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Original Research Article

Serum Magnesium: A Novel predictor of diabetic nephropathy

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Abstract: Type 2 diabetes accounts for approximately 90 to 95% of all diagnosed cases of diabetes. Multi-system effects of diabetes mellitus such as retinopathy, nephropathy, neuropathy and cardiovascular diseases are important public health concerns. The Objective is to estimate level of serum magnesium in the development and progression of DM Type 2 and its complications. In Methodology retrospective study includes total 150 participants among them 50 patients are of Diabetic nephropathy (Complicated diabetic patients), 100 uncomplicated diabetics' patients and 100 age and sex matched healthy control. Fasting and post-prandial blood samples were collected from all participants for estimation of FBS, PPBS, Blood urea, serum creatinine, and HbA1C and serum magnesium. Urine sample was also analyzed for proper identification of diabetic nephropathy patients. In Results the Hypomagnesaemia is found in diabetic nephropathy patients when compared to uncomplicated diabetic patients. In Conclusion this study concluded that low serum magnesium plays a major role in the development and progression of DM Type 2 and its complications.
Keywords: Type 2 DM, Diabetic Nephropathy, Micro vascular changes, Serum Magnesium

INTRODUCTION

Diabetes mellitus is a metabolic disease which is caused by absolute or relative insulin deficiency. About 10% of the Indian population suffers from this disease. Various factors play a role in the aetiopathogenesis and in the glycaemic control among the type 2 diabetic patients [1]. The chronic hyperglycemic condition is associated with long term damage, dysfunction and failure of various organs especially eyes, kidneys, nerves, heart and blood vessels. Complications of diabetes mellitus include acute complications that are generally a reflection of altered energy homeostasis either from hyperglycemia (diabetic ketoacidosis and non-ketotic hyper osmolar syndrome) or hypoglycemia and chronic microvascular complications consisting of retinopathy, nephropathy, neuropathy and angiopathy[5]. Diabetic Nephropathy, also known as Kimmelstiel Wilson Syndrome or nodular diabetic glomerulosclerosis is a progressive kidney disease caused by angiopathy of capillaries in the kidney glomeruli. It is characterized by nephrotic syndrome and diffuse glomerulosclerosis. It is due to longstanding diabetes mellitus [6]. Low serum Magnesium (Mg) have been reported in individuals with poor glycemic control, coronary artery disease, hypertension, diabetic retinopathy, nephropathy and neuropathy [7].

MATERIAL AND METHODS

This Retrospective study was conducted at Geetanjali Medical college and Hospital, Udaipur, Rajasthan from 2011-2012 .This study Includes 100 healthy controls, 100 uncomplicated diabetic subjects and 50 patients with diabetic nephropathy.

Fasting and post prandial Blood sample as well as urine sample was collected from all the subjects in the collection room of clinical Central Laboratory of Geetanjali Medical College and Hospital, Udaipur. Blood sample was investigated for various parameters like Fasting Blood Sugar, Post Prandial Blood Sugar, HbA_1C, Urea, Creatinine and Magnesium after the separation of serum.

Blood sugar, HbA_1C, Urea and Creatinine were estimated on fully automated biochemistry analyser Roche Cobas C 311 while magnesium was estimated by Erba Chem 5 plus V2 semi autoanalyser. Following methods were employed for different parameters:-

1. Fasting and Post prandial Blood Sugar – Glucose oxidase peroxidase Method
2. HbA_1C - Turbidimetric Inhibition Immunoassay Method

3. Blood Urea- Urease Enzymatic Method
4. Serum Creatinine - Jaffe's Method
5. Serum Magnesium- Calmagite Method

Urine sample was analysed for sugar and protein using Chemistrix- AGpH multi-reagent strips (Biolab Diagnostics). The results were recorded according to the colour chart provided by the manufacturer.

RESULTS

Mean values of FBS, PPBS, HbA_1C, Blood Urea and Serum Creatinine for control, uncomplicated diabetics and diabetic nephropathy were as follows-

Table 1: Various biochemical parameter level in Control, Uncomplicated Diabetics and Diabetic Nephropathy

Parameters	Control (N=100)	Uncomplicated Diabetics (N=100)	Diabetic Nephropathy (N=50)
Fasting Blood Sugar (mg/dl)	95±12	170.88±77.8	173.3±65.8
Post Prandial Blood Sugar(mg/dl)	115±9.95	196.07±77.89	201±66.01
HbA1c (%)	5.59±0.37	7.80±2.12	8.51±1.93
Blood Urea (mg/dl)	26.01±9.19	32.29±12.35	84.28±58.13
Serum Creatinine (mg/dl)	0.815±0.15	1.69±0.56	3.06±3.48

The mean values of FBS, PPBS, HbA_1c, Blood Urea and Serum Creatinine of control group when compared to uncomplicated diabetic group were found to be much significantly higher in uncomplicated diabetic group($p< 0.1$ and 0.001).

The mean values of all above parameters were also found to be significantly higher in diabetic nephropathy groups when compared to uncomplicated diabetics ($p<0.01$, 0.001 and 0.0001). But a highly significant relation was found when the values of diabetic nephropathy group were compared against controls ($p<0.001$ and 0.0001).

Table 2: Showing t -values and p- values of different biochemical parameters in different groups

Parameters	t- value	p-value
Fasting Blood Sugar	9.595 [a] 11.521 [b] 0.188 [c]	<0.001 [a] <0.01 [b] <0.01 [c]
Post Prandial Blood Sugar	10.372 [a] 12.83 [b] 0.383 [c]	<0.001 [a] <0.001 [b] <0.001 [c]
HbA_1c	10.257 [a] 14.56 [b] 1.976 [c]	<0.001 [a] <0.0001 [b] <0.01 [c]
Blood Urea	4.119 [a] 9.812 [b] 8.579 [c]	<0.001 [a] <0.001 [b] <0.001 [c]
Serum Creatinine	1.055 [a] 6.463 [b] 6.353 [c]	<0.01 [a] <0.001 [b] <0.0001 [c]

a= control v/s Uncomplicated Diabetics
b= Control v/s Diabetic Nephropathy
c= Uncomplicated Diabetics v/s Diabetic Nephropathy

- The mean concentration of Serum magnesium in controls was 2.13 ±0.31 mEq/L, in uncomplicated diabetes was 1.69±0.56 mEq/L while in diabetic nephropathy was 1.50±0.55 mEq/L.
- Table 3 shows that serum magnesium values were lowest in Diabetic Nephropathy when compared to rest of the two groups.
- Serum Magnesium values in uncomplicated diabetic subjects were lowers when compared

to controls but higher than those of diabetic nephropathy subjects.

- 26% of uncomplicated diabetic subjects were recorded for low serum magnesium levels (<1.3 mEq/L) i.e. Hypomagnesemia, while 40% of diabetic nephropathy subjects had hypomagnesemia.

Table 3 also shows that uncomplicated diabetic patients have hypomagnesemia ($p<0.001$) when compared.

Table 3: Showing Serum magnesium level in different group

Parameters	**Control (N=100)**	**Uncomplicated Diabetics (N=100)**	**Diabetic Nephropathy (N=50)**
Serum magnesium(mEq/L)	2.13 ±0.31	1.69 ± 0.56	1.50 ± 0.55
t-value	6.866 [a]	8.923 [b]	1.986 [c]
p-value	<0.001 [a]	< 0.001 [b]	< 0.01 [c]

Table 4: Urine examination of Diabetic patients

Concentration	Uncomplicated Diabetics (N=100)		Diabetic Nephropathy (N=50)	
	Urine Sugar	Urine Protein	Urine Sugar	Urine Protein
Nil	58%	74%	38%	6%
Trace	3%	11%	12%	6%
Sugar=250 to 1000 mg/dL Protein=30to 300 mg/dL	39	15	48%	88%
Sugar>2000 mg/dL Protein > 2000 mg/dL	0%	0%	2%	0%

- Table 4 shows that 39% of uncomplicated diabetic subjects had glucosurea (sugar concentration between 250 to 1000 mg/dL) while 48% diabetic nephropathy patients showed the same.
- Microalbuminuria (albumin concentration 30 to 300 mg/dL) was found in 15% uncomplicated diabetic subjects while 88% diabetic nephropathy subjects had microalbuminuria.
- Urine sugar > 2000 mg/dL was found only in 2% of diabetic nephropathy patients.

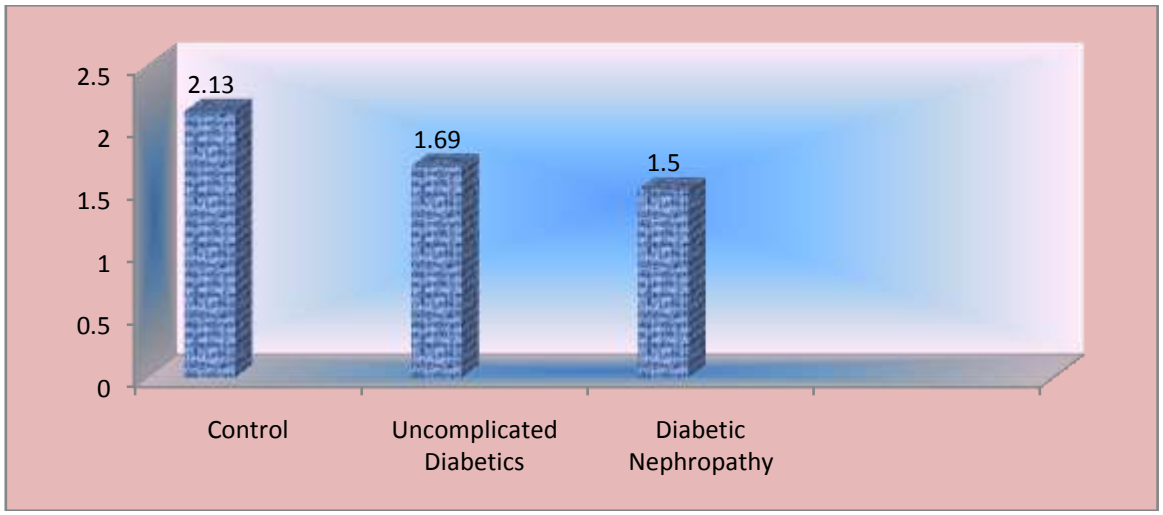

Fig 1: Showing Serum Magnesium (mEq/L) level in different groups

DISCUSSION

The observations in the present study revealed a definite lowering of serum magnesium in uncomplicated diabetic patients and more over patients who had diabetic nephropathy were found to have lowest concentration of serum magnesium. These observations are similar to many other workers [9]. Consequently it is suggested that hypomagnesemia as a possible risk factor in the development and progression of diabetic nephropathy.

The present study also shows a strong association between hypomagnesemia and diabetes. Many previous studies have also supported this fact [10].

The exact cause of diabetic hypomagnesemia is still unknown but it may result from poor oral intake, poor gastrointestinal absorption and enhanced renal magnesium excretion. Diabetic autonomic neuropathies that may reduce oral intake and gastrointestinal absorption include esophageal dysfunction, gastro paresis, and diarrhea [11]. In patients with diabetes, the ultra filterable magnesium load may be enhanced by glomerular hyperfilteration, recurrent excessive volume repletion after hyperglycemia induced osmotic diuresis, recurrent metabolic acidosis associated with diabetic ketoacidosis and hypoalbuminemia. The last two conditions may increase the serum ionized magnesium fraction and hence ultra filterable magnesium load and subsequent urinary loss.

It is also proposed that under the shadow of hypomagnesemia there is excessive production of reactive oxygen species and reactive nitrogen species which is reflected by elevated lipid peroxides and nitric oxide end products concomitant with dwindled antioxidants and suggest their association with late complications in Type 2 diabetes mellitus (nephropathy, retinopathy and neuropathy) [12].

Many studies have shown that lower serum magnesium concentration is associated with faster renal function deterioration in DM 2 patients [13]. The exact reason of the impact of hypomagnesemia on diabetic nephropathy is not well understood but it is believed that magnesium deficiency may promote the development of diabetic nephropathy via cell membrane transport disruption and subsequent intracellular depletion of myo-inositol [14]. In addition it is also conceivable that significant microalbuminuria and overt proteinuria among patients with diabetic nephropathy may contribute to renal magnesium wasting as a result of protein bound magnesium loss. Therefore, it is plausible that magnesium deficiency has specific pathogenic significance in type 2 diabetic nephropathy; however the exact role of magnesium deficiency in type 2 diabetic nephropathy warrants further investigation.

Many workers also have documented that the oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetics with decreased serum magnesium levels [15] and have also shown that it has beneficial effect on delaying diabetes and its late complications [16, 17]. Hence further studies on oral magnesium supplementation to prevent late complications of diabetes will be interesting and helpful.

In our study it was found that 88% of diabetic nephropathy subjects had microalbuminuria while 15% of uncomplicated diabetic subjects had the same. Thus these results also validate microalbuminuria as sensitive predictor of kidney damage in DM type 2.

CONCLUSION

The study successfully revealed that hypomagnesaemia has a principal role in the development of diabetes mellitus type 2. Moreover, hypomagnesaemia has a key participation in enrooting diabetic nephropathy. Thus, timeouts estimation of serum magnesium would definitely be helpful for proper estimation and treatment of diabetic nephropathy.

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