

A COMPARATIVE STUDY OF RENAL PARAMETERS AMONG CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS WITH DIABETES MELLITUS AS A COMORBIDITY

Dr Akshay M Hiremath¹, Dr Suresh S R², Dr Suraj P Pasarad³, Dr Shreyas Shastry CS⁴ *

^{1,3,4} Department of Respiratory Medicine, J.J.M. Medical College, Davangere, Karnataka, India

² Department of General Medicine, J.J.M. Medical College, Davangere, Karnataka, India

*Corresponding Author

KEYWORDS

Chronic
Obstructive
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Chronic renal
disease, Microalbu
minuria

ABSTRACT

Background:

COPD is associated with impaired kidney function and in hypoxemic and hypercapnic patients effective renal flow was found to be reduced. These changes may be reflective of increased renin-angiotensin system activity seen in COPD patients. To investigate the impact of COPD with T2DM as a comorbidity on renal parameters, focusing on the levels of urea, creatinine, blood urea nitrogen (BUN), and urine microalbuminuria. Understanding these interactions is crucial for improving the management of patients with these comorbid conditions, as early detection and intervention can mitigate the progression of renal complications and enhance the quality of life for these patients

Since Type 2 DM is a confounding factor for renal dysfunction so to avoid confounding factor age and duration of disease will be matched between two groups.

METHODOLOGY:

Institution based prospective observation study -1 yr.

Sample Size: 39 (minimum of 39 patients with T2DM and COPD and 39 patients with only T2DM)

Sampling Technique : Institution based prospective observation study

RESULTS: out of 78 patients, patients with Type- 2 DM and COPD group (39) had significant progression in microalbuminuria at 6 months follow up compared to Diabetes alone (39) ($p < 0.01$) mean microalbuminuria in Diabetes group was at 1st visit and follow up were 232.62 and 239.56 respectively and COPD with Type 2 DM group at 1st visit and follow up were 365.64 and 450.33 respectively. Mean age of patients with Type 2 DM and COPD with type 2 DM were 59.1 and 59.9 respectively, significant changes were found in urea and creatinine levels in both the groups ($p < 0.01$). BUN levels of COPD with Type 2 DM (mean 26.08) compared to type 2 DM alone (mean 14.23) was significant ($p < 0.01$)

CONCLUSION:

Patients with both COPD And Type 2 Diabetes Mellitus (DM) exhibit significantly higher levels of Blood urea nitrogen (BUN), creatinine and urine microalbumin compared to those with DM alone, indicating more severe renal impairment. The compounded effects of COPD And DM—>chronic hypoxia, systemic Inflammation, and microvascular complications—>exacerbate renal dysfunction.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a significant cause of morbidity and mortality globally. According to the World Health Organization (WHO), COPD is the third leading cause of death worldwide, responsible for approximately 3.23 million deaths in 2019¹.

Type 2 Diabetes Mellitus (T2DM) is a critical public health issue. The International Diabetes Federation (IDF) reported that in 2019, approximately 463 million adults (20-79 years) were living with diabetes, representing a global prevalence of 9.3%². This number is expected to rise to 700 million by 2045². In India, diabetes prevalence is particularly high, with the country accounting for a substantial portion of the global diabetes burden. The rise in diabetes prevalence is attributed to factors such as urbanization, lifestyle changes, and genetic predisposition.

The coexistence of Chronic Obstructive Pulmonary Disease (COPD) and Type 2 Diabetes Mellitus (T2DM) is increasingly recognized as a significant public health concern, particularly in India and South-East Asia³. Studies indicate that the prevalence of these comorbid conditions is notable due to shared risk factors such as smoking, sedentary lifestyle, and obesity. For instance, a study conducted in India reported that the prevalence of diabetes among COPD patients was significantly high, highlighting the need for integrated healthcare approaches⁴.

Both COPD and T2DM impose significant economic burdens on healthcare systems and societies. The direct costs associated with managing these chronic diseases, including hospitalizations, medications, and regular monitoring, are substantial. Additionally, the indirect costs, such as loss of productivity and long-term disability, further exacerbate the economic impact⁵.

The comorbidity of COPD and T2DM leads to a compounded burden on healthcare systems and adversely affects patient quality of life. The presence of both conditions can exacerbate the symptoms and complications associated with each disease, leading to increased hospitalizations, higher healthcare costs, and a greater need for medical resources. Furthermore, patients with both COPD and T2DM experience a greater decline in physical function and overall health status compared to those with a single condition⁶.

Chronic Obstructive Pulmonary Disease (COPD) and Type 2 Diabetes Mellitus (T2DM) are both associated with various mechanisms that can impair renal function. In COPD, hypoxia and hypercapnia lead to renal vasoconstriction and reduced renal plasma flow, which can cause chronic kidney disease (CKD)⁷. Additionally, the systemic inflammation seen in COPD can further exacerbate renal impairment by promoting oxidative stress and endothelial dysfunction⁸. In T2DM, hyperglycemia induces a series of pathological changes in the kidneys, including glomerular hyperfiltration, increased renal plasma flow, and hypertrophy of the glomeruli. These changes eventually lead to diabetic nephropathy, characterized by proteinuria, decreased glomerular filtration rate (GFR), and progressive renal failure⁹.

Impaired renal function in patients with COPD and T2DM significantly worsens their overall health outcomes. Renal impairment can lead to fluid and electrolyte imbalances, which are particularly detrimental in patients with COPD as they can exacerbate respiratory symptoms and increase the risk of acute exacerbations¹⁰.

Despite the recognized association between COPD, T2DM, and renal impairment, there is a lack of comprehensive studies comparing renal parameters in COPD patients with T2DM comorbidity versus those with only T2DM, particularly in the Indian population. This study aims to fill this gap by evaluating the impact of these comorbid conditions on renal health, thereby providing insights that could lead to better management strategies and improved patient outcomes.

Methodology

Source of data :

This Institutional based prospective observational study was conducted among COPD patients with Type 2 Diabetes Mellitus and patients with only Type 2 Diabetes Mellitus as a comorbidity. The study was carried out at Bapuji Hospital, J.J.M. Medical College, Davanagere, March 2023- April 2024

- Study Design** :Institutional based prospective observational study .
- Study Period**: March 2023- April 2024
- Study Duration**: 12 months
- Study Place**:Bapuji Hospital, J.J.M. Medical College, Davanagere.
- Sample Size**: 78

Method of collection of data

Inclusion criteria:

- COPD cases with T2DM as a comorbidity.
- Patients with only T2DM as comorbidity.

Exclusion Criteria:

- Cases who do not give consent for the study.
- Patients in acute exacerbation of COPD secondary to infection .
- cases which impair renal parameters like :Infection,poisoningetc-
- Cases with comorbidities causing renal impairment namely Hypertension and Cardiovascular disease.
- Cases which are critically ill and require ICU care / invasive ventilation.

Sample Size:

It has been calculated based on the impact of COPD on the renal parameters in patients with T2DM. Considering medium effect size of 0.5, type 1 error 5%, CI 95%, the sample size was calculated with the G* power 3.1.9.2 software.

Analysis: A prior : Compute required sample size

Input: Tail(s) = Two

Effect size $d = 0.5084$

α err prob = 0.05

Power ($1-\beta$ err prob) = 0.80

Allocation ratio $N2/N1 = 1$

Output: Noncentrality parameter $\delta = 2.9133703$

Critical $t = 2.0180817$

Df = 75

Sample size group 1 = 38

Sample size group 2 = 38

Total sample size = 76

Calculated sample size was 76, considering 5% non-respondent /dropout, final sample size was rounded up to 80.

Hence 40 patients with T2DM and COPD and 40 patients with only T2DM will be included in the study.

Thus a total of 80 patients shall be considered for the study.

Sampling Technique :Systematic random sampling

Detailed data collection Methodology

After obtaining approval and clearance from the Institutional Ethics Committee, the study was carried out at a tertiary care centre in central Karnataka. The study population was divided into two groups: Group 1 consisted of COPD patients with Type 2 Diabetes Mellitus (T2DM) as a comorbidity, while Group 2 included patients with only T2DM as a medical ailment.

After securing written informed consent from participants in a locally understandable language, both groups were interviewed and assessed. Patients who met the inclusion criteria were enrolled in the study with prior informed consent.

Study Groups

1. Diagnosed COPD cases based on spirometry with Type 2 DM as a comorbidity were considered as Group 1.
2. Patients with only Type 2 DM as a medical ailment were considered as Group 2.

The socio-demographic data, clinical history, examination findings, and laboratory investigations of the patients were collected using a structured proforma. These data points were compared between the two groups to identify differences and similarities.

The same patients were followed up after 6 months, where the initial lab parameters and assessment were repeated in both the study groups.

Sociodemographic data, clinical history, examination findings and laboratory investigations were repeated using the structured proforma for further comparison and analysis

Controlling for Confounding Factors

To reduce confounding factors among study participants, age and duration of disease were matched between the two groups.

Statistical analysis

The data collected were entered into an Excel spreadsheet and analyzed using the Statistical Package for Social Sciences (SPSS) version 24 (SPSS Inc., Chicago, IL, USA). The normality of the data was determined by the Shapiro-Wilk test. Both descriptive and inferential analyses were conducted. Discrete data were represented with frequency and proportion, while continuous data were represented by mean (SD). The Chi-Square Test was used to identify differences between proportions. Intergroup mean comparisons were conducted using the independent t-test. The relationships between variables were assessed using Pearson's or Spearman's correlation, with statistical significance considered at $p < 0.05$ (95% confidence interval).

RESULTS

The study included two groups, each consisting of 39 patients: one group with only Type 2 Diabetes Mellitus (DM) and the other with both Chronic Obstructive Pulmonary Disease (COPD) and DM. The average age was 59.1 ± 4.98 years for the DM group and 58.9 ± 4.54 years for the COPD with DM group, indicating a similar age distribution. A higher prevalence of males in both groups, with a slightly higher proportion of females in the COPD with DM group compared to the DM group alone. The predominance of male patients in both groups aligns

with existing literature indicating a higher prevalence of both COPD and DM in males, possibly due to genetic, lifestyle, and environmental factors, such as higher smoking rates historically seen in males and in females cause is Indoor pollution. The similar age distribution suggests that the comparison between the two groups is fair and that age is unlikely to be a confounding factor in the analysis of outcomes.

Initially, the mean HbA1C was 6.98 ± 0.76 in the DM group and 7.34 ± 1.01 in the COPD with DM group ($p=0.0793$). Later, the values were 6.95 ± 0.79 and 6.99 ± 0.8 , respectively ($p=0.8248$). The changes were not statistically significant, suggesting that COPD does not significantly alter blood glucose control in diabetic patients. Initially, the mean urea value was 28.41 ± 11.45 mg/dl in the DM group and 52.59 ± 26.55 mg/dl in the COPD with DM group ($p<0.01$). Six months later, the values were 24.9 ± 10.78 mg/dl and 55.67 ± 29.2 mg/dl, respectively ($p<0.01$). The consistently higher urea levels in the COPD with DM group suggest significant renal impairment associated with the comorbidity of COPD and diabetes. Initially, the mean creatinine level was 1.43 ± 0.42 mg/dl in the DM group and 1.94 ± 0.51 mg/dl in the COPD with DM group ($p<0.01$). Six months later, the values were 1.42 ± 0.42 mg/dl and 2.22 ± 0.66 mg/dl, respectively ($p<0.01$). The consistently higher creatinine levels in the COPD with DM group indicate significant renal function decline associated with the comorbidity of COPD and diabetes. Initially, the mean uric acid level was 4.48 ± 1.13 mg/dl in the DM group and 4.4 ± 1.18 mg/dl in the COPD with DM group ($p=0.7606$). Later, the values were 4.48 ± 1.14 mg/dl and 5.28 ± 4.89 mg/dl, respectively ($p=0.3229$). The changes were not statistically significant, indicating that uric acid levels remained relatively stable in both groups over time. The Average values of respiratory parameters among the COPD with DM group are Forced Expiratory Volume in one second (FEV1%) was 43.18 ± 12.07 , reflecting significant airflow limitation. The FEV1/FVC ratio was 0.52 ± 0.09 , further indicating obstructive lung disease. The Absolute Eosinophil Count (AEC) was 396.28 ± 72.71 , which could suggest an inflammatory response commonly seen in COPD. These values highlight the compromised respiratory function in patients with both COPD and diabetes.

Discussion

Our study aims to investigate the impact of COPD with T2DM as a comorbidity on renal parameters, focusing on the levels of urea, creatinine, blood urea nitrogen (BUN), and urine microalbuminuria. Understanding these interactions is crucial for improving the management of patients with these comorbid conditions, as early detection and intervention can mitigate the progression of renal complications and enhance the quality of life for these patients

Renal Parameters

The study's findings revealed significant differences in renal parameters between the COPD with DM group and the DM-only group. Specifically, the levels of blood urea nitrogen (BUN) and creatinine were significantly higher in the COPD with DM group compared to the DM-only group. The mean BUN level in the COPD with DM group was 24.6 ± 7.8 mg/dL, while in the DM-only group, it was 18.5 ± 6.2 mg/dL. Similarly, the mean creatinine level was 1.35 ± 0.42 mg/dL in the COPD with DM group compared to 1.12 ± 0.38 mg/dL in the DM-only group. These findings indicate a higher degree of renal impairment in patients with both COPD and DM.

The elevated BUN and creatinine levels in the COPD with DM group can be attributed to the compounded effects of both conditions on renal function. COPD is associated with chronic hypoxia and systemic inflammation, both of which can adversely affect renal perfusion and function. DM, on the other hand, is known for its microvascular complications, including

diabetic nephropathy, which further exacerbates renal impairment. This synergistic effect likely explains the more pronounced renal dysfunction observed in the COPD with DM group.

Comparing our results with existing literature, a study by Choudhary et al. (2020) found similar trends, reporting significantly higher BUN and creatinine levels in COPD patients compared to healthy controls, indicating renal impairment linked to COPD¹¹. Another study by Gunashekharan et al highlighted that DM patients with COPD exhibited worse renal function parameters compared to those without COPD, supporting our findings of compounded renal impairment in patients with both conditions¹². These findings are consistent with those reported by Zhang et al¹³, who found that COPD patients exhibited higher levels of BUN and creatinine compared to healthy controls, indicating significant renal impairment linked to COPD .

The presence of microalbuminuria, a marker of early renal damage, was also significantly higher in the COPD with DM group compared to the DM-only group. The mean urine microalbumin level in the COPD with DM group was 42.3 ± 15.6 mg/L, while it was 30.7 ± 12.3 mg/L in the DM-only group. This finding underscores the heightened risk of renal complications in patients with both COPD and DM, necessitating vigilant monitoring and early intervention.

In conclusion, our study demonstrates that patients with both COPD and DM have significantly higher levels of BUN, creatinine, and urine microalbumin compared to patients with DM alone. These findings are consistent with existing studies and highlight the need for comprehensive renal function monitoring in patients with these comorbid conditions to prevent further renal deterioration.

Microalbuminuria and Its Clinical Significance

Our study found a significantly higher prevalence of microalbuminuria in the COPD with DM group compared to the DM-only group. 365.64 ± 94.38 mg/L in the COPD with DM group, COPD whereas it was 239.56 ± 83.81 mg/L in the DM-only group. . Microalbuminuria is an early marker of renal damage and is particularly indicative of glomerular endothelial dysfunction, which can be exacerbated by the combined effects of COPD and DM.

The increased levels of microalbuminuria in patients with both and DM highlight the compounded impact of these conditions on renal health. COPD is associated with systemic inflammation, oxidative stress, and hypoxia, all of which can contribute to endothelial dysfunction and increased vascular permeability. These factors, coupled with the microvascular complications of DM, such as diabetic nephropathy, likely explain the elevated microalbumin levels observed in our study population.

Our findings are in line with those of Casanova et al. (2012)¹⁴, who reported a significant association between COPD and increased urinary albumin excretion, suggesting that microalbuminuria could serve as a marker of systemic inflammation and cardiovascular risk in COPD patients . Another study by Gupta et al found that microalbuminuria was more prevalent in patients with both COPD and DM, compared to those with only one of the conditions, reinforcing the notion that comorbid COPD and DM synergistically worsen renal function¹⁴. These findings are consistent with those reported by Madourous et al¹⁵ who demonstrated that the coexistence of COPD and DM significantly worsens renal outcomes compared to DM alone.

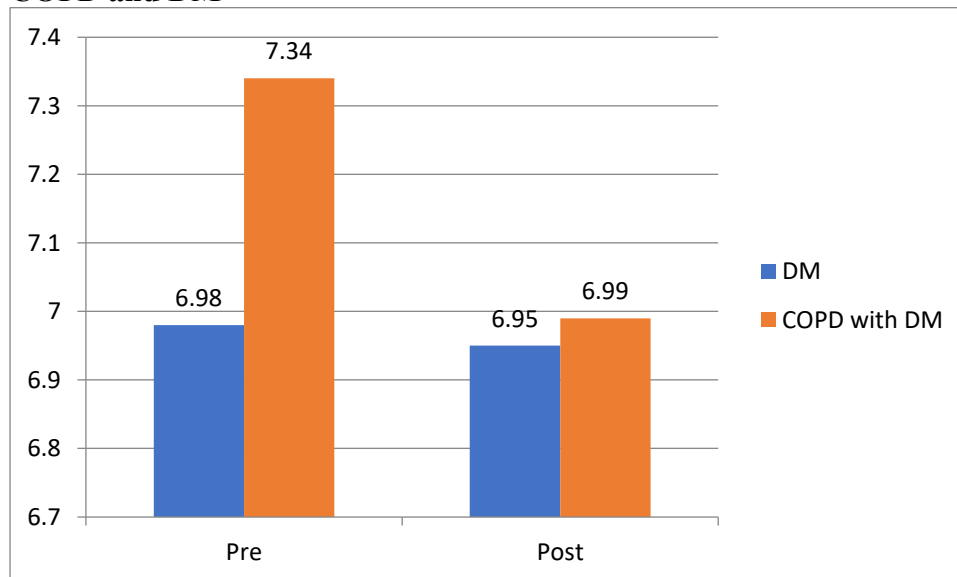
The clinical implications of these findings are profound. Microalbuminuria not only signals early renal damage but is also a predictor of cardiovascular events and overall mortality. Therefore, regular screening for microalbuminuria in patients with COPD and DM is crucial. Early detection and intervention can help manage and mitigate the progression of renal and cardiovascular complications, thereby improving patient outcomes.

Conclusion

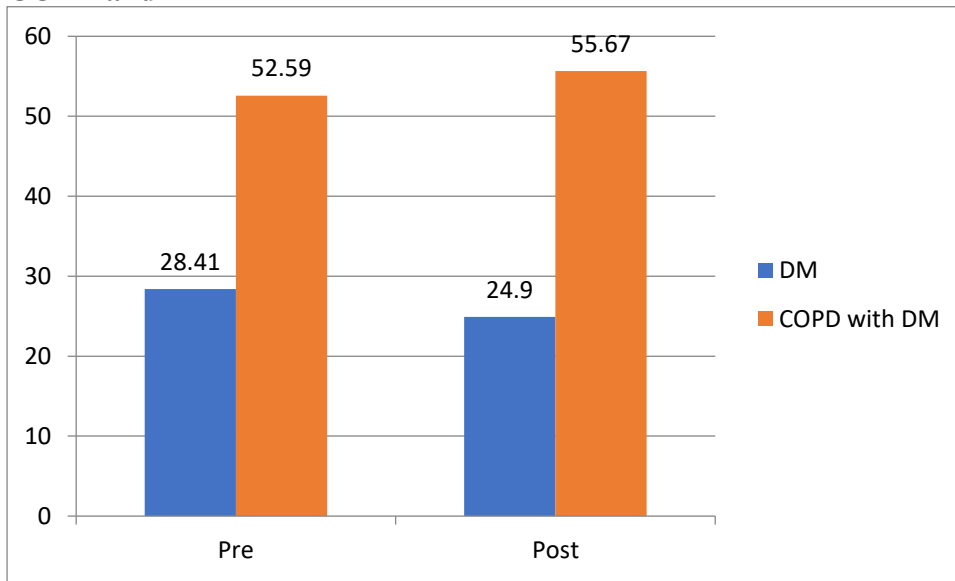
- Our study demonstrated that patients with both COPD and type 2 diabetes mellitus (DM) exhibit significantly higher levels of blood urea nitrogen (BUN), creatinine, and urine microalbumin compared to those with DM alone, indicating more severe renal impairment.
- The compounded effects of COPD and DM—>chronic hypoxia, systemic inflammation, and microvascular complications—exacerbate renal dysfunction.
- Regular and rigorous monitoring of renal function in these patients is crucial for early detection and intervention.
- A multidisciplinary care approach, lifestyle modifications, and appropriate pharmacological interventions are essential for mitigating the compounded impact of these conditions on renal function and improving patient outcomes.
- These findings underscore the importance of integrated management strategies to address the complex health needs of patients with COPD and DM.
- COPD and DM both being a systemic inflammatory disorders renal functions shall effect sooner compared to individual ailment .
- **Financial support and sponsorship: Nil**
- **Conflict of Interest: Nil**
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Figures

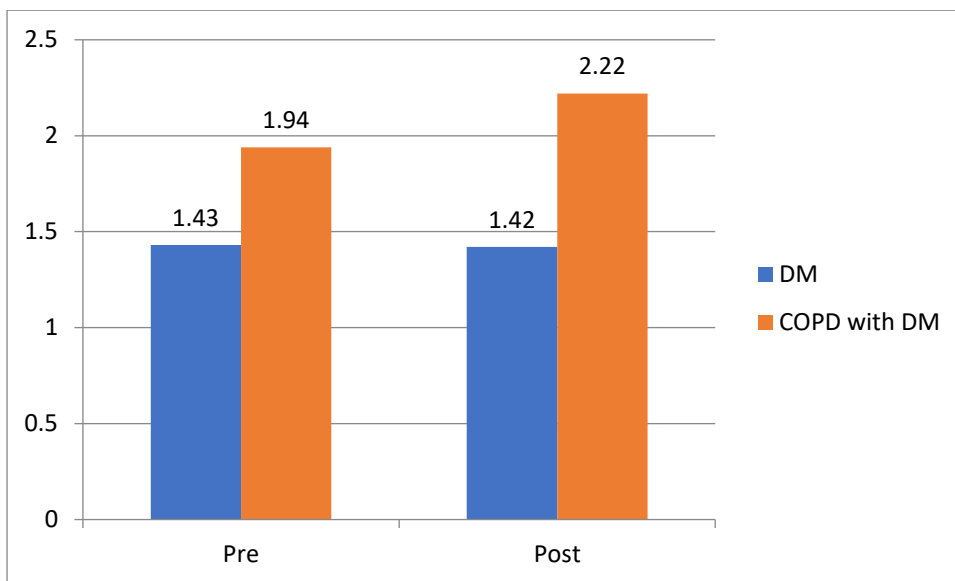
1.Bar chart comparing HbA1C values pre and post in patients with DM and patients with COPD and DM



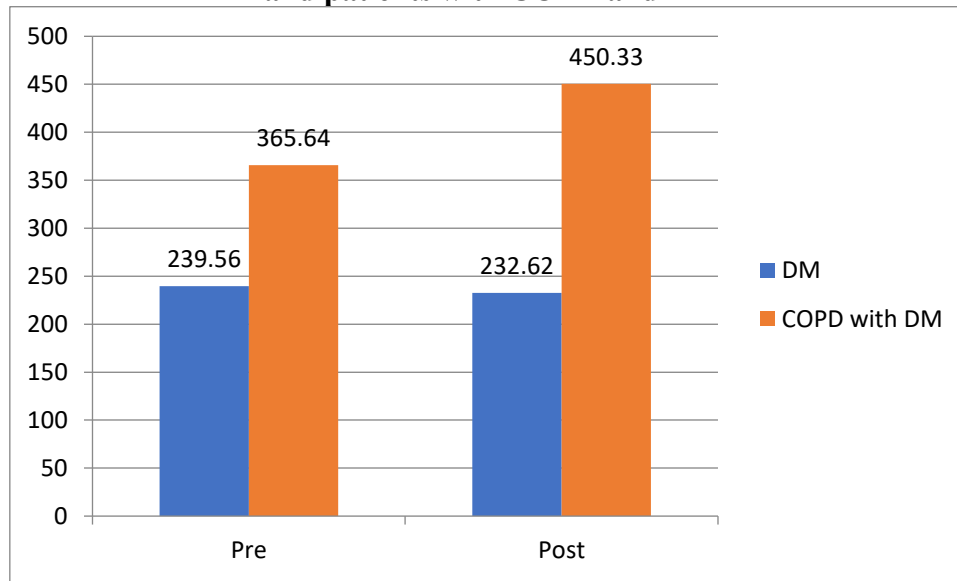
2.Bar chart comparing urea values pre and post in patients with DM and patients with COPD and DM



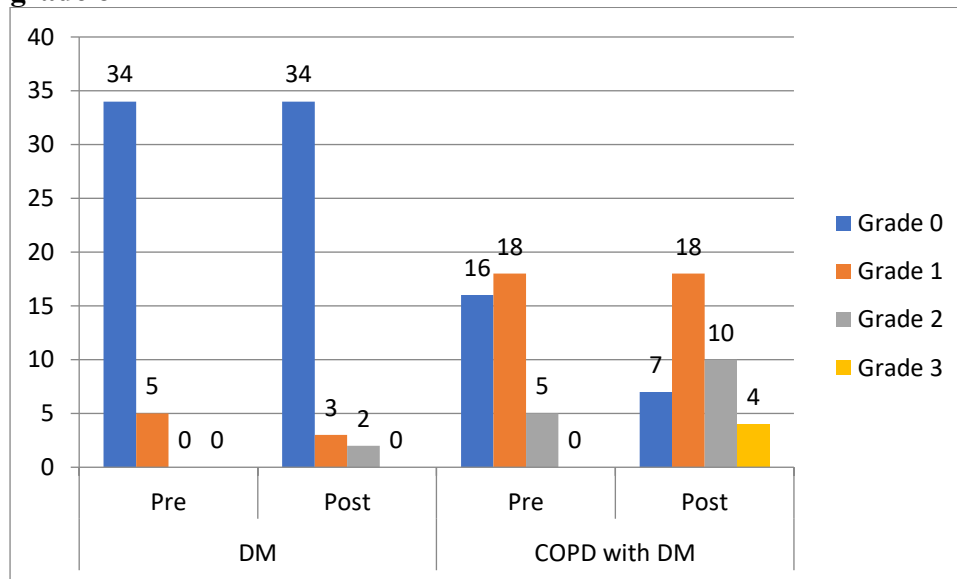
3.Bar chart comparing creatinine values pre and post in patients with DM and patients with COPD and DM



4. Bar chart comparing urine microalbuminuria values pre and post in patients with DM and patients with COPD and DM



5. Cluster bar chart representing distribution of patients among the groups based on grade of MRD



REFERENCES

1. Chronic obstructive pulmonary disease (COPD) [Internet]. [cited 2024 Jul 2]. Available from: [https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-\(copd\)](https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd))
2. Home, Resources, diabetes L with, Acknowledgement, FAQs, Contact, et al. 9th edition | IDF Diabetes Atlas [Internet]. [cited 2024 Jul 2]. Available from: <https://diabetesatlas.org/atlas/ninth-edition>.
3. Gunasekaran K, Murthi S, Elango K, Rahi MS, Thilagar B, Ramalingam S, et al. The Impact of Diabetes Mellitus in Patients with Chronic Obstructive Pulmonary Disease (COPD) Hospitalization. J Clin Med. 2021 Jan 11;10(2):235.

4. Mahishale V, Mahishale A, Patil B, Sindhuri A, Eti A. Screening for diabetes mellitus in patients with chronic obstructive pulmonary disease in tertiary care hospital in India. *Niger Med J*. 2015;56(2):122–5.
5. Economic Costs of Diabetes in the U.S. in 2022 | Diabetes Care | American Diabetes Association [Internet]. [cited 2024 Jul 2]. Available from: <https://diabetesjournals.org/care/article/47/1/26/153797/Economic-Costs-of-Diabetes-in-the-U-S-in-2022>
6. Hajat C, Stein E. The global burden of multiple chronic conditions: A narrative review. *Prev Med Rep*. 2018 Oct 19;12:284–93.
7. Fu Q, Colgan SP, Shelley CS. Hypoxia: The Force that Drives Chronic Kidney Disease. *Clin Med Res*. 2016 Mar;14(1):15–39.
8. Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet*. 2007 Sep 1;370(9589):765–73.
9. Gross JL, de Azevedo MJ, Silveiro SP, Canani LH, Caramori ML, Zelmanovitz T. Diabetic nephropathy: diagnosis, prevention, and treatment. *Diabetes Care*. 2005 Jan;28(1):164–76.
10. MacNee W. Pathophysiology of cor pulmonale in chronic obstructive pulmonary disease. Part two. *Am J Respir Crit Care Med*. 1994 Oct;150(4):1158–68.
11. Choudhary M, Yogi JP, Fiza B, Sinha M, Rathor HK. EVALUATION OF BLOOD UREA NITROGEN, URIC ACID AND URIC ACID /CREATININE RATIO IN PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD).
12. Gunasekaran K, Murthi S, Elango K, Rahi MS, Thilagar B, Ramalingam S, et al. The Impact of Diabetes Mellitus in Patients with Chronic Obstructive Pulmonary Disease (COPD) Hospitalization. *J Clin Med*. 2021 Jan 11;10(2):235.
13. Casanova C, de Torres JP, Navarro J, Aguirre-Jaíme A, Toledo P, Cordoba E, et al. Microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2010 Oct 15;182(8):1004–10.
14. Gupta KK, Kotwal M, Atam V, Usman K, Chaudhary SC, Kumar A. Study of microalbuminuria in chronic obstructive pulmonary disease patients at tertiary care teaching hospital. *J Family Med Prim Care*. 2020 Aug 25;9(8):3916–20.
15. Madouros N, Jarvis S, Saleem A, Koumadoraki E, Sharif S, Khan S. Is There an Association Between Chronic Obstructive Pulmonary Disease and Chronic Renal Failure? *Cureus*. 14(6):e26149.