

To Determine Correlations of HbA1c And Lipid Indices with Oxidative and Inflammatory Markers, Lung Function (FEV₁, FEV₁/FVC), and Functional Capacity (6-minute walk test) in COPD Patients: A Review

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) involves not only airflow limitation but also systemic metabolic, oxidative, and inflammatory changes. This review evaluates associations of glycosylated hemoglobin (HbA1c) and lipid indices with oxidative stress, inflammation, lung function, and functional capacity. Elevated HbA1c reflects glycemic dysregulation that worsens oxidative and inflammatory pathways, while atherogenic lipid profiles correlate with oxidative injury, reduced antioxidant defenses, and lower spirometric values (FEV₁, FEV₁/FVC). Markers like malondialdehyde (MDA) and TBARS are elevated, whereas superoxide dismutase (SOD) is diminished. Functional capacity, assessed by the six-minute walk test, declines with these systemic processes, linking metabolism to COPD progression.

KEYWORDS: COPD, MDA, SOD, TBARS, 6MWT.

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INTRODUCTION

COPD is determined as a major cause of morbidity and mortality globally. Almost all forms of smoking products are significantly associated with COPD. In non-smokers, especially women, an exposure to biomass fuels, smoke is an important factor¹. In COPD, there is airflow obstruction which causes air trapping and hyperinflation due to which patient is unable to exhale forcefully which causes decline in FEV₁ values. Also, respiratory muscle weakness contributes to loss in FEV₁ FEV₁/FVC ratio is generally used to define the presence or absence of airflow limitation. An impaired exercise Tolerance is the main feature in COPD².

Between metabolic dysfunction, oxidative stress, and systemic inflammation, which could adversely affect lung function parameters such as forced expiratory volume in one second (FEV₁), FEV₁/FVC ratio, and functional capacity assessed by the 6MWT³. Beyond structural lung changes, patients often experience chronic inflammation and oxidative stress, which stimulate a cascade of comorbid processes. Oxidative stress arises from an imbalance between pro-oxidant molecules (like reactive oxygen species) and antioxidant defenses⁴.

MATERIAL AND METHODS

A comprehensive literature search was performed in PubMed, Scopus, Web of Science, and Google Scholar using keywords related to COPD, HbA1c, lipid indices, oxidative stress, inflammatory markers, lung function, and 6MWT. Both original studies and reviews in English were considered. After screening for relevance, a total of 193 articles were included in this review.

Discussion:

HbA1c and Oxidative–Inflammatory Burden

In COPD, where oxidative and inflammatory drivers are already elevated, an elevated HbA1c may exacerbate lung injury and systemic inflammation, potentially influencing lung function and exercise tolerance⁶. Elevated glucose levels activate nuclear factor kappa-light chain enhancer of activated B cell (NF- κ B), a transcription factor that promotes the expression of pro-inflammatory cytokines such as TNF- α , IL-6, and CRP. These inflammatory mediators not only impair signaling, contributing to insulin resistance, but also damage vascular endothelium⁷.

1. Lipid Indices and Oxido-Inflammatory Status

COPD patients frequently display dysregulated lipid profiles. Atherogenic indices such as elevated LDL/HDL, triglyceride/HDL, and non-HDL cholesterol correlate positively with oxidative markers like MDA and TBARS negatively with antioxidant activity such as SOD and total antioxidant capacity⁸. Lipid peroxidation is initiated when reactive oxygen species attack polyunsaturated fatty acids in cellular membranes, triggering chain reactions that generate lipid hydroperoxides and various secondary products such as malondialdehyde (MDA) and 4-hydroxy 2-nonenal⁹.

2. Lung Function (FEV₁ and FEV₁/FVC)

Spirometric indicators of airflow limitation specifically lower FEV₁ and FEV₁/FVC—are consistently correlated with higher oxidative (e.g., MDA, TBARS,) and inflammatory markers (CRP, IL-8, leukotrienes, isoprostanes)¹⁰. Those symptoms usually preceded the classical definition of COPD that needs the spirometric clarification of FEV₁/FVC < 0.7¹¹.

3. Functional Capacity (6-Minute Walk Test)

Functional capacity, as measured by the 6MWD, is a direct reflection of integrated cardiopulmonary, vascular, and muscular performance. Evidence shows that increased oxidative stress and inflammation correlate with reduced 6MWD¹². Although direct correlations between lipid indices or HbA1c and 6MWD are less commonly reported, it is plausible that metabolic dysfunction and systemic oxidative-inflammatory burden impair muscular endurance, oxygen utilization, and overall exercise tolerance¹³.

4. Physiological Basis of Functional Capacity (6MWT)

The 6MWT evaluates the aerobic capacity and endurance of an individual. The distance walked during the test correlates with peak oxygen uptake, although not as precisely as treadmill or cycle ergometer tests. The simplicity of the test lies in its ability to integrate the response of multiple systems¹⁴:

5. Integrated Insights and Implications

1. **HbA1c**:- as a marker of chronic glycemia, may contribute to oxidative stress and systemic inflammation, compounding COPD pathophysiology.
2. **Atherogenic lipid indices**: - especially in severe COPD, are correlated with oxidative injury and inflammatory biomarkers, while being negatively associated with lung function and prognosis.
3. **Oxidative stress markers**: - (MDA, TBARS,) and inflammatory mediators (CRP, IL-8, leukotriene B₄) are consistently elevated in COPD, particularly with greater airflow limitation. They likely mediate tissue damage and systemic dysfunction¹⁵.
4. **Spirometric decline**: - (reduced FEV₁ and FEV₁/FVC) tracks with escalating oxidative and inflammatory stress, reflecting lung structural disruption.
5. **Reduced functional capacity**: - (lower 6MWD) likely reflects cumulative effects of metabolic derangements, oxidative-inflammatory injury, and respiratory compromise¹⁶.

6. Hypothetical Correlation Patterns

HbA1c: Positive correlation with oxidative and inflammatory markers; negative correlation with FEV₁, FEV₁/FVC, and 6MWD.

Lipid Indices: (LDL/HDL, TG/HDL, non-HDL, Atherogenic index of plasma): Positive correlation with oxidative/inflammatory markers; negative correlation with lung function and functional capacity¹⁷.

Oxidative markers: (MDA, TBARS,): Negative correlation with lung function and 6MWD.

Inflammatory markers: (CRP, IL-8,): Similar negative correlations with FEV₁ and 6MWD. These relationships suggest multiple potential mechanisms: metabolic dysfunction (HbA1c and lipids) may aggravate oxidative and inflammatory damage, which in turn undermines pulmonary mechanics and physical capacity¹⁸.

CONCLUSION

Chronic obstructive pulmonary disease sits at the crossroads of metabolic, oxidative, inflammatory, respiratory, and functional domains. Elevated HbA1c and atherogenic lipid profiles reflect systemic metabolic stress, which likely fuels oxidative and inflammatory mechanisms already active in COPD. These processes are intertwined with declining lung function (lower FEV₁, FEV₁/FVC) and diminished functional capacity (reduced 6MWT).

REFERENCES

1. Barnes PJ. Chronic obstructive pulmonary disease: A growing But Neglected Global epidemic. Plos Med. 2007;4(5):e112.
2. Miyamoto S, Nagaya N, Satoh T, Kyotani S, Sakamaki F, Fujita M, et al. Clinical correlates and prognostic significance of six-minute walk test in patients with primary pulmonary hypertension: comparison with cardiopulmonary exercise testing. Am J Res Crit Care Med. 2000 Feb 1;161(2):487-92.

3. Okeleji LO, Ajayi A F, Gege Grace , Aremu V Epidemiologic evidence linking oxidative stress and pulmonary function in healthy populations 2021 Jan 29;7(2):88–99. doi: 10.1016/j.cdtm.2020.11.004
4. Barnes J Peter, Yoo C G Oxidative Stress in Chronic Obstructive Pulmonary Disease 2022 May 13;11(5):965. doi: 10.3390/antiox11050965.
5. S Sabitha, V Shreelaxmi, Agarwal Vinayak, NS Delna, Pillai Ajita Biomarkers of Oxidative Stress and Their Clinical Relevance in Type 2 Diabetes Mellitus Patients: A Systematic Review 2024 Aug 10;16(8):e66570. doi: 10.7759/cureus.66570.
6. Anghel Lucreția , Ciubară Anamaria, Patraș D, Chronic Obstructive Pulmonary Disease and Type 2 Diabetes Mellitus: Complex Interactions and Clinical Implications J. Clin. Med. 2025, 14(6), 1809; <https://doi.org/10.3390/jcm14061809>
7. González Patricia , Lozano Pedro, Ros Gaspar, Solano Francisco Hyperglycemia and Oxidative Stress: An Integral, Updated and Critical Overview of Their Metabolic Interconnections Int.J.Mol.Sci.2023,24(11),9352; <https://doi.org/10.3390/ijms24119352>
8. Ivanovska B Z, Stojković J, Dokikj D, Anastasova S, Zejnel Sead The Level of Cholesterol in COPD Patients with Severe and Very Severe Stage of the Disease J Med Sci .2016 May 24;4(2):277–282. doi: 10.3889/oamjms.2016.063
9. Markelić Ivona, Hlapčić I, Rogić Dunja, Rako Ivana, Samaržija M Lipid profile and atherogenic indices in patients with stable chronic obstructive pulmonary disease Nutr Metab Cardiovasc Dis 2021 Jan 4;31(1):153-161. doi: 10.1016/j.numecd.2020.07.039
10. Zhai J, Voraphani N, Imboden Medea, Keidel Dirk, Liu C, Stern, Debra Circulating biomarkers of airflow limitation across the life span J Allergy Clin Immunol. 2024 Jan 20;153(6):1692–1703. doi: 10.1016/j.jaci.2023.12.026.
11. Hoesterey Daniel, Das Nilakash , Janssens Wim, Buhr Russell G, Spirometric indices of early airflow impairment in individuals at risk of developing COPD: Spirometry beyond EFV1/FVC Volume 156,September 2019, pages 58-68 <https://doi.org/10.1016/j.rmed.2019.08.004>.
12. Araujo A S, Roscani M G , Trimer R , da Silva A L G, Silva A B Distance travelled in the six-minute walk test in patients with chronic obstructive pulmonary disease as a predictor of mortality BMC Pulm Med 2025 May 23;25:258. doi: 10.1186/s12890-025-03721-x.
13. Casano H A. Matos , Ahmed Intisar, Anjum Fatima Six-Minute Walk Test national library of medicine July 7, 2025.
14. Aalstad LT, Hardie JA, Espehaug B, Thorsen E, Bakke PS, Eagan TML, Frisk B. Lung hyperinflation and functional exercise capacity in patients with COPD - a three-year longitudinal study. BMC Pulm Med. 2018 Dec 06;18(1):187. [PMC free article] [PubMed]
15. Barnes Peter J. , Oxidative stress-based therapeutics in COPD Volume 33, June 2020, 101544 <https://doi.org/10.1016/j.redox.2020.101544>
16. Agarwala P, Salzman SH. Six-Minute Walk Test: Clinical Role, Technique, Coding, and Reimbursement. Chest. 2020 Mar;157(3):603-611. [PMC free article] [PubMed]
17. Nosrati, M.; Safari, M.; Alizadeh, A.; Ahmadi, M.; Mahrooz, A. The Atherogenic Index Log (Triglyceride/HDL-Cholesterol) as a Biomarker to Identify Type 2 Diabetes Patients with Poor Glycemic Control. Int. J. Prev. Med. 2021, 12, 160.
18. Kumar Meet , Goit Shambhu Nath The Impact of Metabolic Syndrome on Pulmonary Function Assessments International Journal of Toxicological and Pharmacological Research 2023; 13(1); 270-275 on www.ijtp.com