ORIGINAL ARTICLE

ASSOCIATION OF SERUM MAGNESIUM AND SERUM CALCIUM LEVELS IN ACUTE MYOCARDIAL INFARCTION ASSOCIATED WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

This study was done to see the association of serum magnesium and serum calcium in acute myocardial infarction with type 2 diabetes mellitus. This cross sectional study was done on 50 diagnosed patients of acute myocardial infarction with type 2 diabetes and 50 acute myocardial infarction patients without type 2 diabetes mellitus in the department of Biochemistry, Dhaka Medical College, Dhaka from July 2014 to June 2015. Adult patients of acute myocardial infarction with type 2 diabetes mellitus aged between 35 to 60 years, both male and female, attending CCU of Dhaka Medical College Hospital & National Institute of Cardiovascular Diseases and Hospital were selected as the study subjects according to selection criteria. Informed written consent from all study subjects was taken after full explanation of the procedure. The serum magnesium and serum calcium and fasting plasma glucose of study subjects were assessed. The serum magnesium and serum calcium levels were statistically compared to observe the relation with patients of acute myocardial infarction with or without type 2 diabetes mellitus. Serum magnesium showed negative significant correlation ($r=-0.710$; $p=0.001$) with fasting plasma glucose of the study patients ? and negative correlation ($r=-0.266$; $p=0.062$) in patients with AMI with diabetes mellitus. Serum calcium showed negative significant correlation ($r=-0.746$; $p=0.001$) with fasting plasma glucose of the study patients ? and negative significant correlation ($r=-0.431$; $p=0.002$) in patients with acute myocardial infarction with diabetes mellitus. The hypomagnaesemia and hypoglycaemia were observed in patients with acute myocardial infarction with type 2 diabetes mellitus with statistical significance. It is very much important to evaluate these parameters as early as possible on arrival of the patients in hospital to reduce cardiac death. Because hypomagnaesemia and hypocalcaemia in the initial phase of post-acute myocardial infarction is very critical, as ventricular tachyarrhythmia, sudden cardiac death and reinfection and neuromuscular disturbance are the usual outcomes.

Key words: Acute myocardial infarction, Type 2 diabetes mellitus, Serum magnesium, Serum calcium, Troponin I, Reinfarction

Introduction

Ischemic heart disease (IHD) is the leading cause of morbidity and mortality worldwide[1]. Acute myocardial infarction (AMI) is the most life-threatening disease in emergency hospital admissions[2]. The risk for coronary heart disease (CHD) among diabetic subject is greater by a factor of 2 to 4 compared to non-diabetic subjects[3].

Type 2 diabetes mellitus is a heterogeneous disorder caused by a combination of genetic factors related to impaired insulin secretion, insulin resistance and environmental factors such as obesity, overeating, lack of exercise, and stress as well as aging[4]. It is typically a multifactorial disease involving multiple genes and environmental factors to varying extents[5].

Magnesium is the fourth most common cation in the body and the second most common intracellular cation after potassium. It has a fundamental role as a cofactor in more than 300 enzymatic reactions involving energy metabolism and nucleic acid synthesis[6].

A deficiency of magnesium and calcium may result in an increased neuromuscular and cardiac excitability and in excess they may lead to depressed muscular performance or paralysis. Hypomagnesemia and hypocalcemia occur frequently in diabetic patients especially with poor glycemic control. Diabetic patient with hypomagnesemia and hypocalcemia are at an increased risk of cardiac death and cause major complication in acute myocardial infarction. The present study was designed to explore the relation of serum magnesium and serum calcium in AMI with type 2 diabetic patients.

Materials and Methods

This cross-sectional study was conducted in the Department of Biochemistry, Dhaka Medical College (DMC), Dhaka, Bangladesh during July 2014 to June 2015. Patients with acute myocardial infarction with or without type 2 diabetes mellitus were the study population.

Total 100 patients of acute myocardial infarction with or without type 2 diabetes mellitus attending the coronary care unit (CCU) of DMCH & NICVD, Dhaka were selected as per inclusion and exclusion criteria for this study by purposive sampling. Fifty AMI patients with type 2 diabetes (Group I) and 50 AMI patients without type 2 diabetes (Group II) were selected.

Diagnosed acute myocardial infarction (diagnosis based on ECG and troponin I) with or without type 2 diabetes mellitus patients aged between 35-60 years, both male and female, were included in this study. Patients with history of surgery or trauma, associated with any infectious disease and inflammatory disorders, who were taking calcium containing drugs or any drugs which interfere calcium metabolism, or who had taken these drugs within the previous 30 days and patients with any debilitating disease such as chronic kidney disease, COPD, malignancy, autoimmune disease, malnutrition, liver disease, thyroid dysfunction and patients with pregnancy were excluded from the study.

Methods

- Diagnosed acute myocardial infarction with or without type 2 diabetic patients of both sexes in CCU of DMCH & NICVD were taken as study subjects.
- Informed written consent was taken from each patient who fulfilled the criteria.
- Initial evaluation of the patients by taking history, general examination and clinical examination were recorded in preformed data collection sheet.

- Demographic profile and pulse, BP, body weight were measured. Drug history was taken regarding calcium containing drug or any drugs which interfere in calcium metabolism, within the previous 30 days.
- Serum magnesium and serum calcium levels were determined by photoelectric colorimetric method as per instruction of the manufacturer.
- All information was properly noted in the preformed data sheet.

Collection and preservation of samples

Five milliliters of overnight fasting venous blood was drawn from each subject with all aseptic precautions and immediately transferred to a dry clean test tube after removing the needle to prevent hemolysis and allowed to clot. Then the sample was centrifuged and serum was collected in a microcentrifuge tube and appropriately labelled and preserved at -20°C to transport to Biochemistry department of DMC. Sample was used for the measurement of fasting plasma glucose, serum magnesium and serum calcium. Reference values of target parameters are mentioned below.

Parameters	Reference values
Serum calcium	9–11 mg% 2.5 mmol/L
Serum magnesium	1.8–3.6 mg% 1.5 mmol/L
Fasting plasma glucose	<6.1 mmol/L

Procedure of data analysis

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Chi-Square test was used to analyze the categorical variables. Student t-test was used for continuous variables. Pearson's correlation coefficient was used to test the relationship between the groups. P value <0.05 was considered as statistically significant.

Results

This cross-sectional study was carried out in the Biochemistry Department, DMCH, Dhaka during the period from July 2014 to June 2015. The aim of the study was to observe and compare the serum magnesium and serum calcium levels in patients of acute myocardial infarction with and without type 2 diabetes mellitus. Fifty AMI patients with type 2 diabetes and fifty AMI patients without type 2 diabetes were selected for this study.

Table I shows distribution of the study subjects according to age and sex. Almost half (48.0%) patients belonged to age >55 years in group I and 22(44.0%) in group II. The mean age was found 54.2 ± 5.7 years in group I and 50.3 ± 8.9 years in group II. Almost two-thirds (64.0%) patients were male in group I and 35 (70.0%) in group II. The study groups were age and sex matched.

Table I: Distribution of the study subjects by age and sex (n=100)

Baseline characteristics	Group-I (n=50)		Group-II (n=50)		P values
	Number	Percentage	Number	Percentage	
Age (in years)					
≤40	0	0.0	13	26.0	
41–45	7	14.0	6	12.0	
46–50	8	16.0	6	12.0	
51–55	11	22.0	3	6.0	
>55	24	48.0	22	44.0	
Mean±SD	54.2±5.7		50.3±8.9		[a]0.001[s]
Range (min-max)	41–60		35–60		
Sex					
Male	32	64.0	35	70.0	[b]0.523[ns]
Female	18	36.0	15	30.0	

s= significant, ns= not significant
aP value reached from unpaired t-test
bP value reached from chi square test

Table II shows blood pressure of the study patients. Mean systolic pressure was found 129.1±34.2 mm Hg in Group I and 131.8±33.5 mm Hg in Group II. The mean diastolic pressure was found 77.1±19.6 mm Hg in Group I and 84.0±16.1 mm Hg in Group II. The difference of mean blood pressures between two groups was not statistically significant (p>0.05) .

Table II: Distribution of the study patients by blood pressure (n=100)

Blood pressure (mm Hg)	Group-I (n=50)		Group-II (n=50)		P values
	Number	Percentage	Number	Percentage	
Systolic					
<140 (normal)	35	70.0	32	64.0	
≥140	15	30.0	18	36.0	
Mean±SD	129.1±34.2		131.8±33.5		0.690[ns]
Range (min-max)	80–220		70–190		
Diastolic					
<90 (normal)	32	64.0	25	50.0	
≥90	18	36.0	25	50.0	
Mean±SD	77.1±19.6		84.0±16.1		0.057[ns]
Range (min-max)	50–120		60–110		

ns= not significant
P value reached from unpaired t-test

Table III shows laboratory investigations of the study patients. Mean fasting plasma glucose was found 11.9±2.7 mmol/L in Group I and 4.2±0.8 mmol/L in Group II. The mean serum magnesium was found 1.3±0.2 mmol/L in Group I and 1.9±0.3 mmol/L in Group II. The mean serum calcium was found 8.2±0.5 mmol/L in Group I and 9.3±0.5 mmol/L in Group II.

Table III: Distribution of the study patients by laboratory investigations (n=100)

Laboratory investigations	Group-I (n=50)	Group-II (n=50)	P values
	Mean ±SD	Mean ±SD	
Fasting plasma glucose (mmol/L)	11.9 ±2.7	4.2 ±0.8	0.001 s
Range (min-max)	7.8−20	2.8−5.8	
Serum magnesium (mmol/L)	1.3 ±0.2	1.9 ±0.3	0.001 s
Range (min-max)	1.0−1.7	1.3−2.5	
Serum calcium (mg/dL)	8.2 ±0.5	9.3 ±0.5	0.001 s
Range (min-max)	7.4−9.5	8.1−10.5	

s= significant ($p<0.05$)
P value reached from unpaired t-test

Figure 1 shows the correlation between serum magnesium and fasting plasma glucose concentration of study subjects. Figure 2 shows the correlation between serum calcium and fasting plasma glucose concentration. Figure 3 shows the correlation between serum magnesium and fasting plasma glucose of AMI patients with diabetes mellitus. Figure 4 shows the correlation between serum magnesium and fasting plasma glucose of AMI patients without diabetes mellitus. Figure 5 shows the correlation between serum calcium and fasting plasma glucose concentration of AMI patients with diabetes mellitus. Figure 6 shows the correlation between serum calcium and fasting plasma glucose concentration of AMI patients without diabetes mellitus.

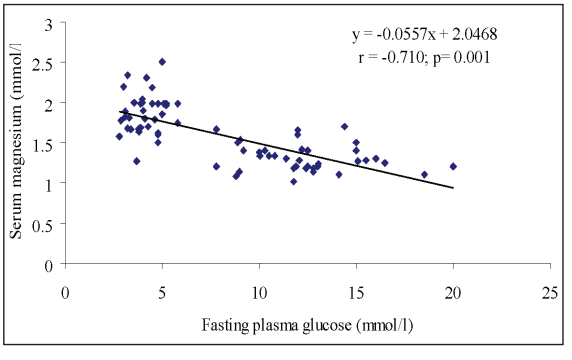

Fig 1. Scatter diagram showing negative (strong) significant correlation (r=-0.710; p=0.001) between serum magnesium and fasting plasma glucose of the study patients

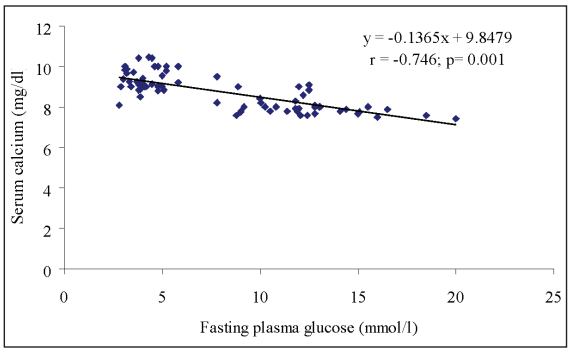

Fig 2. Scatter diagram showing negative (strong) significant correlation (r=-0.746; p=0.001) between serum calcium and fasting plasma glucose of the study patients

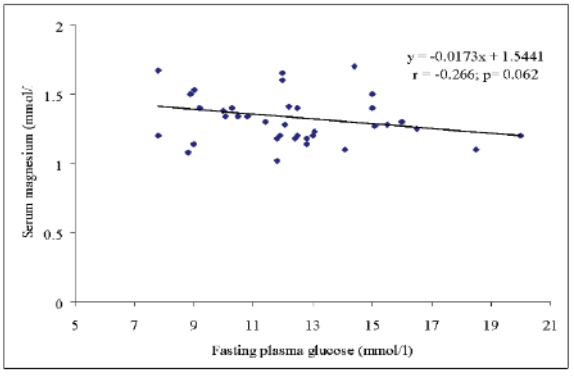

Fig 3. Scatter diagram showing negative (weak) correlation (r= -0.266; p=0.062) between serum magnesium and fasting plasma glucose of patients of AMI with diabetes mellitus

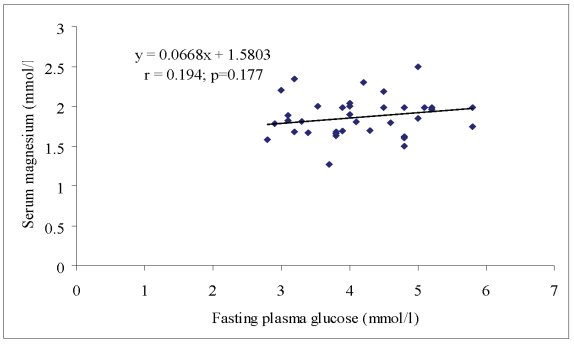

Fig 4. Scatter diagram showing positive (negligible) correlation (r=0.194; p=0.177) between serum magnesium and fasting plasma glucose of patients of AMI without diabetes mellitus

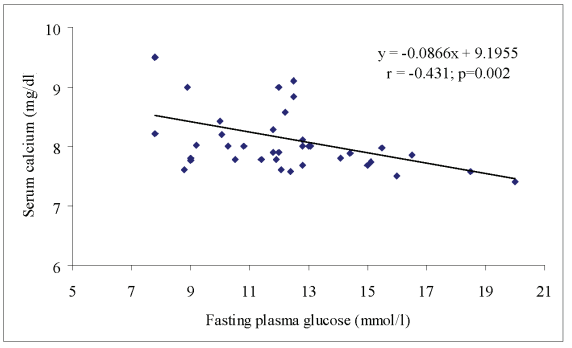

Fig 5. Scatter diagram showing negative (moderate) significant correlation (r= -0.431; p=0.002) between serum calcium and fasting plasma glucose of patients of AMI with diabetes mellitus

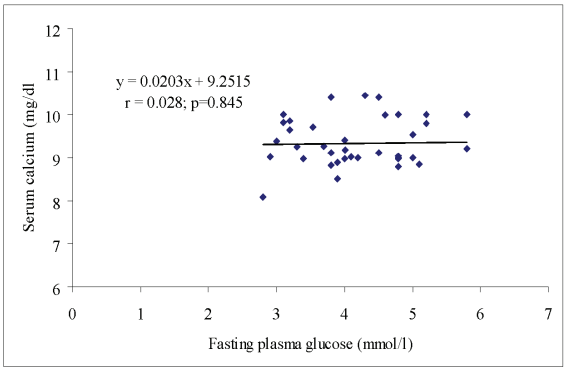

Fig 6. Scatter diagram showing positive (negligible) correlation (r=0.028; p=0.845) between serum calcium and fasting plasma glucose of patients of AMI without diabetes mellitus

Discussion

This cross-sectional study was carried out with an aim to estimate serum magnesium, serum calcium, fasting plasma glucose in AMI patients with and without type 2 diabetes mellitus and also to compare serum magnesium and serum calcium between AMI patients with and without type 2 diabetes mellitus.

A total of 100 acute myocardial infarction patients with or without type 2 diabetes mellitus aged 35-60 years of both sex attending the coronary care unit (CCU) of DMCH & NICVD,

Dhaka during July 2014 to June 2015 were included in this study. Among them 50 patients having acute myocardial Infarction (AMI) with diabetes mellitus were considered as Group I and rest 50 patients having acute myocardial infarction (AMI) without diabetes mellitus were considered as Group II. In the present study it was observed that almost half of the patients belonged to age >55 years-in Group I 24(48.0%) and in group II 22(44.0%). The mean age was found 54.2±5.7 years in Group I and 50.3±8.9 years in Group II. The difference of mean ages between two groups was statistically significant ($p<0.05$). Mane et al[7] showed the mean age was 55.2±10.2 years in case group and 48.3±11.6 years in control group. Similar age range was also observed by Kiranmai et al[8]. In another study, Waltia et al[9] showed the mean age was 61.3±10.3 years in diabetics and 58.3±7.2 years in control group, which is higher than it is in the current study. The higher age may be due to geographical variations, racial, ethnic differences, genetic causes and different lifestyles may have significant impacts on these diseases.

In this study, it is observed that mean fasting plasma glucose is 11.9±2.7 mmol/L (from 7.8–20.0 mmol/L) in group I and 4.2±0.8 mmol/L (from 2.8–5.8 mmol/L) in group II. The mean serum magnesium is 1.3±0.2 mmol/L (from 1–1.7 mmol/L) in group I and 1.9±0.3 mmol/L (from 1.3–2.5 mmol/L) in group II. The mean serum calcium is 8.2±0.5 mg/dL (from 7.4–9.5 mg/dL) in group I and 9.3±0.5 mg/dL (from 8.1–10.5 mg/dL) in group II. The mean difference between groups is statistically significant ($p<0.05$). On a hyperglycemic day, an i.v. infusion of 20% glucose was started at the end of a euglycaemic baseline period, increasing blood glucose concentration from 5.3 mmol/L to 12.3 mmol/L[9]. Waltia et al[9] showed the mean (±SD) plasma magnesium concentrations of the diabetics and controls were 0.77±0.08 and 0.83±0.07 mmol/L, respectively ($p<0.05$). Plasma magnesium concentrations were below the normal reference range in 37.6% of the diabetic patients and 10.9% of the control subjects ($p<0.05$). Mane et al[7] showed that the blood levels of plasma FBS in cases was found 112.77±41.89 mg/dL as compared with control values 85.57±12.08 mg/dL. The mean serum magnesium was found 2.26±0.24 mmol/L in control and 1.98±0.32 mmol/L in case group. This was found to be statistically significant ($p<0.001$). In another study Kiranmai and Lakshmi[8] found that the mean serum magnesium was 1.08±0.26 mmol/L in controls and 0.68±0.24 mmol/L in diabetes group. The mean serum calcium was found 9.45±1.13 mg/dL in control and 8.35±1.0 mg/dL in diabetes group. The mean serum magnesium was statistically significant ($p<0.05$) between two groups. Geiger & Wanner[10] mentioned in their study one common feature in patients with type 2 diabetes mellitus (T2DM), hypertension and low levels of high-density lipoprotein cholesterol (HDL-C) appears to be a deficiency of magnesium. T2DM is often associated with hypomagnesaemia and incidence rates of 13.5-47.7% have been reported by Pham et al[11]. Hypomagnesaemia can be defined as serum magnesium concentrations ≤0.65 mmol/L (1.6 mg/dL) or ≥2 SD below the average in the general population[12,13]. Hereditary factors, poor dietary intake, autonomic dysfunction, altered insulin metabolism, glomerular hyperfiltration, osmotic diuresis, recurrent metabolic acidosis hypophosphataemia and hypokalaemia may all

contribute to hypomagnesaemia in diabetic patients[11]. In epidemiological studies, an inverse correlation between magnesium intake and the risk of developing diabetes mellitus was found[14-16]. The Women's Health Study enrolled a cohort of 39 345 US women aged at least 45 years. During a follow up period of 6 years, on average, 918 women developed T2DM. The trial results support a protective role for higher magnesium intake and a reduced risk of developing T2DM, in particular in the subgroup of overweight women[16].

In this series negative (weak) correlation ($r=-0.266$; $p=0.062$) between serum magnesium and fasting plasma glucose of patients of AMI with diabetes mellitus was observed. In this present study it was observed that there is positive (negligible) correlation ($r=0.194$; $p=0.177$) between serum magnesium and fasting plasma glucose of patients of AMI without diabetes mellitus. Kim et al[17] and Sales & Pedrosa[18] showed a significant negative correlation between magnesium and fasting plasma glucose. Similar findings was also observed in the study of Mishra et al[19] which revealed a significant negative association between serum magnesium and fasting plasma glucose.

In this current study it was observed that there is negative (moderate) significant correlation ($r=-0.431$; $p=0.002$) between serum calcium and fasting plasma glucose of patients of AMI with diabetes mellitus. In this present study it was observed that there is positive (negligible) correlation ($r=0.028$; $p=0.845$) between serum calcium and fasting plasma glucose of patients of AMI without diabetes mellitus. Hypoglycaemia was seen in 43% of our patients with type 2 diabetes. Findings of current study is consistent with another study which showed that hypocalcaemia was associated with the development of type 2 diabetes.[8]

In this study the disturbance in serum magnesium and serum calcium levels, i.e., hypomagnesaemia and hypocalcaemia were observed in patients with AMI with type 2 diabetes mellitus with statistical significance. The estimation of serum magnesium and serum calcium levels in patients with acute myocardial infarction with type 2 diabetes mellitus should be done as early as possible on arrival of the patients in emergency department to reduce the post AMI complications such as ventricular tachyarrhythmia, sudden cardiac death and re-infarction in diabetic patients.

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References

1. Costa e Silva R, Pellanda L, Portal V, Maciel P, Furquim A, Schaan B. Transdisciplinary approach to the follow-up of patients after myocardial infarction. Clinics (Sao Paulo) 2008; 63(4): 489-496.
2. McDaniel MC, Willis P, Walker BB. Tlaque necrotic core content is greater immediately distal to bifurcations compared to bifurcations in the proximal lad of patients with CAD. Am J Cardiol 2008; 102(8): 242.
3. Haffner SM, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Mortality from Coronary Heart Disease in Subjects with Type 2 Diabetes and in Nondiabetic Subjects with and without Prior Myocardial Infarction.N Eng J Med 1998; 339: 229-234.

4. Kaku K. Pathophysiology of type 2 diabetes and its treatment policy. JMAJ 2010; 53(1): 41-46.

5. Holt GI. Diagnosis, epidemiology and pathogenesis of diabetesmellitus an update for Psychiatrists. Br J Psychiatry 2004; 184: s55-s63.

6. Fawcett WJ, Haxby EJ, Male DA. Magnesium Physiology and pharmacology. BRJ Anesth 1999; 83: 302-320.

7. Mane M, Chaudhari GR, Reddy EP. Hypomagnesaemia in Diabetic Patients and Biochemical action on the cardiovascular system. Int J Biol Med Res 2012; 3(1): 1273-1276.

8. Kiranmai P, Lakshmi NV. Comparative study of serum magnesium, calcium, potassium and sodium levels in diabetics and hypertensives with acute myocardial infarction. IOSR Journal of Pharmacy and Biological Sciences 2015; 10(2): 10-14.

9. Waltia MK, Zimmermann MB, Spinas GA, Hurrell RF. Low plasma magnesium in type 2 diabetes. Swiss Med Wkly 2003; 133: 289-292.

10. Geiger H, Wanner C. Magnesium in disease. Clin Kidney J 2012; 5: i25–i38.

11. Pham PC, Pham PM, Pham SV, Miller JM, Pham PT. Hypomagnesemia in patients with type 2 diabetes. Clin J Am Soc Nephrol 2007; 2: 366–373.

12. McNair P, Christensen MS, Christiansen C, Madsbad S, Transbol I. Renal hypomagnesaemia in human diabetes mellitus: its relation to glucose homeostasis. Eur J Clin Invest 1982; 12(1): 81–85.

13. Pham PC, Pham PM, Pham PA, Pham SV, Pham HV, Miller JM et al. Lower serum magnesium levels are associated with more rapid decline of renal function in patients with diabetes mellitus type 2. Clin Nephrol 2005; 63: 429–436.

14. Kao WH, Folsom AR, Nieto FJ, Mo JP, Watson RL, Brancati FL. Serum and dietary magnesium and the risk for type 2 diabetes mellitus: The Atherosclerosis Risk in Communities Study. Arch Intern Med 1999; 159(18): 2151–2159.

15. Lopez-Ridaura R, Willett WC, Rimm EB, Liu S, Stampfer MJ, Manson JE et al. Magnesium intake and risk of type 2 diabetes in men and women. Diabetes Care 2004; 27(1): 134–140.

16. Song Y, Manson JE, Buring JE, Liu S. Dietary magnesium intake in relation to plasma insulin levels and risk of type 2 diabetes in women. Diabetes Care 2004; 27(1): 59–65.

17. Kim DJ, Xun P, Liu K, Loria C, Yokota K, Jacobs DR et al. Magnesium intake in relation to systemic inflammation, insulin resistance, and the incidence of diabetes. Diabetes Care 2010; 33: 2604–2610.

18. Sales CH, Pedrosa LFC. Magnesium and diabetes mellitus: Their relationship. Clin Nutr 2006; 25: 554–562.

19. Mishra S, Padmanaban P, Deepti GN, Sarkar G, Sumathi S, Toora BD. Serum Magnesium and Dyslipidemia in Type 2 Diabetes Mellitus. Biomedical Research 2012; 23(2): 295-300.