Original Research Article

Association of serum iron and magnesium levels with lipid profile in type 2 diabetic patients

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Abstract

Background: With around 350 million cases in 2014, type 2 diabetes mellitus (T2DM) is one of the most frequent diseases throughout the world. This number is predicted to increase dramatically in the coming years, resulting in serious health and economic challenges. Chronic hyperglycemia found in diabetes mellitus contributes to the development of oxidative stress associated with increased production of reactive oxygen species and lipid peroxidation[2]. Oxidative stress may occur due to changes in plasma and intracellular concentrations of some minerals, such as magnesium and iron[3,4]. As prevalence of DM in India is continuously increasing, present study is designed to explore the association of serum iron and magnesium in Type 2 Diabetes with the fasting sugar and lipid profile and compare it with the controls. **Study design:** A case-control study includes total of 63 type 2 diabetes mellitus patients and 38 healthy individuals. Fasting blood glucose, lipid profile, iron serum and Magnesium levels were assessed. **Results:** The present study results showed statistically significant increased serum iron levels and hypomagnesium in type 2 diabetes mellitus patients. Our study shows significant negative association between Serum Magnesium levels with fasting plasma glucose and lipid profile. Serum iron depicted significant positive relation with fasting glucose and lipid profile.
Key Word: serum iron, magnesium levels.

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INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia which is characterized by either deficiency in the secretion or action of insulin or both[5]. Diabetes Mellitus is most common endocrine disease and its metabolic derangement is frequently associated with permanent and irreversible functional and structural changes in the cells of the body. The hyperglycaemic effect enhances the non-enzymatic glycosylation of proteins and accumulation of polyol such as Sorbitol and these end products of the advanced glycosylation, cause irreversible changes and this process culminates in cellular damage which includes long term damage, dysfunction and failure of various organs, eyes, kidneys, nerves and heart and blood vessels.[6] It has been known that an imbalance of micronutrients participates in the formation of reactive oxygen species and advanced glycation end products. These Oxidative free radicals increase the peroxidation of low-density lipoprotein (LDL) thereby increasing its uptake by macrophages with increased foam cell formation and atherosclerosis, though other mechanisms may exist[7]. Although the mechanism of protein glycoxidation remains unclear, the process is accelerated and potentiated by Reactive Oxygen Species (ROS) under oxidative stress conditions[8]. Iron is a vital mineral for cell homeostasis, which activity is linked to chemical characteristics and oxidation state, with participation in Fenton and Haber-Weiss reactions. It has been shown that ROS formation is enhanced by the presence of trace redox-active metals[9, 10]. Iron is a strong pro-oxidant and this property, while essential for its metabolic functions, makes iron potentially

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hazardous because of its ability to participate in the generation of powerful oxidant species such as hydroxyl radical . This association of increased level of oxidative stress with high body iron levels can increase the risk of type 2 diabetes mellitus patients[11]. Another important element in glucose metabolism is magnesium. It has a fundamental role in carbohydrate metabolism in general and in Insulin action in particular. Magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes as well as on the evolution of complications such as retinopathy, arterial atherosclerosis and nephropathy[12]. Reduced Mg levels were also associated with an increased prevalence of arrhythmias in DM2 obese subjects[13], and with a more rapid decline of renal function. Moreover, hypomagnesemia is currently considered an accurate predictor of progression of diabetic nephropathy[14,15]. Although various elements are closely linked to the progression of diabetes and its co-morbidities, the aim of our study is to ascertain the difference in serum iron and magnesium concentrations and its effect on lipid metabolism between healthy individuals and type 2 diabetes mellitus patients.

Study design and methodology

This was a case-control study conducted at Annapoorna Medical College and Hospital, Salem. The study was approved by the institutional ethical committee. The study group comprised of sixty three previously diagnosed type 2 diabetes mellitus patients as cases and thirty eight age and sex matched apparently healthy individuals as controls. Each individual enrolled in study underwent a detailed history, clinical examination and laboratory examination designed for the study. Subjects with a history of pregnancy and lactation, anemia, those on mineral and iron supplements, drugs like aminoglycosides, amphotericin B, Cetuximab, cyclosporine, digoxin, diuretics and chronic disorders of the liver, kidney, and cardiovascular system, endocrine disorders, established psychiatric disorder and on antidepressant and/or antipsychotic therapy, malignancy were excluded from the study. After obtaining consent from the patient, Venous blood samples were obtained after at least 10 h of overnight fasting for the estimation of glucose, total cholesterol, triglycerides, HDL, iron, and magnesium and these parameters were estimated using standard kits in Erba EM 200 fully automated clinical chemistry analyser. LDL was calculated by formula. The reference serum magnesium level is 1.3-2.5 mEq|L. The reference serum iron level is 60-160 µg/dL and for female 35-145 µg/dL. Anthropometric measurements were taken. Body mass index (BMI) was calculated as weight divided by height squared (kg/m2) and waist hip ratio was calculated. Statistical analysis was performed using SPSS version 25. Data were expressed in Mean ± SD. Statistical tests like independent t-test, and correlation coefficient 'r' were applied whenever found suitable and necessary. The P-value less than 0.05 were considered as significant.

RESULTS AND OBSERVATION

Table 1 shows that the mean age was 50 ± 13 (37-63) years in control group (n = 38) and 47 ± 9 (34-71) years in type 2 diabetes (n=63) in our study population. The mean body mass index was 25.09 ± 1.77 kg/m2 in control group and 26.01 ± 1.99 kg/m2 in type 2 diabetes patients and BMI of type 2 diabetes patients were found to be more than the controls ($p<0.001$). The mean waist hip ratio was 0.91± 0.04 in control group and 0.92 ± 0.14 in type 2 diabetes patients and there was no statistical significance. Table 1 shows there was a significant rise ($p < 0.001$) of fasting plasma glucose, triglycerides, total cholesterol, and LDL-cholesterol in type 2 diabetes patients in comparison with controls. There was no significant fall in HDL-cholesterol in type 2 diabetes than controls. Table 2 shows that the serum iron was significantly high in type 2 diabetes patients when compare to control group and table 3 shows significant positive correlation of serum iron with fasting glucose, cholesterol, triglycerides and LDL-c. However, the concentrations of serum iron in this study were within the recommended normal values in both groups. And also table 2 shows that the serum magnesium was found to be significantly lower in type 2 diabetes patients than controls and table 3 shows there was a significant negative correlation between serum magnesium with fasting blood glucose and lipid parameters in type 2 diabetes patients when compared to control group

Table 1: Demographic and clinical characteristics of the study population

Parameters	Control n= 38 Mean ± SD	Cases n= 63 Mean ± SD	t-test	p-value
Age	50 ± 13	47 ± 9	1.126	0.26
BMI	25.09 ± 1.77	26.01 ± 1.99	-2.345	< 0.05
WHR	0.91± 0.04	0.92 ± 0.14	-0.386	0.71
GLU-F	84.45 ± 9.26	146.21 ± 42.27	-8.862	< 0.001
Cho	180.05 ± 33.22	256.60 ± 53.69	-7.913	< 0.001
TGL	176.16 ± 80.26	241.30 ± 71.73	-4.227	< 0.001
LDL	123.18 ± 19.86	167.933 ± 43.21	-7.345	< 0.001
HDL	41.45 ± 5.10	43.22 ± 9.39	-1.071	0.28

Table 2: Serum iron and magnesium status of type 2 diabetes patients and control

Parameters	Control n= 38 Mean ± SD	Cases n= 63 Mean ± SD	t-test	p-value
Fe	98.05 ± 24.31	139.94 24.38	± -8.371	< 0.001
Mg	1.829 ± 0.4368	1.359 0.5104	± 4.728	< 0.001

Table 3: Pearson's correlation between serum iron and magnesium with fasting glucose and lipid profile in type 2 diabetes patients and control groups

Parameters	Serum iron (µg/dL)		Serum magnesium (µg/dL)	
	Control	cases	Control	cases
	Fasting Glucose			
r	.032	0.288**	-.176	-.033*
p	.850	.001	.292	.019
	Total Cholesterol			
r	.059	0.343**	-.217	-.219**
p	.727	.001	.192	.025
Triglycerides				
r	.032	.253**	-.052	-.293**
p	.850	.015	.755	.018
	HDL-C			
r	-.128	-.046	.157	.120
p	.444	.783	.345	.351
	LDL-C			
r	.255	.344**	-.279	-.247*
p	.122	.006	089	.013

*significant p value; Pearson's correlation coefficient, r

DISCUSSION

Diabetes Mellitus (DM), a major global health issue which not only decrease life quality and expectancy, but are also becoming a problem regarding the financial burden for health care systems[16]. Therefore every effort should be made to reduce the diabetes burden. Glucose, in the presence of reactive oxygen species (ROS), acts as an as an oxidative agent and drives deleterious processes in Diabetes Mellitus. And also the formation of reactive oxygen species (ROS) is an inevitable by product of metabolism. Oxidative stress induced by an abundance of ROS or failure in the anti oxidative machinery, is the cause of much pathology. Moreover, Lipid oxidation is a major harmful consequence of ROS formation, as it reflects irreversible oxidative changes of membranes[17, 18]. Although there are various causes for the ROS formation and oxidative stress, it may occur due to changes in plasma and intracellular concentrations of some minerals, such as magnesium and iron [3,4]. In this present study we have observed a statistically significant frequency of increased serum iron in the type 2 diabetic patients when compared to the controls. However, the concentrations of serum iron in this study were within the recommended normal values in both groups, but serum iron was significantly increased in the diabetic subjects when compared to control group. In addition to this, there is significant positive correlation with serum iron with total cholesterol, triglycerides and LDL-cholesterol in type 2 diabetic patients whereas it is not correlating with HDL-cholesterol in our study population. Although the exact molecular mechanism of iron-related pathology in diabetes and dyslipidemia is not yet clearly understood, many studies have shown that an ability of iron to induce oxidative stress and inflammation is likely to be involved in the pathogenesis[19-23] . Iron in excess increases lipid peroxidation that modifies fatty acid profile of the cellular membranes leading to damages of organelles and mitochondrial dysfunction[24,25]. This finding is consistent with a Study done by Grotto which shown that high iron levels induce the production of free radicals which promote DNA damage and interact with unsaturated fatty acids, inducing lipid peroxidation [26]. As shown by Jiang Li *et al.* that serum ferritin levels are significantly associated with lipid parameters, independent of glucose metabolism disorders and components of metabolic syndrome (MetS) [27]. In this present study we observed a statistically significant hypomagnesemia in the type 2 diabetic patients when compared to the control groups. Hypomagnesemia is a common observation in studies assessing patients with type 2 diabetes [28,29]. And as shown by Fabiane *et al.* that reduced plasma levels of magnesium in patients with type 2 diabetes appears to be one of the factors involving diabetes pathophysiology [30]. In the present study we have also observed that there was negative correlation of serum magnesium with fasting

glucose, total cholesterol, triglycerides and LDL-cholesterol. This finding is consistent with study done by Dong *et al.*, recent meta-analysis of 13 prospective cohort studies involving 536,318 participants and 24,516 cases; it has clearly indicated the inverse association between Mg intake and T2D risk [31]. Some mechanisms have been proposed to clarify the relationship between magnesium deficiency and iron metabolism in patients with type 2 diabetes. Accordingly, results of some studies suggest that magnesium deficiency is involved in the induction of hemolysis, contributing to iron release which is, in turn, a pro-oxidant nutrient enhancing the production of reactive oxygen species and the synthesis of inflammatory markers[32,33]. At normal levels, magnesium is described to have a protective effect on damage caused by iron overload, reducing hemolysis and the release of free iron[33]. Inverse correlations between erythrocyte magnesium and plasma iron and ferritin in diabetic patients may indicate mechanisms triggered by the body to protect diabetic patients from increased iron levels and to prevent a more vulnerable oxidative state which could promote changes and damage. Similarly, it has been reported that reduced erythrocyte magnesium levels are associated with increased iron in several tissues[33], and low dietary intake of magnesium in rats induces increased iron absorption and reduced number of red blood cells[32]. Animal experiments found that Mg deficiency was associated with reduced glucose uptake and utilization in insulin-sensitive tissues, thus promoting insulin resistance and the development of diabetes[34, 35]. Furthermore, randomized controlled trials including non-diabetic individuals found improvement in insulin sensitivity together with increased levels of serum Mg after Mg supplementation [36].

CONCLUSION

The present study results provide evidence that increased serum iron levels and hypomagnesium were significantly associated with fasting glucose and dyslipidemia in type 2 diabetes patients. Further studies, especially well-designed observational and cohort studies and randomized trials, are warranted to provide stronger evidence and establish a causal inference.

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