation Is Worsening Of Dyspnea, Which Is Caused By These Changes. Other Symptoms Include Increased Coughing And Wheezing, As Well As An Increase In The Amount And Purulence Of Sputum. [10]

Although Serum Creatinine (Scr) Is Frequently Utilized For The Detection And Evaluation Of Kidney Impairment, There Are Usually No Appreciable Changes In Scr In Early Phases Of

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Received: 29-Oct-2025, Manuscript No. JRMR - 5218**; Editor Assigned:** 01-Nov-2025 **; Reviewed:** 14-Nov-2025, QC No. JRMR - 5218 **; Published:** 21-Nov-2025, **DOI:** 10.52338/jrmr.2025.5218
Citation: Doaa Gadallah. Early Detection Of Renal Injury In Elderly Patients With Chronic Obstructive Pulmonary Disease. Journal of Respiratory Medicine and Research. 2025 November; 14(1). doi: 10.52338/jrmr.2025.5218.
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Injuries In The Kidney. An Increase In Scr Levels Frequently Indicates That The Kidneys Have Already Sustained An Irreparable And Quickly Developing Injury. Scr Levels Is Impacted By A Wide Range Of Parameters, Such As Age, Sex, Food, Muscle Mass, Drugs, And Other Factors.[11] More Rapid And Sensitive Biological Markers Are Therefore Required.

One Well-Known Member Of The Cystatin Superfamily, Notably Family Ii, Is Serum Cystatin C (Cys-C). It Is Widely Dispersed In Different Body Fluids And Is Uninterruptedly Secreted By Nucleated Cells Throughout The Body. It Works As A Soluble, Non-Glycosylated Inhibitor Of Cysteine Proteases. Numerous External Stimuli Have Little Effect On Its Steady-State Secretion And Excretion. The Renal Proximal Tubules, Which Do Not Secrete Cys-C Themselves, Completely Reabsorb And Metabolize Cys-C, Which Can Easily Cross The Glomerular Filtration Membrane. It Is A Great Biomarker For Determining The Glomerular Filtration Rate (GFR) Because Of This Feature.[12] According To Earlier Research, Serum Cys-C Levels May Provide A More Reliable Indicator Of GFR Than Creatinine Levels Since They Are Only Influenced By GFR.[13–15] A Low-Molecular-Weight Protein, Beta-2 (B2) Microglobulin (B2-Mg) Is Easily Filtered Throug The Glomerular Membrane And Then Processed In The Renal Tubules.[16] It Is Produced, Synthesized, And Released At A Steady Rate In A Healthy Population.About 99 Percent Of B2-Mg Is Reabsorbed And Metabolized In The Proximal Tubule After Passing Through The Glomerulus. This Biomarker Has Been Used To Track Glomerular Activity As Well As To Assess Tubular Function. According To Earlier Research, B2-Mg Might Be A More Accurate Indicator Of Acute Renal Damage Than Serum Creatinine (Scr) .[17]

Investigating The Function Of Cys-C And B2-Mg As Indicators For Detection Of Early Kidney Injury In Older Individuals With Stable COPD And During Exacerbations Is The Goal Of Our Study.

MATERIALS AND METHODS

Study Design And Setting

In The Present Prospective Comparative-Cross-Sectional Study, 49 Patients With Stable COPD Were Recruited From An Outpatient Clinic Between September 2023 And March 2024, While 86 Cases With Acute Exacerbations Were Admitted To The Respiratory Department At Sohag University Hospital.

In Line With The 2024 Gold (Global Initiative For Chronic Obstructive Lung Disease), COPD Exacerbation Features Dyspnea And/Or Cough And Sputum That Worsen Over <14 Days.[18]

Patients With COPD Who Are Not Currently Having An Exacerbation Of Their Condition Are Said To Have Stable COPD. These Individuals May, However, Have Persistent COPD Symptoms Of Variable Severity Or Have Recently Undergone Exacerbations Followed By Recovery To A New Baseline.[19] Based On The Oxygen Partial Pressure (PaO2) Readings From The Arterial Blood Gas Study Performed At Admission, Three Groups Of Cases Were Formed: Group A Had PaO2 Levels Above 60 mmHg But Below 80 Mm Hg, Which Indicated Mild Hypoxemia; Group B Had PaO2 Levels Above 40 mmHg And Up To 60 mmHg, Which Indicated Moderate Hypoxemia; And Group C Had PaO2 Levels At Or Below 40 mmHg, Which Indicated Severe Hypoxemia.[7]

Ethics Approval And Consent To Participate

The Present Study Received Approval From The Sohag Faculty Of Medicine's Medical Research Ethics Committee. The Institutional Review Board Registration Number Of The Study Was Soh-Med-23-06-04pd.

Inclusion And Exclusion Criteria

All Patients With A Clinically Confirmed Diagnosis Of COPD, Post-Bronchodilator Spirometry, FEV1/FVC < 70%, And Who Were Admitted To Our Department Throughout The Study Period Were Included In The Trial, As Were Cases Over 65 And Those Who Signed An Informed Consent Form.

Patients With Cardiovascular Diseases, Multiple Organ Failures, Primary Or Secondary Renal Diseases, Cancer, Hematological Disorders, Cerebrovascular Diseases (CVD), Patients Who Had Received Nephrotoxic Medications Within Six Weeks Prior To Admission, Patients Who Refused To Participate In The Study, And Patients Who Showed Clinical And/Or Radiographic Signs Of Other Pulmonary Conditions Other Than COPD Were All Excluded.

Data Collection Method

Every Patient Underwent The Following: Taking A History, Which Included Respiratory Symptoms Like Coughing, Dyspnoea, Etc.; Recording Other Information, Including Blood Pressure, Sex, Age, Body Mass Index (BMI), Smoking Index, Number Of Exacerbations Per Year, And Severity Of Exacerbation; And Performing A Clinical Examination And Radiological Evaluation, Which Included Chest Radiography, Echocardiography, High Resolution Computed Tomography Scanning Of The Chest, And Abdominal Ultrasound To Examine The Urinary System, Including Kidneys, Ureters, And Bladder. The Measurements Of The Serum Level Of Creatinine, Cystatin C And B2 Microglobulin Were Carried Out On Admission.

Method Of Measurement Of Serum Creatinine

Creatinine In Serum Or Urine Is Measured By The Jaffe's Reaction, Which Uses Creatinine And Picric Acid To Quantitatively Produce An Orange Color In An Alkaline Medium. After The Passage Of 15 Minutes At Room Temperature, Incubation For Color Development, The Color Was Measured At 520 Nm [20]. Adult Males Typically Have

0.6–1.2 mg/dl Of Creatinine, While Adult Females Typically Have 0.5–1.1 Mg/Dl.

Method Of Measurement Of Serum Cystatin C

As Directed By The Manufacturer, Serum Cystatin C Was Measured Using A Particle-Enhanced Immuneturbidimetric Test On A Cobas 6000 Analyzer (Roche Diagnostics, Indianapolis, In, Usa). The Assay Is A Two-Reagent System That Has An Eight-Week Stability Period. Reagents 1 And 2 Are A Buffer And A Suspension Of Latex Particles Coated With Polyclonal Antibodies Specific To Rabbit Anti-Cystatin C, Respectively. This Method Involves Mixing The Sample With Reagent 1 In A Cuvette Rotor, Then Adding Reagent 2. The Usual Amount Of Cystatin C (Male: 0.71-1.21 Mg/L, Female: 0.61-1.05 Mg/L) [21]Is Tested 10 Minutes After The Agglutination Reaction Begins (546 Nm For Primary Wavelength And 700 Nm For Secondary Wavelength). [22]

Method Of Measurement Of Serum B2 Microglobulin

Following The Recommendations Of The Company **[22]**, The Measurement Of The Serum B2 Microglobulin Was Carried Out Using An Immunoturbidimetric Assay On A Cobas 6000 Analyzer (Roche Diagnostics, Indianapolis, In, Usa). The Normal Range For B2 Microglobulin Is Between 07 And 2.1 Mg/L. **[22]**

Statistical Analysis

The Data Were Collected And Tabulated. Data Were Statistically Analysed Using The Spss Package V. 27. Testing Normality Using The Shapiro-Wilk Test Revealed That The Quantitative Variables Are Not Normally Distributed (P-Value Of Normality Test Was Less Than 0.005), So Non-Parametric Analysis Was Done. The Quantitative Variables Were Expressed In Terms Of Mean±Standard Deviation, Whereas The Categorical Variables Were Given In Frequency And Percent. In Addition, The Mann–Whitney Test Was Utilized To Make Comparisons Between Two Groups, And Kruskal–Wallis Non-Parametric Tests Were Used For Comparison Of Three Or More Groups Because The Data Was Not Normally Distributed. To Assess The Correlation Between The B2 Micro-Globulin, Cystatin C And Other Possible Factors, Spearman's Rho Was Used.

Linear Regression Model Was Done To Investigate The Different Predictors For Acute Renal Injury. We Started With Univariate Linear Regression For Both The Level Of B2 Micro Globulin And Cystatin C Separately For All Variables Included In The Study And The Variables With Significance Were Included In The Multivariate Linear Regression Analysis Was Done To See The Possible Predictors In The Whole Study.

RESULTS

135 Patients With Copd Were Included In The Study; 85 Of Them Were Men, And Their Mean Age Was 68.2±4.51 Years. Cases Were Classified Into Two Categories: Those With Stable COPD (49, Or 36.3% Of The Total) And Those With Acute Exacerbation Of COPD (86, Or 63.7%).

The Groups Under Study Were Compared In **Table 1.** Regarding Demographic Data, Gender And Body Mass Index Did Not Significantly Differ Between The Groups Under Study, But The Groups Had A Difference With Statistical Significance In Age Between The Groups; AECOPD Cases Were Older Than Stable Copd Cases (P Value 0.01). In Terms Of Arterial Blood Gas, The AECOPD Cases Had Statistically Significant Lower PaO2 (58.1¡16.2) And Higher PaC02 (58.1¡18) Values Than Those With Stable COPD (P Value = 0.001 For Both). The Mean Blood Levels Of B2 Microglobulin And Cystatin C Were Substantially Greater In AECOPD Patients Than In Stable COPD Patients (P Value = 0.001 For Both). However, There Were No Statistically Significant Differences In The Levels Of Serum Creatine Between Both Groups. Compared To Stable COPD Cases, AECOPD Cases Had Significantly Higher Systolic And Diastolic Blood Pressure Levels (P Value = 0.001 For Both). Aecopd Patients With Normal Oxygen Tension (16 Cases) And Those With Hypoxemia (70 Cases) Were Compared In Table (2). The Authors Noticed No Significant Differences Concerning Bmi, Sex, Age, Or Serum Creatinine Level, But They Differed Significantly In Terms Of Acute Kidney Injury Markers (B2 Microglobulin And Cystatin C) (2.01±0.451 Vs 2.89±0.73, 1.33±0.184 Vs 1.46±0.21, Respectively), With A P Value Less Than 0.05.

Table 1. Comparison between the stable COPD and COPD AE patients:

	All COPD	Stable COPD (n=49)	COPD AE (n=86)	P-value
Age (years)	68.2±4.51	64.7±3.19	70.2±3.91	0.01
Gender (no%) **Female** **Male**	 50(37) 85(63)	 22(44.9) 27(55.1)	 28(32.6) 58(67.4)	 0.15
BMI (kg/m²)	24.8±4.97	23.2±1.38	25.7±5.95	0.18
PO2 (mmHg)	69.9±20.4	90.8±2.06	58.1±16.2	**0.001**
PCO2 (mmHg)	50.4±16.8	38.2±2.93	58.1±18	**0.001**
Creatinine	0.799±0.218	0.808±0.233	0.794±0.211	0.77
β2 micro globulin	2.17±0.981	1.18±0.303	2.73±0.768	**0.001**
Cystatin C	1.25±0.319	0.914±0.165	1.44±0.21	**0.001**
Systolic bl. pressure	124±17.1	114±9.53	129±17.9	**0.001**
Diastolic bl. pressure	78.9±10.2	73.7±8.83	81.9±9.76	**0.001**

The Mann-Whitney U test was used.

The Comparison Of The Hypoxemia Subgroups Is Displayed In The Remaining Section Of **Table (2)**. The Cases Were Distributed To The Following Groups: Although The Mean Level Of B2 Microglobulin And Cystatin C Is Higher With The Severity Of Hypoxaemia, The Authors Observed The Lack Of Any Significant Differences Between The Levels Of These Two Markers And Different Grades Of Hypoxemia For PaO2 Tension Of 60-80 mmHg (Mild Hypoxemia), 40-60 mmHg (Moderate Hypoxemia), And Less Than 40 mmHg (Severe Hypoxemia), Which Included 10 Cases.

Table 2. Comparison among different grades of hypoxaemia in COPD patients with acute exacerbation:

	COPD AE With Normoxemia (n=16)	COPD AE with Hypoxaemia (n=70)	P-value*	Mild hypoxaemia (PaO2 60-80 mmHg) (n=16)	Moderate hypoxaemia (PaO2 40-60 mmHg) (n=44)	Severe hypoxaemia (PaO2 <40 mmHg) (n=10)	P-value+
Age (years)	69.3±1.53	70.5±4.25	0.505	69.6±4.59	70.5±4.3	71.8±3.42	0.382
Gender (no%) **Female** **Male**	 8(50) 8(50)	 20(28.6) 50(71.4)	 0.105	 6(37.5) 10(62.5)	 10(22.7) 34(77.3)	 4(40) 6(60)	 0.367
BMI (kg/m2)	29.6±8.78	24.9±4.75	0.16	26.7±4.76	24.1±4.49	25.32±5.44	0.183
PaO2 mmHg	83.9±3.76	52.2±11.5	**0.001**	67.9±6.5	50.31±5.52	35.2±4.49	**0.001**
PaCO2 mmHg	42.8±4.75	60.6±17.7	**0.001**	53.1±12.02	61.54±19.1	68.8±15.5	**0.028**
S. Creat.	0.762±0.205	0.801±0.213	0.625	0.825±0.3	0.757±0.13	0.96±0.28	0.079
β2 micrglobulin.	2.01±0.451	2.89±0.73	**0.001**	2.69±0.905	2.94±0.68	2.99±0.63	0.465
Cystatin C	1.33±0.184	1.46±0.21	**0.005**	1.45±0.33	1.46±0.14	1.49±0.22	0.261
Systolic bl. Pressure	128±8.56	130±19.5	0.89	133±12.4	128±21.8	134±18.4	0.198
Diastolic bl. Pressure	85±5.16	81.1±10.4	0.096	85±11.5	79.5±9.87	82±10.3	0.277

* Mann-Whitney U test +Kruskal-Wallis non-parametric among hypoxemic groups

The Relationship Between Various Factors And B2 Micro Globulin Is Displayed In **Table (3)**. In Patients Experiencing An Acute Exacerbation, A Significantly Negative Correlation Was Found Between B2 Microglobulin And Partial Arterial Tension Of Oxygen (PaO2) (R=-0.785 And P Value < 0.001), While There Was A Significant Positive Correlation Between B2 Microglobulin And Cystatin C (R= 0.539 And P-Value < 0.001) And PaCO@ (R= 0.137 And P-Value < 0.001).

Table 3. Correlation between different parameters and B2 micro globulin:

	Stable COPD (49 pt.)		A.E. COPD with normal PaO2 (16 pt)		A.E. COPD with hypoxaemia (70 pt)	
	Spearman rho (r)	**P-value**	**Spearman rho (r)**	**P-value**	**Spearman rho (r)**	**P-value**
Cystatin C	0.013	0.928	0.687	**0.003**	0.539	**< 0.001**
Serum creatinine	0.103	0.48	0.21	0.435	0.064	0.6
PaO2	-0.246	0.088	-0.785	**< 0.001**	-0.268	**0.025**
PaCO2	0.458	0.001	0.785	**0.259**	0.137	**<0.001**
Systolic BP	0.136	0.35	0.466	0.069	0.063	0.606
Diastolic BP	0.06	0.63	0.22	0.414	0.008	0.949

Spearman's rho was used.

In A Similar Analysis, We Found That In Patients Experiencing Acute Exacerbation, There Was A Significant Negative Correlation With Partial Arterial O2 Tension (PaO2) (R=-0.161 And P-Value = 0.045) And A Significant Positive Correlation With B2 Micro-Globulin (R= 0.539 And P-Value < 0.001) And PaCO2 (R= 0.003 And P-Value < 0.001) **(Table 4)**.

Table 4. Correlation between different parameters and Cystatin C:

	Cystatin C					
	Stable COPD (49 pt.)		A.E. COPD with normal PaO2 (16 pt)		A.E. COPD with hypoxaemia (70 pt)	
	Spearman rho (r)	P-value	Spearman rho (r)	P-value	Spearman rho (r)	P-value
β2 micro-globulin	0.013	0.928	0.687	**0.003**	0.539	<0 .001
S. creatinine	0.268	0.062	0.8	0.551	0.1	0.374
PaO2	-0.15	0.27	-0.161	**< 0.001**	-0.113	0.035
PaCO2	0.166	0.25	0.8	0.978	0.003	< 0.001
Systolic BP	0.03	0.84	0.316	0.233	0.081	0.504
Diastolic BP	0.113	0.44	0.555	0.55	0.15	0.205

Spearman's rho was used.

The Multivariate Linear Regression Analysis Model To Look Into Potential Factors For The Level Of B2 Microglobulin Was Displayed In **Table 5**.Significant Predictors Of The Rise In B2 Microglobulin Levels Included Age, Cystatin C, PaO2 Tension, And The Degree Of Hypoxemia.The Amount Of B2 Micro-Globulin Increased By 0.015 For Every Unit Drop In Oxygen Tension.

Table 5. Multivariate logistic Linear regression analysis of possible predictors for the level of β2 micro-globulin:

	Univariate linear regression		Multivariate linear regression			
	Coefficient (B)	P value	Coefficient (B)	95%CI		P value
				Upper	Lower	
Age	0.0903	**0.001**	-0.027	-0.052	-0.003	**0.025**
Cystatin C	2.48	**0.0001**	1.479	1.007	1.951	**< 0.001**
PO2	-0.036	**0.001**	-0.015	-0.026	-0.003	0.011
PaCO2	0.0271	**0.0001**	-0.006	-0.014	9.72	0.086
Systolic BP	0.021	**0.001**	-2.39	-0.007	0.0069	0.948
Diastolic BP	0.026	**0.0001**	0.006	-0.005	0.0184	0.297
Having AECOPD	1.54	**0.001**	0.188	-0.57	0.2018	0.341
Severity of hypoxaemia	1.5	**0.001**	0.403	-0.83	0.0259	**0.045**
Sex 'female'	0.45	**0.015**	-0.066	-0.2615	0.128	0.503

The Multivariate Linear Regression Analysis Model Employed In Order To Look Into Potential Factors For The Amount Of Cystatin C Was Displayed In **Table 6**.The Presence Of AECOPD, Female Patients, And B2 Microglobulin Were Significant Predictors Of Increased Cystatin C Levels, Although The Presence And Severity Of Hypoxemia Were Not.

Table 6. Multivariate logistic Linear regression analysis of possible predictors for the level of Cystatin C.

	Univariate linear regression		Multivariate linear regression			
	Coefficient (B)	P value	Coefficient (B)	95%CI		P value
				Upper	Lower	
Age	0.034	**0.0001**	0.0058	-0.002	0.014	0.157
β2 micro-globulin	0.263	**0.001**	0.159	0.108	0.21	**< 0.001**
PO2	-0.016	**0.001**	0.00173	-0.0021	0.005	0.378
PaCO2	0.007	**0.001**	-5.704	-0.0031	0.002	0.661
Systolic BP	0.005	**0.001**	7.705	-0.002	0.0024	0.948
Diastolic BP	0.007	**0.004**	-0.0026	-0.006	0.0012	0.181
Having AECOPD	0.525	**0.001**	-0.31104	-0.426	-0.195	**< 0.001**
Severity of Hypoxaemia	0.445	**0.001**	-0.01662	-0.159	0.125	0.818
Sex: Female	0.17	**0.002**	0.088	0.026	0.151	**0.006**

DISCUSSION

COPD Has Negative Clinical Consequences For Numerous Organs. Aecopd Patients Often Suffer From Acute Kidney Injury (AKI), Which Is Associated With Worse Prognosis And Higher Use Of Medical Resources. [25]

In Patients Experiencing AECOPD, AKI Is Shown To Be An Independent Risk Factor For In-Hospital Death. [26] According To A Study By Barakat Mf et al., The Prevalent Level Of AKI Among Cases Experiencing Aecopd Amounted To 1.9%, Whereas The Incidence Of AKI In People Experiencing Chronic Obstructive Lung Disease (COPD) Was 128 Instances Per 100,000 Person-Years. [27] Additionally, Compared To Patients Without AKI, People Experiencing AECOPD With AKI Showed A 1.80-Fold Higher Chance Of Dying Within The First Six Months After A COPD Exacerbation. [27]

Serum Creatinine (Scr) And Blood Urea Nitrogen (BUN) Values Are Known To Vary Only When Renal Function Has Already Been Severely Damaged, Making Them Unreliable Indicators Of Renal Impairment, Especially In Its Early Stages. [11]. On The Other Hand, Beta-2-Microglobulin (B2-Mg) And Cystatin C (Cys-C) Are Both Tiny Molecules Whose Levels Inside The Body Don't Change In Response To Environmental Influences. The Renal Tubular Epithelium Is Where These Compounds Are Mainly Reabsorbed Before Being Broken Down And Eliminated Through Urine.

When Renal Tubular Injury Occurs, The Reabsorption Of Both Cystatin C (Cys-C) And Beta-2-Microglobulin (B2-Mg) Decreases, Resulting In Increased Serum Levels [28]. In Order To Detect Acute Renal Injury Among Cases With Chronic Obstructive Pulmonary Disease (COPD), We Investigated The Possibility Of Using Cys-C And B2-Mg As Biological Markers.

Serum Creatinine Levels In This Study Were Found To Be Within The Normal Range, And There Were No Discernible Differences Between The Stable COPD And AECOPD Groups. This Finding Matches The Findings Of A Study Conducted By Chen D et al., Which Found That Serum Creatinine (Scr) In Patients With AECOPD Is Not A Good Indicator Of Acute Kidney Damage (AKI). [29] This Implies That Scr Is Not A Reliable Indicator Of Kidney Injury In Its Early Stages. This Restriction Is Justified Because Of Creatinine's Half-Life, Which Can Range From 4 To 24 To 72 Hours When Gfr Declines, Limiting Its Usefulness As An Indicator Of The Renal Function. Furthermore, After A Major Renal Damage, It Could Take 24 To 36 Hours For Serum Creatinine Levels To Rise. [30] Moreover, Muscular Activity And The Quantities Produced In The Kidneys, Liver, And Pancreas All Affect Creatinine Production. [31]

When We Measured Cystatin C (Cys-C) And B2-Microglobulin (B2-Mg), We Found That Individuals With AECOPD Had Considerably Higher Average Serum Levels Of Both Biomarkers Than Patients With Stable COPD. This Observation Is Consistent With Zhang D.'S Study, Which Found Statistically Significant Variations In Cys-C And B2-Mg Levels Throughout The AECOPD Cohort Compared To The Control Group. [7] Our Findings Also Support Those Of Chen D et al., Who Found Cystatin C To Be A Strong Independent Predictor Of Acute Kidney Injury (AKI) Among AECOPD Patients (Or 5.22; 95% Ci 2.49–10.95; $P < 0.001$). [29] The Reason For This Phenomenon Is That Cases With AECOPD Frequently Have Lower Muscle And Fat Mass [32], Which Results In A Real Drop-In Glomerular Filtration Rate (GFR), Which Is Accurately Represented By Cystatin C. Cystatin C Has A Half-Life That Is Almost 50% Shorter Than Creatinine, And Unlike Other Indicators, Its Levels Are Unaffected By Dietary Protein Intake, Age, Sex, Or Muscle Mass. [33] As A Result, Serum Levels Of Cystatin C Might Increase Before Creatinine [34], Usually Within 24 To 48 Hours Of Even Minor Renal Damage. [35]

Those With Hypoxemia And AECOPD Had Significantly Higher Levels Of Acute Kidney Damage Markers, Notably B2 Micro-Globulin And Cystatin C, Than Those With Normal Oxygen Levels. Additionally, It Was Discovered That The Degree Of Hypoxemia Was Correlated With Increased Average Amounts Of Cystatin C And B2 Microglobulin. This Finding Is Consistent With Zhang D.'S Study, Which Showed That Levels Of Cystatin C And B2 Micro-Globulin Increased Gradually As Hypoxia Increased, With Statistically Significant Differences Across The Different Groups In Numerous Comparisons [7].

According To The Results, Glomerular Hemodynamic Changes Brought On By Prolonged Hypoxia May Be Linked To The Renal Damage Shown In The Research Groups. [7] Because Hypoxemia Activates Vasoactive Substances Such As Endothelin And Angiotensin Ii, It Might Improve Renal Vascular Resistance, Which Can Reduce The Flow Of Renal Blood. [37] Hypoxia Can Also Cause Renal Tubular Epithelial Cells And Mesenchymal Cells To Differentiate Into Fibroblasts Or Trigger Apoptosis, Which Can Result In Tubulointerstitial Fibrosis And Either Cause Or Exacerbate Renal Damage. Those Processes Work Together To Cause Kidney Impairment In Those Who Are Impacted. Furthermore, The Release Of Inflammatory Mediators And Cytokines Might Be Markedly Increased During Acute Exacerbations. [38]

A Substantial Negative Correlation Was Found Between B2 Microglobulin And The Partial Arterial Tension Of Oxygen (PaO2), But B2 Microglobulin Levels And Both Cystatin C And PaCO2 Positively Correlated. Furthermore, Cystatin C Levels Showed A Strong Negative Association With PaO2 And A Positive Correlation With B2 Micro-Globulin And PaCO2. These Results Are In Line With Zhang D.'S Study, Which Found That Cystatin C Levels Had A Negative Association With PaO2 And A Positive Correlation With hs-CRP, PaCO2, Serum Creatinine (Scr), And Blood Urea Nitrogen (BUN). Additionally, B2 Microglobulin Levels Had A Negative Correlation With PaO2 And A Positive Correlation With hs-CRP, PaCO2, Scr, And BUN [7]. The Results Of The Multivariate Linear Regression Analysis

On B2 Micro-Globulin Levels Showed That Increased Cystatin C Levels, Growing Older, And The Existence And Degree Of Hypoxemia Were All Significant Predictors Of Higher B2 Micro-Globulin Levels. In Particular, There Was A 0.015 Rise In B2 Micro-Globulin Levels For Every Unit Drop In Oxygen Tension. Furthermore, Being Female, Having B2 Micro-Globulin Levels, And Experiencing Exacerbations Were All Significant Predictors Of Cystatin C Levels.

Our Study's Limitations Were Mostly Brought On By Its Single-Center Design, Which Could Provide Results That Are Different From Those Found In Other Places, And Its Limited Sample Size, Which Might Result In Less Accurate Findings. Further Investigation Is Required To Examine How The Medication Being Delivered Affects The Levels Of Beta-2 Microglobulin And cystatin C, Particularly When Diuretics Are Used In Patients With Decompensated Cor Pulmonale.

CONCLUSION

Elderly Individuals With Aecopd Frequently Experience Acute Kidney Injury, Which Is Positively Correlated With The Severity Of Hypoxemia And Hypercapnia. Cys-C And B2-Mg Can Be Used As Sensitive Markers To Detect Renal Impairment Early In Older Adults With AECOPD. The Factors That Predicted An Increase In B2 Microglobulin Levels Were Age, The Degree Of Hypoxemia, And An Increase In Cystatin C Level. However, Higher B2 Microglobulin Levels, COPD Exacerbation, And Female Cases Were Predictors Of Elevated Cystatin C. Therefore, Addressing Risk Factors And Detecting Renal Impairment Early Can Improve The Outcome For Individuals With COPD.

Abbreviations:

COPD: Chronic Obstructive Pulmonary Disease;
HF: Heart Failure;
DM: Diabetes Mellitus; Ckd: Chronic Kidney Disease;
AKI: Acute Kidney Injury;
AECOPD: Acute Exacerbation Of Copd;
Scr: Serum Creatinine; Cys-C: Cystatin C;
GFR: Glomerular Filtration Rate;
β2-Mg: Beta-2 (β2) Macroglobulin;
CVD: Cerebrovascular Diseases And PaO2: Oxygen Partial Pressure.

Authors' contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Morsi SN, Gadallah D, and Dongol EM. The first draft of the manuscript was written by Morsi SN and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.
Conflicts Of Interest: The Researchers Declare That They Do Not Have Conflicts Of Interest.
Acknowledgements: Not Applicable.
Funding: Non

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