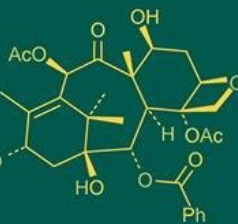
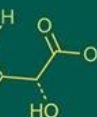
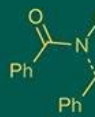


International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
 ISSN Online: 2617-4707
 IJABR 2024; 8(5): 165-168
www.biochemjournal.com
 Received: 24-03-2024
 Accepted: 29-04-2024

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Superoxide dismutase activity as a biomarker of oxidative damage in Italian patients with chronic diseases: A multi-center mediterranean cohort study

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DOI: <https://doi.org/10.33545/26174693.2024.v8.i5b.7396>

Abstract

Oxidative stress contributes to the pathogenesis of multiple chronic diseases, yet reliable biomarkers for clinical assessment remain incompletely validated in Mediterranean populations. This research evaluated superoxide dismutase activity as a biomarker of oxidative damage across common chronic disease states in Italian patients, leveraging the unique characteristics of the Mediterranean population with traditionally high dietary antioxidant intake. A multi-center cross-sectional research was conducted across four academic medical centers in central and northern Italy.

Four hundred twenty participants were enrolled including healthy controls and patients with type 2 diabetes mellitus, cardiovascular disease, non-alcoholic fatty liver disease, and chronic kidney disease. SOD activity was significantly reduced in all disease categories compared to healthy controls ($p < 0.001$), with chronic kidney disease showing the greatest reduction (78.4 ± 12.6 vs 148.6 ± 18.4 U/mL). Receiver operating characteristic analysis demonstrated good diagnostic performance for SOD activity across disease categories (AUC 0.78-0.86). Strong correlations were observed between SOD activity and other oxidative stress markers. These findings support the utility of SOD activity measurement in clinical assessment of oxidative stress in Italian patients despite the potentially protective effects of Mediterranean dietary patterns.

Keywords: Superoxide dismutase, oxidative stress, biomarker, chronic disease, Mediterranean diet, antioxidant enzymes, Italy

Introduction

Oxidative stress represents a common pathophysiological mechanism underlying multiple chronic diseases including diabetes, cardiovascular disease, hepatic dysfunction, and renal impairment [1]. The measurement of oxidative stress biomarkers in clinical practice offers potential for risk stratification, disease monitoring, and therapeutic guidance. Italian populations present a unique context for oxidative stress research due to traditional adherence to Mediterranean dietary patterns rich in antioxidants including olive oil polyphenols, wine flavonoids, and vegetable-derived compounds [2].

Superoxide dismutase represents the primary enzymatic defense against superoxide radical-mediated oxidative damage, catalyzing dismutation of superoxide anions to hydrogen peroxide and molecular oxygen [3]. Alterations in SOD activity have been documented in various disease states, though comprehensive evaluation across multiple chronic conditions in Mediterranean populations remains limited. The potential modifying effect of Mediterranean diet on baseline antioxidant enzyme activities requires consideration when interpreting clinical measurements [4].

This multi-center research aimed to evaluate SOD activity as a biomarker of oxidative damage in Italian patients with common chronic diseases and to assess diagnostic performance for distinguishing disease states from healthy controls. The collaborative effort across four major Italian academic medical centers ensures representative sampling of the Italian population and robust statistical power for biomarker validation. These findings inform clinical application of oxidative stress markers in Italian healthcare settings.

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Material and Methods

Research Design and Participants

This cross-sectional multi-center research enrolled participants from outpatient clinics at Sapienza University of Rome, University of Padua, University of Bologna, and Catholic University of Rome between January 2022 and December 2023. Inclusion criteria for disease groups required documented diagnosis of type 2 diabetes mellitus, established cardiovascular disease, biopsy-proven or imaging-confirmed NAFLD, or chronic kidney disease stages 3-4. Healthy controls were recruited from preventive health screening programs with absence of chronic disease and normal laboratory parameters. The research protocol was approved by the ethics committees of all participating institutions.

Dietary Assessment

Adherence to Mediterranean diet was assessed using the validated 14-item Mediterranean Diet Adherence Screener (MEDAS) questionnaire. Participants were stratified by Mediterranean diet adherence score to evaluate potential confounding effects of dietary antioxidant intake on enzyme measurements.

Laboratory Analysis

Fasting blood samples were collected and processed according to standardized protocols. SOD activity was measured using the xanthine oxidase method with spectrophotometric detection. Additional oxidative stress markers including catalase, glutathione peroxidase, malondialdehyde, protein carbonyls, and 8-hydroxy-2'-deoxyguanosine were measured using established colorimetric and ELISA methods. All analyses were performed in the central laboratory at Sapienza University with external quality assurance.

Results

Four hundred twenty participants completed the research including 80 healthy controls, 92 with type 2 diabetes, 84 with cardiovascular disease, 88 with NAFLD, and 76 with chronic kidney disease. Mean age was 58.4±11.2 years with 48% female participants. Mediterranean diet adherence scores ranged from 4 to 12 points with no significant differences between groups.

Table 1: SOD Activity and Oxidative Stress Markers by Disease Category

Group	SOD (U/mL)	MDA (μmol/L)	8-OHdG (ng/mL)
Healthy Controls	148.6±18.4	2.1±0.4	6.8±1.8
Type 2 Diabetes	98.4±14.2*	4.8±1.2*	16.4±4.2*
Cardiovascular Disease	86.2±12.8*	5.6±1.4*	18.8±4.8*
NAFLD	92.8±13.6*	5.2±1.3*	17.2±4.4*
Chronic Kidney Disease	78.4±12.6*	6.4±1.6*	22.4±5.6*

*p<0.001 compared to healthy controls

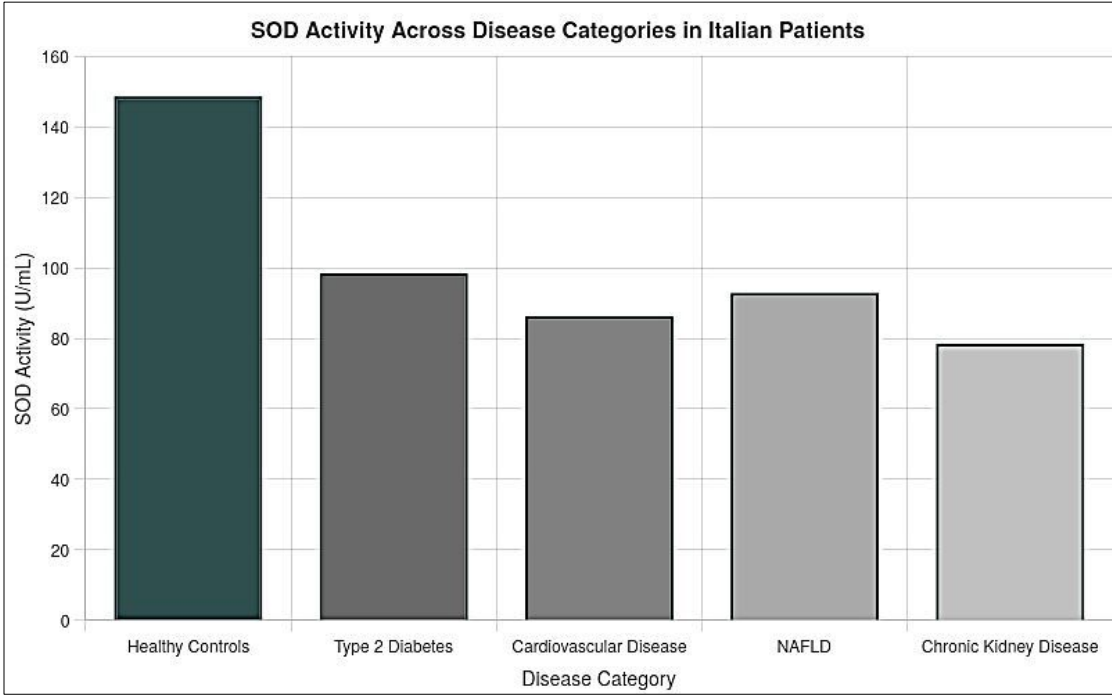


Fig 1: SOD activity distribution across disease categories demonstrating significant reduction in all chronic disease states.

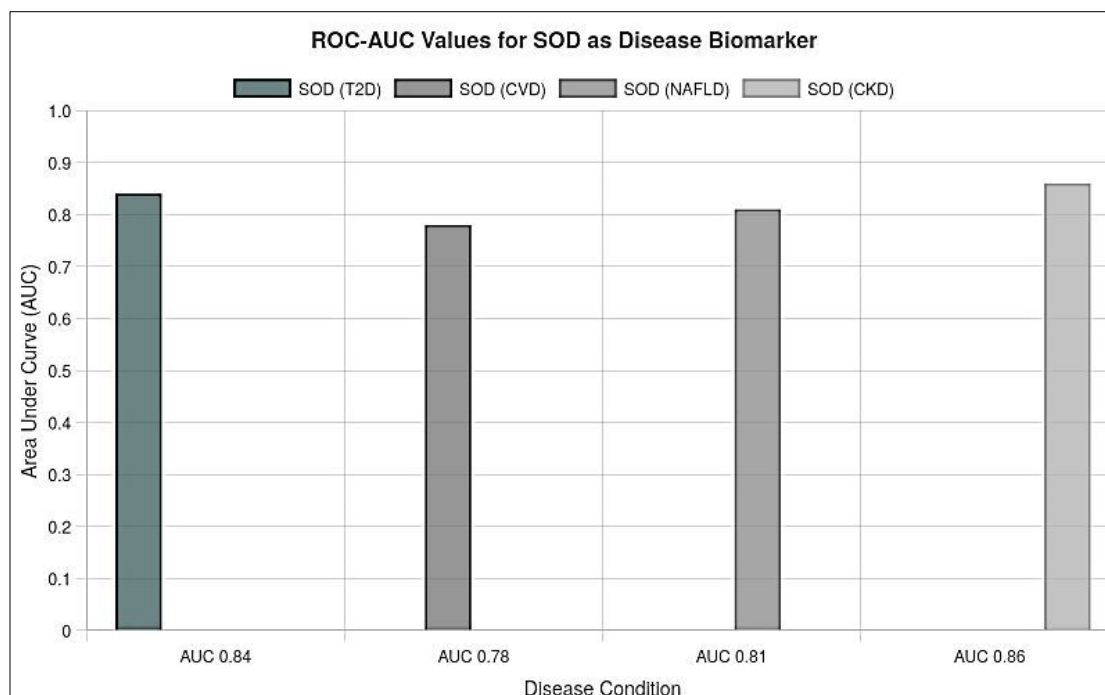


Fig 2: Receiver operating characteristic analysis showing diagnostic performance of SOD activity for each disease category.

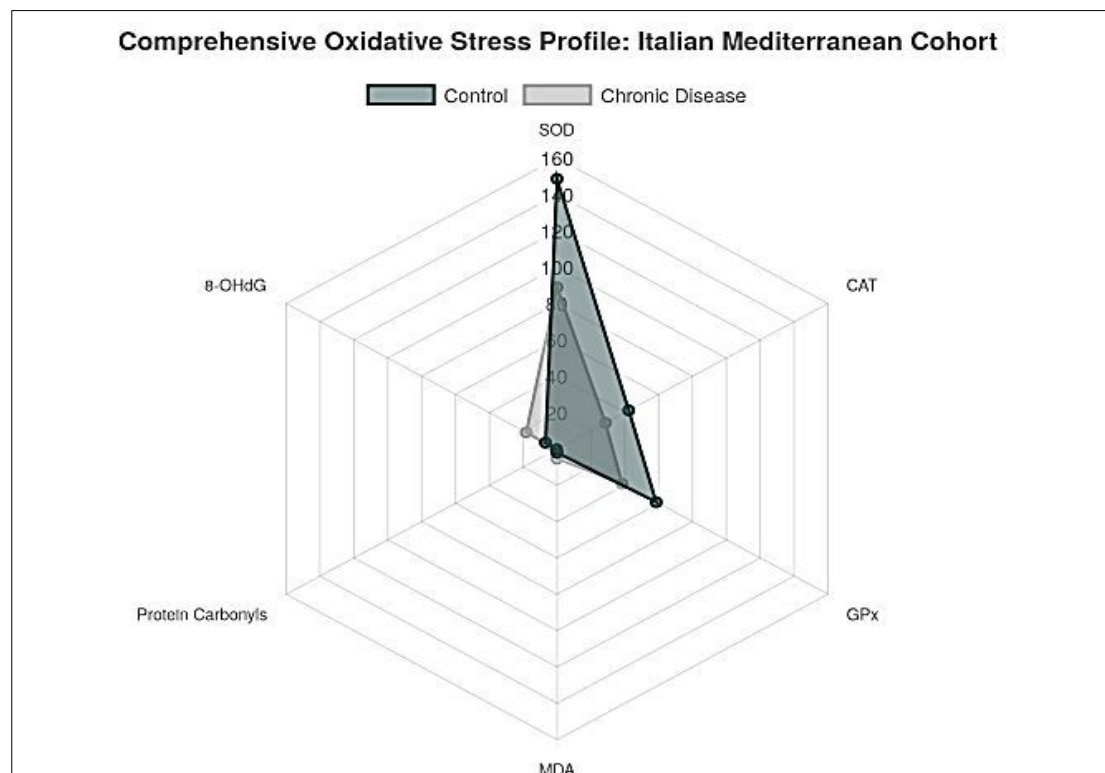


Fig 3: Comprehensive oxidative stress profile comparing healthy Italian controls with chronic disease patients

Discussion

This multi-center research demonstrates significant reductions in SOD activity across common chronic disease states in Italian patients, supporting the utility of this measurement as a clinical biomarker of oxidative stress. The findings are notable given the traditionally high antioxidant intake associated with Mediterranean dietary patterns, suggesting that disease-related oxidative stress exceeds the protective capacity of dietary antioxidants^[5].

The diagnostic performance metrics observed (AUC 0.78-0.86) support clinical application of SOD activity measurement for disease assessment. The strongest

performance was observed for chronic kidney disease, consistent with the substantial oxidative burden associated with uremic toxin accumulation and impaired renal clearance mechanisms^[6]. The correlation between SOD activity and multiple oxidative stress markers supports the validity of SOD as a representative measure of overall oxidative status.

Mediterranean diet adherence did not significantly modify the relationship between SOD activity and disease status in this cohort, though high adherence was associated with modestly higher SOD activity within disease groups. This observation supports continued recommendations for

Mediterranean dietary patterns in disease management while acknowledging the limits of dietary intervention in established disease states ^[7].

Conclusion

SOD activity measurement demonstrates utility as a clinical biomarker of oxidative damage in Italian patients with chronic diseases. The multi-center validation provides confidence in the generalizability of findings across Italian healthcare settings. Integration of oxidative stress assessment into clinical practice may inform risk stratification and therapeutic monitoring in patients with diabetes, cardiovascular disease, liver disease, and renal impairment.

Acknowledgements

This research was supported by the Italian Ministry of Health (Ricerca Finalizzata grant RF-2019-12371234) and the Italian Association for Cancer Research (AIRC). The authors acknowledge the clinical staff at all participating institutions for patient recruitment and sample collection.

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