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Correlation of Insulin Resistance with Vitamin D, Ferritin, and TSH Levels

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Abstract:
Insulin resistance (IR) is a key component of metabolic disorders such as type 2 diabetes, obesity, and cardiovascular disease. This cross-sectional study aimed to investigate the relationship between insulin resistance and three biochemical markers: vitamin D, ferritin, and thyroid-stimulating hormone (TSH). 67 participants (39 females, 28 males) were assessed from Misrata, Libya. Insulin resistance was estimated using the Homeostasis Model Assessment (HOMA-IR). The study found a high prevalence of significant insulin resistance among participants, particularly among females. Pearson correlation analysis revealed a moderate positive correlation between TSH and HOMA-IR and a negative correlation between vitamin D and HOMA-IR, while no significant associations were observed with ferritin or age. The findings highlight the potential role of vitamin D deficiency and thyroid function in insulin resistance. These results support the importance of including vitamin D and TSH screening in routine metabolic assessments, especially for populations at risk.

Keywords: Insulin Resistance, Vitamin D, Ferritin, TSH.

Introduction

The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) has become a practical and widely used tool for estimating insulin resistance in both research and clinical settings. Developed by Matthews et al. (1985). Insulin resistance refers to the reduced effective function of insulin in its target tissues, it induces metabolic stress that manifests itself through alteration in mitochondrial function and chronic inflammation, and this, in turn, can result in the inability to properly respond to insulin, which can provoke metabolic syndrome and diseases such as type 2 diabetes, obesity, and cardiovascular disease. Early identification of insulin resistance using HOMA-IR can support timely interventions aimed at reducing the risk of diabetes and cardiovascular diseases, underscoring its clinical relevance (Bhosle et al., 2016). The risk factors involved in developing insulin resistance include inflammation, mitochondrial functional impairment, hyperinsulinemia, lipotoxicity, genetics, and age, isulin resistance is known to create metabolic stress, which is reflected in disrupted mitochondrial function and persistent inflammation. These disturbances can impair the body's ability to respond effectively to insulin, leading to elevated insulin and blood glucose levels. Over time, these changes can contribute to the development of metabolic syndrome and increase the risk of type 2 diabetes, obesity, and cardiovascular diseases. (Ehrampoush et al., 2021). Vitamin D is classically known for its role in calcium and phosphorus balance, but it also acts as a hormone with diverse effects on metabolism. Growing evidence indicates that vitamin D is involved in the regulation of inflammation, insulin secretion, and insulin sensitivity (Fadhel & Khaleel, 2024), Low vitamin D status has been associated with chronic low-grade inflammation, reduced insulin secretion, and impaired insulin sensitivity (Argano et al., 2023). Ferritin is an intracellular protein that stores iron, and serum ferritin is an established marker of body iron stores. In the context of IR and metabolic health, ferritin is also an acute-phase reactant that rises with systemic inflammation. Elevated ferritin levels have drawn attention as a potential indicator of metabolic risk. High-normal ferritin often reflects increased iron stores, which have been linked to adverse metabolic outcomes. Epidemiologic studies and meta-analyses have shown that higher ferritin is associated with hypertension, dyslipidemia, hyperglycemia, central adiposity, and incident type diabets (Abril-Ulloa et al., 2014).

Thyroid hormones are integral to metabolism, and TSH levels reflect thyroid function, which influences glucose and lipid metabolism. Both overt hypothyroidism and hyperthyroidism can contribute to IR through different pathways. hypothyroidism often leads to weight gain, elevated cholesterol, and reduced hepatic glucose output, all of which can worsen insulin sensitivity.
In contrast, hyperthyroidism can cause weight loss but also increases gluconeogenesis and can induce a state of insulin resistance in certain tissues (especially the liver). Even variations of thyroid function within the clinically normal range (so-called euthyroid variation) have been linked to metabolic differences. There is growing evidence that subclinical hypothyroidism (mild TSH elevation with normal T4) is associated with greater risk of metabolic syndrome and insulin resistance (Choi, 2021). Recently, an association of Vitamin D, Ferritin, and TSH hormone with IR based on the HOMA-IR has been proposed, The aim of this study was to investigate the relationship between these four biomarkers.

Material and Methods

This cross-section study was conducted on 67 participants (39 females, 28 males) in Misrata City, Libya. from September 2024 until July 2025. Most of the participants have signs of low vitamin D levels or insulin resistant.

Blood samples were collected by venipuncture, after night time fasting and centrifuged for 10 min at 3000 rpm. fasting blood glucose (FBG) was determined using Mind-ray BS-200 chemistry analyzer (Mindray Bio-Medical Electronics CO., Ltd., Shenzhen, China), vitamin D, ferritin levels, TSH, and insulin levels were determined by chemiluminescence in Mindray CL-900i chemistry analyzer (Mindray Bio-Medical Electronics CO., Ltd).

HOMA-IR was estimated using the following equation:

HOMA-IR = (Fasting insulin in μU/mL × Fasting glucose in mg/dL) / 405

Statistical analysis was performed using IBM SPSS Statistics 25, Data and quantitative analysis were written as mean ± standard deviation SD. An independent sample t-test was used for comparison among males and females groups, and coefficient r (Pearson's correlation) was used to find out the relationship between the studied parameters.

Ethical statement

All participation was voluntary; Informed consent for participation was obtained from all the participants.

Results and Discussion

A total of 67 participants were included in this study, consisting of 39 females and 28 males. The average age across the total sample was 34.49 years (SD = 12.53), ranging from 12 to 75 years. Female participants tended to be older (M = 37.67 ± 13.51) compared to males (M = 30.07 ± 9.59).

The mean HOMA-IR was (4.26 ± 2.32), with values ranging between 0.89 and 11.40. Females exhibited a higher average (4.74 ± 2.37) than males (3.58 ± 2.12), suggesting greater insulin resistance among female participants.

Vitamin D levels were generally low, with an overall mean of (21.37 ± 9.98 ng/mL) (range: 3.19–47.91). Males had higher levels on average (23.24 ± 10.13) than females (20.02 ± 9.78), although both groups remained below optimal thresholds.

TSH concentrations showed minimal variation across sexes. The total sample had a mean of (2.44 ± 1.31 μIU/mL), (range: 0.01–4.95), with males (2.47 ± 1.16) and females (2.41 ± 1.42) showing nearly identical distributions.

Ferritin levels revealed the most striking gender disparity. The total mean was (62.65 ± 82.76 ng/mL), but males recorded significantly higher values (117.14 ± 102.21; range: 10.43–400) compared to females (23.53 ± 26.73;

range: 1.83–129.28), consistent with known physiological differences in iron storage. The descriptive statistics are shown in Table 1.

Table 1 Descriptive Statistics (Mean ± SD and Range) of Age, HOMA-IR, Vitamin D, TSH, and Ferritin Among Male and Female Participants

	Group / Measure	Age	HOMA-IR	Vit D	TSH	Ferritin
Total	(Mean ± SD)	34.49 ± 12.53	4.26 ± 2.32	21.37 ± 9.98	2.44 ± 1.31	63.53 ± 83.08
	(Range)	12–75	0.89–11.4	3.19–47.91	0.01–4.95	1.83–400.0
Male	(Mean ± SD)	30.07 ± 9.59	3.58 ± 2.12	23.24 ± 10.1	2.47 ± 1.16	117.14 ± 102.21
	(Range)	19–55	0.89–11.4	10.3–44.69	0.57–4.73	10.43–400.0
Female	(Mean ± SD)	37.67 ± 13.51	4.74 ± 2.37	20.02 ± 9.78	2.41 ± 1.42	24.02 ± 26.91
	(Range)	12–75	1.12–10.93	3.19–47.91	0.01–4.95	1.83–129.28

Participants were further categorized based on their HOMA-IR scores into three groups according to the reference of analysis method: insulin sensitive (HOMA-IR < 1), insulin resistance (HOMA-IR > 1.9), and significant resistance (HOMA-IR > 2.9). the majority of the sample fell into the significant insulin resistance category. Specifically, 83.6% of participants demonstrated marked insulin resistance, including 87.2% of females and 78.6% of males. A smaller proportion, 14.9% , were classified as having moderate insulin resistance, with similar distributions between females (12.8%) and males (17.9%). Only 1.5% of the total sample were considered insulin sensitive, and this case was reported in a male participant. Notably, none of the female participants were categorized as insulin sensitive. These findings highlight a high prevalence of insulin resistance, particularly among female participants, and reinforce the clinical importance of early metabolic screening in this population.

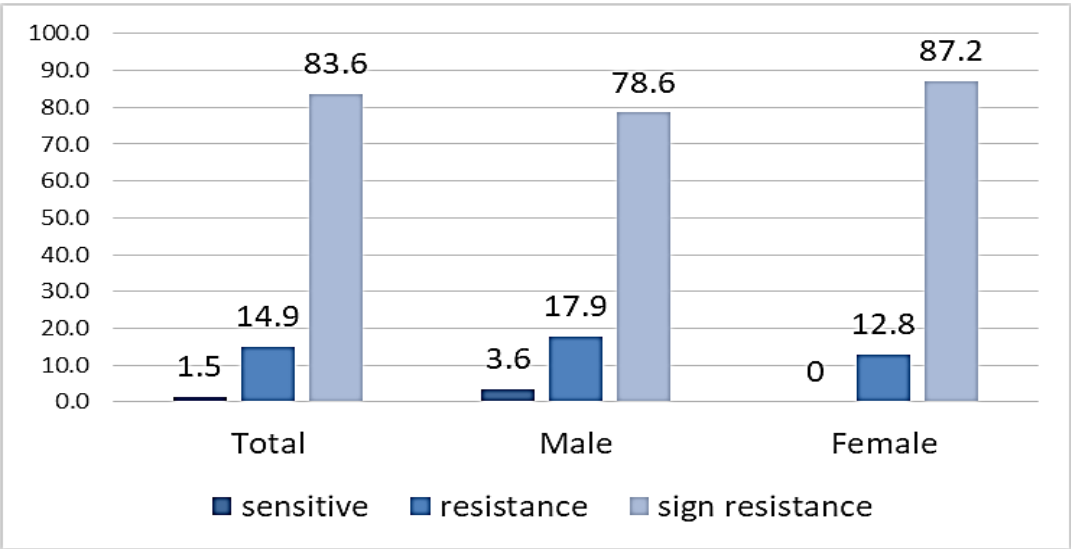

Figure 1: Distribution of Insulin Sensitivity Categories Based on HOMA-IR Levels

Vitamin D status was categorized into three clinical levels: deficiency, insufficiency, and sufficiency. As shown in figure 2, a majority of the participants (56.7%) were classified as vitamin D deficient, with the condition more prevalent among females (64.1%) compared to males (46.4%). A further 25.4% of the total sample were found to have insufficient levels, including 28.6% of males and 23.1% of females. Only 17.9% of participants achieved sufficient vitamin D levels, with a higher proportion among males (25.0%) than females (12.8%). These findings underscore a widespread issue of suboptimal vitamin D status in the study population—particularly among female

participants—raising concerns regarding potential implications for metabolic, musculoskeletal, and endocrine health.

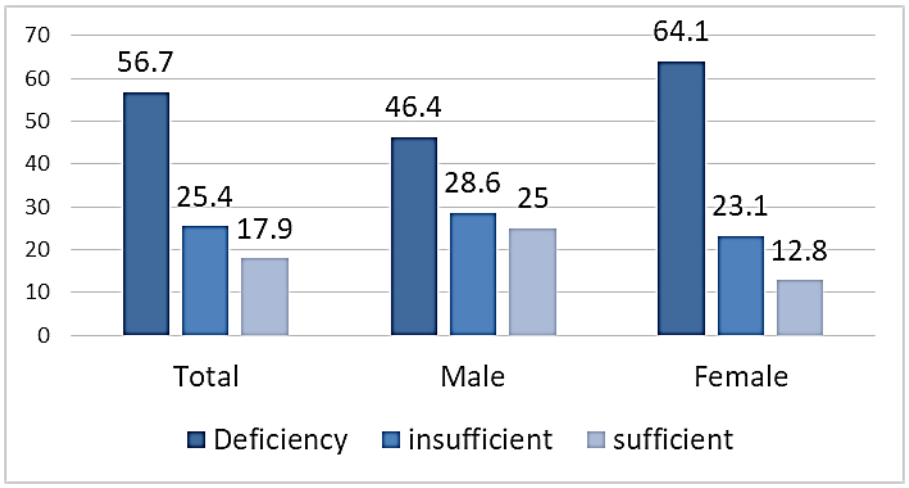

Figure 2. Distribution of Vitamin D Status (Deficiency, Insufficiency, and Sufficiency) by Gender and Total Sample

Regarding thyroid-stimulating hormone (TSH) levels, the majority of participants (94%) were within the normal reference range. All male participants (100%) had TSH levels within normal limits, while 89.7% of females were also classified as normal. Conversely, 6% of the total sample exhibited low TSH levels, all of whom were female (10.3% of female participants). No cases of elevated TSH were reported. These findings suggest that subclinical hyperthyroidism may be present in a small proportion of female participants, whereas males demonstrated uniformly normal TSH levels in this study.

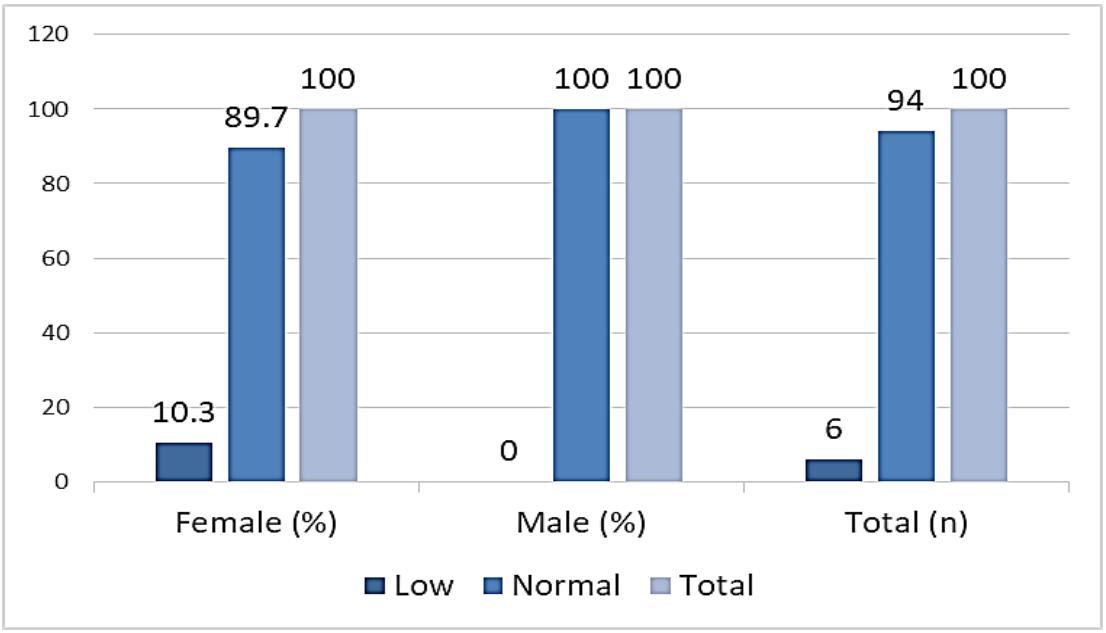

Figure 3. Distribution of TSH Level Classification by Gender and Total Sample (%)

Ferritin levels were classified into two categories: low and normal. Overall, 26.9% of participants exhibited low ferritin concentrations. Notably, this condition was significantly more common among females, with 41.0% affected, compared to only 7.1% of male participants. In contrast, normal ferritin levels were observed in 73.1% of the total sample, including 92.9% of males and 59.0% of females. These results align with the known physiological tendency for females to have lower iron stores than males, potentially due to factors such as menstruation and dietary differences.

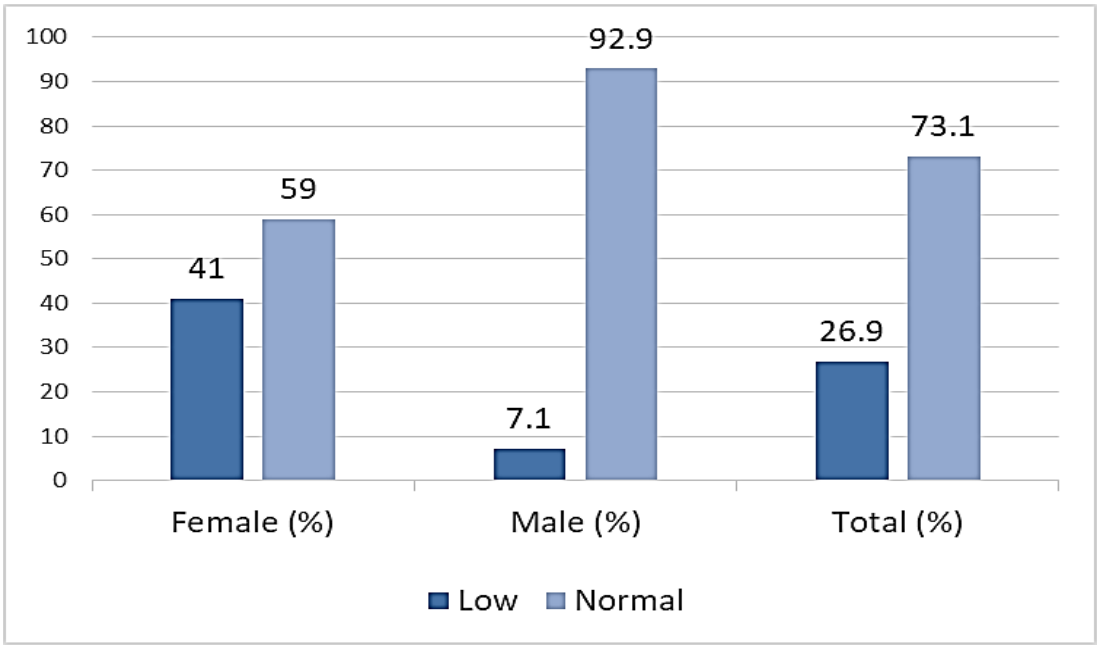

Figure 4. Distribution of Ferritin Levels by Gender and Total Sample (%)

Pearson correlation analysis revealed statistically significant associations between insulin resistance and two key biomarkers. A moderate positive correlation was observed between HOMA-IR and TSH ($r = 0.382$, $p = 0.001$), suggesting that higher TSH levels are significantly associated with influence insulin sensitivity and glucose metabolism.

In contrast, a negative correlation was found between HOMA-IR and vitamin D ($r = -0.242$, $p = 0.048$), indicating that lower vitamin D levels were significantly associated with higher insulin resistance. Although the strength of the correlation was modest, it aligns with emerging evidence that vitamin D plays a role in modulating insulin action and inflammatory pathways.

No significant correlations were found between HOMA-IR and age ($r = 0.161$, $p = 0.194$) or ferritin ($r = 0.101$, $p = 0.417$), suggesting that these factors were not major contributors to insulin resistance in this cohort. These results highlight the potential importance of thyroid and vitamin D status in the metabolic profile of the population and reinforce the need for further investigation into their mechanistic roles in insulin regulation.

Table 2. Correlation between HOMA-IR and (Age, Vitamin D, TSH, and Ferritin)

HOMA-IR	Correlation Coefficient	p value
Age	0.161	0.194
Vit D	-0.242	0.048
TSH	0.382	0.001
Ferritin	0.101	0.417

Independent sample t-tests were conducted to compare the means of HOMA-IR, vitamin D, TSH, and ferritin levels between male and female participants. The results revealed a statistically significant difference in HOMA-IR levels, with females exhibiting higher values ($M = 4.74$, $SD = 2.37$) compared to males ($M = 3.58$, $SD = 2.12$), $t(61.90) = -2.119$, $p = 0.038$. Additionally, a highly significant difference was observed in ferritin levels, where males showed much higher levels ($M = 117.14$, $SD = 102.21$) than females ($M = 23.53$, $SD = 26.73$), $t(29.66) = 4.731$, $p < 0.001$. On the other hand, no statistically significant differences were found in vitamin D levels ($p = 0.195$) or TSH levels ($p = 0.869$) between the sexes. These findings suggest that both insulin resistance and iron storage, as reflected by HOMA-IR and ferritin respectively, differ significantly between male and female individuals, whereas vitamin D and TSH do not appear to show sex-related variation in this sample.

This study explored the relationship between insulin resistance (IR), as measured by HOMA-IR, and selected biomarkers—namely, TSH, vitamin D, ferritin, and age. The findings revealed a statistically significant positive correlation between TSH and HOMA-IR, suggesting that higher TSH levels may be linked to increased insulin resistance. Conversely, vitamin D showed a negative correlation with HOMA-IR, indicating that lower vitamin D levels could be associated with greater insulin resistance. These associations point toward a possible role of thyroid function and vitamin D status in metabolic regulation.

The observed associations are in line with previous research. For instance, Shaik et al. (2019) reported a similar pattern where higher TSH and lower vitamin D were linked to increased HOMA-IR values. Their findings support the idea of an interrelated mechanism connecting vitamin D deficiency, thyroid imbalance, and impaired insulin sensitivity. Likewise, Yücel et al. (2025) found elevated TSH and glucose levels among vitamin D–deficient individuals, although they did not report a direct correlation between vitamin D and insulin resistance. Interestingly, their study did note a strong link between insulin resistance and high ferritin levels—a relationship that was not observed in the present study.

In fact, no significant correlation was found between ferritin and HOMA-IR in our data. This contrasts with studies like those of Wang et al. (2023), who identified ferritin as a key predictor of insulin resistance using machine learning techniques. The discrepancy could be due to differences in sample size, participant characteristics, or confounding variables such as inflammation or iron status that weren't accounted for in the current dataset.

Age also did not show a significant correlation with insulin resistance in this study, which is somewhat unexpected considering that previous large-scale studies have highlighted age as an important risk factor. For example, Wang et al. (2023) incorporated age into their predictive models and found it to be a contributing variable. However, our sample may not have had enough age variation to detect such an effect.

Further support for the relevance of vitamin D comes from Fadhel and Khaleel (2024), who reported strong associations between vitamin D and iron status markers like ferritin and hemoglobin. Although their study didn't focus on insulin resistance, their results suggest that vitamin D may play a broader role in metabolic and hormonal balance.

Taken together, the current findings contribute to the growing body of evidence that vitamin D and thyroid function—particularly TSH—are meaningfully related to insulin resistance. While ferritin and age did not emerge as significant predictors in this sample, the trends observed warrant further investigation in larger, more diverse populations. These insights may have implications for early screening and prevention strategies targeting at-risk individuals.

The results of this study confirm that vitamin D deficiency is a common issue in Libya, particularly among women. Over half of the participants (56.7%) were deficient, which is consistent with findings from Tripoli (55.6%) and Derna (54%) (Ahmed et al., 2023; Eljamay et al., 2022). Similar to previous reports, females in this study had higher deficiency rates than males, reflecting patterns also seen in Benghazi and Misrata.

The proportion of participants with insufficient levels (25.4%) and sufficient levels (17.9%) closely matches earlier studies, suggesting that vitamin D inadequacy remains a widespread concern. Although this study did not explore factors like sun exposure or diet, the gender gap observed aligns with previous research highlighting cultural and lifestyle factors—such as dress style, time spent indoors, and low dietary intake—as contributors to low vitamin D levels (Al-Graiw et al., 2020; Almleeh et al., 2021).

Overall, the current findings support the growing evidence that vitamin D deficiency in Libya is both common and influenced by gender and behavior. This underlines the importance of awareness programs, better supplementation strategies, and early screening—especially for women and at-risk groups.

Moreover, in the present study, low ferritin levels were observed in 26.9% of participants, with a clear gender difference: 41% of females were affected compared to only 7.1% of males. Although this overall percentage is lower than what has been reported in other Libyan studies, the gender gap is consistent. For example, Elawamy et al. (2020) found that 52.4% of their participants had low ferritin, while Elhadi et al. (2023) reported deficiency in 38.5% of women and 10.2% of men. Similarly, Bashir et al. (2020) noted that 34.1% of adolescent girls in Benghazi had iron deficiency.

These differences in prevalence may reflect variations in the study populations and settings, but the pattern is clear: women—particularly those of reproductive age—remain more vulnerable to low iron stores. This is likely

due to factors such as menstruation, low dietary iron intake, and limited use of supplements. Supporting this, Ansari et al. (2022) also found lower average ferritin levels among females (45.35 ng/mL) than males (92.57 ng/mL) in their study. Overall, while the prevalence in our sample is relatively moderate, the consistent gender disparity across studies highlights the need for preventive strategies focused on women's iron health.

Conclusion

This study provides evidence that both vitamin D and TSH levels are meaningfully associated with insulin resistance, as measured by HOMA-IR. While vitamin D showed an inverse relationship, TSH demonstrated a positive association, suggesting that individuals with lower vitamin D or higher TSH may be more susceptible to metabolic disturbances. Although ferritin and age were not significantly correlated with HOMA-IR in this sample, the overall findings underscore the complexity of metabolic regulation and the need for a multifactorial approach in early screening. Given the high prevalence of insulin resistance observed—especially among females—these results emphasize the importance of incorporating endocrine and micronutrient evaluations into preventative healthcare strategies. Future longitudinal studies with larger and more diverse populations are recommended to further clarify these associations and explore potential interventions.

Study Limitations: While the findings of this study offer valuable insights into the relationship between insulin resistance and selected biochemical markers, several limitations should be acknowledged. First, the sample size was relatively small (n = 67), which may limit the generalizability of the results to broader populations. The cross-sectional design also restricts the ability to infer causality between variables—only associations can be reported. Moreover, confounding factors such as physical activity, dietary habits, inflammation markers, and medication use were not controlled or assessed, which might have influenced biomarker levels and HOMA-IR values.

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