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Evaluating Serum Ferritin as a Biochemical Marker of Oxidative Stress in Type 2 Diabetes Mellitus

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Abstract

Elevated blood glucose levels and insulin resistance are two main features of Type 2 Diabetes Mellitus. Arising evidence suggests a mutual influence between iron overload and oxidative stress that impair insulin signaling, damage β pancreatic cells and promotes inflammation thereby contributing significantly to the progression and complications of T2DM, This cross sectional study aims to determine the effect of serum ferritin on T2DM and its correlation with oxidative stress, involving 80 participants, divided equally into diabetic and control group, anthropometric measurements as BMI and biochemical analysis including fasting blood glucose (F.B.G), glycated hemoglobin (HbA1c), insulin level, HOMA IR, serum ferritin and TBARS level were evaluated. The results showed a significant elevation in BMI, F.B.G., HbA1c, insulin levels, HOMA-IR, ferritin levels, and TBARS levels in the diabetic group ($p < 0.05$). Ferritin levels showed a moderate positive correlation with HOMA IR ($r = 0.63$) and FBG ($r = 0.60$). A weaker correlation was observed with HbA1c ($r = 0.4$) and oxidative stress markers ($r = 0.4$). These findings suggest that elevated ferritin may serve as a potential biomarker for insulin resistance and metabolic imbalance in type 2 diabetes mellitus (T2DM), and can also be a biochemical indicator of oxidative stress levels.

Keywords: T2DM; Ferritin; Insulin resistance; HOMA IR; Oxidative stress

INTRODUCTION

Diabetes mellitus is a metabolic condition marked by persistent hyperglycemia, along with disturbances in carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both (Liu et al., 2020). Surfacing evidence indicates an undeniable link between high body iron stores associated with the occurrence of insulin resistance and T2DM. Disturbances in iron metabolism are recognized as an important contributor to the onset and progression of T2DM. However, the exact strength and mechanism of this relationship remain unclear (Kunutsor et al., 2013). Iron is vital for several metabolic enzymes, including those involved in the mitochondrial electron transport chain. Iron assists in ATP production necessary for insulin secretion in β-cells, and plays a role in oxygen transport, indirectly aiding tissue glucose uptake. Serum ferritin, a key iron storage protein, is commonly used as a marker for assessing body iron stores and it varies significantly between sexes, ferritin also functions as an inflammatory marker, high iron stores may

promote lipid peroxidation thereby accelerating free radical generation (Kundu et al., 2013; Feng et al., 2023), Lipid peroxidation involves the oxidative degradation of polyunsaturated fatty acids, generating products such as malondialdehyde (MDA), which is commonly assessed using the thiobarbituric acid reactive substances (TBARS) assay (Tummalacharla et al., 2022). Oxidative stress has been implicated in pancreatic β-cell destruction, leading to impaired insulin secretion, insulin resistance, and ultimately the progression of Type 2 Diabetes Mellitus (T2DM). An imbalance characterized by excessive free radical production and diminished antioxidant defenses reduces the cell's capacity to neutralize reactive species, such as superoxide anions ($O_2^{\bullet-}$) and hydroxyl radicals (•OH) (Ayala et al., 2014; Su, 2022). This oxidative burden, driven by the overproduction of reactive oxygen species (ROS), is considered a central mechanism linking molecular disturbances to insulin resistance, β-cell dysfunction, impaired glucose tolerance, and the eventual development of T2DM.

Understanding the elements affecting the onset and course of T2DM has become increasingly critical. Among its various forms, T2DM represents an impactful and substantial public health challenge in Libya. (Kunutsor et al., 2013), this study aimed to explore the effect of serum ferritin levels on T2DM by examining the correlation between glycated hemoglobin, fasting blood glucose and serum ferritin levels, and to investigate the relationship between serum ferritin and insulin resistance, to assess the level of ROS by measuring malondialdehyde (MDA) using thiobarbituric acid reactive substances (TBARS) assay, Through this study we seek to provide deeper insight into the role of iron metabolism in the development and progression of T2DM.

MATERIALS AND METHODS

A cross-sectional study included 80 subjects, recruited from the diabetic center. Participants were aged between 30 and 60 years. 46 males and 34 females were divided into two age-matched groups: individuals diagnosed with type 2 diabetes mellitus (investigated group) and non-diabetic individuals (control group). Both groups underwent identical biochemical and anthropometric assessments to evaluate parameters related to diabetic profile, and ferritin levels, Participants with clinically significant hepatic, neurological, endocrinological or other major systemic diseases including malignancies were excluded, and patients with acute illness at the time, anemic or underwent repeated blood transfusion were also excluded from the study, participants were provided with detailed information about the study, informed consent was obtained from all participants prior to their inclusion in the study, all collected data were treated with strict confidentiality and participants anonymity was maintained throughout the study, ethical clearance code (NBC 004. H. 24. 1) was obtained from The Libyan National Committee for Biosafety and Bioethics.

Before sample collection, all participants fasted for 8 hours, blood pressure, weight, and height were measured, family history was documented to recognize any potential confounding factors, approximately 12 ml of blood was collected from each patient, and blood samples were immediately placed in an iced container to inhibit metabolic activity and prevent sample degradation. Participants of (FBG ≥ 126 mg/dL and/or HbA1c ≥ 6.5%) were considered as diabetes, individuals with FBG < 120 mg/dL, HbA1c <5.6% with no history of diabetic mellitus were considered controls, with no medication use or other systemic illness.

Biochemical Measurement

Fasting blood glucose was estimated by the hexokinase enzymatic method, and HbA1C was estimated using turbidmetric inhibition immunoassay (TINIA) by the Cobas C 111 analyzer. Insulin levels were estimated using Electrochemiluminescence Immunoassay (ECLIA) using the Cobas e

411 analyzer. Homa IR was calculated via the equation: HOMA-IR = [Glucose (mg/dL) × Insulin (μU/mL)] / 405 (Sama et al., 2021). Ferritin levels were estimated by using an Electrochemiluminescence Immunoassay (ECLIA) on a Cobas e 411 analyzer. Determination of plasma thiobarbituric acid-reactive substances (TBARs) concentrations was done according to (Ohkawa, 1978). The absorbance of the sample was measured against a blank at 532 nm.

Statistical Analysis

Data were calculated using mean and standard deviation (SD). Differences in means between the diabetic group and the control group were evaluated using the independent t-test. While comparisons of medians were performed using the Mann-Whitney U test. Correlation coefficients were applied to examine relationships between variables, with $p < 0.05$ considered statistically significant. Data analysis was carried out using SPSS 26.

RESULTS

The mean ages of both control and investigated were age matched as shown in Table 1, the mean of BMI of the control group was 25.00 kg/m^2 and the mean of BMI of the diabetic group was 28.88 kg/m^2, the difference in BMI of control group and diabetic group was statistically significant indicating higher BMI values in the diabetic group as shown in Table 1.

Table (1). characterization of participants

Variable	Control (n=40)	T2DM (n=40)	P value
Age (years)	42.95 (± 9.97)	42.77 (± 7.09)	
Weight (Kg)	74.17 (± 9.65	86.95 (± 9.7)	
Height (cm)	171.7 (± 8.38)	173.67 (± 9.48)	
BMI (kg/m^2)	25.00 ± (2.93)	28.88 ± (3.16)	Significant

BMI: body mass index, Underweight<18.5**,** Normal weight (18.5-24), Overweight (25-29.5), Obesity > 30, ($p < 0.05$).

The mean HbA1c level of the control group was 5.28%, Meanwhile, in the diabetic group it was 8.37% as described in Table 2, this suggests that the difference in HbA1c of control and diabetic group was statistically significant indicating that the diabetic group showing elevated HbA1c, The mean fasting blood glucose level in the control group was 92.23 mg/dl opposed to 160.32 mg/dl in the diabetic group, reflecting a significant difference among two groups, Similarly, the mean Insulin Level of control group was 6.21 μIU/mL**,** while the diabetic group had significantly higher mean insulin level of 21.87 μIU/mL, the median HOMA IR level of the control group was 1.3 versus the median of diabetic group that was 7.06, suggesting significant statistical difference where the diabetic group had increased levels of HOMA IR, The median serum ferritin level in the control group was 85.8 ng/ml, compared to the diabetic group that was 211.0 ng/ml, reflecting a significant increase in ferritin in the diabetic group.

Table (2). Glycemic control and ferritin levels of the participants

Variable	Control (n=40)	T2DM (n=40)	P value
HbA1c (%)	5.28 (±.477)	8.37 (±1.73)	Significant
F.B.G (mg/dl)	92.23 (±11.05)	160.32 (±50.36)	Significant
Insulin Level (μIU/mL)	6.21 (±2.68)	21.87 (±12.32)	Significant
Homa IR	1.3 (1.1-1.49)*	7.06 (3.96-10.16)*	Significant
Ferritin levels ng/ml	85.8 (62.75–108.85)*	211.0 (41.2–380.9)*	Significant

N.R: normal range, HbA1C: glycated hemoglobin, good control: 4.5-6.3%; fair control: 6.5-8.5%**,** uncontrolled: >8.5%, F.B.G: fasting blood glucose, Homa IR: homeostatic model assessment for insulin resistance, *median (Interquartile Range (Q1–Q3), ($p < 0.05$).

The mean TBARS level in the control group was 0.834 nmol/ml**,** while in the diabetic group, it was 0.897 nmol/ml, as shown in Table 3. This difference is statistically significant with a P value of 0.025, indicating elevated oxidative stress in the diabetic group.

Table (3). Oxidative stress of the control and the diabetic groups

Variable	Control (n=30)	T2DM (n=30)	P value
TBARS (nmol/ml) N.R: (0.006-0.974)	0 .834 (± 0.115)	0.897 (± 0.094	Significant

N.R: normal range, TBARS: thiobarbituric acid reactive substances. ($p < 0.05$).

A moderate positive correlation was found between ferritin level and HOMA IR (r=0.63), as shown in Figure 1.

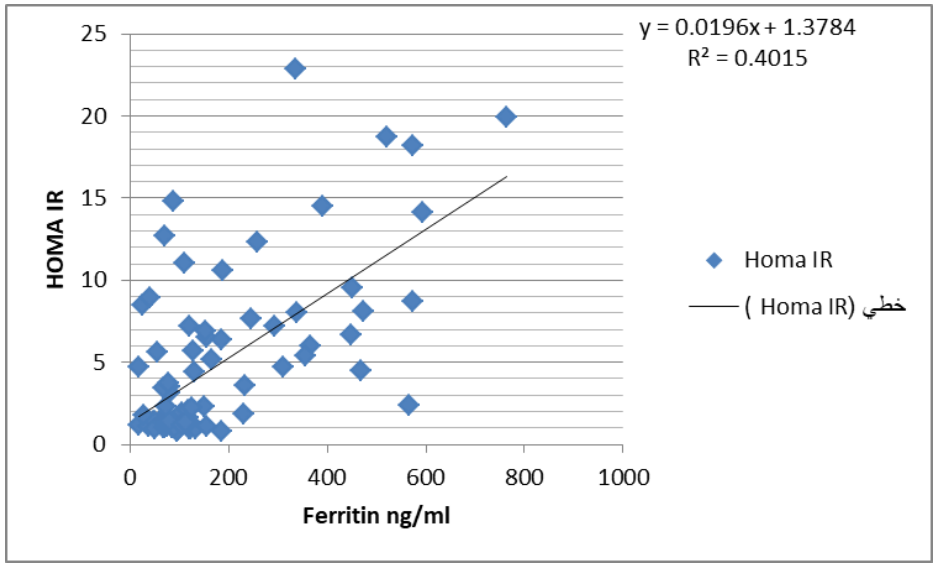

Figure (1). Correlation between ferritin levels and HOMA IR levels

A moderate positive correlation was found between ferritin levels and F.B.G levels (r=0.6) as illustrated in Figure 2.

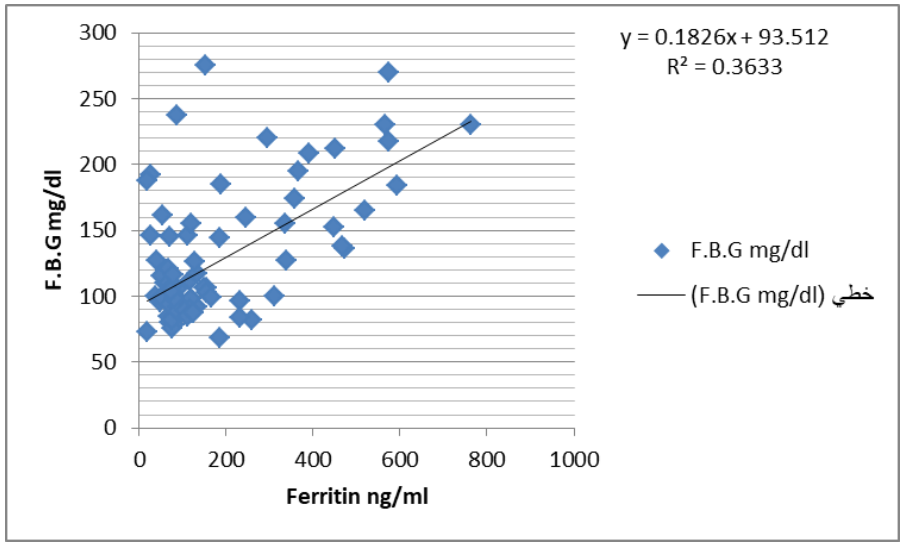

Figure (2). Correlation between F.B.G. and Ferritin levels

A weak correlation between HbA1c and ferritin levels (r=0.4) as in Figure 3.

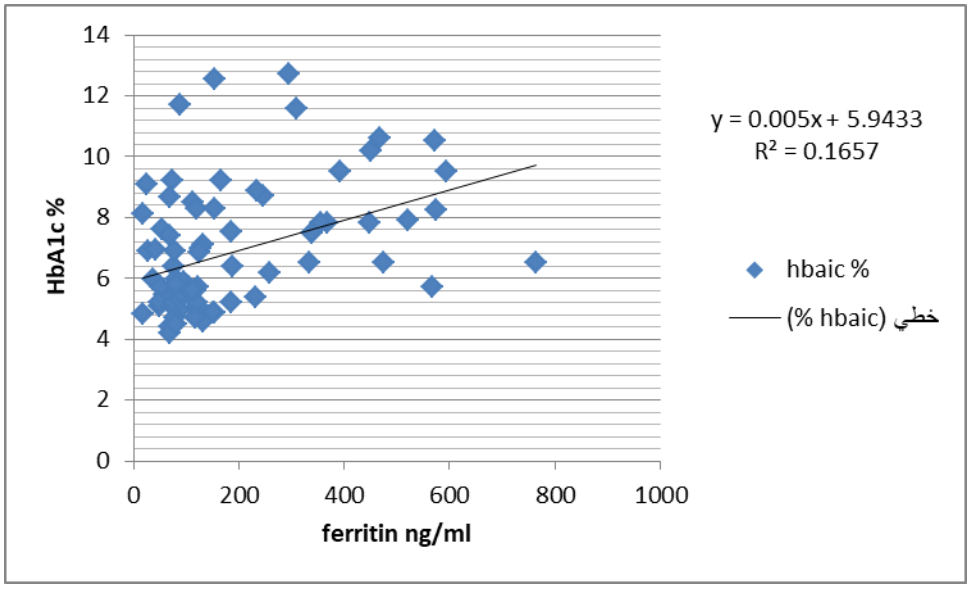

Figure (3). Correlation between HbA1c and ferritin levels

A weak to moderate correlation was observed between ferritin levels and oxidative stress markers.

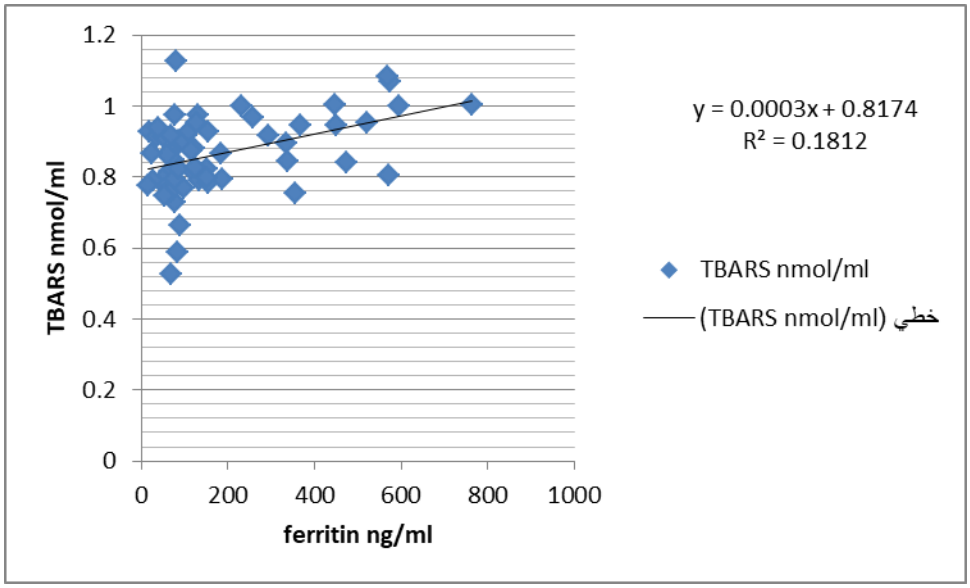

Figure (4). Correlation between TBARS level and ferritin level

DISCUSSION

The study showed that diabetic individuals tended to have higher body weight, while the average height was similar between groups. A notable difference was observed in BMI, with the diabetic group falling into the overweight category. Meanwhile, the control group remained in the normal weight category, this difference was statistically significant emphasizing the association between diabetes and increased BMI as shown in Table 1, this evidence is supported by previous studies indicating that obesity and overweight contribute tremendously to the prevalence of T2DM (Klein

et al., 2022), due to secretion of bioactive substances including pro-inflammatory cytokines like tumor necrosis factor alpha (TNF- α) and interleukin-6 (IL-6) by the Adipose tissue, particularly visceral fat which in turns interfere with insulin signaling pathway leading to impairment of cellular glucose uptake, resulting in elevated blood glucose levels and increase demand on pancreatic β cells to produce more insulin, overtime, this mechanism may fail leading to β cells dysfunction and onset of T2DM (Samuel & Shulman, 2012). Generally, as BMI increases, the chances of developing diabetes also proportionally rise (Klein et al., 2022; Chandrasekaran et al., 2024).

Glycated haemoglobin (HbA1c) is a critical biomarker in the management and diagnosis of diabetes mellitus. The diabetic group exhibited significantly higher HbA1c levels compared to the control group; this difference highlights the variation in the blood glucose regulation, as illustrated in Table 2. In diabetes, chronic hyperglycemia will lead to elevated HbA1c levels which is linked to higher risk of diabetes related complications encompassing renal, neurological, ocular and cardiovascular systems, by estimating HbA1c, we measure the stable glycation of hemoglobin, a process where glucose non-enzymatically binds to the hemoglobin β-chain making it essential parameter to assess long term glycemic control (Sherwani et al., 2016; Xiao et al., 2025). Fasting glucose level monitoring provides critical insight into glycemic control and guides therapeutic decisions**.** In this study, the fasting blood glucose levels were markedly higher in the diabetic group. The current study results reflect impaired glucose regulation in individuals with diabetes. Elevated normal range fasting plasma glucose has been shown to predict the development of T2DM, indicating that glucose production by the liver may become dysregulated even in the early stages of diabetes. There is a strong independent association between fasting plasma glucose levels and the onset of T2DM. The susceptibility to diabetes increases proportionally as fasting plasma glucose increases. These elevations can indicate insulin resistance, impaired insulin secretion, or excessive hepatic glucose production, each of which represents a fundamental mechanism involved in the pathogenesis of T2DM (Xiaoyu et al., 2024).

The diabetic group exhibited substantially higher fasting insulin levels as opposed to the control group. This difference indicates an imbalance in insulin regulation, which reflects the underlying insulin resistance. Elevated fasting insulin levels were connected with an increased risk of developing T2DM. Fasting hyperinsulinemia acts as an initial sign of insulin resistance and impaired glucose metabolism, mainly indicating excessive insulin release by pancreatic β cells. Individuals with elevated fasting insulin levels are more susceptible to developing impaired early-phase insulin secretion, which is an important contributor to the development and progression of T2DM (Park et al., 2021). The diabetic group exhibited markedly elevated HOMA IR levels compared to the control group, reflecting a significant difference in insulin resistance, which indicate a reduced insulin sensitivity in individuals with diabetes, elevated HOMA IR levels were associated with an increased risk of T2DM, which is attributed to insulin resistance & impaired glucose uptake that eventually leads to β cell dysfunction and worsening hyperglycemia (Park et al., 2021; González-González et al., 2022). The dual effect of ferritin as both an indicator of iron overload and inflammation makes it a crucial in assessing metabolic imbalance in diabetes, a statistically significant difference in ferritin levels of the diabetic group was found as shown in Table 2, suggesting a higher iron storage in individuals with diabetes, the association between systemic iron overload and abnormal glucose metabolism was initially noted in conditions such as hereditary hemochromatosis and thalassemia. However, researches demonstrated that regardless of iron overload causes or the specific gene involved, iron overload is associated with higher risk of developing T2DM, excessive dietary iron intake and elevated ferritin referring to excess iron stores may also contribute directly into the pathogenesis of T2DM by promoting both β cell dysfunction and insulin resistance **(**Kundu et al., 2013), elevated ferritin levels are also associated with oxidative stress, in early stages of diabetes, ferritin

may act as a pro-oxidant, catalyzing ROS formation, thereby contributing to cellular damage and insulin resistance (Chaudhari et al., 2021). Persistent elevation in levels of ferritin, along with the extent of these elevations, is strongly associated with diabetes progression **(**Cheng et al., 2024). Ferritin levels showed a moderate positive correlation with HOMA IR (Figure 1), which can be attributed to iron-induced oxidative stress, inflammation, β-cell dysfunction, and hepatic insulin resistance; these mechanisms collectively impair insulin sensitivity, increase insulin secretion, and elevate HOMA IR values (Cho et al., 2017; Kim et al., 2018).

A positive moderate to strong correlation between F.B.G. and ferritin levels was found in this study (Figure 2). Ferritin is an acute-phase reactant, and elevated F.B.G is a sign of poor glycemic control that contributes to systemic inflammation, which in turn stimulates ferritin production (González-González et al., 2022). A weak positive correlation between ferritin levels and HbA1c was also detected, as shown in Figure 3. HbA1c measures the proportion of glycated haemoglobin, mainly influenced by glucose concentration in the blood, the lifespan of red blood cells, and haemoglobin types. Iron levels typically do not have a direct effect on HbA1c (Sherwani et al., 2016).

TBARS level is an effective biomarker for assessing oxidative stress, as it reflects the extent of lipid peroxidation in the body. A significant increase in TBARS levels was observed in the diabetic group, as illustrated in Table 3. This suggests elevated oxidative stress in individuals with diabetes.
Chronic hyperglycemia leads to overproduction of ROS through pathways such as mitochondrial dysfunction and glucose autoxidation (Elfowiris and Banigesh 2022). The excessive ROS generation results in lipid peroxidation, protein damage, and cellular dysfunction, as demonstrated by elevated malondialdehyde in diabetic patients (Yaribeygi et al., 2020). These oxidative results implicated an insulin resistance, β-cell dysfunction, and inflammation, eventually exacerbating complications of T2DM (Chaurasiya et al., 2020). A weak to moderate correlation was detected between oxidative stress and ferritin levels, as illustrated in Figure 4. This can be caused by iron metabolism variations, differences in antioxidant defense, and genetic predisposition. These factors can have a major effect on oxidative stress independently of ferritin. Elevated ferritin levels may not directly contribute to oxidative stress levels. These findings support and are consistent with previous reports (Tiwari et al., 2021).

CONCLUSION

This study demonstrated significant biochemical and physiological disparities between diabetic individuals and non-diabetic controls. The diabetic group exhibited markedly elevated levels of fasting blood glucose, HbA1c, insulin levels, HOMA IR, and ferritin levels, reflecting impaired glycemic control, higher insulin resistance, heightened systemic inflammation, and iron overload. These findings strongly support the hypothesis that T2DM is not solely a disorder of glucose metabolism, but can also be linked to systemic inflammation and iron overload, each of which may contribute to insulin resistance and diabetes related complications.

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ETHICS

Authors should address any ethical issues that may arise after the publication of this manuscript.

Duality of interest: The authors declare that they have no duality of interest associated with this manuscript.

Author contributions: A.B. developed the theoretical formalism, performed the analytic calculations, and performed the numerical simulations. Both A.B and B.C. authors contributed to the final version of the manuscript. B.C. supervised the project.

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REFERENCES

Ayala, A., Muñoz, M. F., & Argüelles, S. (2014). Lipid peroxidation: Production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. *Oxidative Medicine and Cellular Longevity, 2014*, Article 360438. https://doi.org/10.1155/2014/360438

Chandrasekaran, P., & Weiskirchen, R. (2024). The role of obesity in type 2 diabetes mellitus—An overview. *International Journal of Molecular Sciences, 25*(3), 1882. https://doi.org/10.3390/ijms25031882

Chaurasiya, A., Shah, A., & Singh, R. (2020). *Interaction between oxidative stress and diabetes: A mini-review. Journal of Diabetes & Metabolic Disorders, 7*(2), 58–61. https://doi.org/10.15406/jdmdc.2020.07.00201

Chaudhari, R. K., Niraula, A., Gelal, B., Baranwal, J. K., Sarraf, D. P., Maskey, R., & Lamsal, M. (2021). Increased serum ferritin levels in type 2 diabetes mellitus patients: A hospital-based cross-sectional study. *Journal of Universal College of Medical Sciences, 9*(2), Article 24. https://doi.org/10.3126/jucms.v9i02.42009

Cheng, A. N., & Al-Samkari, H. (2024). Impact of iron overload on incidence of diabetes mellitus, cardiac disease, and death in congenital hemolytic anemias. *Blood Advances, 8*(21), 5451–5461. https://doi.org/10.1182/bloodadvances.2024013666

Cho, M. R., Park, J. K., Choi, W. J., Cho, A. R., & Lee, Y. J. (2017). Serum ferritin level is positively associated with insulin resistance and metabolic syndrome in postmenopausal women: A nationwide population-based study. *Maturitas, 103*, 3-7.

Elfowiris, A. and A. Banigesh (2022). "Evaluation of Antioxidant Therapeutic Value of ACE Inhibitor as Adjunct Therapy on Type 2 Diabetes Mellitus Patients with Cardiovascular Disease." *ACS Pharmacology & Translational Science* 5(6): 413-418.

Kim, N. H., Sung, K. C., & Hur, J. (2018). Gender difference in the relationship between the ferritin and homeostasis model assessment of insulin resistance in non-diabetic Korean adults. *Diabetes Research and Clinical Practice, 135*, 42-49.

Klein, S., Gastaldelli, A., Yki-Järvinen, H., & Scherer, P. E. (2022). Why does obesity cause diabetes? *Cell Metabolism, 34*(1), 11–20. https://doi.org/10.1016/j.cmet.2021.12.012

Kundu, D., Roy, A., Mandal, T., Bandyopadhyay, U., Ghosh, E., & Ray, D. (2013). Relation of iron stores to oxidative stress in type 2 diabetes. *Nigerian Journal of Clinical Practice, 16*(1), 100–

105. https://doi.org/10.4103/1119-3077.106776

González-González, J. G., Violante-Cumpa, J. R., Zambrano-Lucio, M., Burciaga-Jimenez, E., Castillo-Morales, P. L., Garcia-Campa, M., Solis, R. C., González-Colmenero, A. D., & Rodríguez-Gutiérrez, R. (2022). HOMA-IR as a predictor of health outcomes in patients with metabolic risk factors: A systematic review and meta-analysis. *Volume 29*, 547–564.

Liu, J., Li, Q., Yang, Y., & Ma, L. (2020). Iron metabolism and type 2 diabetes mellitus: A meta-analysis and systematic review. *Journal of Diabetes Investigation, 11*(4), 946–955. https://doi.org/10.1111/jdi.13216

Park, S. Y., Gautier, J.-F., & Chon, S. (2021). Assessment of insulin secretion and insulin resistance in humans. *Diabetes & Metabolism Journal, 45*(6), 641–654. https://doi.org/10.4093/dmj.2021.0220

Sama, S., Jain, G., Kant, R., Bhadoria, A. S., Naithani, M., & Kumar, A. (2021). Quantifying the homeostatic model assessment of insulin resistance to predict mortality in multi-organ dysfunction syndrome. *Indian Journal of Critical Care Medicine, 25*(12), 1364–1369. https://doi.org/10.5005/jp-journals-10071-24043

Samuel, V. T., & Shulman, G. I. (2012). Mechanisms for insulin resistance: Common threads and missing links. *Cell, 148*(5), 852–871. https://doi.org/10.1016/j.cell.2012.02.017

Sherwani, S. I., Khan, H. A., Ekhzaimy, A., Masood, A., & Sakharkar, M. K. (2016). Significance of HbA1c test in diagnosis and prognosis of diabetic patients. *Biomarker Insights, 11*, 95–104. https://doi.org/10.4137/BMI.S38440

Su, X. (2022). Lipid peroxidation: Types and its determination. *Oxidants and Antioxidants in Medical Science, 11*(6), 1–2.

Tiwari, D. N., Kumar, A., & Mehta, A. (2021). Iron status and oxidative stress biomarkers in adults: A preliminary study. *Agricultural Systems Research, 17*(2), 56-61. https://agris.fao.org/search/en/providers/122535/records/65de4df9b766d82b18fd04eb

Xiaoyu, W., Yuxin, X., & Li, L. (2024). The effects of different intermittent fasting regimens in people with type 2 diabetes: a network meta-analysis. *Frontiers in Nutrition*, 11, 1325894. https://doi.org/10.3389/fnut.2024.1325894

Xiao, Y., Hong, X., Neelagar, R., & Mo, H. (2025). Association between glycated hemoglobin A1c levels, control status, and cognitive function in type 2 diabetes: A prospective cohort study. *Scientific Reports, 15*, Article 5011. https://doi.org/10.1038/s41598-025-53522-1

Yaribeygi, H., Sathyapalan, T., Atkin, S. L., & Sahebkar, A. (2020). Molecular mechanisms linking oxidative stress and diabetes mellitus. *Oxidative Medicine and Cellular Longevity, 2020*, Article ID 8609213. https://doi.org/10.1155/2020/8609213