Association of Serum Magnesium Level with Insulin Resistance in Women with PCOS

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a common hormonal disorder in reproductive-aged women, often associated with insulin resistance (IR), which increases the risk of adverse pregnancy outcomes, type 2 diabetes, cardiovascular disease, and overall health burden. Magnesium (Mg^{2+}), an essential mineral, can become deficient due to low intake, gastrointestinal loss, or increased urinary excretion. In women with PCOS, low magnesium levels may further impair insulin signaling and worsen IR. This study aimed to evaluate the relationship between serum magnesium levels and insulin resistance in women with PCOS. **Methods & Materials:** A cross-sectional study at Bangladesh Medical University (BMU), Dhaka (Oct 2022–Sep 2023), included 120 women (18–40 years) with PCOS. Insulin resistance was assessed via HOMA-IR, categorizing participants into insulin-resistant and non-insulin-resistant groups, and serum magnesium levels were measured. Data were collected through interviews and analyzed using SPSS 27. **Results:** Among the 120 participants, 77 (64.17%) were categorized in Group A with a HOMA-IR level ≥2.1, while 43 (35.83%) were classified in Group B with a HOMA-IR level <2.1. The average serum magnesium concentration was significantly lower in Group A (1.51±0.59 mg/dL) compared to Group B (1.87±0.55 mg/dL; p=0.001). A significant inverse correlation was identified between serum magnesium levels and HOMA-IR (r= -0.301, p = 0.001). **Conclusion:** A low serum magnesium level is found associated with higher risk of insulin resistance in women with PCOS. Future studies should explore the long-term effects of magnesium supplementation on metabolic outcomes in women with PCOS.

Keywords: *PCOS, HOMA-IR, Mg^{2+}.*

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a widespread endocrine disorder that affects a considerable number of women during their reproductive years. Diagnosis is commonly based on the Rotterdam Criteria, which stipulate that a diagnosis of PCOS requires the presence of at least two of the following: oligo/anovulation, clinical or biochemical signs of hyperandrogenism, or polycystic ovaries (≥12 follicles measuring 2–9 mm), excluding other causes of hyperandrogenism as evidenced by ultrasound [1].

Globally, the prevalence of PCOS varies significantly, with estimates ranging from 8% to 13% among different populations [2]. In the USA, the prevalence of PCOS is reported at 5.2% [3]. Conversely, in Bangladesh, there is a prevalence of 6.11% among women attending gynecological clinics and a substantially higher rate of 35.39% among those seeking infertility treatment [4]. Women with PCOS often experience various complications, including menstrual irregularities, infertility, skin disorders, psychological issues, and metabolic disturbances. Insulin resistance (IR) is a prominent metabolic abnormality in this population. It is defined as a reduced glucose response to insulin and may arise from receptor resistance, decreased hepatic clearance, or increased pancreatic sensitivity [5]. Most women with PCOS exhibit insulin resistance due to disrupted insulin receptor signaling, abnormal adipokine secretion, and altered steroid metabolism, often exacerbated by increased abdominal fat [6].

As a compensatory mechanism, hyperinsulinemia develops, further stimulating androgen production in ovarian theca cells [7]. The relationship between insulin resistance and androgen excess is bidirectional. Elevated androgen levels can impair insulin action, creating a feedback loop that exacerbates both conditions [8]. Studies indicate that both obese and non-obese women with PCOS have greater insulin resistance than age- and weight-matched controls. Additionally, oligomenorrheic women tend to exhibit more severe insulin resistance [5].

Magnesium (Mg) plays a crucial role in glucose metabolism and insulin sensitivity. It is involved in over 300 enzymatic reactions, including those related to glucose metabolism and insulin action [9]. The normal range for serum magnesium levels is typically between 1.6 and 2.5 mg/dL [10]. Research suggests that serum magnesium levels are inversely correlated with insulin concentrations, indicating a potential role of magnesium in modulating insulin sensitivity [11]. Magnesium deficiency may contribute to the development of insulin resistance and hinder glucose entry into cells [12]. While some studies indicate lower serum magnesium levels in women with PCOS [9,13].

Research exploring the association between serum magnesium and insulin resistance in this population is limited. This study aims to investigate the relationship between serum magnesium levels and insulin resistance, assessed by the Homeostatic

Model Assessment for Insulin Resistance (HOMA-IR), in women with PCOS. The findings may provide valuable insights for clinical practice and support potential magnesium supplementation strategies to improve insulin sensitivity and reduce the risk of diabetes mellitus and metabolic syndrome in affected women.

METHODS & MATERIALS

This comparative cross-sectional study was conducted in the Department of Obstetrics and Gynecology and the Department of Reproductive Endocrinology and Infertility at Bangladesh Medical University (BMU), Dhaka, Bangladesh, over a period of 12 months from October 2022 to September 2023. Consecutive sampling technique was used to select participants who met the inclusion criteria. A total of 120 women aged 18 to 40 years, diagnosed with polycystic ovary syndrome (PCOS) based on the Rotterdam criteria, were enrolled. Patients with chronic medical conditions such as diabetes, hypertension, thyroid disorders, or chronic renal diseases, as well as women who had been using hormonal medications, hypoglycemic agents, or calcium/magnesium supplements within the last three months were excluded. Data were collected using a semi-structured questionnaire that gathered demographic information, clinical history, and relevant biochemical data. Blood samples were collected from participants after an overnight fast to assess fasting glucose and insulin levels. Fasting glucose was determined using the hexokinase/G-6-PDH method in an automated analyzer (ARCHITECT cSystems), while insulin levels were measured with the ARCHITECT Insulin Reagent Kit utilizing chemiluminescence technology. Insulin resistance was calculated using the homeostasis model assessment of insulin resistance (HOMA-IR) formula: HOMA-IR = fasting insulin (μU/mL) × fasting glucose (mmol/L) / 22.5. The cut-off points for HOMA-IR, used to differentiate insulin resistance in women with polycystic ovary syndrome, is set at a value of 2.1. Participants in the study were categorized into two distinct groups: Group A, which comprised women with PCOS exhibiting insulin resistance (HOMA-IR ≥2.1), and Group B, which included women with PCOS without insulin resistance (HOMA-IR <2.1). Serum magnesium levels were measured using a Beckman Coulter AU analyzer with the colorimetric method, and levels below 1.6 mg/dL were considered low. Statistical analysis was conducted using SPSS software version 27.0. Continuous variables were presented as means and standard deviations, categorical data as frequencies and percentages, with comparisons made using the Chi-square test for categorical variables, the unpaired t-test for continuous variables, and Pearson's correlation to assess the relationship between serum magnesium levels and HOMA-IR. A p-value of <0.05 was considered statistically significant. Ethical approval was obtained from the Institutional Review Board (IRB) of BMU, and written informed consent was acquired from all participants before their enrollment in the study. All blood sample analyses were conducted in the Department of Biochemistry and Molecular Biology, BMU. Additionally, all procedures followed the Declaration of Helsinki guidelines for medical research involving human subjects.

RESULTS

Table I shows the distribution of respondents based on their socio-demographic characteristics. The majority were aged 21 to 30 years (67.5%), with 16.7% aged 20 years or younger and 15.5% between 31 and 40 years. In terms of education, 32.5% completed up to primary level, 30.8% had secondary education, 28.4% held HSC or equivalent qualifications, and 8.3% were graduates or postgraduates. Most participants were housewives (69.2%), followed by wage earners (12.5%), service holders (10.0%) and students (8.3%). Regarding social status, 31.7% were in the lower class, 35.0% in the lower middle class, and 33.3% in the upper middle class.

Table I
Distribution of the PCOS patients according to their socio-demographic characteristics (*n* = 120).

Parameters	Frequency (n)	Percentage (%)
Maternal age (in years)		
≤20	20	16.7
21 – 30	81	67.5
31 – 40	19	15.5
Educational qualifications		
Up to primary level	39	32.5
Secondary/equivalent	37	30.8
HSC/equivalent	34	28.4
Graduate/post-graduate	10	8.3
Occupation		
Housewife	83	69.2
Service holder	12	10.0
Student	10	8.3
Wage earner	15	12.5
Social status according to monthly family income		
Lower class	38	31.7
Lower middle class	42	35.0
Upper middle class	40	33.3

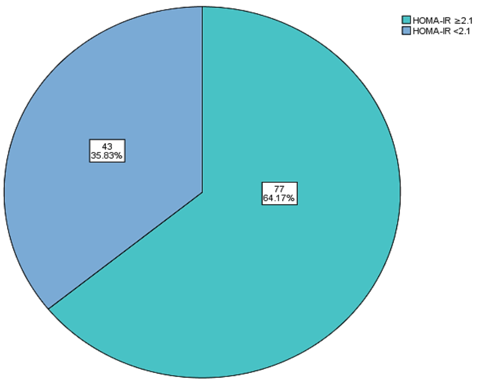

Figure 1 Pie diagram showing distribution of the PCOS patients according to HOMA-IR category (n=120).

Figure 1 illustrates the distribution of the respondents according to HOMA-IR cut-off. Here, 77(64.17%) respondents had HOMA-IR level ≥2.1 (insulin resistant) in comparison to 43(35.83%) of the PCOS patients had HOMA-IR <2.1 (non-insulin resistant).

Table II reveals no statistically significant difference in the age distribution between the two groups (p > 0.05). Obesity was noted in 16.9% of women in group A, compared to 14.0% in group B. The mean (±SD) BMI was marginally higher in group A (26.11±3.86 kg/m²) than in group B (25.81±3.59 kg/m²), though the difference was not statistically significant (p > 0.05).

For age at menarche, 85.7% of group A participants reached menarche at ≥12 years, whereas 79.1% in group B did so (p = 0.383). Regarding parity, nulliparous women were more common in both groups, with 67.5% in group A and 79.1% in group B, but this was not statistically significant (p = 0.179).

Table II
Categorization of the PCOS patients according to age, BMI, obstetric characteristics (n = 120).

Parameters	Group A (n=77) n (%)	Group B (n=43) n (%)	p-value
Age (years)			
18 – 20	17 (22.1)	3 (7.0)	0.072a
21 – 30	47 (61.0)	34 (79.1)	
31 – 40	13 (16.9)	6 (14.0)	
Mean ± SD	25.62 ± 4.90	25.91 ± 4.12	0.749b
BMI (kg/m2)			
Normal (18.5 – 24.9)	23 (29.9)	14 (32.6)	0.855a
Overweight (25.0 – 29.9)	41 (53.2)	23 (53.5)	
Obese (≥30)	13 (16.9)	6 (14.0)	0.658b
Mean ± SD	26.11 ± 3.86	25.81 ± 3.59	
Age at menarche			
<12 years	11 (14.3)	9 (20.9)	0.383a
≥12 years	66 (85.7)	34 (79.1)	
Parity			
Nulliparous	52 (67.5)	34 (79.1)	0.179a
Parous	25 (32.5)	9 (20.9)	

[a]Chi-square test was done to measure the level of significance. [b]Unpaired t test was done to measure the level of significance.

Table III demonstrated that the mean (±SD) magnesium level in group A were signinificantly lower than the group B respondents (1.51±0.59 mg/dl, vs. 1.87±0.55 mg/dL; p=0.001).

Table III
Distribution of PCOS patients according to their serum magnesium levels (n = 120).

Parameters	Group A (n=77) (Mean ± SD)	Group B (n=43) (Mean ± SD)	p-value*
Serum magnesium level (mg/dL)	1.51 ± 0.59	1.87 ± 0.55	0.001b

[b]Unpaired t test was done to measure the level of significance.

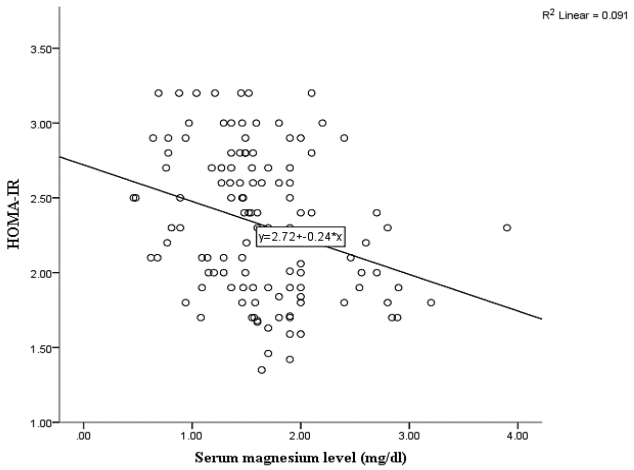

Figure 2 Scatterplot diagram showing correlation between serum magnesium level and HOMA-IR (r= -0.301, p=0.001).

Figure 2 shows a weak negative correlation was observed between serum magnesium level and insulin resistance index (HOMA-IR) in PCOS patients (r= -0.301, p=0.001). Here, R^2 = 0.091 means that approximately 9.1% of the variance in the HOMA-IR can be explained by changes in serum magnesium levels.

Table IV shows that a significantly greater proportion of patients in Group A (63.6%) had serum magnesium levels below 1.6 mg/dL, compared to 32.6% in Group B (p = 0.001). The odds ratio of 3.625 (95% CI: 1.647–7.989) suggests that PCOS patients with lower magnesium levels are over three times more likely to have insulin resistance.

Table IV
Odds ratios (OR) and 95% confidence intervals (CI) for insulin resistance according to serum magnesium levels in PCOS patients (*n* = 120).

S. magnesium level (mg/dl)	Group A n (%)	Group B n (%)	p value	OR (95% CI)
<1.6	49 (63.6)	14 (32.6)	0.001a	3.625
≥ 1.6	28 (36.4)	29 (67.4)		(1.647-7.989)

[a]*Chi square test was done to measure the level of significance.*

DISCUSSION

Insulin resistance is a chronic pathological condition characterized by reduced glucose uptake, particularly in the liver, muscle, and adipose tissues. It is a prevalent issue, affecting approximately 65–70% of women with polycystic ovary syndrome (PCOS) [14]. The aim of this cross-sectional study was to assess the association of serum magnesium levels with insulin resistance in PCOS patients. The study enrolled 120 women with PCOS, all of whom were diagnosed based on the Rotterdam criteria, and their insulin resistance was evaluated through measurements of fasting plasma insulin and glucose levels. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) is often used to assess insulin resistance; however, specific cut-off values may vary based on the population and context. In women with polycystic ovary syndrome PCOS, a HOMA-IR value greater than 2.1 is used to indicate insulin resistance [15]. In this study, 64.17% exhibited insulin resistance (HOMA-IR ≥2.1), similar to the prevalence reported by Tabassum et al. [16].

The majority of participants (67.5%) were aged 21 to 30 years, with comparable mean ages between the insulin-resistant and non-resistant groups of women with PCOS (25.62±4.90 years vs. 25.91±4.12 years; p > 0.05). These demographic characteristics are consistent with the findings of Bhat et al. (2019), who reported similar mean ages for the study and control groups at 28.5 ± 6.15 years and 29.2 ± 5.54 years, respectively [17]. Obesity was found in 16.9% of PCOS patients with insulin resistance and in 14.0% of those with non-insulin resistance. The mean BMI was slightly higher in the insulin-resistant group (26.11±3.86 kg/m²) compared to the non-insulin-resistants (25.81±3.59 kg/m²), but this difference was statistically not significant (p > 0.05). Similarly, Kauffman et al. reported that magnesium levels showed no significant difference between PCOS women with or without insulin resistance, glucose intolerance, or hypertension [9]. Furthermore, the majority of respondents in both groups were nulliparous, echoing Roos et al. findings [18]. The mean serum magnesium level was significantly lower in the insulin-resistant group (1.51±0.59 mg/dL) than in the non-resistant group (1.87±0.55 mg/dL; p=0.001), aligning with previous studies indicating the link between magnesium deficiency and metabolic disorders in PCOS [19]. A moderate negative correlation was observed between serum magnesium levels and HOMA-IR (r=-0.301, p=0.001) indicating that as serum magnesium levels increase, the HOMA-IR scores tend to decrease, and vice versa. Chakraborty et al. documented that woman with polycystic ovary syndrome (PCOS) exhibiting insulin resistance had significantly lower serum magnesium levels (p<0.04), alongside variations in other essential trace minerals. Furthermore, they reported a significant inverse correlation between serum magnesium levels and insulin resistance in this population (r=−0.31; p<0.03), which aligns with the findings of the present study [20]. Moreover, those with magnesium levels below 1.6 mg/dL had a 3.6-fold higher risk of developing insulin resistance (OR=3.625; 95% CI=1.647-7.979), consistent with findings from Chutia and Lynrah, Luo et al. and Hamilton et al. This emphasizes the essential role of magnesium in various metabolic functions, including insulin signaling, glucose uptake, and lipid metabolism [21-23]. A deficiency in magnesium can disrupt these processes, resulting in diminished insulin sensitivity and heightened insulin resistance, which may also exacerbate systemic inflammation and oxidative stress in individuals with PCOS. Contrary to this, Sharifi et al. found no association between magnesium deficiency and IR in individuals with PCOS [24]. Kaufmann et al. also reported no significant difference in serum magnesium levels between women with PCOS and those without; however, the small sample size of the normal population limits the interpretability of their findings [9]. Based on the findings of the present study, it is recommended that the incorporation of magnesium-fortified foods into the diet or the use of parenteral magnesium supplementation could serve as an effective strategy to enhance overall metabolic health in patients with PCOS. Elderawi et al. conducted a randomized controlled trial that demonstrated the efficacy of oral magnesium supplementation in decreasing insulin resistance and improving glycemic control in individuals with type 2 diabetes [25]. These results suggest that magnesium plays a significant role in metabolic regulation and may serve as a valuable intervention for enhancing metabolic health in patients suffering from insulin resistance. Limitations of the current study include the small sample size and its single-centre design, which may limit the generalizability of the results. Additionally, the study did not account for certain confounding factors such as hormonal and environmental factors, which may have influenced the outcomes related to magnesium levels and insulin resistance. Furthermore, the lack of measurement of intracellular magnesium, a more sensitive indicator of magnesium balance, could have affected the findings. Future studies should aim to include larger, multicentre populations and consider a broader range of confounding variables to provide a more comprehensive understanding of the relationship between magnesium and metabolic health in PCOS patients.

CONCLUSION

The study found a significant association between serum magnesium levels and HOMA-IR, concluding that lower serum magnesium concentrations correlate with higher insulin resistance in patients with PCOS.

LIMITATIONS

This study's cross-sectional design prevents causal inference between serum magnesium levels and insulin resistance in PCOS. The sample was drawn from a single tertiary center in Dhaka, limiting generalizability. Dietary magnesium intake, lifestyle factors, and potential confounders such as vitamin D status and medications were not assessed. Additionally, insulin resistance was measured using HOMA-IR rather than gold-standard techniques.

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