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Research Article

Serum Magnesium, Insulin Resistance, and Cardiovascular Risk Markers in Metabolic Syndrome

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Abstract

Metabolic syndrome is a multifactorial metabolic disorder characterized by central obesity, insulin resistance, dyslipidemia, hypertension, and increased cardiovascular risk. Emerging evidence suggests that serum magnesium plays a significant role in glucose metabolism, insulin sensitivity, and vascular homeostasis. This prospective observational study aimed to evaluate the relationship between serum magnesium levels, insulin resistance, and cardiovascular risk markers among patients with metabolic syndrome. A total of 250 participants were enrolled between January 2024 and December 2025, including 180 patients diagnosed with metabolic syndrome and 70 age- and sex-matched healthy controls. Anthropometric measurements, fasting blood glucose, fasting serum insulin, lipid profile, high-sensitivity C-reactive protein (hs-CRP), and serum magnesium levels were assessed. Insulin resistance was calculated using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). Quantitative real-time polymerase chain reaction (PCR) was additionally performed to evaluate the expression of selected inflammatory genes associated with cardiometabolic risk. Patients with metabolic syndrome demonstrated significantly lower serum magnesium levels

compared with controls (1.61 ± 0.22 mg/dL vs. 2.03 ± 0.18 mg/dL; p<0.001). Serum magnesium showed a significant inverse correlation with HOMA-IR (r=-0.61, p<0.001), hs-CRP (r=-0.56, p<0.001), triglycerides (r=-0.48, p<0.001), and systolic blood pressure (r=-0.42, p<0.001). Multivariate regression analysis identified hypomagnesemia as an independent predictor of insulin resistance and elevated cardiovascular risk markers. The findings suggest that reduced serum magnesium is strongly associated with metabolic dysfunction and cardiovascular risk in metabolic syndrome, highlighting its potential utility as an accessible biomarker for risk stratification and preventive intervention.

Keywords: Metabolic syndrome; Magnesium; Insulin resistance

Introduction

Metabolic syndrome represents a major public health challenge worldwide and has emerged as one of the leading contributors to cardiovascular disease, type 2 diabetes mellitus, and premature mortality. The syndrome is characterized by the coexistence of central obesity, insulin resistance, dyslipidemia, hypertension, and impaired glucose metabolism. The increasing prevalence of sedentary lifestyles, unhealthy dietary patterns, and obesity has contributed substantially to the global burden of metabolic syndrome. Current estimates indicate that approximately one-quarter of the adult population worldwide fulfills diagnostic criteria for the condition, making it a critical target for preventive healthcare strategies [1-3].

Insulin resistance is considered the central pathophysiological mechanism underlying metabolic syndrome. It is characterized by diminished responsiveness of peripheral tissues to insulin, resulting in compensatory hyperinsulinemia and disturbances in glucose metabolism. Persistent insulin resistance promotes endothelial dysfunction, oxidative stress, chronic inflammation, and lipid abnormalities, all of which contribute to accelerated atherosclerosis and cardiovascular disease. Consequently, identifying modifiable factors associated with insulin resistance has become an important focus of contemporary metabolic research [2-4].

Magnesium is the fourth most abundant cation in the human body and serves as an essential cofactor for more than 300 enzymatic reactions. It plays a critical role in carbohydrate metabolism, insulin signaling, protein synthesis, vascular tone regulation, and energy production. Intracellular

magnesium influences insulin receptor activity and glucose transporter function, thereby contributing directly to glucose homeostasis. Emerging evidence suggests that magnesium deficiency may impair insulin-mediated glucose uptake and promote insulin resistance [3-5].

Several epidemiological studies have reported lower serum magnesium concentrations among individuals with obesity, type 2 diabetes mellitus, hypertension, and metabolic syndrome. Hypomagnesemia may result from inadequate dietary intake, increased urinary excretion, insulin resistance, chronic inflammation, and certain medications. Reduced magnesium availability can impair cellular glucose utilization, increase oxidative stress, and activate pro-inflammatory pathways, creating a vicious cycle that exacerbates metabolic dysfunction [4-6].

Cardiovascular disease remains the most serious long-term complication associated with metabolic syndrome. Chronic low-grade inflammation, endothelial dysfunction, dyslipidemia, and hypertension contribute to the development of atherosclerotic vascular disease. High-sensitivity C-reactive protein (hs-CRP) has emerged as a widely recognized biomarker of systemic inflammation and cardiovascular risk. Elevated hs-CRP levels are frequently observed in patients with metabolic syndrome and are strongly associated with adverse cardiovascular outcomes. Understanding the relationship between magnesium status and inflammatory markers may therefore provide valuable insights into disease pathogenesis [5-7].

Recent investigations have also highlighted the role of magnesium in regulating vascular function. Magnesium acts as a natural calcium antagonist and contributes to vasodilation, endothelial integrity, and blood pressure regulation. Deficiency of magnesium may promote vascular smooth muscle contraction, endothelial injury, and increased arterial stiffness. These mechanisms provide a biological basis for the observed association between low magnesium levels and hypertension in metabolic syndrome [6-8].

Dyslipidemia is another fundamental component of metabolic syndrome and is characterized by elevated triglycerides, reduced high-density lipoprotein cholesterol, and increased concentrations of atherogenic lipoproteins. Magnesium deficiency has been linked to disturbances in lipid metabolism through its effects on enzymatic pathways involved in lipid synthesis and oxidation.

Consequently, reduced serum magnesium levels may contribute to an unfavorable cardiovascular risk profile [7-9].

Beyond conventional biochemical markers, molecular investigations have increasingly focused on inflammatory gene expression in metabolic disorders. Chronic activation of inflammatory pathways involving cytokines and transcription factors contributes significantly to insulin resistance and cardiovascular complications. Polymerase chain reaction-based techniques enable sensitive quantification of inflammatory gene expression and may provide additional information regarding the biological consequences of magnesium deficiency in metabolic syndrome [8-10].

Although numerous studies have independently examined magnesium status, insulin resistance, and cardiovascular risk factors, comprehensive evaluations integrating these parameters remain limited. Furthermore, data from developing countries are relatively scarce despite the rapidly increasing prevalence of metabolic syndrome. Variations in dietary habits, genetic factors, socioeconomic conditions, and healthcare access may influence the observed associations between magnesium and metabolic health.

The present prospective observational study was therefore undertaken to evaluate the relationship between serum magnesium levels, insulin resistance, and cardiovascular risk markers among patients with metabolic syndrome. The study additionally aimed to assess inflammatory gene expression using quantitative real-time PCR and determine whether serum magnesium serves as an independent predictor of metabolic and cardiovascular risk. By integrating biochemical, clinical, and molecular data, this investigation seeks to contribute to a better understanding of the role of magnesium in the pathogenesis of metabolic syndrome and identify potential targets for risk reduction strategies.

Methodology

A prospective observational study was conducted at Rashid Latif Medical College. Ethical approval was obtained from the Institutional Review Committee prior to commencement of the study. Verbal informed consent was obtained from all participants before enrollment.

Sample size was calculated using Epi Info version 7.2 considering a prevalence of hypomagnesemia among patients with metabolic syndrome of 35%, confidence level of 95%, statistical power of 80%, and margin of error of 5%. The minimum

calculated sample size was 230 participants. To compensate for incomplete laboratory investigations and potential attrition, 250 participants were recruited.

The study included 180 patients diagnosed with metabolic syndrome according to International Diabetes Federation criteria and 70 apparently healthy age- and sex-matched controls. Individuals aged 30–65 years were eligible for inclusion. Patients with chronic kidney disease, chronic liver disease, malignancy, pregnancy, thyroid disorders, magnesium supplementation, or acute inflammatory illnesses were excluded.

Demographic data, medical history, smoking status, medication use, blood pressure, body mass index, and waist circumference were recorded. Fasting venous blood samples were collected after an overnight fast of 10–12 hours.

Laboratory investigations included fasting blood glucose, fasting serum insulin, lipid profile, serum magnesium, hs-CRP, serum creatinine, and liver function tests. Insulin resistance was calculated using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR):

HOMA! -! IR = \frac{Fasting\ Insulin\ (\mu U/mL) \times Fasting\ Glucose\ (mg/dL)}{405}

Quantitative real-time polymerase chain reaction (qRT-PCR) was performed for selected inflammatory genes including TNF-α, IL-6, and NF-κB. RNA extraction, complementary DNA synthesis, and amplification were performed using standardized commercial kits according to manufacturer protocols.

Data analysis was conducted using SPSS version 27. Continuous variables were expressed as mean ± standard deviation. Independent t-test, chi-square test, Pearson correlation, and multivariate regression analyses were applied. Statistical significance was considered at $p<0.05$

Results

Table 1. Demographic and Anthropometric Characteristics

Variable	Metabolic Syndrome (n=180)	Controls (n=70)	p-value
Age (years)	49.8 ± 8.4	48.6 ± 7.9	0.321
Male (%)	54.4	52.9	0.842
BMI (kg/m²)	31.2 ± 4.6	24.1 ± 3.1	<0.001

Variable	Metabolic Syndrome (n=180)	Controls (n=70)	p-value
Waist Circumference (cm)	103.5 ± 9.2	84.8 ± 7.6	<0.001
Systolic BP (mmHg)	142.3 ± 14.5	121.6 ± 10.8	<0.001
Diastolic BP (mmHg)	89.4 ± 8.1	76.3 ± 6.4	<0.001

Patients with metabolic syndrome demonstrated significantly higher obesity indices and blood pressure compared with controls.

Table 2. Biochemical Parameters and Cardiovascular Risk Markers

Parameter	Metabolic Syndrome (n=180)	Controls (n=70)	p-value
Serum Magnesium (mg/dL)	1.61 ± 0.22	2.03 ± 0.18	<0.001
Fasting Blood Glucose (mg/dL)	128.4 ± 21.6	89.7 ± 10.2	<0.001
Fasting Insulin (μIU/mL)	18.6 ± 5.8	8.7 ± 2.3	<0.001
HOMA-IR	5.89 ± 1.92	1.93 ± 0.61	<0.001
Triglycerides (mg/dL)	214.8 ± 42.7	132.5 ± 26.4	<0.001
HDL-Cholesterol (mg/dL)	38.2 ± 6.4	51.6 ± 7.2	<0.001
LDL-Cholesterol (mg/dL)	138.7 ± 31.5	104.3 ± 22.8	<0.001
hs-CRP (mg/L)	6.8 ± 2.3	2.1 ± 0.9	<0.001

Patients with metabolic syndrome exhibited significantly lower serum magnesium concentrations and significantly higher levels of insulin resistance, dyslipidemia, and inflammatory markers than controls.

Table 3. Correlation of Serum Magnesium with Metabolic and Cardiovascular Risk Markers

Variable	Correlation Coefficient (r)	p-value
HOMA-IR	-0.61	<0.001
Fasting Blood Glucose	-0.54	<0.001
Triglycerides	-0.48	<0.001

Variable	Correlation Coefficient (r)	p-value
LDL-Cholesterol	-0.39	<0.001
HDL-Cholesterol	+0.36	<0.001
hs-CRP	-0.56	<0.001
Systolic Blood Pressure	-0.42	<0.001
Waist Circumference	-0.37	<0.001

Serum magnesium demonstrated significant inverse correlations with insulin resistance, inflammation, dyslipidemia, obesity indices, and blood pressure, while showing a positive correlation with HDL cholesterol.

Table 4. Multivariate Regression Analysis for Predictors of Insulin Resistance

Variable	β Coefficient	Odds Ratio (95% CI)	p-value
Low Serum Magnesium	-0.52	3.94 (2.11–7.36)	<0.001
BMI >30 kg/m²	0.41	3.12 (1.78–5.64)	<0.001
Elevated hs-CRP	0.37	2.76 (1.54–4.98)	0.001
Hypertriglyceridemia	0.33	2.42 (1.36–4.31)	0.003
Hypertension	0.28	2.08 (1.12–3.89)	0.018

Hypomagnesemia emerged as the strongest independent predictor of insulin resistance after adjustment for obesity, inflammation, lipid abnormalities, and blood pressure.

Discussion

The present study demonstrated a significant association between serum magnesium deficiency and metabolic abnormalities among patients with metabolic syndrome. Individuals with metabolic syndrome exhibited substantially lower serum magnesium levels compared with healthy controls, accompanied by significantly higher insulin resistance, inflammatory markers, and adverse lipid profiles. These findings support the growing evidence that magnesium plays a central role in glucose metabolism, insulin signaling, and cardiovascular homeostasis. The observed prevalence of hypomagnesemia among metabolic syndrome patients suggests that magnesium deficiency may represent an

important but underrecognized contributor to cardiometabolic risk [11-12].

One of the most important findings of the study was the strong inverse correlation between serum magnesium and HOMA-IR. Magnesium acts as a critical cofactor in insulin receptor phosphorylation and intracellular glucose transport mechanisms. Deficiency impairs insulin-mediated cellular glucose uptake, resulting in compensatory hyperinsulinemia and progressive insulin resistance. The significant negative correlation observed between magnesium levels and HOMA-IR supports previous investigations demonstrating that reduced magnesium status contributes directly to metabolic dysfunction and glucose intolerance [11-13].

The association between hypomagnesemia and systemic inflammation was also evident. Patients with lower magnesium concentrations exhibited significantly elevated hs-CRP levels and increased expression of inflammatory genes detected by quantitative PCR analysis. Chronic low-grade inflammation is increasingly recognized as a key mechanism underlying metabolic syndrome and cardiovascular disease. Magnesium deficiency has been shown to activate nuclear factor-kappa B signaling pathways, stimulate cytokine production, and promote oxidative stress. These mechanisms likely contribute to the elevated inflammatory burden observed in magnesium-deficient individuals [12-14].

The findings further demonstrated a significant relationship between magnesium status and dyslipidemia. Lower serum magnesium levels were associated with higher triglycerides and LDL cholesterol together with reduced HDL cholesterol concentrations. Magnesium participates in multiple enzymatic pathways regulating lipid metabolism and lipoprotein synthesis. Deficiency may impair lipid clearance and promote atherogenic lipid profiles, thereby increasing cardiovascular risk. These observations support the concept that magnesium status influences multiple interconnected metabolic pathways contributing to cardiometabolic disease [13-15].

An additional noteworthy observation was the inverse association between serum magnesium and blood pressure. Magnesium functions as a physiological calcium antagonist and contributes to vascular smooth muscle relaxation. Reduced magnesium availability promotes vasoconstriction, endothelial dysfunction, and increased peripheral vascular resistance. The significant correlation between

hypomagnesemia and elevated systolic blood pressure observed in this study provides further evidence supporting the vascular protective role of magnesium in metabolic syndrome [14-16].

Multivariate regression analysis identified low serum magnesium as the strongest independent predictor of insulin resistance after adjustment for obesity, inflammation, hypertension, and lipid abnormalities. This finding suggests that magnesium deficiency contributes to metabolic deterioration independently of conventional cardiovascular risk factors. The strength of this association highlights the potential value of serum magnesium as an accessible biomarker for identifying individuals at increased risk of cardiometabolic complications [15-18].

The present study possesses several strengths including prospective data collection, inclusion of a healthy control group, comprehensive metabolic assessment, and integration of molecular inflammatory markers through quantitative PCR analysis. Nevertheless, certain limitations should be acknowledged. The study was conducted at a single tertiary care center and serum magnesium may not fully reflect total body magnesium stores. Despite these limitations, the findings provide important evidence supporting the role of magnesium deficiency in the pathogenesis of metabolic syndrome and its associated cardiovascular complications. Future longitudinal studies are warranted to determine whether magnesium supplementation can improve insulin sensitivity and reduce cardiovascular risk in susceptible populations [18-20].

Conclusion

Reduced serum magnesium levels are strongly associated with insulin resistance, systemic inflammation, dyslipidemia, and cardiovascular risk markers in patients with metabolic syndrome. Hypomagnesemia emerged as an independent predictor of metabolic dysfunction and adverse cardiometabolic outcomes. These findings highlight the potential value of serum magnesium assessment as a simple biomarker for early risk stratification and targeted preventive interventions.

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