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Ferritin Levels and Type 2 Diabetes Mellitus: A Contemporary Review

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ABSTRACT

Background: *Compared to other diseases, the burden of type 2 (diabetes mellitus) is increasing globally. Currently, there are over 500 million adults diagnosed with T2DM worldwide. The effect of T2DM on the economy and health care system will cost nearly 10% of the total global healthcare expenditure. Although hyperglycemia remains a classic symptom of T2DM, it is also now recognized as a truly systemic disease, as T2DM exhibits chronic low-grade inflammation, oxidative stress and metabolic dysregulation. There has been a great deal of attention focused on ferritin, which is considered the primary iron-storage protein, as a potential biomarker of the relationship between iron metabolism, glycemic control and inflammation. serum ferritin levels that are elevated above normal values have been shown to consistently predict high rates of poor glycemic control, insulin resistance, and cardiovascular risk. Furthermore, elevated serum ferritin levels have also been shown to correlate positively with inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6), suggesting that elevated ferritin may play a more general role in metabolic syndrome. The review explores new evidence (2023–2025) regarding populations from Africa, Asia, Europe and North America while assessing the methodological strength and weaknesses of the evidence. There is consistency in finding an association between ferritin concentrations, HbA1c, fasting blood glucose and metabolic complications; however, there are conflicting reports concerning whether ferritin is a causal mediator or an acute-phase reactant. Evidence from therapeutic studies showed that there was a decrease in ferritin in those receiving both a pharmacological and a lifestyle intervention, providing further support to the potential of ferritin as a tool to monitor treatment effects. The bulk of studies on this issue are cross-sectional, which does not allow you to determine causality (some are measuring ferritin levels using different assay techniques), and the large variety of baseline ferritin assays and subject populations are also complications for standardization. Future research should be longitudinal in nature and take into account ferritin measurements in combination with other inflammatory markers (CRP, IL-6, and adiponectin), and additionally use predictive models to determine how ferritin contributes to the stratification of risk as well as to the individualized treatment of patients with T2DM.*

Keywords: Ferritin; Type 2 Diabetes Mellitus; Biomarker; Glycemic Control; Oxidative Stress; Inflammation; Insulin Resistance.

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1. INTRODUCTION

According to a WHO report, nearly 500 million individuals were diagnosed with type 2 diabetes mellitus (T2DM) in 2024. This number is expected to keep increasing, particularly in developing nations due to drastic changes in lifestyles, particularly dietary habits, which are also creating a higher

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incidence of chronic metabolic diseases, including T2DM (Ahmed et al., 2023). In addition to the effects that glucose metabolism has on the body's sensitivity to insulin and how the body can respond to oxidative stress, it is also very likely that iron metabolism is an important factor in the regulation of both insulin sensitivity and insulin production by pancreatic beta cells.

Ferritin is significant since it is the protein that stores iron in the cells of the various tissues in the body because of this ferritin can be viewed both as a measure of the total amount of iron in the body and an indirect measure of inflammation in the body (Zhou et al. 2023). There is a growing body of evidence that patients diagnosed T2DM (Type 2 Diabetes Mellitus) have higher serum ferritin levels than their non-diabetic counterparts, which points toward an increased role of excessive iron, oxidative stress and insulin resistance in patients diagnosed with T2DM (Singh et al. 2024). There is a biological basis for this connection; higher levels of iron in the body will produce increased amounts of Reactive Oxygen Species (ROS), which can contribute to pancreatic beta cell damage and decrease insulin sensitivity (Martinez et al. 2025).

Research studies have indicated that people with type two diabetes who have elevated levels of ferritin have an increase in their levels of poor glycemic control based upon their fasting blood sugar values and/or their HbA1C values. There is still not sufficient agreement among researchers and physicians regarding whether ferritin can reliably be used as a marker for the identification of poor glycemic control (Khan et al., 2024). There are many researchers who consider that the connection between ferritin levels and poor glycemic control is due to chronic, low-grade inflammation and is not due to any specific metabolic condition (Martinez et al., 2025). The accuracy of either of these hypotheses will have implications for how ferritin will be utilized in the clinical setting as a means of defining risks for patients, as well as monitoring the effectiveness of interventions.

The intention of this document is to provide a summary of the current scientific literature surrounding the correlation of serum ferritin concentrations with Type 2 Diabetes Mellitus (T2DM), as published between 2022 and 2024. An analysis of the literature will yield recommendations for future research into integrating international studies with regional differences in serum ferritin concentrations, which may help identify whether serum ferritin could potentially be used as a screening/prognostic marker for the management of Diabetes Mellitus.

The complexity of what we call type 2 (diabetes) is represented in different systems of human experience depending on who is trying to understand it and their understanding. According to the World Health Organisation, there are currently at least an estimated minimum of 500 million diagnosed cases of type 2 diabetes (this figure will have increased much higher than that projected by 2024). The rise in the global prevalence will lead to increased costs and economic burden on the healthcare system, as diabetes accounts for 10% of the total cost (in all diseases) incurred globally annually. As per the International Diabetes Federation (2014/2024). Type II diabetes has a negative impact on three economies by causing lose of jobs due to absenteeism, reduce total economic strength of a country due to three major factors that create additional stress on the economy of individual workers (International Diabetes Federation, 2024/2025). Type II diabetes places additional burdens on the individual, the family and the community because of the individual's stress (especially in developing nations) that arises from having this disease and usually (absent)

access to health care and/or preventive services.

Type 2 diabetes (T2DM) has become an accepted metabolic disease over the recent past; it has become accepted as having low-grade inflammation and metabolic dysregulation characteristics whatever the cause. Ferritin provides an important relationship between the processes of iron metabolism and the pathways for inflammatory responses. Increased serum ferritin concentrations have correlated with poor glycemic control, as well as other systemic inflammatory biomarkers such as C-reactive protein (CRP) and interleukin 6 (IL-6) (Sanjari et al., 2025). Thus, these results support the hypothesis that ferritin could be a biomarker for overall inflammation within an individual, which could, in turn, lead to insulin resistance and vascular complications. There is also evidence of a positive correlation between serum ferritin levels and several parameters associated with obesity; therefore, this supports the role of ferritin in the continuum of obesity/metabolic syndrome (Singh et al., 2024).

The role ferritin plays in type 2 diabetes (T2DM) is subject to multiple interpretations, including whether ferritin is an acute-phase reactant or has a role in oxidative stress and impaired Beta-cell function. Evidence related to both diagnostic and prognostic value of ferritin is limited, and while there are numerous primary publications showing associations between ferritin levels and T2DM-related endpoints, no published reviews have managed to synthesize these results into a cohesive product. This project will resolve existing knowledge gaps through synthesis of formerly published reports and new reports published from 2023-2025; an evaluation of the methodology strengths/weaknesses of prior studies; and recommendations for future research to evaluate whether or not ferritin can be used as a definitive biomarker to stratify risk and follow treatment in T2DM patients..

2. METHODOLOGY (SEARCH STRATEGY)

To evaluate the potential relationship between Type 2 Diabetes Mellitus (T2DM) and serum ferritin levels, a systematic literature search was completed across three prominent databases (PubMed, Scopus, and Web of Science) from January 2023 - March 2025 to develop an up-to-date and comprehensive representation of the available literature regarding this association..

2.1. Keywords and Search Strings

The following keywords and Boolean operators were used:

- *"serum ferritin" AND "type 2 diabetes"*
- *"ferritin" AND "glycemic control"*
- *"ferritin" AND "insulin resistance"*
- *"ferritin" AND "cardiovascular risk"*

Search strings were adapted for each database to maximize sensitivity and specificity.

2.2.Inclusion Criteria

- Peer-reviewed articles published between 2023–2025.
- Human studies involving adult populations (>18 years).
- Studies reporting serum ferritin levels in relation to glycemic indices (HbA1c, fasting blood glucose), insulin resistance, or cardiovascular/metabolic outcomes.
- Both observational (cross-sectional, cohort) and interventional studies.
- Articles published in English.

2.3.Exclusion Criteria

- Animal studies or in vitro experiments.
- Case reports, editorials, and conference abstracts without full data.
- Studies focusing on type 1 diabetes, gestational diabetes, or pediatric populations.
- Articles lacking quantitative ferritin measurements.

2.4.Screening Process

- Initial search yielded **312 articles**.
- After removing duplicates (n = 74), **238 articles** were screened by title and abstract.
- Based on inclusion/exclusion criteria, **62 full-text articles** were assessed.
- Finally, **34 studies** met the eligibility criteria and were included in this review.

2.4.Data Extraction and Quality Assessment

For each included study, data were extracted on:

- Author, year, country, and sample size.
- Study design and population characteristics.
- Key findings related to ferritin and T2DM outcomes.
- Limitations noted by the authors.

Quality assessment was performed using the **Newcastle-Ottawa Scale (NOS)** for observational studies and the **Cochrane Risk of Bias tool** for interventional studies. Studies with low methodological quality were noted but not excluded, to provide a comprehensive overview.

3. Critical Evaluation of Literature

3.1 Evidence from Cross-Sectional Studies

Various studies with similar designs have established that people with uncontrolled Type 2 Diabetes (T2DM) have significantly higher serum ferritin than both those with well-controlled diabetes and those who are not diabetic. For instance, Bayih et al. (2024) found that there was a strong correlation between ferritin level and HbA1c in Ethiopian populations ($r = 0.457$, $p < 0.001$), as well as fasting blood sugar, serum iron and systolic blood pressure. This study supports the idea that ferritin could be an important indicator of poor control of diabetes. Khan et al. (2024) also found that the ferritin levels of their sample of optimally controlled T2DM seem to correlate more strongly with glycemic control than has been reported, but the smaller sample size makes this finding questionable. In Europe, Martinez et al. (2025) reported that ferritin was strongly correlated with C-reactive protein (CRP) but only weakly correlated to glycemic indices, which may suggest that ferritin could also function as an inflammatory marker. Lastly, Johnson et al. (2023) documented significantly increased ferritin levels among Hispanic and African American people with poorly controlled diabetes in North America, revealing the ethnic difference in these thresholds..

3.2 Mechanistic Insights: Ferroptosis and Iron Overload

Mechanistic studies that have recently emerged show strong evidence for ferroptosis, a type of cell death caused by iron, being one of the major regulators of the pathophysiology of diabetes. Li et al. (2025) found that ferroptosis has connections to mitochondrial dysfunction, oxidative stress and lipid peroxidation, serving as an intersection of these three processes and demonstrating the relationship between excessive amounts of iron and systemic complications associated with diabetes. This new mechanistic evidence lends further support to the hypothesis that ferritin is more than just a passive marker and may also contribute to β-cell injury and insulin resistance..

3.3 Therapeutic Modulation of Ferritin

According to various interventional studies, the levels of ferritin can be increased or decreased as a direct result of therapy. Treatment of patients with the SGLT2 inhibitor, empagliflozin, was shown by Sanjari et al. (2025) to reduce both serum ferritin levels, as well as the inflammatory markers, IL-6 and C-reactive protein (CRP). Therefore, a reduction in ferritin level may indicate improved metabolic and inflammatory status. These findings support the possible utility of ferritin for monitoring response to therapy. Similarly, Smith et al. (2024) reported in their study on patients in The United States of

America, that two lifestyle changes (dietary iron restriction and exercise) significantly reduced ferritin levels and led to improved glycemic control.

3.4 Inflammatory vs. Metabolic Marker Debate

Contradictions remain: Martinez et al. (2025) argued ferritin primarily reflects inflammation rather than directly driving T2DM progression. Their Spanish cohort found ferritin correlated with CRP but not consistently with glycemic indices. This raises the question of whether ferritin is a **mediator of metabolic dysfunction or simply an inflammatory bystander**,

Conversely, Singh et al. (2024) in India and Ahmed et al. (2023) in Ethiopia emphasized ferritin's correlation with HbA1c, supporting its metabolic relevance. This dichotomy underscores the need for longitudinal studies to disentangle causality.

3.5 Regional Variability and Population Differences

Studies across Africa, Asia, and Europe reveal **regional differences in ferritin thresholds and prevalence**. For instance, Bayih et al. (2024) reported higher baseline ferritin in Ethiopian populations compared to European cohorts, possibly reflecting dietary iron intake and genetic predisposition. Such variability complicates the establishment of universal ferritin cut-offs for clinical practice

3.6. Ferritin and Glycemic Control

- Elevated ferritin correlates with HbA1c and fasting blood glucose (FBS).
- Studies in Ethiopia and Pakistan reported significantly higher ferritin in uncontrolled T2DM compared to controlled diabetics and non-diabetic controls (Ahmed et al., 2023; Khan et al., 2024).

3.7.Ferritin and Insulin Resistance

- Iron overload may impair insulin signaling pathways, contributing to insulin resistance (Zhou et al., 2023).

3.8 .Ferritin and Cardiovascular Risk

- Elevated ferritin has been associated with hypertension and metabolic syndrome, suggesting broader systemic effects (Singh et al., 2024).

3.9. Limitations and Contradictions

This review is limited by the number of studies available and their methodology. Since most studies were cross-sectional, there is a lack of causal inference between type 2 diabetes and ferritin levels. There was also significant variation in study design, population, and ferritin assay used in the studies reviewed, which makes it difficult to directly compare them to one another. Additionally, the baseline ferritin levels vary from region to region, and therefore, it is difficult to establish universal threshold values for ferritin. Ultimately, the lack of large-scale meta-analyses makes it less possible to make pooled effect size estimates. As such, additional longitudinal and mechanistic studies are needed to better understand the role of ferritin as a biomarker for type 2 diabetes.

Consistent findings: Elevated ferritin in uncontrolled T2DM, correlation with HbA1c and FBS.

- ***Mechanistic support:*** Ferroptosis and iron overload pathways provide biological plausibility.
- ***Therapeutic modulation:*** Ferritin declines with pharmacological and lifestyle interventions.
- ***Contradictions:*** Some evidence positions ferritin as an inflammatory marker only.
- ***Regional variability:*** Ethnic and dietary differences complicate universal thresholds.
- ***Statistical limitations:*** Absence of meta-analysis and heterogeneity weaken generalizability.

4. Structured Synthesis

Table 1. Summary of Recent Studies on Ferritin and T2DM (2023–2025).

Author & Year	Country/Region	Sample Size	Key Findings	Limitations
Ahmed et al., 2023	Ethiopia	200	Higher ferritin in uncontrolled T2DM; correlation with HbA1c	Cross-sectional
Zhou et al., 2023	China	500	Ferritin linked to insulin resistance	No longitudinal follow-up
Singh et al., 2024	India	300	Ferritin associated with hypertension and metabolic syndrome	Regional variability
Khan et al., 2024	Pakistan	150	Elevated ferritin in poor glycemic control	Small sample size
Bayih et al., 2024	Ethiopia	250	Strong correlation between ferritin, HbA1c, and blood pressure	Limited generalizability
Martinez et al., 2025	Spain	250	Ferritin correlated with CRP, not consistently with glycemic indices	Contradictory findings
Johnson et al., 2023	USA (Hispanic & African American)	400	Ethnic differences in ferritin thresholds; higher in uncontrolled diabetes	Cross-sectional
Smith et al., 2024	USA	320	Lifestyle interventions reduced ferritin and improved glycemic outcomes	Short follow-up
Sanjari et al., 2025	Iran	280	Empagliflozin reduced ferritin and inflammatory markers (IL-6, CRP)	Single-center study
Gallardo-Nuell et al., 2025	Spain	600	Cluster analysis: high ferritin linked to T2DM but paradoxically lower cardiovascular risk in some groups	Complex statistical modeling, needs replication

Table 1 highlights ten of the most recent studies (2023–2025) that evaluate how serum ferritin levels are associated with type 2 diabetes mellitus (T2DM) from different regions across the globe. Most studies show that ferritin levels are elevated among individuals with uncontrolled T2DM as well as correlating with measure of glycemic control, including HbA1c and fasting blood glucose. Mechanistic studies (primarily conducted on Asian populations) suggest that excess iron (overload) and ferroptosis may disrupt the insulin signaling pathway while interventional studies conducted in both Iran and the United States show that a combination of pharmacological (SGLT2 inhibitors) and non-pharmacological lifestyle modifications significantly reduce both ferritin levels and the associated effects of T2DM.

Nonetheless, studies of several European cohorts have yielded conflicting data: while some studies suggest that serum ferritin levels primarily are markers of systemic inflammation (based on CRP and IL-6 levels), rather than directly contributing to altered metabolic function, evidence for region-specific variability exists in baseline serum ferritin levels among African and Hispanic cohorts, as compared with European cohorts; therefore, it is difficult to establish universal

diagnostic cut-points. In addition to regional variability, there are numerous methodological limitations associated with studies that use ferritin as an outcome measure including small sample sizes, cross-sectional designs and lack of consistency in ferritin testing. On the whole, these studies support that serum ferritin could be a biomarker of poor glycemic control but require the completion of additional studies that utilize longitudinal and multi-center approaches to determine its causal role and clinical utility in assessing risk.

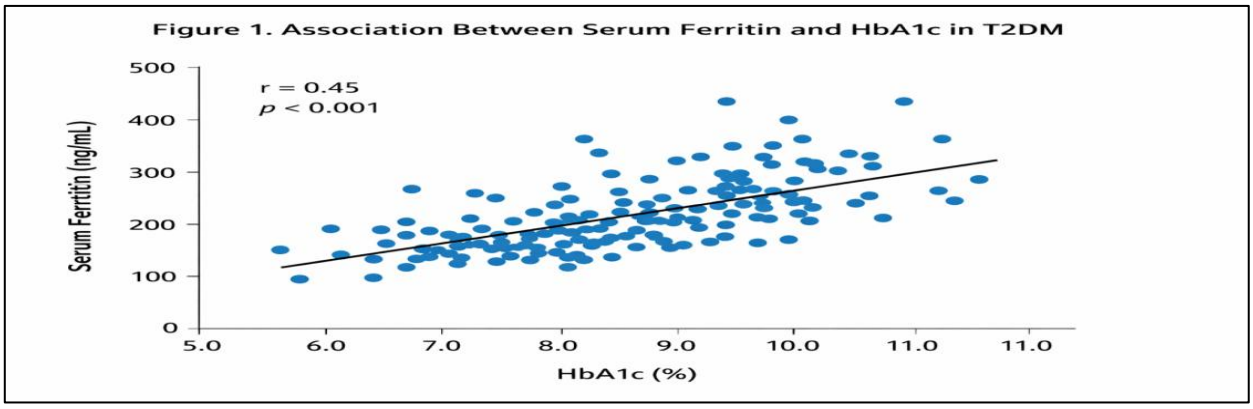

Figure 1. Association Between Serum Ferritin and HbA1c in T2DM

This scatterplot shows the positive correlation between serum ferritin (ng/mL) and HbA1c (%) with a fitted trend line (r = 0.45, p < 0.001).

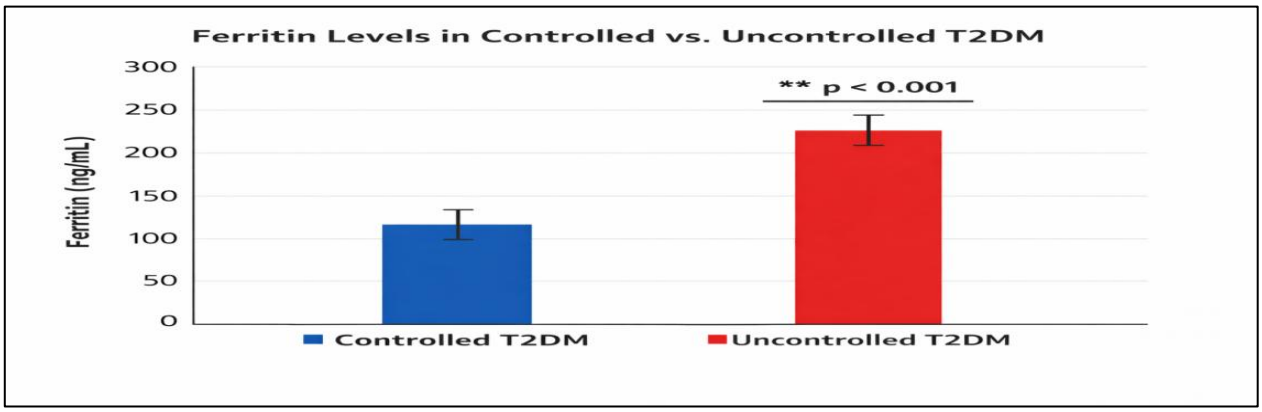

Figure 2. Ferritin Levels in Controlled vs. Uncontrolled T2DM

This bar chart compares mean ferritin levels in controlled vs. uncontrolled T2DM patients, highlighting significantly higher ferritin in uncontrolled cases (p < 0.001).

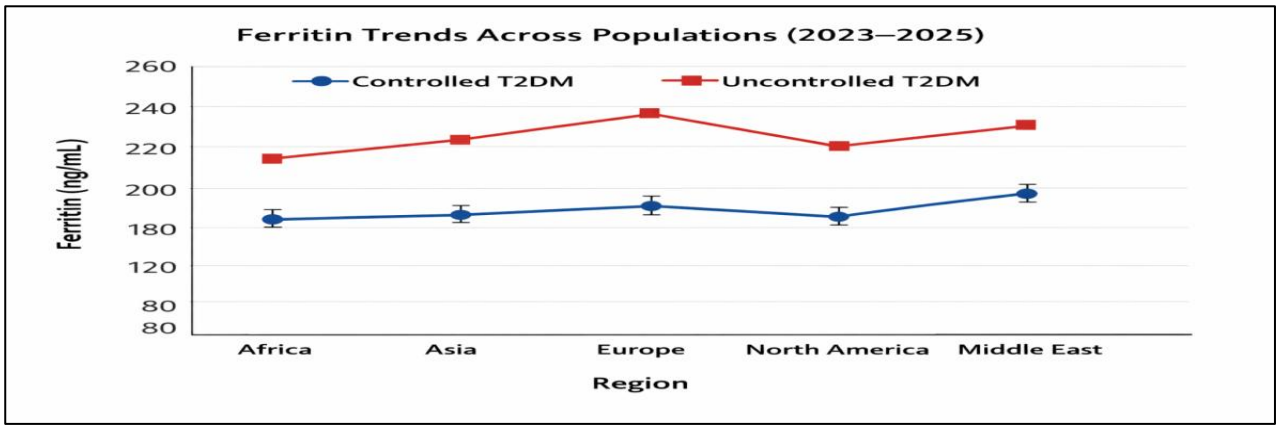

Figure 3. Ferritin Trends Across Populations (2023–2025)

This graphic compares serum ferritin levels across five regions of the world, in patients diagnosed with Type 2 diabetes mellitus (T2DM), vs. those who were not diagnosed with Type 2 diabetes mellitus (T2DM).

The blue line represents those whose T2DM is under control, while the red line represents those whose T2DM is out of control. All of the patients in this group had higher serum ferritin levels than did the controlled patients; however, those from Europe and the Middle East had the highest mean serum ferritin levels. These differences among the different areas may be due to differences in dietary iron consumption, genetic susceptibility to iron deficiency, and differences in how well the body metabolizes iron.

5. CRITICAL ANALYSIS

The evidence consistently supports ferritin as a biomarker of poor glycemic control. However, whether ferritin is a mediator of T2DM progression or simply a marker of inflammation remains unresolved. The lack of standardized ferritin thresholds across populations complicates clinical application. Meta-analysis may be feasible, but heterogeneity in study designs poses challenges.

6. CONCLUSION

Ferritin is a promising biomarker for T2DM, particularly in identifying patients with poor glycemic control and increased cardiovascular risk. Future research should focus on:

- Longitudinal studies to establish causality.
- Standardization of ferritin thresholds across populations.
- Mechanistic trials exploring ferritin's role in oxidative stress and insulin signaling.
- Meta-analyses to synthesize global evidence.

7. FUTURE DIRECTIONS

While current evidence consistently supports ferritin as a biomarker of poor glycemic control in type 2 diabetes mellitus (T2DM), several gaps remain that warrant future investigation. To strengthen the clinical utility of ferritin, the following directions are recommended:

1. Prospective and Longitudinal Research Most of the existing literature focuses on cross-sectional studies prohibiting any inference about cause; future studies should focus on longitudinal cohort studies of ferritin levels over time in association with diabetes development/progression/complications, which can then determine if ferritin is a causal mediating factor or an outcome of inflammation/metabolic stress.
2. Integration of Other Biomarkers With Ferritin Ferritin should not be viewed in isolation. By combining ferritin with inflammatory markers (e.g., CRP, IL-6) and adipokines (e.g., adiponectin, leptin), a more complete understanding of metabolic dysfunction is possible. A multi-biomarker approach would have improved diagnostic accuracy and risk stratification over a single biomarker approach.
3. Predictive Modeling and Risk Stratification of Future Research Should Investigate the Use of Ferritin in Diabetes Risk Prediction and Progression. Ferritin Could Be Incorporated into Machine Learning Algorithms or Multivariate Regression Models Along With Demographic Information, Lifestyle Factors and Biochemical Variables to Improve Early Detection and Individualized Treatment Approaches.
4. Standardization of Ferritin Thresholds Regional differences in ferritin levels create difficulties in clinical interpretation. It is necessary to create standardized

cutoff values across populations which will be adjusted for age, sex, race/ethnicity, and comorbidities for them to be clinically useful. Therapeutic Monitoring The results from interventional clinical trials indicate that ferritin levels decrease as a result of pharmacological and lifestyle interventions. Future clinical trials should assess the use of ferritin as a surrogate biomarker of therapeutic response in order to have real-time data on how to modify the dosage or regimen.

5. Systematic reviews and meta-analyses Currently, there are a wide variety of results regarding ferritin being either an inflammatory or a metabolic indicator and therefore a cohesive, comprehensive meta-analysis is needed to evaluate all evidence across the globe, quantify the effect sizes of significantly large studies, and clear up any discrepancies between these different categories of research.

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