ORIGINAL ARTICLE

EVALUATION OF ASSOCIATION OF SERUM MAGNESIUM WITH DYSLIPIDAEMIA IN DIABETIC NEPHROPATHY – A CASE CONTROL STUDY

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ABSTRACT

Aim: The objectives of this study were to estimate Serum magnesium and lipid profile in type II diabetes mellitus without complications, diabetic nephropathy & healthy controls. To correlate Serum magnesium and lipid profile in cases and controls.

Materials & Methods: The study was done on 50 clinically diagnosed diabetic nephropathy; 50 Type II diabetics without complications; and 50 age & sex matched healthy controls. Serum Magnesium, Fasting Blood sugar (FBS), lipid profile and spot urine microalbumin were estimated. Data obtained was analyzed for Mean, standard deviation, 'p' value and 'r' value.

Results: We observed highly significant decrease in magnesium (p <0.001) and dyslipidaemia in diabetic nephropathy compared to diabetics without complications and controls.

Conclusion: Hypomagnesaemia occurs in diabetics due to osmotic diuresis. Decreased Mg progresses the dyslipidaemia in Diabetic nephropathy leading to further complications like CRF & coronary artery diseases.

Keywords: Diabetic nephropathy, Dyslipidaemia, Magnesium

INTRODUCTION

The prevalence of diabetes is rising all over the world due to change in life style, obesity and physical inactivity. Unlike in the West, where older persons are most affected, diabetes in Asian countries is disproportionately high in young to middle-aged adults. This could have long-lasting adverse effects on a nation's health and economy, especially for developing countries. The International Diabetes Federation (IDF) estimated that total number of people in India with diabetes around 50.8 million in 2010, rising to 87.0 million by 2030. Approximately 285 million people worldwide (6.6%) in the 20–79 year age group had diabetes in 2010 and by 2030, 438 million people (7.8%) of the adult population, is expected to have diabetes [1]. Type II diabetes is the most common form of diabetes mellitus and the leading cause of morbidity and mortality. Diabetes is associated with microvascular and macrovascular complications, of which Diabetic nephropathy is the most common. Diabetic nephropathy is defined by increased urinary albumin excretion (UAE) in the absence of other renal diseases. Diabetic nephropathy is categorized into 2stages: microalbuminuria (UAE > 20 μg/min and < 199 μg/min) & macroalbuminuria (UAE >200μg/min) [2]. Hyperglycemia, increased blood pressure levels, and genetic predisposition are the main risk factors for the development of diabetic nephropathy. Elevated serum lipids, smoking habits and the amount and origin of dietary protein also seem to play a role as risk factors. In patients with type II diabetes, screening for microalbuminuria should be performed at diagnosis and yearly thereafter.

Magnesium (Mg) is an important intracellular cat ion that is distributed into three major compartments: mineral phase of bones (65%), intracellular space (34%) and extracellular fluid (1%) [3,4,5]. Magnesium serves as a cofactor for all enzymatic reactions that require ATP e.g-Kinases, activates neuromuscular excitability and cell permeability, regulates ion channels and mitochondrial function, and an important factor in both cellular and humaral immune reactions [6]. Intracellular Mg deficiency may affect the insulin sensitivity & further progresses development of insulin resistance [7,8]. Hypomagnesaemia may be directly related with some micro and macro vascular complications observed in diabetes, such as nephropathy, cardiovascular disease, retinopathy and neuropathy [8,9,10]. Magnesium depletion has atherogenic potential.

Insulin resistance has a central role in the development of diabetic dyslipidaemia and the main cause of the three cardinal features of diabetic dyslipidaemia is the increased free fatty-acid release from insulin resistant fat cells. The increased flux of free fatty acids into the liver in the presence of adequate glycogen stores promotes triglyceride production, which in turn stimulates the secretion of apolipoprotein B (ApoB) and VLDL cholesterol. The impaired ability of insulin to inhibit free fatty-acid release leads to enhanced hepatic VLDL cholesterol production, which correlates with the degree of hepatic fat accumulation [11]. Diabetic nephropathy has been reported to have significantly higher plasma concentrations of Very Low Density Lipoprotein (VLDL), Low Density Lipoprotein (LDL), Triglycerides (TG) and lower HDL. Dyslipidaemia influences on the formation of glomerular lesions, especially focal glomerular sclerosis and it is proposed that dyslipidemia may promote the progression of chronic renal disease and progression of diabetic nephropathy [12].

Magnesium play a role in the release of insulin. Magnesium supplementation may result in beneficial effect on the lipid profile of diabetic patients and also prevents its progression to complications[5]. So in view of all the above, the present study is undertaken to study the relationship between serum Magnesium and lipid profile in Healthy subjects, Type II Diabetes without complications and Diabetes with nephropathy patients. Objective was to estimate Serum magnesium and lipid profile in healthy subjects, type II diabetes mellitus without complications & diabetic nephropathy. To correlate Serum magnesium and lipid profile in cases and controls.

MATERIALS AND METHODS:

This case control study was conducted for a period of one year, on age matched 50 healthy subjects, 50 Type II diabetes mellitus without complications and 50 clinically diagnosed Diabetic nephropathy patients. Patients informed consent & Institutional Ethical clearance was obtained.

Sample Collection: Blood sample: 4 ml of overnight fasting venous blood was collected aseptically from antecubital vein for estimations. 1ml in fluoride containing tube & 3ml in plain tube. Serum was separated by centrifugation at 3000 rpm for 10 min and was stored at 4°C until analysis. Urine sample: Spot urine sample collected in sterile container.

Materials: The present study included 150 subjects both male and female with mean age 53 ± 10 years. Fifty were healthy controls, fifty were Type II diabetes (FBS > 126mg/dl, PPBS > 199mg/dl) [13] and fifty were diabetic nephropathy (Microalbuminuria +ve) subjects. Exclusion criteria includes age <30yrs & >60yrs, other diabetic complications, hypertension, liver diseases, gastroenteritis, lipid lowering drugs, diuretics and any other medications.

Methods: Estimations were done in Semiautoanalyser Erba Chem-7, Blood Glucose by GOD-POD method [14]. Serum Magnesium by Chlorophosphonazo-III method [15], Serum Total Cholesterol by CHOD-PAP method [16], Serum Triglycerides by GPO-PAP method [17], LDL was calculated by Friedwald's formula [18], Serum HDL by Immunoturbidimetric method [19], Spot urine Microalbumin by Immunoturbidimetric method [20]

Statistical Analysis

The results were expressed as mean ± standard deviation. ANOVAs test was used to compare mean values. Pearson's correlation coefficient for association between the parameters was done using the statistical package of social sciences (SPSS-17, Chicago, USA)

RESULTS

In our study we found statistically significant increased blood sugar ($p < 0.05$) in type II diabetes mellitus when compared with controls and highly significant increased blood sugar ($p < 0.001$) in diabetic nephropathy patients when compared with controls. Serum magnesium is significantly decreased ($p < 0.05$) in type II diabetes and highly significantly decreased ($p < 0.001$) in diabetic nephropathy patients when compared to controls.

Table-1: Mean and Standard deviation of various parameters in controls and cases

Parameters (mg/dl)	Controls	Diabetes Mellitus	Diabetic nephropathy
FBS	89 ± 14	144 ± 21*	236 ± 26**
PPBS	112 ± 18	196 ± 23*	318 ± 31**
Magnesium	2.34 ± .49	1.76 ± .34*	1.5 ± 0.30**
Urine Micr-oalbumin#	27.80 ±5.13	55.10 ±22.80*	86.14 ±54.8**
TC	157 ± 45	183 ± 56*	284 ± 81**
TG	107 ± 38	180 ± 90*	326 ± 140***
LDL	98 ± 18	170 ± 23*	181 ± 41**
HDL	47 ± 17	36 ± 10*	35 ± 16*

#μg/mg; Statistically significant *p<0.05, **p<0.001, ***p<0.0001

Table-2: Correlation between serum magnesium and Lipid profile

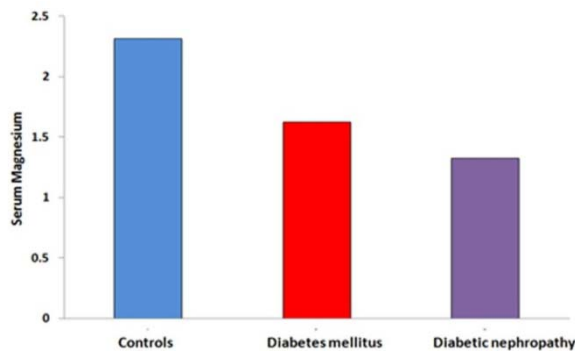|	TC	TG	LDL	HDL
Correlation coefficient	-0.704	-0.617	-0.51	+0.52
P value	< 0.001	< 0.0001	< 0.01	< 0.01
Significance	HS	HS	S	S

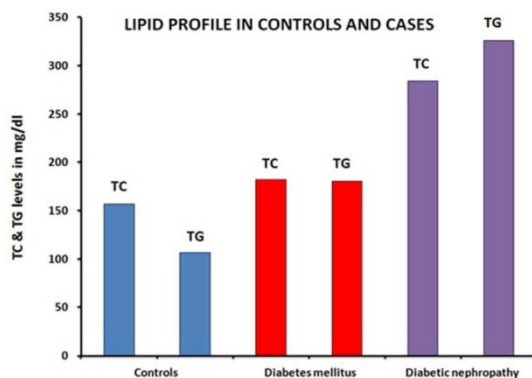**Fig 1: Serum Magnesium in Control and Casers**

Fig 2: Lipid Profile in case and control group

The table-I reveals mean ± SD of FBS (236±26), PPBS (318±31), Microalbumin (86.14 ± 54.8), serum Magnesium (1.5 ± 0.30), TC (284±81), TG (326±140), LDL (181±41), HDL (35±16) differ significantly ($p < 0.001$) in Diabetic nephropathy compared to Type II Diabetes and healthy controls (Figure 1 & Fig 2).

In this study table-2 shows highly significant inverse (negative) correlation of serum Mg with Total cholesterol ($p < 0.001$) ($r = - 0.704$) and Triglycerides ($p < 0.0001$) ($r = - 0.617$) and significant negative correlation ($p < 0.01$) with LDL & significant positive correlation with HDL were found in Diabetic nephropathy patients.

DISCUSSION

This work was done to study the association or relation of serum magnesium with lipid profile and lipid indices in Diabetic nephropathy. In our present study the serum values of Magnesium, lipid profile and indices showed statistically significant difference when compared in healthy subjects, Type II Diabetes & Diabetic nephropathy. The principle findings of the present study were significant negative correlation of serum Mg with serum cholesterol and Triglycerides & also non significant correlation of serum Mg with LDL & HDL were observed.

Microalbuminuria is mild elevated levels of albumin in urine. The increased level of albumin in urine is proportional to the duration of hyperglycemia which results to nephropathy. Microalbuminuria is strongly associated with vascular disease suggesting it as a marker of vascular or endothelial damage [21,22,23].

Magnesium is necessary for several enzymes that play an important role in glucose metabolism. The hypomagnesaemia in diabetic nephropathy due to Poor dietary intake, impaired absorption of magnesium, increased urinary loss due to hyperglycemia, osmotic diuresis, defective Mg reabsorption from renal tubules and loss of plasma protein bound Mg. Magnesium depletion is said to reduce the insulin sensitivity, thereby increasing the risk of secondary complications. Hyperglycemia leads to decreased cellular Mg levels. Hypomagnesaemia leads to collagen and ADP-induced platelet agreeability and also decreased function of Mg dependent enzymes, kinases and oxidative stress [23,24].

Magnesium deficiency also has a role in the perturbation of lipid metabolism of diabetic patients. Hypomagnesaemia inhibits prostacyclin receptor function, producing an imbalance between prostacyclin and thromboxane effects. Hypomagnesaemia can increase platelet reactivity, increase vascu-

lar and adrenal responses to angiotensin II, enhance thromboxane A2 (TXA2) release, and lead to organ damage from free radicals [4,5].

Hypomagnesaemia causes dyslipidaemia by decreasing activity of lipoprotein lipase, LCAT and increasing HMG COA reductase enzyme. The lipid changes are attributed to increased Free Fatty Acids flux secondary to insulin resistance [11]. The characteristic features of diabetic nephropathy are high TC, TG, LDL and low HDL levels. Dyslipidaemia has significant deleterious role in the initiation and progression of renal injury by causing microvascular damage leading to glomerulosclerosis and tubulointerstitial damage in Diabetic nephropathy and also for CVD [12,24].

Like other studies [4,5,6,26] it observed significant low serum Magnesium levels and Dyslipidaemia in diabetic nephropathy compared to Type II Diabetes mellitus without complications and healthy subjects.

CONCLUSION

Hypomagnesaemia in type II diabetes causes dyslipidaemia which leads to atherogenesis and diabetic complications like Diabetic nephropathy, so regular monitoring of serum magnesium and lipid profile along with Mg supplementation in Type II Diabetes mellitus may prevent its progression to further complications like nephropathy. Evaluation of serum Mg should be included in routine testing.

REFERENCES

1. Ramachandran A, AK Das, SR Joshi, CS Yajinik, S Shah, KM Prasanna Kumar. Current status of Diabetes in India and Need for Novel Therapeutic Agents. JAPI 2010; 58 (3): 1-7.

2. Jorge L. Gross, Mirela J, Sandra P. et al. Diabetic Nephropathy:Diagnosis, prevention and treatment. Diabetes care 2005; 28 (1): 176-188.

3. Sasmita Mishra, P. Padmanaban, G.N. Deepti, G.Sarkar, S. Sumathi, B.D. Toora. Serum Magnesium and Dyslipidemia in Type-2 Diabetes Mellitus. Biomedical Research 2012; 23 (2): 295-300.

4. Hamid Nasri, Hamid-Reza Baradaran. Lipids in association with serum magnesium in diabetes mellitus patients. Bratisl Lek Listy 2008; 109(7): 302-306.

5. Hamid Nasri. Lipids in association with serum magnesium in diabetes mellitus patients. Acta Angiol 2006 ; 12(4): 149–154.

6. Phuong-Chi T. Pham, Phuong-Mai T. Pham, Son V. Pham, Jeffery M. Miller and Phuong-Thu T. Pham. Hypomagnesemia in Patients with Type 2 Diabetes. Clinical journal of the American Society of Nephrology 2007; 2: 366-373.

7. Kenji Ueshima. Magnesium and ischemic heart disease: a review of epidemiological, experimental, and clinical evidences. Magnesium Research 2005; 18(4): 275-284.

8. Rasic-Milutinovic Z, Perunicic-Pekovic G, Pljexa S, Dangic A, Libek V, Bokan Lj, Cankovic-Kadijevic M. Magnesium deficiency in type 2 diabetes. Hippokratia 2004; 8 (4): 179-181.

9. Cristiane Hermes Sales, Lucia de Fatima Campos Pedrosa. Magnesium and diabetes mellitus: Their relation. Clinical Nutrition 2006; 25: 554–562

10. Monika K. Wältia, Michael B. Zimmermanna, Giatgen A. Spinasb, Richard F. Hurrel. Low plasma magnesium in type 2 diabetes. Swiss Med Wkly 2003; 133: 289 – 292.

11. Arshag D Mooradian. Dyslipidemia in type 2 diabetes mellitus. Nature Clinical Practice Endocrinology & Metabolism 2009; 5: 150-159.

12. Fauci, Kasper, Hauser, Longo, Loscalzo and Jameson et al. Harrison`s Principles of internal medicine. 18th edition; Mc Graw Hill medical publishing division; 2012: 508-513.

13. Kaplan L. A, Pesce A. J. Carbohydrates and Metabolite, In Clinical Chemistry: Theory, Analysis and Co-relation. 1984: 1032-1040.

14. Tietz, N.W. Fundamentals of Clinical Chemistry, W. B. Saunders Co., Philidelphia 1976: 919-920.

15. Allain C. C, Poon L.S, Chan C.S.G, Richmond W and Fu P. Clinical Chemistry 1974; 20: 470-471.

16. McGowan MW, et al. Clinical Chemistry 1983; 29: 538 - 539.

17. Rifal, N. and Warnick, G.R.Ed. Laboratory Measurement of lipids, lipoproteins and apolipoproteins. AACC Press, Washington, DC, USA 1994.

18. Schmidtz, A., et al. Diabetic Medicine 1988;5 (126): 112-117

19. Haeckel, R. et al. Clinical Chemistry 1981; 27(1): 179-183.

20. Tiffany, T.O. Jansen J, Burtis C. A, Scott C. D. Clinical Chemistry 1972; 18: 829-830.

21. Bonnet. F, Cooper. M. E. Potential influence of lipids in diabetic nephropathy: insights from experimental data and clinical studies. Diabetes & Metabolism 2000; 26: 254-264.

22. Vasudevan , Sreekumari, Kannan Vaidyanathan. Textbook of Biochemistry for Medical Students, 6th edition 2011: 292-296. .`

23. Farah Aziz Khan, Mohd. Fareed Khan, et al. Estimation of serum copper and magnesium levels in diabetic nephropathy patients. Asian Journal of Biological and Life Sciences 2013; 2 (1): 23-26.

24. Vamsi Krishna Chittimoju and Sujatha Pasula. Study of serum magnesium, HBA1C and Microalbuminuria in diabetic retinopathy. International Journal of Pharma and Bio Siences 2013; 4(3): 501-509.

25. Ismail M, Yosif Kh, Kamil M et al. Micro Albuminuria and Hyper Lipidemia in long standing Diabetes Mellitus. ARPN Journal of Science and Technology 2013; 3 (6): 574-577

26. Jha P, Das BKL, Shrestha S, et al. Glycemic status lipid profile and proteinuria in Diabetic Nephropathy. Journal Nepal Med Assoc 2010; 49 (178): 143-146.