International Journal of General Medicine

Dovepress
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ORIGINAL RESEARCH

Role of Zinc and Magnesium in Glycemic Status Among the Saudi Population

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Purpose: Certain trace minerals, such as zinc (Zn) and magnesium (Mg), may play a role in glucose regulation and insulin signaling pathways. However, population data from the Middle East are scarce and may differ in terms of dietary and metabolic profiles from those previously studied. We examined the association of circulating and dietary Zn and Mg with prediabetes, insulin resistance, and β-cell function in Saudi adults.

Methods: A cross-sectional study of 1009 Saudi adults aged ≥ 18 years (861 participants with normoglycemia, 148 participants with prediabetes) recruited from Riyadh and Almadinah cities, Saudi Arabia. Demographic data, anthropometry, fasting glucose, insulin, serum Zn and Mg were measured. Dietary intakes were estimated from two 24-h recalls and a validated food-frequency questionnaire. Insulin resistance and β-cell function were assessed with HOMA-IR and HOMA-β. Between-group differences, partial correlations, and multivariable logistic and linear regression (adjusted for age, sex, BMI, physical activity, energy, dietary supplement use, and lipid profile) analyses were conducted.

Results: Compared to participants with normoglycemia, those with prediabetes had higher Serum Zn (119.9 ±33.5 vs 112.4 ±23.3 µg dL, P<0.001), whereas serum Mg was not significantly different. Fasting glucose, insulin, and HOMA-IR were all elevated in prediabetes (P<0.001). Low serum Mg (<1.7 mg dL) was independently associated with higher odds of prediabetes (OR =1.9, 95% CI 1.3–2.8).

Conclusion: Lower serum magnesium was linked to higher odds of prediabetes, while higher serum Zn was associated with greater insulin resistance; dietary Zn showed no significant associations. Given the low prevalence of Zn deficiency, intake–status associations may be attenuated. Mg status appears more consistently tied to glucose regulation, highlighting the need for targeted nutrition strategies and further research on zinc's metabolic role.

Keywords: zinc, magnesium, diet, mineral deficiency, diabetes, prediabetes

Introduction

Diabetes mellitus is a major public health concern worldwide, with continuously rising prevalence rates.[1] A systematic review and meta-analysis found that more than one in ten adults (about 537 million people) worldwide had diabetes in 2021, and projected that about 783 million adults worldwide will have diabetes by 2045.[2] Saudi Arabia also faces an alarming burden, with the International Diabetes Federation reporting a prevalence of diabetes, predominantly type 2 diabetes mellitus (T2DM), of 23.1% in 2024, making it one of the highest rates globally.[3]

The progression of T2DM begins with a stage known as prediabetes, characterized by impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT).[4] A meta-analysis showed that about 70% of adults with prediabetes progress to T2DM within ten years if preventive measures are not implemented.[5] In Saudi Arabia, the World Health Organization reported that around 3 million Saudis had T2DM in 2016, with another 3 million being prediabetic, emphasizing the substantial public health concern in this population.[6]

Genetic predisposition and lifestyle behavior are major contributors to the development of T2DM.[1] Modifiable factors such as sedentary lifestyle, obesity, and dietary habits can contribute to the risk of T2DM, with growing attention on trace

Received: 16 September 2025
Accepted: 6 December 2025
Published: 17 December 2025

mineral status as an additional, potentially modifiable risk factor.[7–9] Some trace minerals, such as zinc (Zn) and magnesium (Mg), have been implicated in glucose regulation and insulin signaling pathways.[10,11] Recent umbrella and meta-analyses show that Zn supplementation improves fasting glucose, Hemoglobin A1c, fasting insulin, and homeostatic model assessment of insulin resistance (HOMA-IR) in adults with or at risk for type 2 diabetes.[12] A systematic review and meta-analysis limited to single-intervention Zn trials, together with two-sample Mendelian randomization, supports a likely causal effect on fasting glucose, Hemoglobin A1c, and HOMA-IR, while noting limited power in included studies.[13]

Zn is involved in a variety of critical metabolic processes, including the maintenance of insulin receptors, as a cofactor for important enzymes involved in the antioxidant defense system, a contributor to pancreatic β-cell function, and for regulating glucose homeostasis.[14] Zn deficiency is frequently linked to atherosclerosis, insufficient carbohydrate utilization, and insulin resistance.[15] Similarly, Mg contributes significantly to glucose homeostasis as an essential cofactor for enzymes involved in glucose metabolism and insulin signaling pathways.[16] Mg deficiency can result in a variety of abnormalities, including impaired lipid metabolism, IGT, and insulin resistance.[17]

Systematic reviews of both randomized controlled trials and observational studies suggest an inverse association between serum Mg levels and diabetes risk, and some report glycemic improvements with Mg supplementation[18,19] as well as a beneficial effect, or an inverse association between serum Zn level or supplementation and T2DM or glycemic control.[11,13] However, other reviews found no impact of Mg supplementation on fasting glucose[20,21] or the relation between Zn status or supplementation and T2DM.[20,22]

The literature gap is particularly notable in Saudi Arabia. Given that dietary and metabolic profiles of Saudi adults may differ from those of Western and Asian populations previously studied,[23,24] further research in this population is warranted. To date, no studies have examined the association between serum and dietary Zn and Mg levels and prediabetes specifically in Saudi adults. This study thus aims to examine the relationship between circulating and dietary Zn and Mg with prediabetes, insulin resistance, and β-cell function specifically in Saudi adults.

Materials and Methods

Study Design

A population-based, cross-sectional study was conducted in Riyadh and AlMadinah cities in Saudi Arabia. All study procedures comply with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist. The protocol was approved by the King Saud University Institutional Review Board (approval No. KSU-IRB-21-314), in compliance with the Declaration of Helsinki. Written informed consent was obtained from all participants after a full explanation of the study aims and procedures. Participants had the right to withdraw from the study at any time.

Participants

Participants were recruited between December 2021 and December 2023 through advertisements posted on various social-media platforms, and via the King Saud University mailing lists, and shared at local primary-care clinics. Saudi adults aged ≥ 18 years were eligible to participate. We excluded individuals with physician-diagnosed diabetes, type 1 or type 2, or using any glucose-lowering medication, for example insulin or oral agents, those with diseases that may affect their dietary intake (eg, Crohn's disease, ulcerative colitis), those with renal failure and liver failure, history of malignancies, medical conditions such as acute diarrhea, chronic diarrhea, short bowel syndrome, and acrodermatitis enteropathy that affect Mg or Zn absorption, excretion, or redistribution, those using medications that inhibit Mg or Zn absorption or increase Mg excretion, those using Zn or Mg supplementation, and pregnant or lactating females. Of a total of 1172 individuals screened, 163 were excluded yielding 1009 recruits (Supplementary Figure 1).

Outcome Definitions

Participants were classified as having prediabetes (n=148) or normoglycemia (n=861). Prediabetes was defined using the American Diabetes Association 2023 criteria: IFG (5.6–6.9 mmol/L^{-1}) or IGT (2-h oral glucose tolerance test 7.8–11.0 mmol/L^{-1}).[25]

Data Collection

Lifestyle and Sociodemographic Questionnaire

Trained personnel administered a structured health history questionnaire to collect data on age, sex, marital status, income, education, smoking, and medical history. Physical activity (PA) was assessed using the Arabic Global Physical Activity Questionnaire (GPAQ v2).[26] Metabolic Equivalent of Task (MET)-minutes week^{-1} were computed and categorized as low (< 600), moderate (600–2999) or high (≥ 3000 MET-min week^{-1}).

Anthropometry

Using standardized methods, participants' weight (kg) and height (cm), with light clothing and without shoes, were recorded to the nearest 0.1 kg and 0.5 cm, respectively. Weight was measured using Bioelectrical Impedance Analysis (BIA) (Body Composition Analyzer; In Body 570, Seoul, South Korea). Height was measured using a digital stadiometer (Seca 274, Hamburg, Germany). All participant measurements were recorded twice, and the average was calculated. Body Mass Index (BMI) was calculated by dividing the weight by the square of the height in meters.[27]

Dietary Assessment

Participants completed two 24-h dietary recalls using the multiple-pass method and standard food models to aid in estimating portion sizes.[28] The first 24-hour recall was collected in person for intake on a weekday. The second 24-hour recall was collected via a phone call for intake on a weekend day. Habitual intake was assessed with a previously validated semi-quantitative food frequency questionnaire (FFQ) developed by Samman et al[29] that was modified and validated by Alsufiani et al to assess the dietary intake of Zn and Mg among Saudi adults.[30] When discrepancies occurred between nutrient intakes estimated from the 24-h recalls and the FFQ, the FFQ data were used to represent habitual (long-term) intake, while the latter were used to capture recent (short-term) intake patterns. This approach follows established dietary assessment practice, where FFQs reflect usual intake over months.[31]

The FFQ consisted of 133 food items, including common foods and composite dishes consumed by Saudi adults, such as Jareesh, Saleeq, Marasia, and Kabsah. The FFQ included questions about the frequency of consumption (daily, weekly, and monthly) of the food items. Specifically, the questionnaire contains 64 food items out of the 133 with high Zn content, most consumed by the Saudi population. It also included specific questions about sodium, sugar, oil, supplementation, and frequency of restaurant consumption.[32]

Correlations between dietary Zn and Mg estimates from the FFQ and the mean of the two 24-h recalls were high (r = 0.72 for Zn and r = 0.68 for Mg), indicating good agreement between the two dietary assessment methods in ranking participants' intakes.

Because no national food composition database is available for Saudi Arabia, the US Department of Agriculture (USDA) Food and Nutrient Database was used as the most practical and regionally applicable source available to analyze the dietary intake results. After data collection, dietary intake was analyzed using ESHA Food Processor SQL Software (ESHA Research, Salem, UT, USA) to calculate average food intake in grams per day based on frequencies and portion sizes.

Blood Sampling

A trained phlebotomist collected 10 mL of fasting venous blood from each participant during the same week as the first dietary interviews. For glucose, gray-top tubes containing a glycolysis inhibitor were used. We used sodium fluoride with citrate buffer and EDTA. Plasma was separated within 30 minutes of phlebotomy, 1200 × g for 15 minutes at 4°C, then stored at −80°C. Glucose concentrations were measured using the BS 240 Chemistry Pro analyzer (inter-assay CV = 1.6%). Insulin levels were determined by chemiluminescence using the CL 1200 I instrument (inter-assay CV = 4.2%). Serum Zn was analyzed with the Agilent 7900 inductively coupled plasma mass spectrometer (ICP-MS) using 0.8 mL of serum (inter-assay CV = 3.1%). Mg concentrations were measured using the BS 240 Chemistry Pro with the xylidyl blue method (inter-assay CV = 2.4%).

Low serum magnesium was defined as <1.7 mg/dL, corresponding to the lower limit of standard clinical reference used to define hypomagnesemia.[33] Low serum Zn was defined as <82 µg/dL, consistent with population-level thresholds used in nutritional status assessments.[34]

HOMA-IR and β-cell function (HOMA-β) was calculated using the Matthews equations for HOMA-IR and HOMA-β, respectively.[35] The formulas used were as follows:

$$HOMA-IR=\frac{\left(\text{fasting insulin}\mu\ \text{UmL}^{-1}\times\text{fasting glucosemmol L}^{-1}\right)}{22.5}$$

$$HOMA-\beta=\frac{\left(20\times\text{fasting insulin}\ \mu\text{U mL}^{-1}\right)}{\left(\text{fasting glu cos e mmol L}^{-1}-3.5\right)}$$

Statistical Analysis

Statistical analyses were conducted using SPSS version 28 (IBM Corp., Armonk, NY, USA). Data normality was tested using the Shapiro–Wilk test. Descriptive statistics were presented as means ± SD or medians (IQR) for continuous variables and as frequencies (%) for categorical variables. Independent *t*-tests or Mann–Whitney *U*-tests for continuous variables and chi-square tests for categorical variables were used for between-group comparisons.

Pearson or Spearman correlation analysis was used to assess the relationship between serum Zn and Mg levels and measures of glucose regulation, depending on the distribution of variables.

Multivariable logistic regression analyses were applied to estimate the odds of prediabetes and low serum Zn and Mg, and log-transformed dietary Zn and Mg intakes (to improve normality). Linear regression analysis was also done in total participants to assess the relationship between fasting glucose levels, HOMA-IR, HOMA-β and both serum and log-transformed dietary Mg and Zn. We fit two prespecified models sequentially. Model 1 was adjusted for age (continuous), sex (categorical), while Model 2 adjusted for Model 1 variables plus education (categorical), smoking status (categorical), BMI (continuous), dietary supplement use (categorical), and physical activity (categorical).

Selected covariates were adjusted for, driven by literature indicating their association with both micronutrient status and glucose metabolism, including studies on age and sex differences in trace mineral status and diabetes risk,[36] education level as a determinant of dietary quality and nutrient intake,[37] smoking and its association with impaired micronutrient absorption and altered glucose metabolism,[38] BMI as a predictor of micronutrient bioavailability and insulin resistance,[39] dietary supplement use since they may contain Zn or Mg,[19] and physical activity's role in modulating insulin sensitivity and nutrient requirements.[40]

Results

Participant Characteristics

A total of 1009 participants were included in the analysis, comprising 148 individuals with prediabetes and 861 individuals with normoglycemia (Table 1). Participants with prediabetes were significantly older, with a mean age of 35.2 ±14.1 years, compared to 30.6 ±11.3 years in the control group (P<0.001). BMI was also significantly higher in the prediabetes group, averaging 29.0 ± 5.8 kg/m^2, compared to 26.3 ±6.1 kg/m^2 among individuals with normoglycemia (P<0.001). In terms of gender distribution, a greater proportion of the prediabetes group were females (51.4% vs 35.3%, P<0.001).

Metabolic and biochemical assessments revealed differences between participants with prediabetes and normoglycemia (Table 1). Serum Zn levels were significantly higher in individuals with prediabetes, averaging 119.9 ± 33.5 µg/dL, compared to 112.4 ± 23.3 µg/dL (P<0.001). In contrast, serum Mg levels were not significantly different (P=0.17). Fasting glucose, insulin, and HOMA-IR values were all significantly higher among participants with prediabetes (P<0.001 for all).

Correlation Analysis

Serum Zn was positively associated with fasting insulin levels (R =0.11, P=0.001), and HOMA-IR (R =0.12, P<0.001) (Table 2). Dietary Zn was positively correlated with BMI (R = 0.11, P=0.001). Serum Mg was not correlated with HOMA-IR. Dietary Mg intake was inversely correlated with fasting insulin (R = −0.09, P=0.004) and HOMA-IR (R = −0.09, P=0.006).

Table 1 Baseline Characteristics of Study Participants, n=1009

Parameters	Normoglycemia	Prediabetes	P-value
N	861	148	
Age (years)	30.6 ± 11.3	35.2 ± 14.1	<0.001
BMI (kg/m^2)	26.3 ± 6.1	29.0 ± 5.8	<0.001
Female	304 (35.3)	76 (51.4)	<0.001
Male	557 (64.7)	72 (48.6)	
Glucose (mmol/L)	4.9 (4.6–5.2)	5.9 (5.7–6.2)	<0.001
Insulin (μIU/mL)	8.9 (6.4–12.7)	12.3 (8.2–16.8)	<0.001
HOMA-IR	2.0 (1.3–2.8)	3.2 (2.2–4.4)	<0.001
HOMA-β	33.3 (22.6–47.7)	38.8 (24.8–54.7)	0.003
Serum Mg (mg/dL)	1.8 ± 0.4	1.7 ± 0.5	0.17
Serum Zn (μg/dL)	112.4 ± 23.3	119.9 ± 33.5	<0.001
Dietary Zn (mg/1000kcal)	3.7 (2.9–4.6)	3.7 (3.0–4.7)	0.95
Dietary Mg (mg/1000kcal)	105.1 (84.8–129.6)	109.5 (86.0–134.7)	0.89
Tolal Energy intake (kcal/day)	4011 (646)	3796 (702)	0.16
Education			
High school or less	28.1	27.4	0.32
Bachelor	58.0	56.9	
Postgraduate studies	13.9	15.7	
Smoking	9.6	14.8	0.12
Physical activity (min/week)	259.2 (150.1)	224.0 (308.3)	0.23

Note: Data presented as Mean ± SD for normal variables and median (Quartile 1 – Quartile 3) for non-normal variables; P<0.05 considered significant.
Abbreviations: BMI, body mass index, HOMA-IR, homeostatic model assessment of insulin resistance, HOMA-β, homeostatic model assessment of β-cell function, kcal, kilocalorie, magnesium, Zn, zinc.

Table 2 Correlation Between Serum Magnesium, Serum Zinc, Dietary Magnesium, Dietary Zinc and Select Parameters Among All Participants, n=1009

Parameters	Serum Magnesium		Serum Zinc		Dietary Magnesium		Dietary Zinc	
	R	P-value	R	P-value	R	P-value	R	P-value
Serum Mg (mg/dL)			−0.11	0.001	−0.03	0.41	0.09	0.007
Serum Zn (μg/dL)	−0.11	0.001			−0.03	0.31	0.04	0.27
Dietary Mg	−0.03	0.41	−0.03	0.31			0.54	<0.0001
Dietary Zn	0.09	0.007	0.04	0.27	0.54	<0.0001		<0.0001
Age (years)	0.05	0.10	−0.18	<0.0001	0.27	<0.0001	0.13	<0.0001
BMI (kg/m^2)	−0.02	0.49	−0.07	0.04	0.09	0.006	0.11	0.001
Glucose (mmol/L)	0.06	0.08	0.05	0.10	0.00	0.99	0.03	0.35
Insulin (μIU/mL)	−0.01	0.80	0.11	0.001	−0.09	0.004	−0.06	0.07
HOMA-IR	0.01	0.84	0.12	<0.0001	−0.09	0.006	−0.04	0.26
HOMA-β	−0.03	0.34	0.11	0.001	−0.11	0.001	−0.07	0.03

Note: Data presented as Pearson Correlation Coefficient (R); P<0.05 considered statistically significant.
Abbreviations: BMI, body mass index, HOMA-IR, homeostatic model assessment of insulin resistance; HOMA-β, homeostatic model assessment of β-cell function; Mg, magnesium; Zn, zinc.

Among participants with normoglycemia, serum Mg and Zn were inversely correlated ($R = -0.16$, $p < 0.001$) (Supplementary Table 1). Among participants with prediabetes, serum Zn was positively correlated with insulin ($R = 0.20$, $p = 0.02$) and HOMA-IR ($R = 0.21$, $p = 0.01$), while dietary Mg intake was inversely correlated with fasting insulin ($R = -0.29$, $p < 0.001$) and HOMA-β ($R = -0.30$, $p < 0.001$) (Supplementary Table 2).

Table 3 Odds of Having Prediabetes in Relation to Serum and Dietary Magnesium and Zinc

	Crude		Model 1		Model 2	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Low Serum Mg (< 1.7 mg/dL)	1.6 (1.1–2.3)	0.02	1.8 (1.2–2.7)	0.003	1.9 (1.3–2.8)	0.002
Log Dietary Mg (mg/1000 Kcal)	1.1 (0.3–3.6)	0.94	0.6 (0.2–2.1)	0.39	0.6 (0.2–2.4)	0.51
Low Serum Zn (<82.0 µg/dL)	0.6 (0.2–1.6)	0.35	0.7 (0.2–1.7)	0.39	0.6 (0.2–1.6)	0.28
Log Dietary Zn (mg/1000 kcal)	1.6 (0.6–4.6)	0.36	0.9 (0.3–2.6)	0.81	1.0 (0.3–3.0)	0.95

Notes: Model 1 was adjusted for age, sex, and BMI. Model 2 adjusted for Model 1 and education, smoking status, BMI, dietary supplement use, and physical activity.
Abbreviations: BMI, body mass index; CI, confidence interval; kcal, kilocalorie; Mg, magnesium; OR, odds ratio; Zn, zinc.

Risk Analysis for Prediabetes

Participants with low serum Mg levels (<1.7 mg/dL) had significantly higher odds of prediabetes (Table 3). The crude odds ratio was 1.6 (95% CI: 1.1–2.3, P=0.02) and increased to 1.8 (95% CI: 1.2–2.7, P=0.003) after adjusting for age, sex, and BMI (Model 1), and to 1.9 (95% CI: 1.3–2.8, P=0.002) after controlling for additional dietary and lifestyle variables (Model 2). No significant associations were found between dietary Mg intake and prediabetes in any model. Similarly, low serum Zn levels (<82 µg/dL) and dietary Zn intake were not significantly associated with prediabetes.

Relationship Between Mg, Zn and Glucose Regulation

For the relationship between dietary Mg and fasting glucose levels, the crude regression coefficient was −0.01 (standard error = 0.02), corresponding to a standardized Beta of −0.03 and a non-significant p-value of 0.42 (Supplementary Table 3). For serum Mg, the coefficient was 0.006 (standard error= 0.005), with a Beta of 0.04 and a p-value of 0.220, indicating no statistically significant association.

Discussion

This study investigated the relationship between dietary and serum Zn and Mg levels and prediabetes, insulin resistance, and β-cell function in Saudi adults. While both serum and dietary measures were examined, the relationships with glycemic indices differed; serum Zn was positively associated with insulin and HOMA-IR, dietary Zn showed no significant associations, and dietary Mg was inversely related to insulin and HOMA-IR. This pattern is partly consistent with the literature, where dietary and circulating mineral levels show modest correlations due to homeostatic regulation, absorption variability, and differences in short- versus long-term exposure measures.[41]

Compared with global reference values, mean serum Zn concentrations in our sample were within the normal range (>82 µg/dL).[34] Median Zn intake in our sample (~3.7 mg/1000 kcal) was below the WHO and the Institute of Medicine Recommended Dietary Allowance (RDA) for adults (8 mg/day for women, 11 mg/day for men),[42] consistent with reports of suboptimal Zn intake in many populations worldwide.[16,43]

Our results did not support the hypothesized inverse relationship between serum Zn and prediabetes. Participants with prediabetes had higher serum Zn concentrations and elevated fasting glucose, insulin, and HOMA-IR. The positive association between serum Zn and both insulin and HOMA-IR aligns with several population studies that link higher circulating Zn with impaired fasting glucose and insulin resistance.[44–46] Zn is required for insulin storage and secretion, yet excess Zn (>120 µg/dL) may promote leptin resistance and β-cell hypersecretion, ultimately worsening insulin sensitivity.[47,48] Given the complexity of Zn metabolism, it is important to distinguish between sources and measures: serum Zn reflects short-term status, whereas dietary Zn intake reflects habitual exposure and is influenced by bioavailability.[49]

Intervention studies show mixed results. An umbrella review of randomized trials reported that Zn supplementation lowered fasting glucose, insulin, and HOMA-IR,[12] particularly in populations with low baseline Zn status. However, findings are inconsistent. Lim et al observed lower Zn in prediabetes and better insulin sensitivity at higher Zn levels,[50] and Ahn et al documented an inverse relation between Zn and HOMA-IR only in men.[51] The latter study speculated that sex hormones and differences in Zn transporter expression may underlie these sex-specific associations. These short-term supplementation studies in metabolically healthy adults have failed to replicate the glycemic benefits observed in

deficient or at-risk populations, highlighting possible effect-modifiers such as baseline Zn status, dose, and intervention length. The sex-specific heterogeneity noted in earlier cohorts, where inverse correlations between serum Zn and HOMA-IR were observed in men, was not evident in our Saudi sample, although the current study was not powered for detailed sex-stratified analyses.

Mean serum Mg was at the lower end of the reference range (1.7–2.3 mg/dL),[33] with median Mg intake (~105–110 mg/1000 kcal) below the RDA (320 mg/day for women, 420 mg/day for men),[52] compatible with other Middle Eastern studies.[18,53] Mean serum Mg was not statistically different between groups; however, the association between low serum Mg (Mg<1.7 mg/dL) and prediabetes is consistent with a 2021 systematic review showing significantly lower circulating Mg in adults with prediabetes versus controls[18] and previous observational studies.[54] Mg supplementation trials also show mixed results; a double-blind crossover trial of participants with insulin-treated T2DM reported no improvement in insulin sensitivity after six weeks of oral Mg supplementation.[55] On the other hand, a recent pilot trial using highly bioavailable deep-seawater Mg in participants with prediabetes demonstrated significant reductions in HOMA-IR.[56] These differences may be attributed to the chemical form of Mg, baseline deficiency status, and the degree of dysglycemia at study entry. Mg serves as a cofactor for the insulin-receptor tyrosine-kinase and key enzymes in glycolysis and the Krebs cycle; hypomagnesaemia therefore impairs post-receptor insulin signaling, promotes oxidative stress and enhances urinary Mg wasting, establishing a vicious cycle of insulin resistance and Mg depletion.[57]

Mg supports insulin receptor signaling and glucose uptake. It is a required cofactor for tyrosine kinase activity of the insulin receptor and for ATP-dependent steps in the PI3K/Akt pathway.[58] Experimental work shows that physiological Mg^{2}+ augments Akt activation and promotes GLUT4 translocation, increasing insulin-stimulated glucose uptake in adipocytes. Insulin also enhances renal Mg reabsorption by stimulating the epithelial Mg channel TRPM6 in distal convoluted tubule via PI3K and Rac1, and genetic variants that blunt insulin-induced TRPM6 activation are linked to impaired glucose tolerance.[59,60]

Serum Mg reflects metabolic dysregulation through renal losses and transporter regulation. Hyperglycemia and insulin resistance increase urinary Mg wasting and reduce TRPM6-mediated reabsorption, so lower serum Mg is common in prediabetes and type 2 diabetes and associates with insulin resistance in meta-analyses.[61] In contrast, serum Zn is a negative acute-phase reactant and is largely albumin-bound, so inflammation and circulating free fatty acids can lower serum Zn irrespective of intake or tissue stores, and co-secretion of Zn with insulin plus reduced hepatic insulin clearance can raise circulating Zn. These features increase noise for Zn in cross-sectional glycemic analyses. In our largely Zn-replete sample, serum Mg is therefore a more reliable correlate of dysglycemia than serum Zn.[18]

Implications

From a policy and practice perspective, targeted screening for low Mg status in high-risk individuals, and the consideration dietary interventions to improve Mg intake in populations where habitual intake is below recommended levels may provide potential benefit. Taken together, data from this study suggest that trace mineral status may play a role in early dysglycemia, however, they also highlight differential patterns: higher serum Zn was associated with higher insulin and HOMA-IR, whereas both serum and dietary Mg were associated with more favorable insulin sensitivity indices. These findings are consistent with literature indicating that Zn homeostasis is tightly regulated and may not always mirror dietary intake,[62] whereas Mg status is more closely linked to habitual intake and may be more responsive to dietary modification.[63] Ethnic dietary patterns, genetic variation in mineral-transport proteins such as ZnT8 and TRPM6/7, and differences in assay methodology[64,65] may influence these relationships and should be considered in future work.

Strengths and Limitations

The current study is the first to investigate the association between serum and dietary Zn and Mg with prediabetes in Saudi Arabia. Data collection accuracy was enhanced through in-person interviews, in-depth health history questionnaires, and repeated measurements of anthropometric data. To reduce confounding effects, we excluded pregnant and lactating women, and participants using Zn or Mg supplements. We used plasma Mg concentration as a biomarker to assess dietary Mg levels,

aiming to reduce possible biases stemming from dietary evaluations. This approach helps mitigate systematic measurement errors in diet exposure.[66] Another strength is the high correlation between dietary Zn and Mg estimates collected from the FFQ and the mean of the two 24-h recalls, supporting the validity of our dietary intake assessment methods in this population. In addition, use of the multiple-pass method for dietary recalls and inclusion of both weekday and weekend recalls are methodological strengths, reducing random error compared to a single recall.[67]

Although we used validated questionnaires such as 24-hour recall, FFQ, yet errors caused by recall bias may affect the interpretation of the results as previous studies show that participants often overestimate their intake of healthy foods such as fruits and vegetables and underestimate less healthy items, which could lead to misclassification of Zn and Mg intake.[68,69] This systematic error may attenuate or inflate observed associations between dietary minerals and glycemic control. Furthermore, our participants were Zn-replete, only 0.2% percent met the predefined deficiency cutoff. Low deficiency limits variability, which can attenuate intake-status associations. External validity is therefore restricted to Zn-replete adult populations. Effects may differ where deficiency is more common. Also, we could not fully account for inflammation, which can lower plasma or serum Zn during the acute-phase response, so any residual confounding likely attenuates associations. Additionally, reverse causality is plausible. Pancreatic beta cells co-secrete Zn with insulin into the portal vein. Co-secreted Zn suppresses hepatic insulin clearance by inhibiting clathrin-mediated insulin endocytosis, so higher insulin secretion or reduced clearance can raise both circulating insulin and Zn, creating positive cross-sectional associations between serum zinc and insulin or HOMA-IR that are unrelated to intake. We did not measure C-peptide, so we could not estimate hepatic insulin clearance.[70] In later diabetes, increased urinary zinc loss can lower circulating zinc, which may invert associations by disease stage.[71] Finally, the cross-sectional study design in this research study limits the establishment of a cause-and-effect relationship.

Conclusion

This study is the first to examine the relationship between both dietary and serum Zn and Mg levels with glycemic indices in Saudi adults, providing novel insight into trace mineral status in this population. Our findings show low serum magnesium was associated with higher odds of prediabetes. Serum zinc was positively related to insulin and HOMA-IR, dietary zinc showed no association, and dietary magnesium was inversely related to insulin and HOMA-IR. Zinc deficiency was rare, about 0.2%, which likely reduced intake–status correlations.

These findings matter for prevention. Screening for low magnesium in adults at risk for dysglycemia may aid early identification. From a public health perspective, these findings may inform dietary guidelines, fortification programs, and targeted nutrition interventions in Saudi Arabia aimed at diabetes prevention. Routine Zn supplementation for glycemic control is not supported in zinc-replete settings.

This study is cross-sectional, from two Saudi cities, and used serum biomarkers. We did not include inflammation markers, so residual confounding is possible. Reverse causality cannot be excluded, for example higher insulin can raise circulating Zn. Prospective and interventional studies in Gulf populations should test whether correcting magnesium deficiency improves insulin resistance and should evaluate zinc biology with C-peptide, inflammation markers, kidney function, and transporter gene variation.

Acknowledgments

The author(s) declare that financial support was received for the research and/or publication of this article. We acknowledge the Ongoing Research Funding Program number (ORF-2025-559), King Saud University, Riyadh, Saudi Arabia.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. We acknowledge the Ongoing Research Funding Program number (ORF-2025-559), King Saud University, Riyadh, Saudi Arabia.

Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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