

Original Research Article

Study of serum magnesium levels in pre-diabetics and its correlation to body mass index

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ABSTRACT

Background: Diabetes is a growing public health burden across the world, particularly in the developing countries. Homeostasis of the trace elements such as magnesium has been found to play an important role in the pathogenesis of diabetes and diabetic complications. Studies had found out an association between serum magnesium and incident diabetes; where diabetes may induce urinary magnesium loss. But in pre-diabetes, serum glucose levels are below the threshold for urinary magnesium wasting and hence unlikely to influence serum magnesium levels. This study was done to assess their serum magnesium levels and find its correlation.

Methods: This cross sectional study was done among 120 pre-diabetic subjects. Pre-diabetes was diagnosed as per ADA guidelines and body mass index was calculated according to Asian guidelines of BMI. Serum magnesium levels were done for all of them and statistically analysed to correlate the serum magnesium with body mass.

Results: The present study observed that 69 out of 120 pre-diabetics, 57.5% have low magnesium levels. This study showed that 57.5% of pre-diabetics is having normal body mass index, out of which more than half of them are having normal serum magnesium. But out of 12 obese pre-diabetics, 11 were having low serum magnesium 91.6%. (P value 0.026 which is statistically significant).

Conclusions: This study observed that serum magnesium levels are low in Pre-diabetics. Significant hypomagnesemia has been seen in pre-diabetics with high BMI compared to those with normal BMI.

Keywords: BMI, Hypomagnesemia, Pre-diabetes; Serum magnesium

INTRODUCTION

The prevalence of diabetes mellitus is increasing worldwide and recent estimates indicates that one out of three people will develop diabetes during their lifetime.¹ Hence it is important to identify modifiable risk factors. One such potential modifiable risk factor is serum magnesium. Magnesium is a co factor in glucose transport, insulin sensitivity and insulin secretion providing a molecular basis for its involvement in the pathogenesis of pre-diabetes and diabetes mellitus.¹

Hypomagnesemia is defined as serum magnesium concentrations <1.6 mg/dl in the general population.² Hypomagnesemia causes altered cellular glucose transport, altered insulin-insulin receptor interactions, reduced insulin secretion and defective post receptor insulin signalling thus aggravates insulin resistance.²

Patients with diabetes shows urinary magnesium loss, caused by high sugars, hyperfiltration or a direct effect of insulin on magnesium channels in the kidney.¹ In contrast, in pre diabetes, serum glucose levels are below

the threshold for urinary magnesium loss and hence unlikely to influence serum magnesium levels.¹ Type 2 diabetes mellitus is associated with hypomagnesemia and incidence rates of 12-47% is been reported.^{3,4}

Only few studies about serum magnesium levels in pre-diabetes are available, and hence the need for this research. This study aimed to find out the serum magnesium levels in pre-diabetes and its correlation to body mass index.

Objectives of the study were to study the serum magnesium levels in pre-diabetes patients, to correlate body mass index with serum magnesium in pre-diabetes patients.

METHODS

Source of data

A cross sectional study was done for 1 year (January 2018 to January 2019) on pre-diabetic volunteers who were willing to participate in the study and individuals who were detected to be pre-diabetic during routine investigations in Father Muller medical college hospital (IP OR OP) were included in the study.

After ethical committee approval, a total of 120 subjects fulfilling the selection criteria were included in this study after getting a written informed consent.

Inclusion criteria

Individuals above 18 years of age who got detected to be pre-diabetic were included in the study.

Exclusion criteria

Patients with known co-morbidities such as Diabetes mellitus, Chronic kidney disease, Chronic liver disease, Malabsorption syndrome, Thyroid disorders, chronic diarrhoea, chronic pancreatitis, Drug therapy patients taking diuretics and magnesium containing antacids and Chronic Alcoholics and smokers were excluded from the study.

Methodology

Diagnosis of pre-diabetics as per ADA guidelines (FBS 100-125 mg/dl or PPBS 140-200 mg/dl or HbA1c 5.7-6.4%).

BMI was calculated for all the pre-diabetic individuals (according to Asian guidelines of BMI, where BMI = Weight in Kg/Height in m², where obese is > 25kg/m² according to Asian guidelines), then the serum magnesium levels were assessed (serum magnesium ≥ 1.6 mg/dl is considered normal).

The following investigations will be done in all cases – FBS and PPBS using COBAS 6000 apparatus by Hexokinase enzyme method and Serum Magnesium measured using COBAS 6000 apparatus by photoelectric calorimetry and HbA1c using BIORAD TURBO. Variant V-II by immune-turbidometry.

Data collected were analyzed by using frequency, percentage, mean, standard deviation, t-test, chi-square test, pearson correlation coefficient and odds ratio.

Statistical analysis

All the statistical data were analysed using Statistical Package for Social Sciences version.20 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as mean + S.D. Inferential statistics were computed using Chi-square test and student “t” test.

Sample size estimation

Sample size was calculated using the formula given below

$$n = Z\alpha^2 * P(1-P) / e^2$$

$$p=2.9\%, e=3\%, Z\alpha=1.96 \text{ at } 95\% \text{ CI, } n=120$$

RESULTS

A total 120 subjects who fulfilled the criteria were studied.

Age

Out of 120 study subjects (Pre-diabetics) included in the study, the maximum number of participants were in the age group of 51 - 60 years of age. The mean age of the participants was 54.83 with the age ranging from 26 years to 89 years (Table 1).

Table 1: Frequency distribution of subjects based on age.

Age (in years)	Number	Valid percent
≤ 30	6	5
31-40	13	10.8
41-50	22	18.3
51-60	41	34.2
61-70	25	20.8
>70	13	10.8
Total	120	100

Gender

Out of the total 120 pre-diabetics, 74 (61.7%) were males and 46 (38.3%) were females.

Table 2: Distribution of subjects based on gender.

Gender	Number	Valid percent
Males	74	61.7
Females	46	38.3

Occupation

68 pre-diabetics (i.e. 56.6%) are leading a sedentary life style. 26.6 % of pre-diabetics leading moderate and 16.6% leading heavy work life style (Table 3).

Table 3: Distribution of subjects based on occupation.

Occupation	Number	Valid percent
Sedentary	68	56.66
Moderate	32	26.6
Heavy	20	16.6
Total	120	100

Body mass index

According to Asian guidelines of BMI, 69 out of 120, i.e. 57.5 % of all pre-diabetics are having normal BMI. 51 pre-diabetics were found to have high body mass index. (42.5%), 32.5% of all pre-diabetics are having overweight and 10% of pre-diabetics are obese, with an average BMI of 23.07 kg/m² (Table 4).

Table 4: Distribution of subjects based on BMI (Asian Guidelines).

BMI (Kg/m ²)	Number	Valid percent
Normal (18.5-22.9)	69	57.50
Overweight (23-24.9)	39	32.50
Obese (more than 25)	12	10
Total	120	100

Serum magnesium

51 out of 120 pre-diabetics, 42.5 % have normal serum magnesium. 69 out of 120 pre-diabetics, i.e. 57.5% of them have low serum magnesium levels. The mean serum magnesium levels were found to be 1.6 mg/dl (Table 5). 68 (56.6%) pre-diabetics are leading sedentary life, out of which 46 subjects (67.6 %) were having low magnesium levels (Table 6) which is statistically significant (p-value 0.033).

Table 5: Distribution of subjects based on serum magnesium.

Serum magnesium	Number of subjects	Valid percent
<1.6 mg/dl	69	57.5
≥1.6 mg/dl	51	42.5
Total	120	100

Table 6: Comparison of occupation and serum magnesium.

Occupation	Serum Magnesium		Total	Chi square test	P value
	<1.6 (low magnesium)	≥1.6 (normal magnesium)			
Sedentary	46	22	68	6.85	0.033
Moderate	15	17	32		
Heavy	8	12	20		
Total	69	51	120		

Table 7: Comparison of BMI and serum magnesium.

BMI	Serum Magnesium		Total	Chi square test	P value
	<1.6 (low magnesium)	≥1.6 (normal magnesium)			
Normal (18.5-22.9)	34 (49.2%)	35 (50.7%)	69 (100%)	7.294	0.026
Overweight (23-24.9)	24 (61.5%)	15 (38.5%)	39 (100%)		
Obese (>25)	11 (91.70%)	1 (8.3%)	12 (100%)		
Total	69 (57.50%)	51 (42.50%)	120		

Table 8: Comparison of FBS, PPBS, HbA_{1C} and BMI with magnesium using t-test.

		N	Mean	Std. deviation	t test	P value
FBS	≥1.6 (normal magnesium)	51	111.540	5.7222	2.951	0.004
	<1.6 (low magnesium)	69	115.157	7.1902		
PPBS	≥1.6 (normal magnesium)	51	144.400	13.1335	3.779	0.003
	<1.6 (low magnesium)	69	154.171	14.5263		
HbA _{1C}	≥1.6 (normal magnesium)	51	6.096	0.1884	0.404	0.687
	<1.6 (low magnesium)	69	6.110	0.1866		
BMI	≥1.6 (normal magnesium)	51	22.6	1.41	2.297	0.023
	<1.6 (low magnesium)	69	23.4	2.1		

Out of 69 pre-diabetics with normal BMI, 50.7 % were found to have normal serum magnesium. Out of 39 overweight pre-diabetics, 24 has got low magnesium (61.5%). Out of 12 obese pre-diabetics, 11 were having low serum magnesium (91.7%) (p value.0.026 which is statistically significant, Table 7). Significant hypomagnesemia has been found in pre-diabetics with high BMI. Using standard deviation and t test, serum magnesium levels were low with high FBS, PPBS, HbA_{1c} and BMI and its statistically significant in all except for HbA_{1c} (p value 0.687 , Table 8)

Table 9: Pearson correlation coefficient of various parameter.

Various parameter	Pearson correlation	P value
BMI	-0.113	0.22
FBS	-0.266	0.003
PPBS	-0.289	0.001
HbA1c	-0.049	0.592

Pearson correlation coefficient showed a negative correlation for serum magnesium with FBS, BMI, HbA_{1c} and PPBS in pre diabetic patients (r= -0.266, -0.113, -0.049,-0.289) i.e. higher the FBS, PPBS, HbA_{1c} and BMI, lower the serum magnesium (Table 9).

Table 10: Odds ratio.

Variables	Odds ratio	95% C.I.for odds ratio		P value
		Lower	Upper	
BMI	1.321	1.037	1.682	0.024
HbA_{1c}	0.436	0.043	4.415	0.483
PPBS	1.054	1.019	1.090	0.002
FBS	1.073	1.005	1.147	0.036
Age	1.004	0.972	1.037	0.792
Gender	0.600	0.255	1.412	0.292

In the present study among 120 pre-diabetics, 51 individuals i.e. 42.5% were either overweight or obese and of them more than half i.e. 35 individuals (68.6%) were having low magnesium level, while among those who were of normal BMI, 50.7% were having normal magnesium level. This difference in the serum magnesium level between overweight/obese individuals as compared to those who were not overweight or obese (normal BMI) was found to be statistically significant (OR=1.321(1.037-1.682) p=0.024) Table 10.

DISCUSSION

Pre-diabetes

Pre-diabetes can be defined as a condition in which blood sugar is high, but not high enough to be termed as diabetes mellitus. It can be impaired glucose tolerance, which means higher than normal blood sugar after a meal

or impaired fasting glucose which means higher than normal blood sugar in the morning before eating.⁵ The estimated prevalence of pre-diabetes was 6.3% and obesity was significantly associated with elevated pre-diabetes prevalence.⁶

Magnesium

Magnesium is the fourth most abundant cation in our body. It is one of the important components of many food items like grains, nuts, and green leafy vegetables.⁷ Magnesium is a co-factor in several pathways including glucose transport, insulin sensitivity and insulin secretion. Hypomagnesemia can induce altered cellular glucose transport, reduced insulin secretion, defective post receptor insulin signalling and altered insulin receptor interactions and thus aggravating insulin resistance.⁸ Insulin by itself does not influence the serum magnesium concentration but in hyperglycaemic state, insulin causes rapid intracellular uptake of glucose. This process causes an increase in the phosphorylation by sodium potassium ATPase on the cell membrane. Since magnesium is a co factor for sodium potassium ATPase, magnesium is consumed, which subsequently decreases the serum magnesium concentration.^{9,10} One third of body magnesium is bound to plasma proteins, the remaining two thirds, which is diffusible or ionized, appears to be the biologically active component.¹⁷ In normal man, daily magnesium intake should be between 240 and 480 mg to maintain an adequate magnesium balance.²⁶

Hereditary factors, poor dietary intake, autonomic dysfunction, altered insulin metabolism, glomerular hyperfiltration, osmotic diuresis, hypophosphatemia and hypokalemia all contributes to hypomagnesemia in diabetic patients.^{16,18} Intracellular magnesium deficiency leads to decrease in tyrosine kinase activity of insulin receptors and impairment in insulin action, resulting in insulin resistance. Hypomagnesaemia (<1.6 meq) is a well recognized clinical syndrome characterized by muscular symptoms (gross muscular tremor, ataxia, tetany), psychiatric manifestations (agitation, confusion and hallucinations) and cardiological signs (low-voltage T-wave at the ECG).^{18,19}

Our study includes 120 pre-diabetics whose serum magnesium levels and BMI were assessed to find the correlation between them. In the study we found out 120 pre-diabetics ranging from 26-89 years, with mean age of 54.83 years with maximum participants in the age group of 51-60 years. But In a population based cohort study done by Kieboom et al in Netherlands, the mean age of pre-diabetes was 64.7 years.¹ Among the total 120 pre-diabetics included in the study, 74 (61.7%) were males and 46 (38.3%) were females whereas 50.4 % were females in the study done by Kieboom et al.¹ The study revealed that 68 pre-diabetics (i.e. 56.6%) are leading a sedentary life style and 26.6% of pre-diabetics leading moderate and 16.6% leading heavy work life style. Our study showed that 69 out of 120, i.e. 57.5 % of all pre-

diabetics are having normal BMI and 51 pre-diabetics were found to have high body mass index (42.5%). 32.5% of all pre-diabetics are overweight and 10% of the pre-diabetics are obese.

The present study showed average BMI of 23.07 kg/m² in pre-diabetics with hypomagnesaemia. A cross sectional study done among pre-diabetics in Lebanon showed individuals with hypomagnesaemia have an average BMI of 27.5 kg/m².²³ Our study observed that hypomagnesaemia was present among 69 pre-diabetics (57.5%) and 51 pre-diabetics were having normal serum magnesium. In a case control study done in Chennai, serum magnesium levels were found to be lower in cases with pre-diabetes when compared to non-diabetic controls.²¹ In the cross sectional study done in Lebanon, among individuals with pre-diabetes, 73.3% had hypomagnesaemia.²³ The range of serum magnesium in pre-diabetics in the present study is 1.30 to 2.40 mg/dl with mean value of 1.6 mg/dl whereas in a study done by Kieboom et al, the range of serum magnesium is 0.82 to 2.9 mg/dl with mean serum magnesium value of 1.52 mg/dl.¹ In a case control study done in Chennai, mean serum magnesium in pre-diabetes was 1.49 mg/dl.²¹

The average FBS, PPBS and HbA1C in the present study was 113.65 mg/dl, 150.1 mg/dl and 6.1% respectively which is in concurrence with the Chennai study.²¹ The present study shows that there is no significant association between age and serum magnesium level. These findings are in concurrence with the study done in Lebanon.²³ Out of 74 pre-diabetic males, 48 were found to have low serum magnesium (64.9%). Out of 46 pre-diabetic females, 21 were found to have low serum magnesium (45.7%). The present study found out that low magnesium levels have significantly higher proportion of males (p-value 0.026) but we have not taken equal number of male and female patients. In the population based cohort study done in Netherlands by Kieboom et al, hypomagnesaemia was found to be more prevalent among females.¹

In the study done in Lebanon, the Pearson Chi-Square Test showed that Magnesium levels did not correlate with gender (p=0.45).²³ Among the 120 pre-diabetics in our present study, 68 (56.6%) subjects are leading sedentary life, out of which 46 subjects (67.6%) were having low magnesium levels which is statistically significant (p value 0.033). Significant hypomagnesaemia was found in individuals who are leading sedentary lifestyle which is in concurrence with other studies.

Out of 69 pre-diabetics with normal BMI, 50.7% were found to have normal serum magnesium. Out of 39 overweight pre-diabetics, 24 have got low serum magnesium (61.5%). Out of 12 obese pre-diabetics, 11 were having low serum magnesium (91.7%). So the present study shows that among 69 pre-diabetics (i.e. 0.57.5%) who is having normal body mass index, more than half of them are having normal serum magnesium,

whereas out of 12 obese pre-diabetics, 11 were having low serum magnesium; 91.7% (p-value.0.026 which is statistically significant).

In this study, Pearson correlation coefficient showed a negative correlation for serum magnesium with FBS, PPBS, BMI and HbA_{1c} in pre-diabetic patients. Higher the FBS, PPBS, BMI and HbA_{1c}, lower the serum magnesium. These findings are in concurrence with the cross sectional study done in Lebanon.²³ Significant hypomagnesaemia has been observed in individuals with high BMI (P value of 0.026) in this study. The study done in Najran University, KSA showed that serum magnesium decreases with an increase in BMI.²² Higher the BMI and lower the serum magnesium, worse the glycemic control.^{22,25}

CONCLUSION

Serum magnesium levels are found to be low in pre-diabetics. Significant hypomagnesaemia is observed in pre-diabetics with high body mass index. Further studies will be needed to elaborate on this association, monitoring the diets and physical activity in a larger population. It also remains to be proven whether there are any benefits, if magnesium supplementations are given in pre-diabetics.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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