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ORIGINAL ARTICLE

Indicators of Metabolic Imbalance in Seemingly Healthy individuals: Serum Antioxidant Enzyme (SOD, CAT, GPx)

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ABSTRACT

Metabolic imbalance is a preclinical mechanism that silent process that follows the development of overt disease and is tightly associated with the oxidative stress and the low-grade chronic inflammation. The objective of the study was to examine the association between the serum antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), and the metabolic, inflammatory, and physiological biomarkers in seemingly healthy adults. The study was a cross-sectional analytical study of 180 adults (20-55 years). The biochemical and physiological parameters were analyzed (28 in total, which included the markers of oxidative stress), such as SOD, CAT, GPx, total antioxidant capacity (TAC), malondialdehyde (MDA), and GSH/GSSG ratio), glycemic indices (fasting blood glucose (FBG), HbA1c, insulin, and HOMA-IR), lipid profile (total cholesterol (TC), LDL, HDL, triglycerides (TG), and atherogenic index of plasma (AIP)), inflammatory markers (hs-CRP, IL-6, TNF-α), adipokines (leptin and adiponectin), anthropometric indices (BMI, waist circumference, body fat percentage), and blood pressure. There were notable changes in the antioxidant enzyme activity of those people with early metabolic aberrations. SOD and GPx also exhibited strong negative relationships with BMI, triglycerides, HOMA-IR, hs-CRP, and IL-6 ($p < 0.01$), which showed that the lower the metabolic status, the less the antioxidant protection. Conversely, CAT activity showed a compensatory increment at the initial phases of metabolic disequilibrium. The multivariate regression analysis found HOMA-IR, AIP, and IL-6 to be the independent predictor of reduced antioxidant capacity. These results imply that serum antioxidant enzyme can be used as an early integrative biomarker to indicate the presence of subclinical metabolic dysregulation in otherwise healthy people.

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1- INTRODUCTION

The metabolic, hormonal, inflammatory and molecular regulatory pathways interact in a complex manner to provide metabolic homeostasis which ensures the maintenance of appropriate energy balance and cellular functioning [1]. Disruption of these interdependent systems can cause a phenomenon called metabolic imbalance which is an early preclinical phase that is antecedent to the emergence of metabolic disorders such as insulin resistance, obesity, type 2 diabetes mellitus and cardiovascular diseases [2]. It is important to note that such disturbances can take place in individuals that seem to be clinically well, whereas there are biochemical and molecular changes that are already subtle, yet occurring [3].

Oxidative stress is one of the most significant processes that accompany the development of metabolic imbalance and occurs due to a disproportion between the generation of reactive oxygen species (ROS) and the neutralizing power of the antioxidant defense system of the body [4]. Whilst ROS are normal physiological byproducts of cell metabolism with important functions in intracellular signaling, high levels of ROS can lead to lipid, protein and nucleic acid damage that results in cellular dysfunction and metabolic imbalances [5]. A number of important metabolic and inflammatory pathways have been strongly correlated with oxidative stress. High ROS concentrations may also impair insulin signaling and lead to the onset of insulin resistance, as well as facilitating lipid peroxidation and adipocyte dysfunction [6]. Moreover, oxidative stress may trigger the activation of inflammatory signaling pathways, specifically by the activation of transcription factors such as NF- 8B, which promote the expression of pro-inflammatory cytokines, including tumor necrosis factor- alpha (TNF- 8B) and interleukin- 6 (IL- 6). These inflammation effects also increase the metabolic imbalances and lead to the development of metabolism disorders [7]. Simultaneously, an effective endogenous antioxidant defense mechanism mediates cellular protection against oxidative damages. The main enzymatic antioxidants are superoxide dismutases (SOD), catalase (CAT), and glutathione peroxidase (GPx) acting in synergy to counter the reactive oxygen species, and to preserve the redox balance in cells [8]. These enzymes are partly regulated by redox-sensitive transcriptional regulators like Nrf2 that is a key mediator of antioxidant response signaling, and cell defence against oxidative damage [9]. Although there has been increased awareness of oxidative stress as an underlying cause of metabolic dysfunction, the majority of the past researches have involved patients with known metabolic illnesses [10]. Conversely, there is a dearth in the literature on how antioxidant defense mechanisms relate to the occurrence of early metabolic disturbances in seemingly healthy populations, in which subtle physiological changes may be antecedents of clinical disease over a number of years [11].

In turn, early biomarkers that are resilient to indicate the interactivity between oxidative stress and metabolic control and inflammatory, thus, is of critical importance in amplifying early diagnosis and prevention mechanisms. The enzymes present in serum as antioxidants may be considered potential biomarkers because the level of their activity is a marker of the redox condition of the entire body and the adaptation of the body to metabolic-related stress factors [12]. Accordingly, the present study aims to evaluate whether serum antioxidant enzymes—particularly SOD, CAT, and GPx—can serve as integrative early indicators of metabolic, inflammatory, and molecular imbalance in apparently healthy individuals. By examining their relationships with metabolic and inflammatory parameters, this study seeks to provide further insight into the early biological processes underlying metabolic dysregulation [13].

2- MATERIALS AND METHOD

2.1 Study Design and Population

The current analytical cross-sectional study will be carried out between January and December 2025 in primary care centers and preventive clinics across Kirkuk. Eligibility criteria were designed to recruit a stable metabolically population of apparently healthy adults (90 males and 90 females) aged between 20-55 years to achieve a total of 180 participants. The subjects had to be free of chronic diseases, had not smoked, and did not have antioxidant supplements or drugs that could interfere with oxidative stress biomarkers. Patients who had diabetes mellitus, cardiovascular disease, chronic liver or kidney disease, chronic inflammatory disease, or were pregnant were screened out to avoid possible confounding factors. The Ethical Committee of University of Kirkuk approved the study protocol and all participants were informed and gave informed consent before being enrolled in the study.

2.3 Anthropometric and Physiological Measurements

The anthropometric and physiological measurements were acquired in a standardized way. Calibrated scales and stadiometers were used to measure the body weight and height, and the body mass index (BMI) was calculated by dividing the weight in kilograms by the height in meters squared (kg/m2). A non-stretchable measuring tape was used to measure the waist circumference (WC) at the location between the iliac crest and the lower edge of the final rib. Bio electrical impedance analysis was used to determine body fat percentage under standard conditions. A validated automated sphygmomanometer was used to record systolic and diastolic blood pressure (SBP and DBP) when the participants had at least 5 minutes of rest in a seated position [14].

2.4 Blood Sample Collection

Following the 10 -12 hours of an overnight fast, 10 mL of venous blood was taken out of each participant under aseptic conditions. The samples were subdivided into plain tubes, on which serum separation was done and whereas the EDTA-containing tubes were used when the need arose to do further biochemical tests. The serum was centrifuged and then aliquoted to evaluate antioxidant, metabolic, lipid, and hormonal markers, and whole blood in EDTA tubes was stored to be further used in molecular tests. All the serums were kept at -80 o C pending additional biochemical analysis [15].

2.5 Biochemical Analyses

A. Oxidative Stress Markers

The SOD activity was calculated by the pyrogallol autoxidation inhibition method, whose principle is that the enzyme inhibits the pyrogallol autoxidation activity. The activity of catalase (CAT) was determined by the rate of decomposition of hydrogen peroxide spectrophotometrically [16]. The performance of Glutathione peroxidase (GPx) was measured in the context of the NADPH oxidation method in which the reduction in the NADPH absorbance is a measure of enzyme activity [17]. A commercially available colorimetric assay kit was used to determine total antioxidant capacity (TAC) based on the instructions of the manufacturer. The amount of lipid peroxidation, expressed in terms of malondialdehyde (MDA) was determined using the thiobarbituric acid reactive substances (TBARS) assay [18]. An enzymatic recycling approach was done to determine the reduced-to-oxidized glutathione ratio (GSH/GSSG) [19].

B. Glycemic Profile

The glucose oxidase enzyme method evaluated the level of fasting blood glucose (FBG). The measurement of glycated hemoglobin (HbA1c) was performed using high-performance liquid chromatography (HPLC) [20]. Sandwich ELISA was used to measure the fasting insulin levels. The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was used as a measure of insulin resistance; this was calculated as (FBG × fasting insulin)/ 22.5. The insulin sensitivity was also measured by Quantitative Insulin Sensitivity Check Index (QUICKI) which was computed as $1/[\log(\text{fasting insulin}) + \log(\text{FBG})] = 1/1 + [\log(\text{insulin}) + \log(\text{BG})]$ [21].

C. Lipid Profile

An enzymatic colorimetric measurement of total cholesterol was done. A direct enzymatic assay was used to measure high-density lipoprotein cholesterol (HDL-C) and the Friedewald formula was used to compute low-density lipoprotein cholesterol (LDL-C). Enzymatic analysis of triglycerides was done. The difference between the total cholesterol and HDL-C was used as non-HDL cholesterol. Atherogenic index of plasma (AIP) was computed as the logarithmic of triglycerides/HDL-C which is used to measure cardiovascular risk [22].

D. Inflammatory Markers

ELISA was used to determine the level of high-sensitivity C-reactive protein (hs-CRP). Interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) were measured by commercial ELISA kits based on the instructions of the manufacturers. The level of serum ferritin was identified by immunoassay [23].

E. Hormonal and Adipokine Assessment

The leptin and adiponectin serum concentrations were determined by ELISA kits. The ELISA methodology was used to determine cortisol levels. The concentration of thyroid-stimulating hormone (TSH) was analyzed with a chemiluminescent immunoassay [24].

2.6 Statistical Analysis

The SPSS (version 26) was used to conduct statistical analysis. The normality of data was checked before the analysis. mean ± SD were used to portray continuous variables. Group comparisons were done using independent t-test as this is appropriate. Pearson correlation and multiple linear regression were used. A p-value < 0.05 was taken as being significant.

3- RESULTS AND DISCUSSION

Table 1 summarizes the baseline characteristics of the study participants and Figure 1 illustrates the same. The research samples were 180 seemingly healthy adults (90 men and 90 women) with a mean age of 36.4 ± 8.2 years of age. Although there is no known diagnosed metabolic disease, the average body mass index (BMI) (27.1 ± 3.9 kg/m2) shows a tendency towards the overweight.

Table (1): Baseline Demographic, Anthropometric, and Clinical Characteristics of the Study Participants

Parameter	**Mean ± SD / n (%)**
Age (years)	36.4 ± 8.2
Male/Female	90/90
BMI (kg/m²)	27.1 ± 3.9
Overweight (BMI 25–29.9)	68 (38%)
Obesity (BMI ≥30)	47 (26%)
Waist Circumference (cm)	92.5 ± 10.4
Body Fat %	28.2 ± 7.1
SBP/DBP (mmHg)	123 ± 14 / 79 ± 9

As Table 1 indicates, a significant percentage of participants was overweight (38%), or even obese (26%), indicating that there are early anthropometric risk factors related to metabolic disorders. Unwanted adiposity and especially central fat is dynamically active and leads to the release of pro-inflammatory cytokines and adipokines [25]. High waist circumference (92.5 + 10.4 cm) and body fat percentage (28.2 + 7.1) demonstrated in Figure 1 are also the signs of the central adiposity as it is highly associated with the insulin resistance and cardiometabolic risk. Also, the mean rates of blood pressure (123 ± 14 / 79 ± 9 mmHg) were close to the upper limit implying that there might have been some early changes in the vascularity [26].

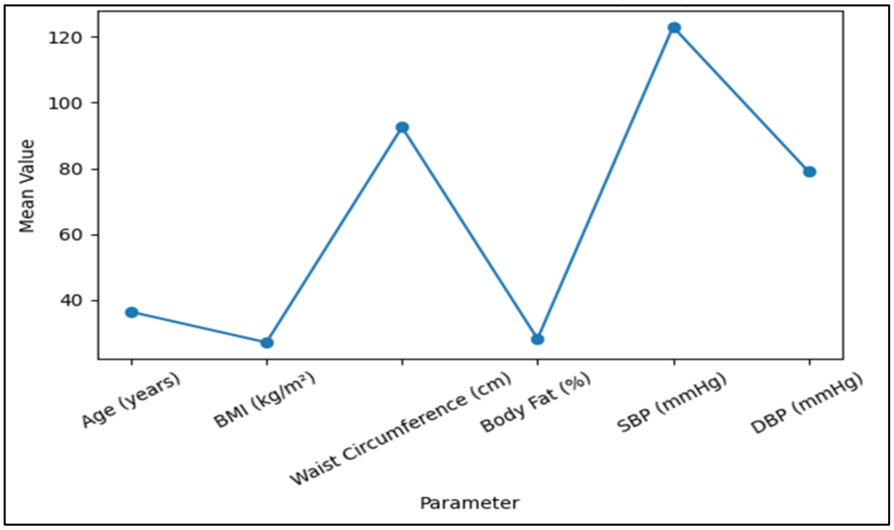

Fig (1): Distribution of Anthropometric and Physiological Parameters in the Study Population

These results imply that a clinically healthy person can have the presence of concealed risk factors associated with metabolism [27].

3.1 Oxidative Stress Markers

It was also found that there was significant difference in the biomarkers of oxidative stress in the two groups as showcased in Table 2 and Figure 2. The SOD, GPx, TAC and GSH/GSSG ratio indicating poor response to antioxidant defense were found in much lower concentrations in the respondents of the borderline metabolic profile.

Table (2): Comparison of Oxidative Stress Biomarkers between Normal and Borderline Metabolic Profiles

Marker	**Normal Metabolic Profile**	**Borderline Metabolic Profile**	**p-value**
SOD (U/mL)	5.82 ± 0.74	4.91 ± 0.63	<0.01
CAT (U/mL)	48.3 ± 6.1	52.7 ± 7.4	0.03
GPx (U/mL)	71.5 ± 8.9	63.2 ± 7.8	<0.01
TAC (mmol/L)	1.42 ± 0.21	1.19 ± 0.17	<0.01
MDA (µmol/L)	2.04 ± 0.35	2.68 ± 0.41	<0.01
GSH/GSSG Ratio	12.3 ± 3.1	8.6 ± 2.7	<0.01

These decreases in antioxidant markers as illustrated in Table 2 are evidence of an imbalance between formation of reactive oxygen species (ROS) and the antioxidant response [28]. The metabolic derangements such as hyperglycemia, lipid abnormalities, and mitochondrial dysfunction could be more likely to produce an excess of ROS [29].

Interestingly, the borderline group showed significantly higher catalase (CAT) activity (Table 2, Figure 2), which can be attributed to the compensatory mechanism of the higher levels of oxidative stress as catalase is one of the essential agents in the degradation of hydrogen peroxide [30].

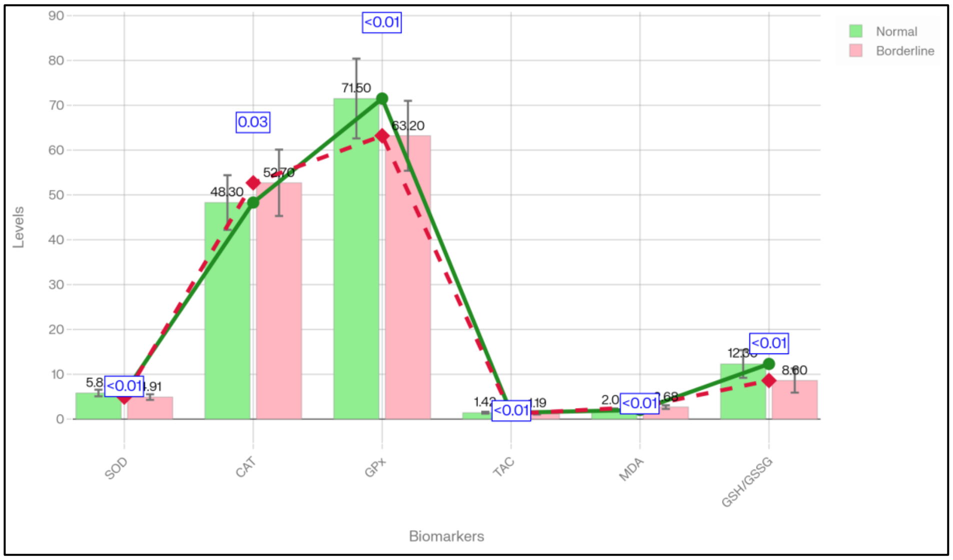

Fig (2): Comparison of Oxidative Stress Biomarkers between Normal and Borderline Metabolic Profiles

Moreover, MDA levels are very high (Figure 2), which means that lipid peroxidation and membrane damage are increased. The simultaneous existence of antioxidant capacity decline and oxidative damage is a strong indication of the presence of oxidative imbalance in individuals with early metabolic disturbances [31].

3.2 Glycemic Profile

The glycemic data in Table 3 and Figure 3 demonstrated the presence of considerable changes in the glucose metabolism in the subjects with borderline metabolic status. Table 3 demonstrates that the level of fasting blood glucose (FBG) and HbA1c is significantly increased in the borderline group, which also means that the glucose homeostasis was dysregulated early [32].

Table (3): Comparison of Glycemic Parameters between Normal and Borderline Metabolic Profiles

Marker	Normal Metabolic Profile	Borderline Metabolic Profile	p-value
FBG (mg/dL)	88.5 ± 9.2	102.3 ± 11.4	<0.01
HbA1c (%)	5.2 ± 0.4	5.9 ± 0.5	<0.01
Insulin (µIU/mL)	8.6 ± 2.3	13.7 ± 3.1	<0.01
HOMA-IR	1.9 ± 0.6	3.5 ± 0.9	<0.01
QUICKI	0.36 ± 0.02	0.31 ± 0.02	<0.01

Moreover, there was a significant increase in fasting insulin levels, as well as in HOMA-IR (Figure 3), indicating the existence of insulin resistance. On the contrary, QUICKI levels were greatly decreased, which once again proves the impaired insulin sensitivity [33].

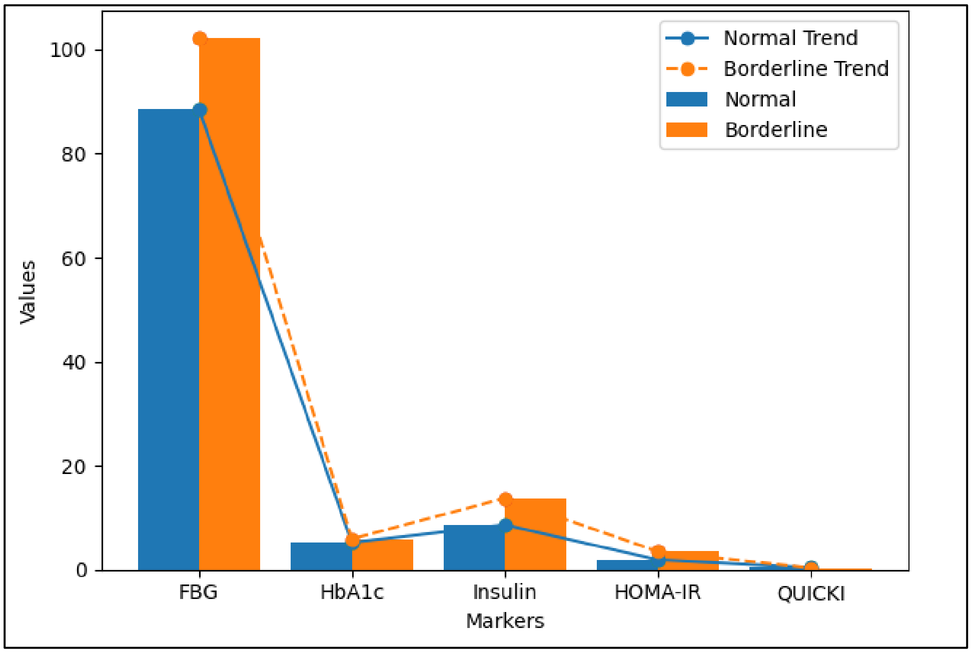

Fig (3): Comparison of Metabolic Markers in Normal vs. Borderline Profiles

These results are in accordance with the changes of the oxidative stress, which is observed in Figure 2 because hyperglycemia is known to increase ROS-generation, and it disrupts insulin-signaling (pathways) [34]. The fact that there is compensatory hyperinsulinemia shows that the pancreatic 8 cells are acting in reaction to the lowered insulin sensitivity. All these findings indicate that physiological problems with glucose metabolism can happen at an insidious phase, before the actual manifestation of diabetes [35].

3.3 Lipid Profile

The results of the lipid profile that have been summarized in Table 4 and Figure 4 indicated a much more atherogenic pattern in the borderline metabolic group. Table 4 demonstrates that the total cholesterol, LDL-C, triglycerides, non-HDL cholesterol and AIP were high, whereas the level of HDL-C was low [36].

Table (4): Comparison of Lipid Profile Parameters between Normal and Borderline Metabolic Profiles

Marker	**Normal**	**Borderline**	**p-value**
Total Cholesterol (mg/dL)	178 ± 25	210 ± 28	<0.01
LDL-C	104 ± 21	135 ± 24	<0.01
HDL-C	51 ± 8	43 ± 7	<0.01
Triglycerides	125 ± 30	187 ± 36	<0.01
Non-HDL	127 ± 22	167 ± 27	<0.01
AIP	0.23 ± 0.08	0.38 ± 0.10	<0.01

These changes are early dyslipidemia related to insulin resistance and augmented adiposity. High triglycerides and LDL-C levels promoting atherosclerotic' plaque development and low HDL-C levels undermining reverse cholesterol transport and antioxidant protection, respectively [37].

Recurring Atherogenic Index of Plasma (AIP) as shown in Figure 4 is also an indication that there is high cardiovascular risk. It is important to note that such lipid disorders can also lead to the presence of oxidative stress and inflammation, which underlines the interdependence of metabolic disorders [38].

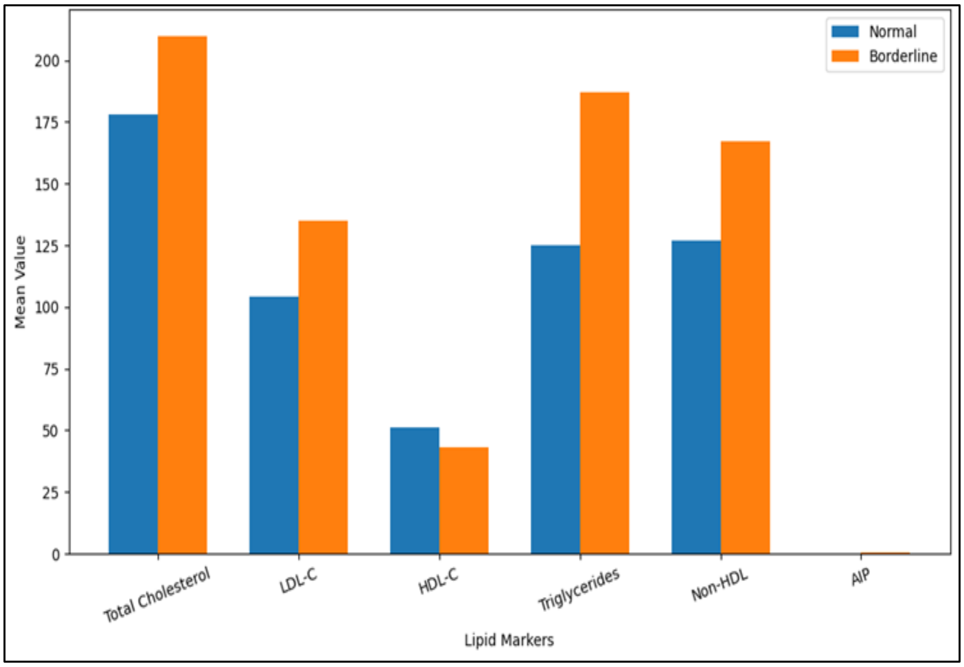

Fig (4): Comparison of Lipid Profile Markers between Normal and Borderline Groups

3.4 Inflammatory Markers

Table 5 and Figure 5 outline inflammatory biomarkers that show a substantial enhancement of the systemic inflammation in the borderline metabolic group [39]. Hs-CRP, IL-6, TNF-α as well as ferritin levels were all significantly higher than those of the normal group (Tab 5) [40].

Table (5): Comparison of Inflammatory Biomarkers between Normal and Borderline Metabolic Profiles

Marker	Normal	Borderline	p-value
hs-CRP (mg/L)	1.8 ± 0.7	3.5 ± 1.2	<0.01
IL-6 (pg/mL)	2.3 ± 0.9	5.6 ± 1.5	<0.01
TNF-α (pg/mL)	3.1 ± 0.8	5.2 ± 1.1	<0.01
Ferritin (ng/mL)	89 ± 24	118 ± 30	<0.01

Adipose tissue, especially visceral fat, is a type of active endocrine organ that releases pro-inflammatory cytokines. The cytokines can disrupt insulin signaling pathways and cause insulin resistance [41].

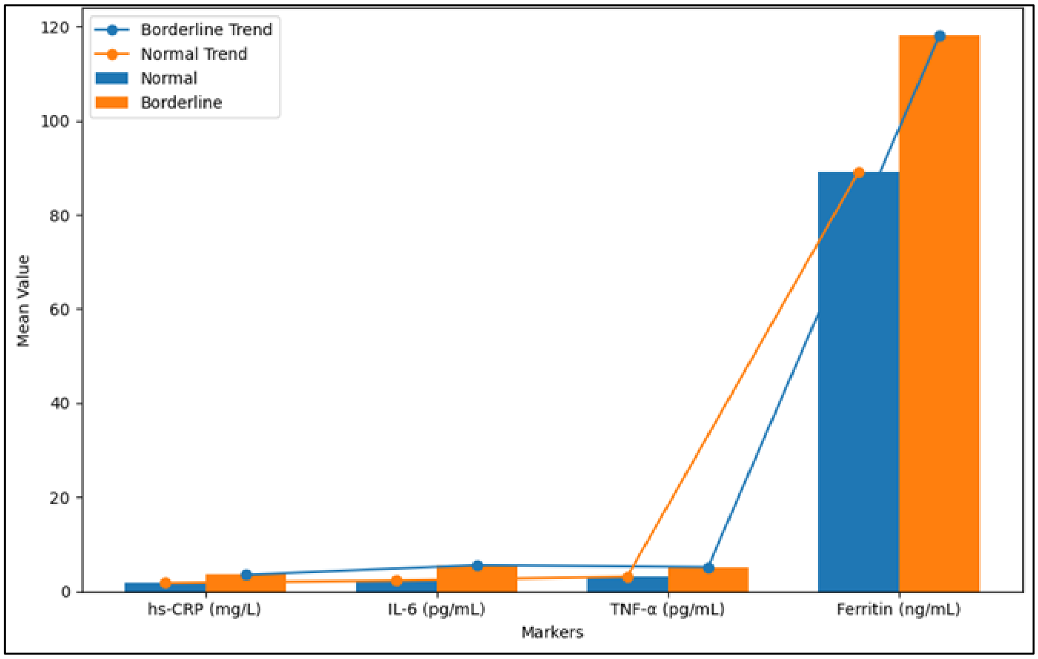

Fig (5): Comparative Analysis of Inflammatory Biomarkers between Normal and Borderline Groups

The high levels of hs-CRP as shown in Figure 5 give substantial evidence of systemic inflammatory activation [42]. Further, IL-6 and TNF-α are important in enhancing an inflammatory response, connecting the inflammation with the oxidative stress and lipid abnormality discussed in Figure 2 and 4 [43].

3.5 Hormonal and Adipokine Markers

Table 6 and Figure 6 were the delivered hormonal and adipokine profile, which demonstrated serious changes in the endocrine system of the borderline metabolic group. Leptin concentration was elevated significantly (as indicated in Table 6), which is probably because of the mass of adipose tissue and appearance of leptin resistance.

Table (6): Hormonal and Adipokine Profile in Normal and Borderline Metabolic Groups

Marker	**Normal**	**Borderline**	**p-value**
Leptin (ng/mL)	12.5 ± 4.3	21.2 ± 5.1	<0.01
Adiponectin (µg/mL)	8.2 ± 2.1	5.6 ± 1.7	<0.01
Cortisol (µg/dL)	14.2 ± 3.5	17.1 ± 4.0	0.02
TSH (µIU/mL)	2.1 ± 0.7	2.5 ± 0.9	0.07

Conversely, there were minimal adiponectin levels (Figure 6). With its effects on the promotion of insulin sensitivity and anti-inflammatory properties, low adiponectin levels could be an additional contributor of the described metabolic abnormalities [44].

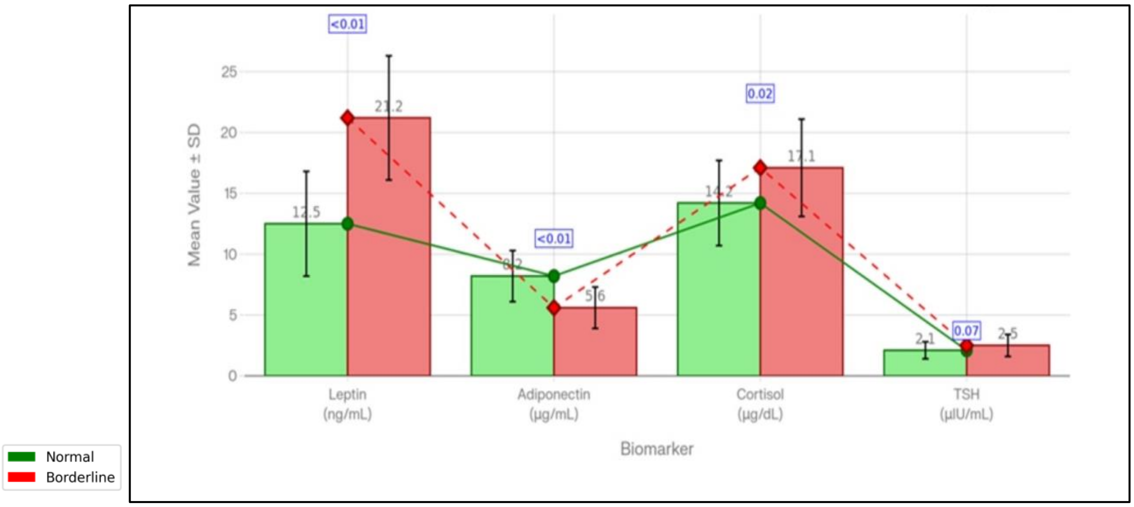

Fig (6): Comparison of Biomarkers between Normal and Borderline Metabolic Profiles

The level of cortisol was also highly increased (Table 6), which implies the stimulation of the hypothalamic–pituitary–adrenal (HPA) axis. Persistent cortisol could foster the development of fatty tissues in the viscose and metabolic imbalance [45]. Even though the TSH levels were a bit higher, the difference was not very significant, which showed that the thyroid functioning played less of a role in this situation [46].

Overall, these results point to the role of adipokine imbalance and neuroendocrine changes in the initial metabolic malfunctions [47].

4- CONCLUSION

Overall, the current work shows that people possessing borderline metabolic profiles have premature and interrelated imbalances in oxidative, metabolic, inflammatory and hormonal pathways even in the absence of overt clinical disease. The subsequent loss in antioxidant defenses and increased lipid peroxidation, insulin resistance, dyslipidemia and low-grade inflammation are indicative of a state of subclinical metabolic dysregulation. These findings verify the thought that metabolic imbalance precedes the clinical symptom development by a great distance and the importance of early biochemical screening. Preventive measures that focus on targeting these initial changes could be a key opportunity to mitigate the chances of metabolic syndrome, type 2 diabetes, and cardiovascular diseases.

REFERENCES

[1] Müller, L., Di Benedetto, S., & Müller, V. (2025). From homeostasis to neuroinflammation: Insights into cellular and molecular interactions and network dynamics. *Cells, 14*(1), 54.

[2] Yang, Q., Cai, Y., Guan, Y., Wang, Z., Guo, S., Qiu, S., & Zhang, A. (2025). Metabolic phenotypes: Molecular bridges between health homeostasis and disease imbalance. *Computational and Structural Biotechnology Journal.*

[3] Lee, J., & Kim, H. J. (2022). Normal aging induces changes in the brain and neurodegeneration progress: Review of the structural, biochemical, metabolic, cellular, and molecular changes. *Frontiers in Aging Neuroscience, 14,* 931536.

[4] Afzal, S., Abdul Manap, A. S., Attiq, A., Albokhadaim, I., Kandeel, M., & Alhojaily, S. M. (2023). From imbalance to impairment: The central role of reactive oxygen species in oxidative stress-induced disorders and therapeutic exploration. *Frontiers in Pharmacology, 14*, 1269581.

[5] Manoharan, R. R., Prasad, A., Pospíšil, P., & Kzhyshkowska, J. (2024). ROS signaling in innate immunity via oxidative protein modifications. *Frontiers in Immunology, 15*, 1359600.

[6] Liu, S., Liu, J., Wang, Y., Deng, F., & Deng, Z. (2025). Oxidative stress: Signaling pathways, biological functions, and disease. *MedComm, 6*(7), e70268.

[7] Guo, Q., Jin, Y., Chen, X., Ye, X., Shen, X., Lin, M., ... & Zhang, J. (2024). NF-κB in biology and targeted therapy: New insights and translational implications. *Signal Transduction and Targeted Therapy, 9*(1), 53.

[8] Rao, M. J., Duan, M., Zhou, C., Jiao, J., Cheng, P., Yang, L., ... & Zheng, B. (2025). Antioxidant defense system in plants: Reactive oxygen species production, signaling, and scavenging during abiotic stress-induced oxidative damage. *Horticulturae, 11*(5), 477.

[9] Hammad, M., Raftari, M., Cesário, R., Salma, R., Godoy, P., Emami, S. N., & Haghdoost, S. (2023). Roles of oxidative stress and Nrf2 signaling in pathogenic and non-pathogenic cells: A possible general mechanism of resistance to therapy. *Antioxidants, 12*(7), 1371.

[10] Kuwait, Z.I., Mousa, T.A.H. (2026). A Comparative Biochemical Study of Oxidative Stress and Lipid Profiles in Patients with Acute MyocardialInfarction. Dijlah Journal of Medical Sciences, 3(1): 152-162.

[11] Zou, H., Zhang, S., Cui, X., Xu, H., Zhou, Z., Cheng, D., ... & Dong, X. (2025). Advancements in the investigation of the mechanisms underlying cognitive aging. *Biogerontology, 26*(4), 158.

[12] Liu, S., Liu, J., Wang, Y., Deng, F., & Deng, Z. (2025). Oxidative stress: Signaling pathways, biological functions, and disease. *MedComm, 6*(7), e70268.

[13] Liu, S., Liu, J., Wang, Y., Deng, F., & Deng, Z. (2025). Oxidative stress: Signaling pathways, biological functions, and disease. *MedComm, 6*(7), e70268.

[14] Norton, K. I. (2018). Standards for anthropometry assessment. In *Kinanthropometry and exercise physiology* (pp. 68–137). Routledge.

[15] Alkubaisi, M. R., & Tahir, N. T. (2023). Dyslipidemia poses a significant risk of many complications for type 2 diabetes mellitus patients: Article review. *NTU Journal of Pure Sciences, 2*(3).

[16] Ekozin, A., Otuechere, C. A., & Adewuyi, A. (2022). Apocynin-loaded silver nanoparticles display potent in vitro biological activities and mitigate pyrogallol-induced hepatotoxicity. *Chemico-Biological Interactions, 365*, 110069.

[17] Sattar, A. A., Matin, A. A., Hadwan, M. H., Hadwan, A. M., & Mohammed, R. M. (2024). Rapid and effective protocol to measure glutathione peroxidase activity. *Bulletin of the National Research Centre, 48*(1), 100.

[18] Wang, J. H., Lee, S. B., Lee, D. S., & Son, C. G. (2021). Total antioxidant capacity in HBV carriers: A promising biomarker for evaluating hepatic fibrosis—A pilot study. *Antioxidants, 10*(1), 77.

[19] Karimi Galougahi, K., Antoniades, C., Nicholls, S. J., Channon, K. M., & Figtree, G. A. (2015). Redox biomarkers in cardiovascular medicine. *European Heart Journal, 36*(25), 1576–1582.

[20] Chaila, M. Z., Viniegra, M., Gagliardino, J. J., Martínez, A., Simesen de Bielke, M. G., Frusti, M., ... & Commendatore, V. F. (2022). Glycated hemoglobin measurement: Comparison of three methods versus high performance liquid chromatography. *Journal of Diabetes Science and Technology, 16*(3), 724–731.

[21] Ogbodo, E. C., Onah, C. E., Amah, A. K., Okeke, C. S., Obiorah, M. O., Okezie, A. O., ... & Meludu, S. C. (2024). Assessment of fasting plasma glucose, insulin, insulin resistance, and glycated haemoglobin as markers of glycemic control in apparently healthy older adults in Nnewi. *Indian Journal of Forensic and Community Medicine, 11*(2), 49–55.

[22] Ribeiro, R. M., Ribeiro, D. D. S. F., Cota, L. O., Carvalho, A. M., de Oliveira Gobesso, A. A., & Faleiros, R. R. (2023). Comparison between the direct method and Friedewald's formula for the determination of low-density lipoprotein cholesterol serum levels in horses. *Journal of Equine Veterinary Science, 122*, 104230.

[23] Abdullah, A. H. (2025). Peripheral inflammation as a biomarker of disease activity in relapsing-remitting MS. *Neurosignals, 32*(1), 1–10.

[24] Alshammary, R. A., Alshammary, A. G., Hameed, W. M., & Al-Karawi, A. S. (2025). Multisystem effects of obesity: Dysregulation of leptin, thyroid hormones, autoantibodies, immune, and neurological responses. *The Egyptian Journal of Immunology, 32*(4), 101–109.

[25] Zorena, K., Jachimowicz-Duda, O., Ślęzak, D., Robakowska, M., & Mrugacz, M. (2020). Adipokines and obesity: Potential link to metabolic disorders and chronic complications. *International Journal of Molecular Sciences, 21*(10), 3570.

[26] Liu, A. B., Lin, Y. X., Meng, T. T., Tian, P., Chen, J. L., Zhang, X. H., ... & Su, G. H. (2024). Associations of the cardiometabolic index with insulin resistance, prediabetes, and diabetes in US adults: A cross-sectional study. *BMC Endocrine Disorders, 24*(1), 217.

[27] Stefan, N., & Schulze, M. B. (2023). Metabolic health and cardiometabolic risk clusters: Implications for prediction, prevention, and treatment. *The Lancet Diabetes & Endocrinology, 11*(6), 426–440.

[28] Afzal, S., Abdul Manap, A. S., Attiq, A., Albokhadaim, I., Kandeel, M., & Alhojaily, S. M. (2023). From imbalance to impairment: The central role of reactive oxygen species in oxidative stress-induced disorders and therapeutic exploration. *Frontiers in Pharmacology, 14*, 1269581.

[29] González, P., Lozano, P., Ros, G., & Solano, F. (2023). Hyperglycemia and oxidative stress: An integral, updated, and critical overview of their metabolic interconnections. *International Journal of Molecular Sciences, 24*(11), 9352.

[30] Anwar, S., Alrumaihi, F., Sarwar, T., Babiker, A. Y., Khan, A. A., Prabhu, S. V., & Rahmani, A. H. (2024). Exploring therapeutic potential of catalase: Strategies in disease prevention and management. *Biomolecules, 14*(6), 697.

[31] González, P., Lozano, P., Ros, G., & Solano, F. (2023). Hyperglycemia and oxidative stress: An integral, updated, and critical overview of their metabolic interconnections. *International Journal of Molecular Sciences, 24*(11), 9352.

[32] Yu, E. Y. W., Ren, Z., Mehrkanoon, S., Stehouwer, C. D., van Greevenbroek, M. M., Eussen, S. J., ... & Wesselius, A. (2022). Plasma metabolomic profiling of dietary patterns associated with glucose metabolism status: The Maastricht Study. *BMC Medicine, 20*(1), 450.

[33] Reynoso-Roa, A. S., Gutiérrez-Rubio, S. A., Castillo-Romero, A., García-Iglesias, T., Suárez-Rico, D. O., Becerra-Orduñez, K. M., ... & García-Cobián, T. A. (2025). Performance of the triglyceride-glucose (TyG) index for early detection of insulin resistance in young adults: Comparison with HOMA-IR and QUICKI in Western Mexico. *Diabetology*, *6*(11), 141.

[34] González, P., Lozano, P., Ros, G., & Solano, F. (2023). Hyperglycemia and oxidative stress: An integral, updated, and critical overview of their metabolic interconnections. *International Journal of Molecular Sciences, 24*(11), 9352.

[35] Skelin Klemen, M., Kopecky, J., Dolenšek, J., & Stožer, A. (2024). Human beta cell functional adaptation and dysfunction in insulin resistance and its reversibility. *Nephron, 148*(2), 78–84.

[36] Ma, L., Sun, F., Zhu, K., Han, Q., & Sun, Q. (2024). The predictive value of atherogenic index of plasma, non-high-density lipoprotein cholesterol (non-HDL-C), non-HDL-C/HDL-C, and lipoprotein combine index for stroke incidence and prognosis in maintenance hemodialysis patients. *Clinical Interventions in Aging*, 1235–1245.

[37] Alcover, S., Ramos-Regalado, L., Girón, G., Muñoz-García, N., & Vilahur, G. (2025). HDL-cholesterol and triglycerides dynamics: Essential players in metabolic syndrome. *Antioxidants, 14*(4), 434.

[38] Assempoor, R., Daneshvar, M. S., Taghvaei, A., Abroy, A. S., Azimi, A., Nelson, J. R., & Hosseini, K. (2025). Atherogenic index of plasma and coronary artery disease: A systematic review and meta-analysis of observational studies. *Cardiovascular Diabetology, 24*(1), 35.

[39] López-Villatoro, J. M., Díaz-Marsá, M., De la Torre-Luque, A., MacDowell, K. S., Prittwitz, C., Leza, J. C., & Carrasco, J. L. (2023). Inflammatory and oxidative endophenotypes in borderline personality disorder: A biomarker cluster analysis. *The World Journal of Biological Psychiatry*, *24*(7), 587–594.

[40] Nisar, M., & Iqbal, M. U. N. (2021). Influence of hs-CRP, IL-6, and TNF-α and its role in dyslipidemia and type 2 diabetes in the population of Karachi, Pakistan. *Pakistan Journal of Pharmaceutical Sciences*, *34*.

[41] Yan, K. (2024). Recent advances in the effect of adipose tissue inflammation on insulin resistance. *Cellular Signalling, 120*, 111229.

[42] Kandelouei, T., Abbasifard, M., Imani, D., Aslani, S., Razi, B., Fasihi, M., ... & Sahebkar, A. (2022). Effect of statins on serum level of hs-CRP and CRP in patients with cardiovascular diseases: A systematic review and meta-analysis of randomized controlled trials. *Mediators of Inflammation, 2022*(1), 8732360.

[43] Dama, A., Shpati, K., Daliu, P., Dumur, S., Gorica, E., & Santini, A. (2024). Targeting metabolic diseases: The role of nutraceuticals in modulating oxidative stress and inflammation. *Nutrients, 16*(4), 507.

[44] Choi, H. M., Doss, H. M., & Kim, K. S. (2020). Multifaceted physiological roles of adiponectin in inflammation and diseases. *International Journal of Molecular Sciences, 21*(4), 1219.

[45] Janssen, J. A. (2022). New insights into the role of insulin and hypothalamic–pituitary–adrenal (HPA) axis in the metabolic syndrome. *International Journal of Molecular Sciences*, *23*(15), 8178.

[46] Taylor, P. N., Razvi, S., Pearce, S. H., & Dayan, C. M. (2013). A review of the clinical consequences of variation in thyroid function within the reference range. *The Journal of Clinical Endocrinology & Metabolism, 98*(9), 3562–3571.

[47] Cheon, S. Y., & Song, J. (2025). Neuropsychiatric abnormalities in metabolic disturbances: Interplay of adipokines and neurotransmission. *Molecular Neurobiology, 62*(7), 8824–8842.