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Research Article

A Research Study on Renal Complication in Outpatients: Hypomagnesemia with Hyperglycemia

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ABSTRACT

Objective: The evaluation of the hypomagnesemia correlation with the hyperglycemia and associated renal complication was the objective of this research in outpatients.
Study Design: Case control research study.
Place and Duration of Study: Research was carried out in the period of January, 2016 to August, 2016 at Mayo Hospital, Lahore.
Material and Methods: Both male and female were included in our research in the age of twenty and above years. We included hyperglycemia as subjects and normoglycemiaas controls (63 each) in our research through consecutive sampling technique. We did not include all the patients having malabsorption, adrenal dysfunction, thyroid dysfunction, renal impairment, pregnancy, taking mineral supplement, lactation and acute illness cases. Serum Magnesium (Mg) and Fasting plasma glucose (FPG) levels were measured through ADVIA – 1800 (Siemens Clinical Chemistry Auto-Analyzer) with xylidin and hexokinase blue techniques. Analysis of urine albumin was carried out through Jaffé Kinetic Assay. Creatinine and Albumin ratio was also measured. ACR and FPG were also used for the calculation of the Pearson correlation coefficient "r". Comparison of the mean levels of the serum Mg was carried out in normoglycemicand hyperglycemic groups through T-test.Hypomagnesemia frequency (Serum Mg ≤0.66 mmol/L) was measured too in the subjects of hyperglycemic having T2DM. Significant statistical p-value was observed as (<0.05).
Results: There was a significant invers relation of Serum Mg with FPG and ACR having respectively the values of "r" and p-value as (r=-0.543) & (p=0.001) and ACR (r=-0.474) & (p=0.001).Mean serum Mg level was observed in hyperglycemic and normoglycemic respectively as (0.78 mmol/l) and (0.88 mmol/l) with a significant p-value of (0.001). Hypomagnesemia frequency in T2DM subjects was observed s (18.8%); whereas, we observed no subject having any with pre-diabetes &normoglycemiahaving the incidence of hypomagnesemia.
Conclusion: Hyperglycemia subjects had a significant low levels of mean serum Mg in comparison to the healthy counterparts. There was also an association of hypomagnesemia with diabetic nephropathy and poor glycemic control.

Keywords: Albumin Creatinine Ratio (ACR), Hyperglycemia, Fasting Plasma Glucose (FPG), Hypomagnesemia and (T2DM) Type 2 diabetes mellitus.

INTRODUCTION

There is a high prevalence of the T2DM in chronic metabolic disease which is a threat in itself to the population and burden to the healthcare [1].Metabolism change in the certain T2DM micronutrients plays a significant role in complications and pathogenesis [2]. An important mineral is considered in this regard is Mg which is complexly relating to the carbohydrate metabolism. Homeostasis of Mg is closely regulated through the balance in renal excretionand intestinal absorption [3]. Moreover, determinants of genetics& steroids of sex can possibly modulate the levels of the serum Mg [4]. It is suggested in the numerous research studies

that T2DM can cause the low levels of the Mg serum which affects the diabetes glycemic control and also increases the micro vascular and chronic macro complications.

Interaction of the metabolism in the T2DM and hypomagnesemia is not well-defined and understood. However, insulin action and secretion can be affecting in this regard [5]. A hypomagnesemia evidence can possibly cause transformed glucose transport, transformed post-receptor insulin signaling, decreased pancreatic insulin secretion andinsulin–insulin receptor interactions defect [6]. No relation has been revealed by the numerous research studies in the levels of serum Mg and glycemic control or diabetic control improvement through replacement of Mg [7]. Data has conflict because of various involved population and design of the research studies. The evaluation of the hypomagnesemia correlation with the hyperglycemia and associated renal complication was the objective of this research in outpatients.

MATERIAL AND METHODS

After the formal approval from the institution our case control research was completed in the time span of January, 2016 to August, 2016 at Mayo Hospital, Lahore.WHO calculator was the course of data collection with confidence interval and test power respectively as 95% & 90. Hyperglycemia ratio in the subjects and controls was respectively as 32 and 10 percent. We included hyperglycemia as subjects and normoglycemia as controls (63 each) in our research through consecutive sampling technique. We did not include all the patients having malabsorption, adrenal dysfunction, thyroid dysfunction, renal impairment, pregnancy, taking mineral supplement, lactation and acute illness cases. Blood sample of 3 ml was taken in the fasting of one night, collected in the tube of sample and for FPG to measure Mg level gel tube was used. Clean container was used for the collection of urine sample of 5 – 10 ml. Centifuge process was carried out at 3000 g after the clotting of Mg samples.Analysis of FPG was made after the collection of sample within two hours and analyzed through hexokinase method; whereas, analysis of Mg serum was carried out through blue technique by using (ADVIA – 1800® Siemens Clinical Chemistry Auto-Analyzer). Analysis of urine albumin was carried out through immune-turbidimetric method and measurement of urine creatinine was made through JafféKinetic Assay through same device analyzer. Creatinine and Albumin ratio was also measured. ACR and FPG were also used for the calculation of the Pearson correlation coefficient “r”. SPSS-20 was used for data entry and analysis. Gender was reflected in percentage as it is a qualitative variable, mean and SD were measured for ACR, FPG, age and Mg as they were quantitative variable.Hypomagnesemia frequency (Serum Mg $\leq$ 0.66 mmol/L) was measured too in the subjects of hyperglycemic having T2DM. Significant statistical p-value was observed as (< 0.05). Hyperglycemia group was sub-divided in to pre-diabetes and T2DM respectively as (FPG was in the range of 5.6 – 6.9 mmol/L) &(FPG $\geq$7.0 mmol/L) and hypomagnesemia frequency was also measured in the T2DM subjects.

Table: Baseline characteristics in subject (hyperglycemia) and controls (normoglycemia) (n=126).

Parameter	**Normoglycemia Mean ± SD**	**Hyperglycemia Mean ± SD**	**p-value**
Gender (M/ F)	34/29	33/30	
Age (years)	49.7 ± 11.5	52.8 ± 11.7	0.138
Plasma Fasting Glucose (mmol/L)	5.1 ± 0.3	8.04 ± 2.6	<0.001
Mean serum Magnesium(mmol/L)	0.88± 0.1	0.78± 0.1	<0.001
Albumin Creatinine Ratio (g/mmol)	0.97± 0.5	4.3± 6.2	<0.001
Sample Size (126)			
Correlation Coefficient (r = -0.543)			
Significance Level (<0.001)			

RESULTS

Both male and female were included in our research in the age of twenty and above years. We included hyperglycemia as subjects and normoglycemia as controls (63 each) in our research through consecutive sampling technique. There was a significant invers relation of Serum Mg with FPG and ACR having respectively the values of "r" and p-value as (r = -0.543) & (p = 0.001) and ACR (r = -0.474) & (p = 0.001). Mean serum Mg level was observed in hyperglycemic and normoglycemic respectively as (0.78 mmol/l) and (0.88 mmol/l) with a significant p-value of (0.001). Hypomagnesemia frequency in T2DM subjects was observed s (18.8%); whereas, we observed no subject having any with pre-diabetes &normoglycemia having the incidence of hypomagnesemia.

Male to female ratio was respectively 52% and 48%. Comparison of quantitative variables was carried out for the (Mean ± SD) FPG, age, ACR and Mg as reflected in the Table. We observed higher levels of mean ACR and FPG in hyperglycemia group in comparison to the normoglycemic. No difference was observed in mean age factor for both the groups.

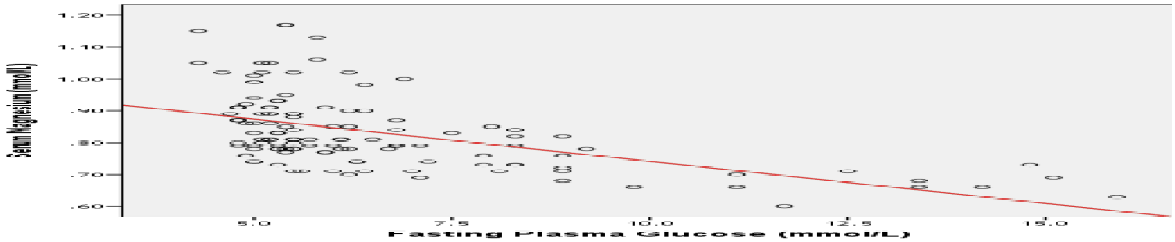

Figure-1: Scatter plot showing the relationship between serum Magnesium (mmol/L) and fasting plasma glucose (mmol/L).

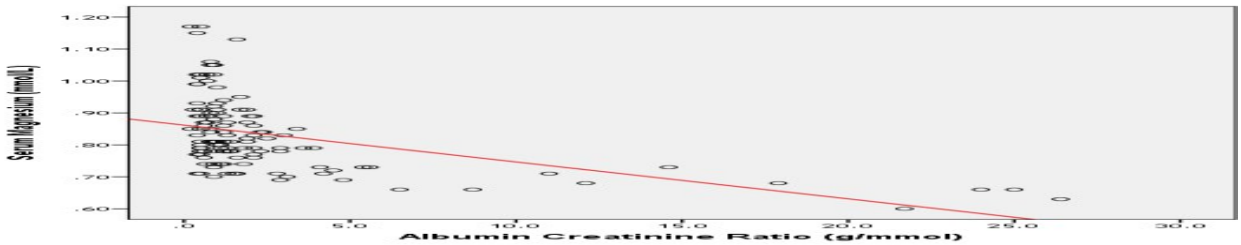

Figure-2: Scatter plot showing the relationship between serum Magnesium (mmol/L) and Albumin

DISCUSSION

A major intracellular cation is Mg which is an important cofactor in more than three hundred enzymes specificallylinked to the Adenosine Triphosphate (ATP) and production of energy. DNA function,regulation of cell permeability, neuromuscular activity and replication requires this and it is also considered crucial as well [3]. Hypomagnesemia is also linked with the inflammation, dyslipidemia, oxidative stress, hypertension, atherosclerosis, impaired coagulation, coronary heart disease and enlarged carotid intimae thickness. Hypomagnesemia can be indicated through level of Mg (1%)available in Extra Cellular Fluid (ECF) [6]. Clinically, we can also define hypomagnesemia that it is a concentration of serum Mg (≤1.6 mg/dl) or (0.66 mmol/L) or (≤2SD) under general population mean value [7].

There is a high prevalence of the T2DM in chronic metabolic disease which is a threat in itself to the population and burden to the healthcare [1]. Metabolism change in the certain T2DM micronutrients (chromium, vanadium and magnesium) plays a significant role in complications and pathogenesis [2]. Complex relation in T2DM metabolic complications and

hypomagnesemia have been shown by numerous authors. We observed that at first, inverse association of serum Mg is prevalent with plasma glucose fasting in the adult population and low levels of Mg are linked with the poor glycemic control; secondly, there is also an inverse association of the ACR with serum Mg and thirdly, hypomagnesemia frequency is higher significantly in T2DM.

According to Longstreet and Yokota back in 2005, in the adult population there is a potent relation in T2DM and levels of Mg serum [9, 10]. Larsson SC and Dong JY (2007 and 2012) presented their two meta-analysis, in which they concluded that an intake of Mg as inversely linked with the DM onset [11, 12].

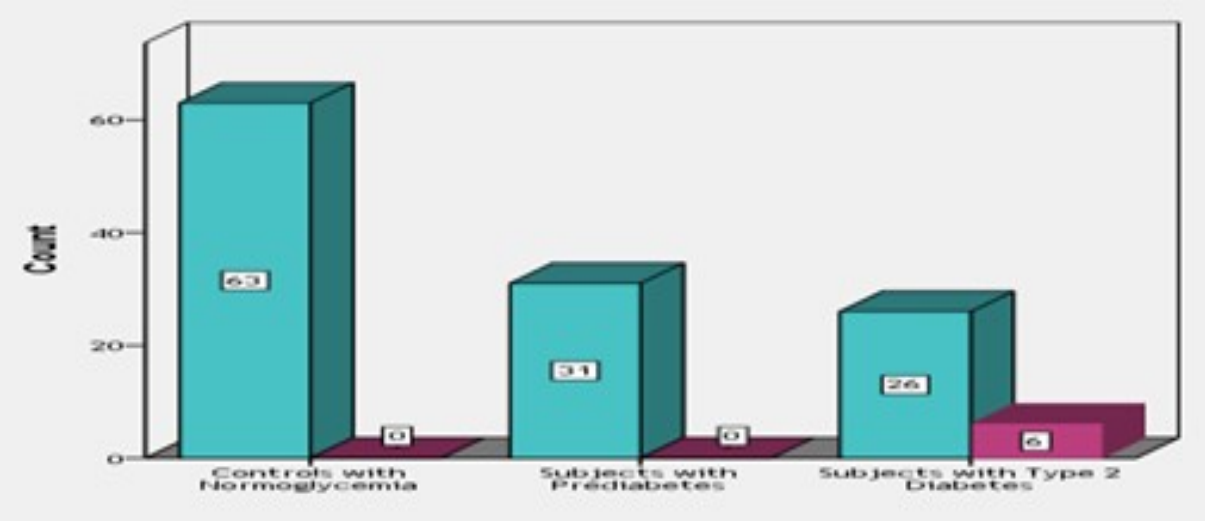

Figure-3: Bar chart showing the frequency of hypomagnesemia among controls with normoglycemia and subjects with hyperglycemia divided into categories of prediabetes and type 2 diabetes mellitus.

It is suggested in the numerous research studies that T2DM can cause the low levels of the Mg serum which affects the diabetes glycemic control and also increases the micro vascular and chronic macro complications. Interaction of the metabolism in the T2DM and hypomagnesemia is not well-defined and understood. However, insulin action and secretion can be affecting in this regard [5]. A hypomagnesemia evidence can possibly cause transformed glucose transport, transformed post-receptor insulin signaling, decreased pancreatic insulin secretion and insulin–insulin receptor interactions defect [6]. No relation has been revealed by the numerous research studies in the levels of serum Mg and glycemic control or diabetic control improvement through replacement of Mg [7]. There is no evidence of research on association of hyperglycemia and hypomagnesemia in Pakistan. Our research uncovers the association of Mg serum level with ACR and hyperglycemia in diabetic control through replacement of Mg and levels of Mg. However, clinical trials outcomes are disagreeingabout Mg supplementation effects on T2DM control and complications related to the metabolism.This may be attributed to the participantsheterogeneity e.g. age differences, Mg balance &glycemic control and race. Small size of the population and varying Mg salts and doses may also be the reason.

We also observed an inverse relation in the ACR and levels of serum Mg which focuses on the hypomagnesemia role in diabetic microvascular problems pathogenesis. According to Pham(2005), there is an association of the low Mg with T2DM patient's faster renal function decline with [8]. However, a research held in Brazil speaks about another microvascular complication i.e. Type I &

II DM subjectsretinopathy, which fails in the demonstration of a significant association between Mg serum level and retinopathy severity.In the outcomes of our research we observed hypomagnesemia in (18.8%) T2DM subjects. However, in the outcomes of other research studies it is reported in the range of 13.5 – 47.7 percent. The contributing cause may include hypomagnesemia, Mg measurements methods and patient cohort heterogeneity. Our research also had few limitations such as Mg serum use in the place of free bioactive to measure the level of Mg,design of the research makes certainty of the relationship between T2DM and Mg status almost impossible.

CONCLUSION

Hyperglycemia subjects had a significant low levels of mean serum Mg in comparison to the healthy counterparts. There was also an association of hypomagnesemia with diabetic nephropathy and poor glycemic control. There was a significant invers relation of Serum Mg with FPG and ACR having respectively the values of "r" and p-value as (r = -0.543) & (p = 0.001) and ACR (r = -0.474) & (p = 0.001). Mean serum Mg level was observed in hyperglycemic and normoglycemic respectively as (0.78 mmol/l) and (0.88 mmol/l) with a significant p-value of (0.001). Hypomagnesemia frequency in T2DM subjects was observed s (18.8%); whereas, we observed no subject having any with pre-diabetes &normoglycemia having the incidence of hypomagnesemia.

RECOMMENDATION

It is recommended that more work is required for the establishment of relation in the use of Mg supplements for T2DM management.

CONFLICT OF INTEREST

No conflict of interest in involved in this research.

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