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ORIGINAL ARTICLE

SERUM MAGNESIUM LEVEL AND INSULIN RESISTANCE IN OBESE VERSUS NON-OBESE ADULT MALES FROM LAHORE, PAKISTAN

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ABSTRACT

Background: Obesity is a worldwide medical menace with a huge health-economic burden. Glucose metabolism can be regulated by cellular magnesium in many ways; by mediating secretions of insulin and enabling receptor interaction of insulin. The objective of this study was to determine correlation between serum magnesium levels and insulin resistance in obese male subjects and compares with non-obese male.

Material and Methods: This cross sectional study was conducted at Central Park Medical College from December 2021 to May 2022 on 40 obese and 40 non-obese males. Homeostasis model assessment for insulin resistance (HOMA-IR) index was used for determining insulin resistance and magnesium levels were assessed by using atomic absorption spectrophotometry.

Results: A significantly low serum magnesium level was found in obese subjects as compared to controls (mean ±SD 1.356 ±0.215 vs. 1.79 ±0.267 mg/dl, $p<0.0001$). A significantly high HOMA-IR index was found in obese group than non-obese group (median (IQR); 3.12(2.65-3.46) vs. 1.61(1.46-1.83; $p<0.0001$).

Conclusion: The study showed significantly lower serum magnesium level and higher insulin resistance in obese men as compared to non-obese. The study has also shown that serum magnesium is negatively correlated with IR. Lower serum magnesium levels and HOMA-IR indices were observed in obese group as compared to non-obese group.

KEY WORDS: Obesity; Magnesium; Insulin Resistance HOMA-IR; Diabetes Mellitus.

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INTRODUCTION

Obesity is a worldwide medical menace with a huge health-economic burden. The metabolic complications of obesity have detrimental effects on human health and there is growing realization that obesity must be curtailed to improve health outcomes. Type 2 diabetes mellitus (type 2 DM), also termed non-insulin dependent diabetes, involves relative insulin insufficiency and insulin resistance (IR).[1] For all age groups, the incidence of diabetes is perceived to rise to 4.4% by the year 2030.[2] Type 2 DM has prevalence in Pakistan of 26.3%.[3] The two main pathological hallmarks of diabetes are in IR and dysfunction of beta cells resulting in hyperglycemia that may lead to type 2 DM.[4] IR is a pathological condition which is featured by decreased physiological reaction of peripheral tissues to insulin. It leads to various metabolic disorders which are collectively known as metabolic syndrome.[5]

Body's glycemic control, IR, metabolic syndrome, and diabetes are observed being improved due to presence of an important mineral i.e. magnesium.[6, 7] Magnesium is second richly available intracellular cation in the human body. Glucose metabolism can be regulated by cellular magnesium in many ways; by mediating secretions of insulin and enabling receptor interaction of insulin. In addition, magnesium facilitates signal transduction via tyrosine kinase

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mediated phosphorylation. It serves as a cofactor for several important enzymatic reactions in metabolic pathways for glucose utilization.[8,9] Reaction of various enzymes concerned with glucose metabolism can be hindered due to decreased magnesium levels. Hypomagnesaemia also obstructs function of insulin receptor via enhanced plasma membrane micro-viscosity culminating in decreased insulin sensitivity.[10]

Some studies have shown that hypomagnesaemia is frequently found in diabetics, and it may be a foregoing disorder in the development of hyperinsulinemia along with IR.[11] Magnesium supplementation is found to be fruitful for treatment of diabetes and it prevents / slows down the development of its chronic complications.[12,13] The objective of current study was to determine magnesium levels and to correlate them with insulin resistance which was calculated using (HOMA-IR) index.

Research Objective:

To asses and compare serum magnesium levels in obese and non-obese population of Lahore.

To asses and compare insulin levels in obese and non-obese population of Lahore.

To asses and compare fasting serum glucose levels in obese and non-obese population of Lahore.

To asses and compare HOMA-IR in obese and non-obese population of Lahore.

To correlate serum magnesium levels with HOMA-IR.

Null Hypothesis:

$H_0$1: There is no statistically significant difference between serum magnesium levels of obese and non-obese local population of Lahore.

$H_0$2: There is no statistically significant difference between serum insulin levels of obese and non-obese local population of Lahore.

$H_0$3: There is no statistically significant difference between fasting serum glucose levels of obese and non-obese local population of Lahore.

$H_0$4: There is no statistically significant difference between HOMA-IR of obese and non-obese local population of Lahore.

$H_0$5: There is no statistically significant correlation between serum magnesium levels and HOMA-IR.

MATERIALS AND METHODS

This cross-sectional study was conducted at Central Park Teaching Hospital Lahore from December 2021 to May 2022. Random convenient sampling technique was employed and a total of 80 participants were recruited after calculating the sample size using WHO sample size calculator and were divided into two groups based on their body mass index in kilograms per meter square. Group I comprised of subjects (n=40) having BMI < 25 kg/m^2 and same no. of subjects were included in group II having BMI >25 kg/m^2 as per WHO guidelines for South Asians. WHO defined values of BMI for South Asians are different in comparison to other populations because they have got high percentage of body fat at lower BMI.[14] According to WHO Asian specific criteria, normal range of BMI is 18.5-22.9Kg/m^2 over weight is ≥23Kg/m^2 and obesity is ≥25Kg/m^2.[15] Subjects with renal / hepatic disorders, uncontrolled blood pressure, and/or any acute infection were not included. On paper written informed consent was taken from all the subjects and ethical approval (CPMC/IRB-No/1303) was obtained from Central Park Research Committee.

Fasting blood samples were taken from all the subjects. Immediate centrifugation of blood samples was done for 10 minutes at 1000 rpm and the serum was preserved at – 20°C for subsequent utilization. Serum magnesium levels were measured by atomic absorption spectrophotometry. Glucose oxidase method was used for measuring serum glucose and serum insulin was estimated using enzyme-linked immunosorbent assay (ELISA). The sample size was calculated by standard formula, considering power of study 90%, β as 0.1, level of significance 0.05 and 95% confidence interval. Insulin resistance was evaluated by fasting level of serum glucose considered in mmol/l and serum insulin in μ IU/ml via HOMA-IR index.

Statistical Analysis

SPSS ver. 21 was employed for analysis of the collected data. Shapiro-Wilk test was applied to check the normality of data. Mean and standard deviation (Mean±SD) were calculated for normally distributed quantitative variables while median and inter-quartile range (IQR) were calculated for non-normally distributed quantitative variables. Independent samples T-test and Mann Whitney U test were performed for observing group mean differences. Spearman's correlation coefficient r was calculated to assess the relationship between serum magnesium and HOMA-IR. A p value less than .05 was considered as significant.

RESULTS

The mean ages for group 1 and 2 were 37.93 $\pm$ 2.82 and 37.93 $\pm$ 5.49, with no significant mean difference on appliance of independent sample t test with p value of .069. Normality of the data was assessed by employing Shapiro Wilk test and further statistics were employed accordingly as explained in table 1. Serum magnesium levels were compared using independent sample t test while other parameters were assessed using Mann Whitney U test.

Table 1. Description of Normality Test based on Shapiro-Wilk Test

	Shapiro-Wilk		
	Statistic	Df	Sig.
Serum magnesium(ng/ml)	.981	80	.264
Fasting plasma insulin	.934	80	.000
Fasting blood glucose (mmol/l)	.958	80	.010
HOMA.IR	.948	80	.003

A low level of serum magnesium was observed in group 2 (obese people) as Mean $\pm$ SD of serum magnesium in Group I (non-obese men; 1.79 $\pm$ 0.267 mg/dl) was higher than that in Group II (obese men; 1.356 $\pm$ 0.215 mg/dl). A statistically significant difference was observed in the serum magnesium levels between the two groups (p=0.0001) (Table 2).

Serum insulin of group I had median IQR value 7.07 (6.43-7.77) μU/ml and in obese group II it was 13.25 (11.7-14.6) μU/ml. Analysis of serum insulin levels among 2 groups showed statistically significant differences (p=0.0001) (Table 3).

In group I, value of median (IQR) serum glucose was 90 (88-94.75) mg/dl and the value was 94 (92-99.5) mg/dl in group II. A statistically significant difference was observed in the fasting serum glucose levels between the two groups (p=0.001) (Table 4).

Median (IQR) of HOMA-IR in group I was 1.61(1.46-1.83) and it was 3.12 (2.65-3.46) in group II. The difference observed in HOMA-IR among two groups was significant (p=0.0001) (Table 5).

An inverse correlation was observed between serum magnesium and HOMA-IR in all the study participants (r = - 0.522, p = <0.0001).

Table 2. Serum Magnesium Levels in Non-Obese and Obese Population of Lahore.

Groups	n	Mean	SD	Mean difference	95% CI of difference		t-value	d.f.	P-value (2-tailed)
					Lower	Upper			
Non-Obese	40	1.7960	0.267	0.444	0.336	0.551	8.193	78	< .00001
Obese	40	1.3520	0.214	Independent-Samples t-test			$H_0$1 rejected at α .05		

Table 3. Serum insulin Levels in Non-Obese and Obese Population of Lahore.

Groups	Median	IQRs	Difference of medians	Mann-Whitney U	Wilcoxon W	Z	p-value (2-tailed)
Non-Obese (n=40)	7.07	6.43-7.77	6.18	.000	820.000	-7.700	.0001
Obese (n=40)	13.25	11.7-14.6		Mann Whitney U test		H_{03} rejected at α 0.05	

Table 4.Fasting Serum Glucose Levels in Non-Obese and Obese Population of Lahore.

Groups	Median	IQRs	Difference of medians	Mann-Whitney U	Wilcoxon W	Z	p-value (2-tailed)
Non-Obese (n=40)	90	88-94.75	4.0	469.000	1289.000	-3.192	.0001
Obese (n=40)	94	92-99.5		Mann Whitney U test		H_{03} rejected at α 0.05	

Table 5. HOMA-IR Scores in Non-Obese and Obese Population of Lahore.

Groups	Median	IQRs	Difference of medians	Mann-Whitney U	Wilcoxon W	Z	p-value (2-tailed)
Non-Obese (n=40)	1.61	1.46-1.83	1.51	2.000	822.000	-7.680	.0001
Obese (n=40)	3.12	2.65-3.46		Mann Whitney U test		H_{04} rejected at α 0.05	

DISCUSSION

The present findings showed significantly lower serum magnesium level and higher insulin resistance in obese males as compared to non-obese. Huerta et al, 2005 and Song et al., 2004 found a negative correlation in between serum magnesium and body BMI in healthy children and adults.[13]

A poor glycemic control was found in patients having hypomagnesaemia in comparison with patients having normal magnesium levels in a study by Dasgupta et al.[16] In diabetes mellitus the magnesium deficiency is not only associated with development of disease but also with severity of the illness.

Hruby et al. in his work on middle aged diabetic Americans, witnessed that higher magnesium intake decreases the threat of progression of disease in high risk patients having insulin resistance and also in pre-diabetics.[17] Multiple factors can cause low serum magnesium levels such as hypovitaminosis D, lower dietary intake of magnesium, and inflammatory conditions in obesity.[18] Obesity predisposes to glucose intolerance and insulin resistance. Magnesium deficiency is thought to be one of the causes for insulin insensitivity in obese persons.[19]

The present work demonstrated an inverse correlation between magnesium levels and HOMA-IR. These results are similar to the findings of Huerta et al., 2005.[20] A reduced tyrosine kinase enzyme action is found at insulin receptor and evidence has linked it to hypomagnesaemia. This reduction in enzyme activity may results in decreased action of insulin and increased insulin resistance. The effect of magnesium in enhancing tyrosine kinase action is through its effect of increasing the affinity of receptor for ATP which is vital step for auto phosphorylation of the of insulin receptor (b-subunits).[21] In a study by Rodriguez and Guerrero-Romero, 2003 showed that magnesium supplementation improved the sensitivity of insulin as well as its metabolic control in patients of type 2 diabetes whom had prior hypomagnesemia.[22]

Lower magnesium level has also been shown to correlate with more worsening of kidney function in patients of type 2 DM.[23] Hata et al. observed that increased intake of magnesium is a noteworthy shielding factor for the occurrence of diabetes type 2 in Japanese population. This effect is especially seen in subjects having poor drinking habits along with IR.[24]

Remarkable improvement in insulin resistance has been observed in diabetics and non-diabetics when magnesium supplements had been given to them.[20] Magnesium intake has also been found to reduce the risk of diabetes but the evidence is mostly from Caucasian people and this effect in Asian population is to be fully enlightened. The findings from the present work are concordant with the previous studies and highlight the crucial role of magnesium in glucose homeostasis in the local population.

CONCLUSIONS

The present study showed significantly lower serum magnesium level and higher insulin resistance in obese men as compared to non-obese. The study has also shown that serum magnesium is negatively correlated with HOMA-IR. Though hypomagnesaemia is frequently found in type 2 DM patients but still magnesium level assessment is not the part of regular clinical practice. Therefore, it is suggested that for a better control over type 2 DM may require regular estimation of serum magnesium and its supplementation wherever required.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	SI, MZS, SIAS
Acquisition, Analysis or Interpretation of Data:	SI, MZS, SIAS, TI, II, SN
Manuscript Writing & Approval:	SI, MZS, SIAS, TI, II, SN

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.