



ORIGINAL RESEARCH PAPER

Medical Science

SERUM MAGNESIUM AND SERUM BILIRUBIN LEVELS IN TYPE 2 DIABETES MELLITUS

KEY WORDS:

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ABSTRACT

Introduction:-

Diabetes mellitus (DM) is one of the most common metabolic disorder and leading cause of death and disability in the world. The incidence of diabetes is increasing globally and in India. Approximately one third of patients with type 2 diabetes have hypomagnesaemia, mainly caused by enhanced renal excretion. Magnesium deficiency is associated with the poor glycemic control. Bilirubin acts like an antioxidant, help to reduce tissue damage and inflammation. Initial studies have shown that in humans with higher levels of Bilirubin are less likely to have DM.

Aim & objectives:-

To study the magnesium and bilirubin levels in uncomplicated type 2 DM and compare with the normal subjects.

Materials & methods:-

This was a comparative case control study carried out in 50 T2DM patients and 50 healthy controls. All these biochemical parameters done on automated chemical analyzer.

Results:-

This study found that, Bilirubin and magnesium levels were significantly lower in T2DM as compared to healthy controls.

Conclusion:-

Poor glycemic control an oxidative stress in diabetes can caused profound damage to the vital organs and hypomagnesaemia can lead to development of complications in diabetes.

Introduction:-

India is diabetic capital of the world over a decade and now it is heading to lead in cardiovascular disease (CVD) also as both diabetes and coronary artery disease (CAD).^[1]

India faces a huge case load of T2DM, which is projected to affect about 69.9 million Indian by the year 2025. [2] T2DM may remain in sub-clinical form for years before diagnosis, which is of great concern for health care providers.^[3]

Direct association of elements in diabetes mellitus has been observed in many research studies. The metabolism of several minerals has been reported to alter in DM and these elements might have specific roles in the pathogenesis and progress of this disease. Of these minerals magnesium is the important one element is the fourth most abundant cation in the body and second in the intracellular environment.^[4]

Hypomagnesaemia may have negative impact on glucose homeostasis and insulin sensitivity in DM patients.

Further, magnesium deficiency has been proposed as a novel factor implicated in the pathogenesis of late diabetic complications.^[5,6]

Magnesium deficiency has been shown to cause endothelial cell dysfunction, inflammation and oxidative stress, which are major contributors to atherosclerosis.^[7]

Bilirubin, a major intracellular product of heme catabolism is traditionally considered as a toxic waste product. However, in 1937, Najib-Farah first postulated possible protective actions of bilirubin thus, it gained the momentum as a potent antioxidant and anti-inflammatory factor on the vascular and has been linked to vaso-occlusive disorders.^[8,9]

An increased expression of heme Oxygenase, an enzyme used to breakdown the hemoglobin into bilirubin, is associated with enhanced insulin sensitivity and glucose metabolism. Further, the antioxidant properties of bilirubin have been postulated to reverse oxidative damage associated with a hyperglycemic state. [10]

Hence, the study was done to evaluate, compare and correlate status of serum bilirubin, magnesium in T2DM patients and healthy controls.

Aim and objectives:-

1. To evaluate effect of poor glycemic control on serum bilirubin levels,
2. To assess the role of blood glucose on serum magnesium levels.

Materials and methods:-

Selection of subjects:-

Patients who visited the department of General Medicine OPD at Mahatma Gandhi Mission Medical College & Hospital, Aurangabad, Maharashtra and those who are already diagnosed as T2DM without any complications. Selection of subjects on the basis of clinical history and WHO criteria with the age ranged between 40-65 years.

inclusion criteria:-

Already diagnosed T2DM patients without any complications on the basis of clinical history and laboratory findings.

Exclusion criteria:-

The patients of diabetes having complications, pregnant and lactating women, subjects currently taking nutritional supplements, magnesium containing laxatives, diuretics/alcohol were excluded, renal failure, acute or chronic myocardial infarction.

Study design:-

A comparative case control study was ranging a period of six months from august 2017 to January 2018.

Study population:-

For this study purpose, individuals were divided into two groups, each group consisted of 50 individual.

- Group I: - consisted of 50 T2DM patients,
- Group II: - Consisted of 50 healthy controls.

All individuals were maintained on antidiabetic treatments like oral hypoglycemic agents.

Laboratory analysis:-

3 ml blood was collected from the subjects and the sample was processed for blood glucose level by Glucose-Oxidase peroxidase method, serum bilirubin estimated by end point Diazo method and serum magnesium investigated by Calmagnite method using

automated chemistry analyzer.

Statistical analysis:-

The data collected during this study, normal continuous variables data was presented as mean ± Standard deviation with 95% confidence interval. This test of significance was calculated by unpaired students't' test between cases and controls. Correlation of biochemical parameters were performed by two tailed Person's correlation. Significance was set at P<0.05. All the statistic analysis was performed by using Minitab 17 software.

Results:-

This was a comparative case control study, conducted on 50 patients with clinically diagnosed T2DM and 50 healthy controls. The mean age in patients of T2DM was 51.36±7.25 and controls were 50.96±8.16 years.

In Table No.1, comparison of mean± SD and P values of FBSL, bilirubin and magnesium in T2DM and controls. The mean S.D. of FBSL in the diabetic population was 157.4±23.4 mg/dl in T2DM & 86.1±12.7mg/dl in controls (p=0.000)

The mean S.D. of serum bilirubin level in the T2DM group was 0.678±0.198 mg/dl and 1.320±0.264 mg/dl in non diabetic group (p=0.000) The mean S.D. of serum magnesium level in the T2DM group was 1.438±0.361 mg/dl and 2.398±0.372 mg/dl in healthy control (p=0.000)

Table No.1 :- Comparison of various parameters between diabetic and healthy controls

Parameters	T2DM (n=50) Mean±SD	Controls (n=50) Mean±SD	P-value
Age	51.36±7.25	50.96±8.16	0.796
FBSL (mg/dl)	157.4±23.4	86.1±12.7	*0.000
Serum bilirubin (mg/dl)	0.678±0.198	1.320±0.264	*0.000
Serum magnesium (mg/dl)	1.438±0.361	2.398±0.372	*0.000

Discussion :-

DM is a complex and multifactorial disease indulging severe insulin dysfunction in conjugation with gross abnormalities in glucose homeostasis, lipid and protein metabolism.

Many trace elements are important for human metabolic function. Numerous studies have demonstrated the essential roles of elements such as magnesium in carbohydrate metabolism.^[11]

In our study there were significantly decreased level of serum magnesium in cases (P=0.000). Similar results were obtained Lecube A[12] etal, Badyal A[13] etal, Chambers EC[14] etal Approximately one-third of subjects with T2DM have hypomagnesaemia mainly caused by enhanced renal excretion.^[15]

Rodriguez-Moran M. etal shows that, magnesium deficiency is associated with poor glycemic control and magnesium supplementation improves insulin sensitivity.^[16]

Magnesium can function as a mild natural calcium antagonist. Hence, the level of intracellular calcium is increased in magnesium deficiency subjects. This increased intracellular calcium may compromise the insulin responsiveness of adipocytes and skeletal muscles leading to the development of insulin deficiency or insulin resistance can affect the tubular absorption of magnesium, leading to hypomagnesaemia in DM subjects.^[17,18]

Corica F etal in their study showed that hypomagnesaemia is highly prevalent in diabetic patients.^[19]

Hypomagnesaemia may be a contributing factor for the long term complications particularly ischemic heart disease, retinopathy, foot ulcer and peripheral neuropathy, foot ulcer and peripheral neuropathy.^[20]

However recent studies, have suggested that, elevated serum total bilirubin may provide protection against stroke, CVD and peripheral vascular disease. Our study, showed significantly decreased levels of serum total bilirubin in T2DM as compared to healthy controls.^[21]

Bilirubin has been regard as a powerful endogenous antioxidant and effects on the vasculature and cytoprotective properties, it stands to reason that, higher total bilirubin levels may be protective against the autoimmune, inflammation related pathology, and oxidative physiological stress associated with development of T2DM.^[22]

Bilirubin acts as a cardioprotective agent by scavenging lipid peroxides and other products of physiological oxidation.^[23]

Current research also suggests that, physiological levels of bilirubin block the production of various free radicals that might hinder the inhibitory responses of the cell to take up the high glucose.^[24]

Conclusion:-

Thus, hypomagnesaemia is a factor in poor glycemic control. It may be advisable in clinical practice to periodically monitor serum magnesium concentration in T2DM. Estimation of antioxidant bilirubin is a less expensive tool, which helps clinicians in effectively controlling and preventing from this dreaded onset of complications in diabetes.

References :-

1. Treeprasertsuk, S., Lopez-Jimenez, F. and Lindor, K.D. (2011) Nonalcoholic Fatty Liver Disease and the Coronary Artery Disease. *Digestive Diseases and Sciences*, 56, 35-45.
2. Sicree R, Shaw J, Zimmet P. Diabetes and impaired glucose tolerance. In: Gan D, editor. *Diabetes Atlas*. International Diabetes Federation. 3rd ed. Belgium: International Diabetes Federation; 2006. p. 15-103.
3. Colin Dayan, Gareth Williams. Disorders of glucose homeostasis. In: David A. Warrell, Timothy M. Cox, Jhon D. Firth editors. *Oxford Textbook of Medicine*, 5th edition, New York, Oxford, 2010, pg. 2003.
4. Farid SM, Abulfaraj TG. Trace mineral status related to levels of glycated haemoglobin of type 2 diabetic subjects in Jeddah, Saudi Arabia. *Medical Journal of Islamic World Academy of Sciences*, 2013, 21(2), 47-56.
5. Xu J, Xu W, Yao H, Sun W, Zhou Q, et al., Associations of Serum and Urinary Magnesium with the Pre-Diabetes, Diabetes and Diabetic Complications in the Chinese Northeast Population, *PLoS ONE*, 2013, 8(2), e56750.
6. Seyoum B, Siraj ES, Saenz C, Abdulkadir J. Hypomagnesaemia in Ethiopians with diabetes mellitus. *Ethnicity & Disease*, 2008, 18, Spring.
7. WeFFI, Trapam V, Simonacci M, Ferre S, Maner JA Magnesium deficiency and endothelial dysfunction is oxidative stress involved? *Magnes Res* 2008;21:58-64.
8. Ho Chan Cho. The relationship among Homocysteine, Bilirubin and Diabetic retinopathy. *Diabetes metab J* 2011; 35: 595-601
9. SeungSeok Han, Ki Young Na, Dong- Wan Chae, Yon Su Kim, Suhnggwon Kim and Ho Jun Chin. High Serum Total Bilirubin Is Associated With The Reduced Risk Of Diabetes Mellitus & Diabetic Nephropathy. *Tohoku J. Exp. Med* 2010; 221:133-140.
10. Ndisang JF, Lane N, Jadhav A. Upregulation of the heme oxygenase system ameliorates postprandial and fasting hyperglycemia in type 2 diabetes. *Am J Physiol Endocrinol Metab* 2009;296(5):E1029-1041.
11. Masood Naila, Baloch Ghulam Hussain, Ghori Rafi Ahmed, Memon Iqbal Ahmed, Anwar Muhammad and Memon Muhammad Sadik. Serum Zinc and Magnesium in Type 2 Diabetic patients. *J Coll Physicians Surg Pak.*, 2009; 19(8), 483-486.
12. Lecube A, Baena-Fustegueras JA, Fort JM, Pelegrí D, Herná ndez C, et al., Diabetes Is the Main Factor Accounting for Hypomagnesaemia in Obese Subjects. *PLoS ONE*, 2012, 7(1), e30599.
13. Badyal A, Sodhi KS, Pandey R, Singh J. Serum Magnesium Levels: A Key Issue for Diabetes Mellitus. *JK SCIENCE*, 2011, Vol. 13(3).
14. Chambers EC, Heshka S, Gallagher D, Wang J, Pi-Sunyer FX, Pierson RN. Serum Magnesium and Type-2 Diabetes in African Americans and Hispanics: A New York Cohort. *Journal of the American College of Nutrition*, 2006; Vol. 25(6), 509-13.
15. Rude RK, Magnesium deficiency and diabetes mellitus Cases and effects, *Postgrad Med*, 1992;217-9,222.
16. Radriguez-Moran M. etal, Oral magnesium supplementation improves insulin sensitivity and metabolic control in T2diabetic subjects. A randomized double-blind controlled trial *Diabetics Care*; 2003;26:1147-52.
17. Altura BT, Altura BM, Endothelium dependent relaxation in coronary arteries requires magnesium ions, *Br J Pharmacol*, 1987,91:419-51.
18. Kim DJ, Xun P, Ltu K, Loria C, Jacobs DR, et al, Magnesium intake in relation to systematic inflammation insulin resistance and the incidence of diabetes , *Diabetes Care*, 2010;33:2604-10.
19. Corica F, Corsonello A, Lentile R, Cucinotta D, Di Benedetto A, Perticone F, et al. Serum ionized magnesium levels in relation to metabolic syndrome in type 2 diabetic patients. *Arch Intern Med*. 1996;156(11):1143-8.
20. Grafton G, Buneo CM, Sheoperd MC, Brown G, Baster MA, Effect of magnesium on sodium dependent Inositol transport. Role for magnesium in etiology of diabetic complications, *Diabetes*, 1992,413-9.
21. Cheriyath P, Gorrepati VS, Peters I, Nookala V, Murphy ME, SroujiN, Fischman D. High total bilirubin as a protective factor for diabetes mellitus: An analysis of NHANES data from 1999-2006. *J Clin Med Res* 2010;2: 201-206.
22. Donath MY, Storling J, Maedler K, Mandrup-Poulsen T. Inflammatory mediators and islet beta-cell failure: a link between type 1 and type 2 diabetes. *J Mol Med* 2003;81(8):455-470.

23. Schwertner, H.A., Jackson, W.G. and Tolan, G. (1994) Association of Low Serum Concentration of Bilirubin with Increased Risk of Coronary Artery Disease. *Clinical Chemistry*, 40, 18-23.
24. Chen YH, Chau LY, Chen JW, Lin SJ. Serum bilirubin and ferritin levels link heme oxygenase-1 gene promoter polymorphism and susceptibility to coronary artery disease in diabetic patients. *Diabetes Care* 2008;31(8):1615-1620.