



Study of Serum Magnesium in Diabetes Mellitus and Correlation with its Microvascular Complications

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Abstract

Aim: The prevalence of diabetes mellitus is on a rising trend. Hypomagnesemia has been reported to occur with increased frequency in patients with type 2 diabetes mellitus. It is frequently overlooked and under treated. We aim to study serum magnesium in diabetes mellitus and correlation with its microvascular complications.

Materials and Methods: This is a hospital based prospective study. 100 patients with diabetes mellitus were included in this study. The study was done with objective of assessing serum magnesium in diabetic patients and its correlation with microvascular complications such as diabetic retinopathy, nephropathy and neuropathy.

Results: Mean age group of our patient was 58.28±8.35 years. Of the 100 total patients, 40 patients had hypomagnesemia. Maximum number of patients occurred in the age group 55–65 years (42.5%). 35 patients had diabetic retinopathy. Among them 27 (75.86%) patients, had hypomagnesemia. 14 patients had diabetic nephropathy, out of this 13 (92.86%) patients had hypomagnesemia. 4 patients had diabetic neuropathy, among them all (100%) had hypomagnesemia.

Conclusion: Low serum magnesium levels are commonly seen in diabetic patients. Hypomagnesemia patients had a higher incidence of retinopathy, nephropathy and neuropathy.

Keywords: Diabetes mellitus, serum magnesium.

Introduction

Diabetic mellitus is a renowned epidemic in the world with nearly 70% of the people with diabetes live in developing countries. The largest numbers are in the Indian subcontinent (65% million) and China. Rates of non communicable diseases like diabetes mellitus have risen in the recent decades and are likely to continue as India's population

ages and urbanises. The largest numbers with diabetes are in the 40 to 59 age group (132 million in 2010) which is expected to rise further. The prevalence of diabetes has risen from 30 million in 1985 to 382 million in 2013. It is estimated that prevalence may rise to 592 million by the year 2035 according to current trends^[1].

Diabetes mellitus affects multiple organ systems and is a cause or a major risk factor for the majority of the dreadful diseases. Chronic complications of diabetes mellitus are divided as vascular and non-vascular complications. Among vascular complications, micro vascular complications are diabetic specific.

Magnesium is the fourth most abundant cation in the human body and second most abundant intracellular cation^[2]. It plays an important role in the carbohydrate metabolism. It serves as a cofactor for all enzymatic reactions that require kinases^[3]. It is a critical element in cellular proliferation and apoptosis and an important cofactor in both cellular and humoral functions^[4].

Hypomagnesaemia has been reported to occur with increased frequency in patients with type 2 diabetes mellitus, but it is frequently overlooked and under treated^[5].

The present study was conducted with an objective to evaluate the serum magnesium in diabetes mellitus and correlation with its micro vascular complication such as Diabetic retinopathy, nephropathy and also neuropathy. With a special interest we included the correlation of HbA1c and its correlation with hypomagnesaemia also in the same study population.

Materials and Methods

100 patients with diabetes mellitus, irrespective of the age and sex, who were admitted in general medicine ward, were randomly selected based on the following inclusion and exclusion criteria.

Inclusion Criteria

Patients who gets admitted in general medical ward with Diabetes Mellitus based on history or medical records.

Exclusion Criteria

1. Chronic diarrhoea (Loose stools more than 4 weeks)
2. Patients with chronic renal failure (based on GFR)
3. Patients on diuretic therapy for more than one month.
4. Patients with history of alcohol abuse as reported by patient or care taker.

From all the patients, detailed history, including the duration and treatment along with clinical examination was carried out. All the findings were recorded in the proforma. Fasting blood sugar, post prandial blood sugar, HbA1c, direct ophthalmoscopy, 24hour urine albumin were measured for all the subjects.

Results

Statistical method analysis was done using chi square test and sample variable t test to compare proportions. Results were considered significant at p value <0.05.

Table: 1 a -Age Distribution and Magnesium Levels

Age (in years)	Percentage	Mean	S.D
45 - 55	41	58.28	8.35
56 - 65	40		
66 - 75	15		
> 75	4		
Total	100		

Table 1-b

Age Group (in year)	Hypomagneseia		Normomagnesemia		Total
	N	%	N	%	%
45 - 55	9	22.5	32	53.3	41
56 - 65	17	42.5	23	38.3	40
66 - 75	10	25.0	5	8.3	15
>75	4	10.0	-	-	14
Total	40	100	60	100	100
Chi-square value	16.11				
Df	1				
'P' value	.001 (Significant)				

The mean age of the study patients was 58.28±8.35 years. In our study maximum number of hypomagnesemia patients occurred in the age group 56 - 65 years (42.5%). All patients who

were more than 75 years old had hypomagnesemia (100%). The chi-square test of association is significant ($\chi^2 = 16.11$, $p = .001$) for age distribution and magnesium levels

Table: 1c Age Distribution

Parameters	Hypomagnesemia	Normomagnesemia	Total
Mean	62.20	55.67	58.28
S.D	9.29	6.52	8.35
't' value	4.13		
Df	98		
'P' value	.001 (Significant)		

The Mean age of patients with hypomagnesemia was 62.20±9.29 years and it was 55.67±6.52 years for Normomagnesemia. There is significant

difference in the age between two categories of magnesium levels, calculated by independent sample 't' test ($t = 4.13$, $P = .001$).

Chart -1: Age Distribution

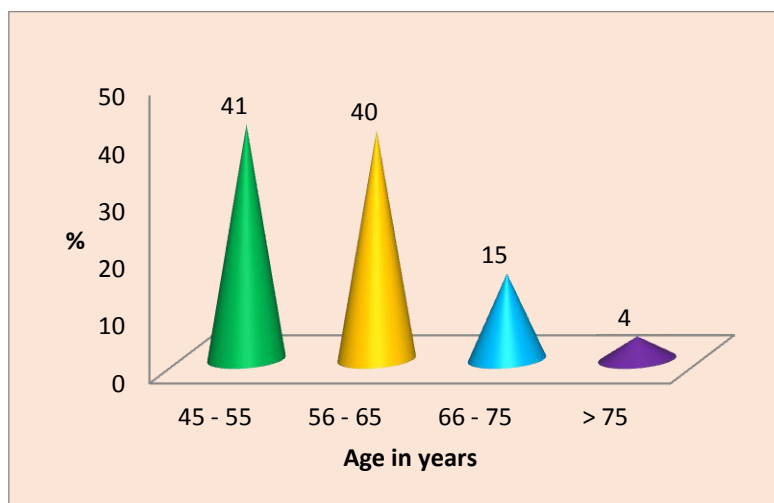


Chart -2: Age Distribution with Hypomagnesemia and Normomagnesemia

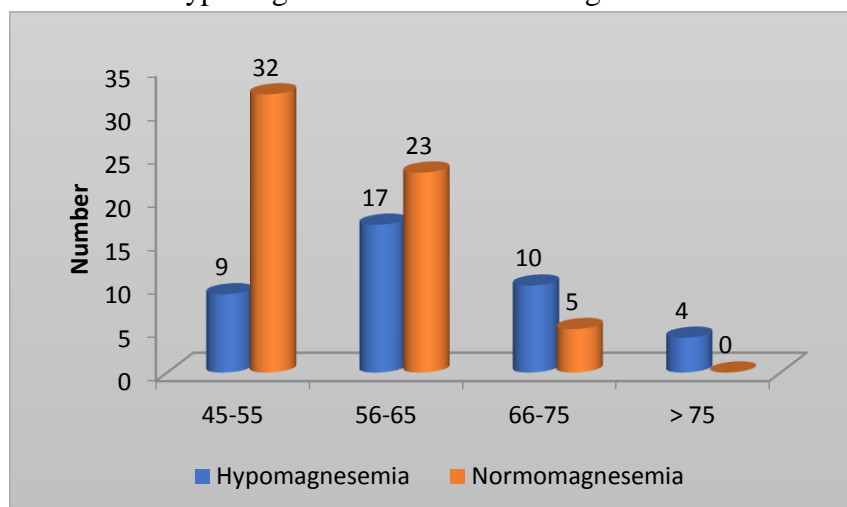


Chart - 3: Prevalence of Hypomagnesemia

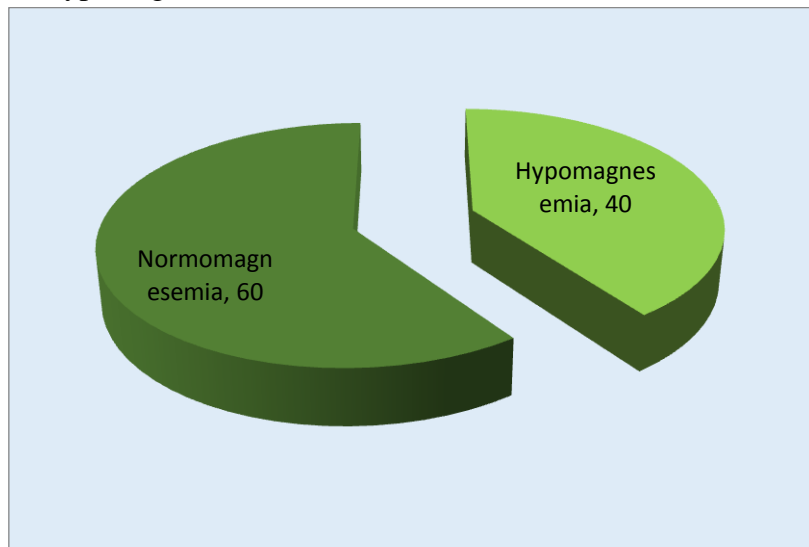


Table: 2a Prevalence of Hypomagnesemia and Neuropathy

	No. of Patients	Patients with Hypomagnesemia	Prevalence
Neuropathy	4	4	100
No Neuropathy	96	36	37.5

Chart - 4: Prevalence of Hypomagnesemia and Neuropathy

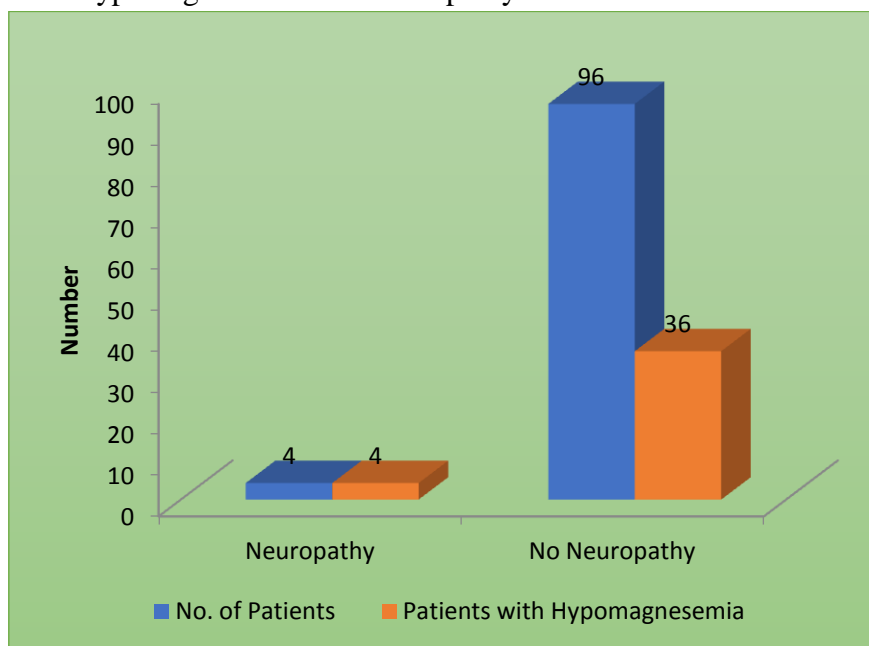


Table 2 b

Neuropathy	Hypo magnesemia		Normo magnesemia		Total
	N	%	N	%	%
Present	4	10	-	-	4
Absent	36	90	60	100	96
Total	40	100	60	100	100
Chi-square value			6.25		
Df			1		
'P' value			.012 (significant)		

The prevalence of hypomagnesemia in patients with neuropathy is 100%. The chi-square test of association is significant ($\chi^2 - 6.25, p = 0.012$).

Table: 3 a -Hypomagnesemia and Diabetic Retinopathy

Retinopathy	No. of Patients	Patients with Hypo magnesemia	Prevalence
NPDR	29	22	75.86
PDR	6	5	83.33
NO Retinopathy	65	13	20

Chart - 5: Hypomagnesemia and Diabetic Retinopathy

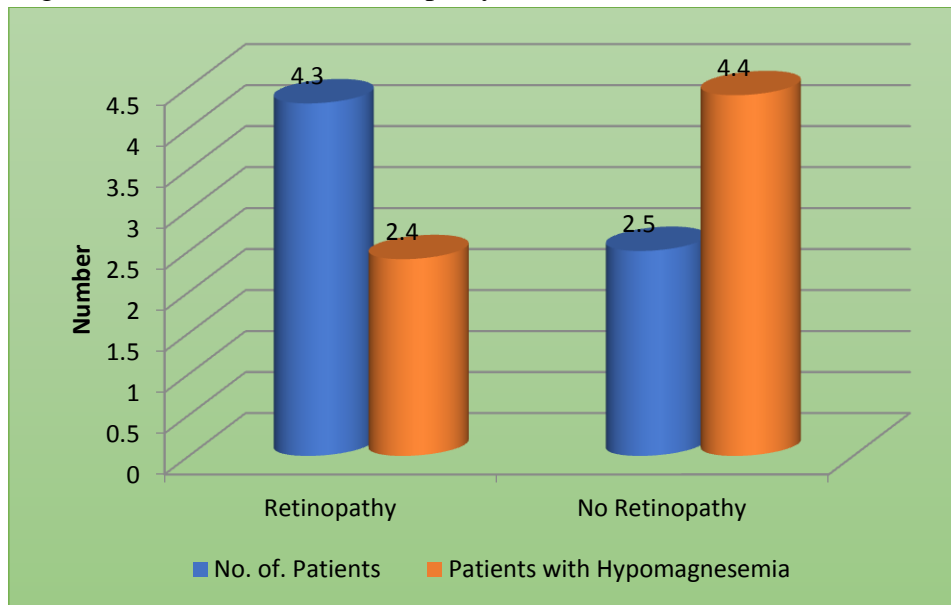


Table 3b

Retinopathy	Hypomagnesemia		Normomagnesemia		Total
	N	%	N	%	%
Present	27	67.5	8	13.3	35
Absent	13	32.5	52	86.7	65
Total	40	100	60	100	100
Chi-square value	30.95				
Df	1				
'P' value	.001 (significant)				

It is inferred from the above table that the hypomagnesemia was observed in 77.14% of patients with retinopathy. The chi-square test of association is statistically significant ($\chi^2 = 30.95$, $p = .001$).

Observations revealed that out of 100 diabetic patients 35 patients had retinopathy. Among these

individuals 27 persons had Low serum magnesium level. Rest of the individuals with retinopathy had normal serum magnesium level using the statistical analysis by chi-square test the association between the presence of Hypomagnesemia with Retinopathy in diabetic patients was found to be significant ($p = 0.001$).

Table: 4a- Hypomagnesemia and Diabetic Nephropathy

Diabetic Nephropathy	No. of patient	Patients with Hypomagnesemia	Prevalence (%)
Nephropathy			
Micro Albuminuria	5	13	92.86
Macro Albuminuria	9		
No Nephropathy	86	27	31.39

Chart - 6: Hypomagnesemia and Diabetic Nephropathy

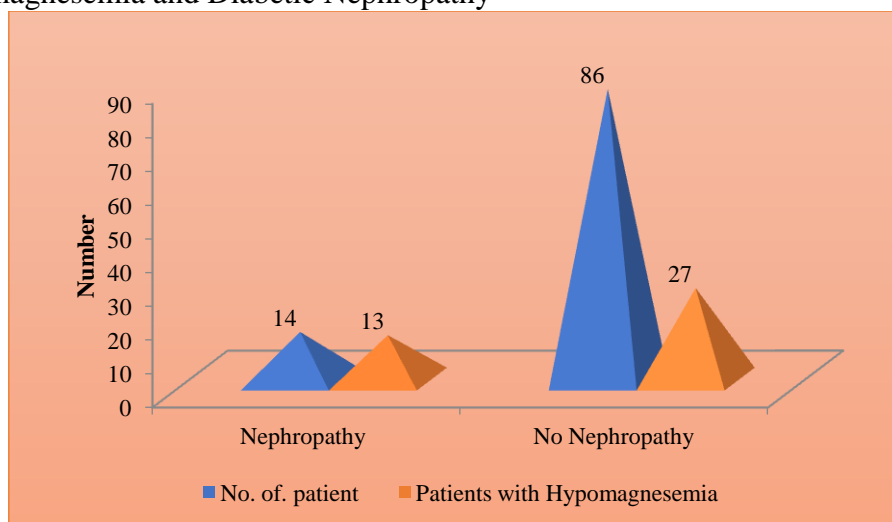


Table 4 b

Diabetic Nephropathy	Hypomagnesemia		Normomagnesemia		Total
	N	%	N	%	
Present	13	32.5	1	1.7	14
Absent	27	67.5	59	98.3	86
Total	40	100	60	100	100
Chi-square value			18.95		
Df			1		
P' value			.001 (significant)		

In our study out of 100 diabetic patients 14 patients had the evidence of nephropathy (14%) out of these diabetic nephropathy patients 13 patients were low serum magnesium level. Presence of normal serum magnesium level

in diabetic nephropathy in our study was low (1.72%). Thus the association between the hypomagnesemia and nephropathy in diabetic patient was found to be statistically significant with the P value of 0.001.

Table: 5a- Prevalence of Hypomagnesemia and HbA1C %

HbA1C (%)	No. of Patient	Patients with Hypo magnesemia	Prevalence
< 6	37	-	-
6 - 7	29	10	34.48
7 - 8	17	16	94.11
8 - 9	13	10	76.92
9 - 10	4	4	100.00

Chart - 7: Prevalence of Hypomagnesemia and HbA1C %

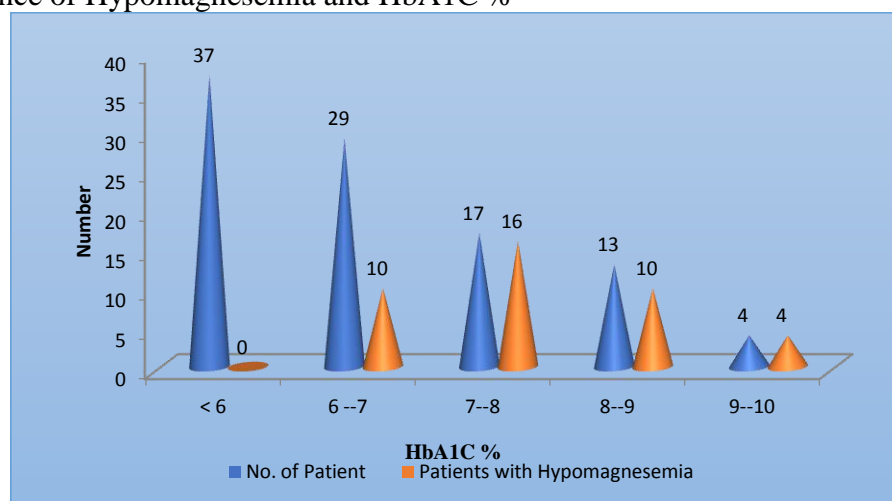


Table 5b

	Hypo magnesemia	Normo magnesemia	Total
Mean	7.74	5.98	6.69
S.D	.86	.62	1.13
't' value		11.93	
Df		98	
'P' value		.001 (Significant)	

The prevalence of hypomagnesimias is higher when HbA1C is more 2 vice versa as shown in table 7. The Mean HbA1C was higher in hypomagnesemia (M = 7.74 ±.86) than in normomagnesemia (M=5.98±.62). The difference is statistically significant (t = 11.93, p = .001). In our study Around 34 patient had, poor glycemic control as evidenced by HbA1C > 7%.

Discussion

Many studies have proven beyond doubt the association between the presence of hypomagnesemia and diabetes mellitus; it has also been proven that hypomagnesemia has been associated with increased incidence of complications in diabetics; hence I found it worthy to take up this study in our settings.

Diabetes & Hypomagnesemia

Previous studies by Rude RK⁶ have reported low serum magnesium status in patients with type 2 DM. The reported prevalence of hypomagnesemia ranged from 13.5% to 47.7% in type 2 DM patients according to Pham PC, Pham PM, Miller JM et al⁷. In our study there were a total of 100 diabetic patients; among them 40 patients had serum Mg below the reference range;. Prevalence of hypomagnesemia in type 2 diabetes mellitus according to our study was similar to that reported by Nadler et al⁸. Walti mk et al⁹ reported that prevalence of hypomagnesemia in type 2 diabetes at 37.6% versus 10.9% in non diabetic controls in a study conducted in, Switzerland; this too is in concordance with our study results;

The causes for the high prevalence of hypomagnesemia in diabetes may be due to increased urinary loss, low dietary intake or impaired magnesium absorption compared to healthy individuals; Mc Nair P, Christiansen MS et al¹⁰ in

their study found excessive urinary magnesium loss in diabetes. Recently defective tubular reabsorption in thick ascending loop of henle is postulated, that results in hypomagnesemia. The reason for the tubular defect is unclear. In diabetes low serum magnesium status due to low dietary intake is unlikely. Only 5.4% of the diabetic groups and 9.1% of the control group in European dietary assessment studies by Walti MK Zimmermann et al¹¹ had intake of magnesium below their individual requirements. In addition type 2diabetes patients with reasonable metabolic control absorb dietary magnesium to a similar extent as healthy controls. In diabetes hyperglycemia and osmotic diuresis may cause excessive urinary loss of magnesium and leads to low serum magnesium status.

Age in Diabetics & Hypomagnesemia

In our study maximum number of diabetics occurred in the age group 45-55 yrs (41 patients); mean age of diabetic patients in our study was 58.28 ; hypomagnesemia occurred maximally in the age group 56-65yrs (42.5%); all patients who were > 70 years old were hypomagnesemic (100%); mean age of hypomagnesemia in our study was 62.20 years; As the age increased the prevalence of hypomagnesemia increased in diabetics; p value was 0.0001 ; according to Yajinick et al¹² and Al Osali ME, Al Qassabi SS et al¹³ proved a significant correlation between age and magnesium levels; also proved a correlation between the male sex and magnesium levels; our study concurred with the above studies with regards to age but not with sex preponderance and magnesium levels;

HbA1c% & Hypomagnesemia

On analyzing the HbA1c % results, we found that 4 patients had values in the range of 9-10% all 4 of them had hypomagnesemia (100 %) 32 patients had a

value in the range 7-8% among them 26 had hypomagnesemia (94.11%). Only 34.48% of the patients who had normal HbA1c values developed hypomagnesemia; the p value for this association is also 0.001 making it statistically significant. This is similar to the study of Tosiello et al¹⁴. Normomagnesemic patients had better control of FBS & HbA1c than the hypomagnesemia groups; this is well supported by the study done by Prabodh, Prakash et al¹⁵.

Diabetic Retinopathy & Hypomagnesemia

In the 100 patients we had, 35 patients were found to have retinopathy, among whom 27 had hypomagnesemia (75.86%); the percentage of hypomagnesemic patients who had retinopathy was 67.5%; the normomagnesemic patients had only 8 % of retinopathy; the p value indicating the association was 0.0001 which was statistically significant; studies which show similar results as ours are McNair et al¹⁶, De walk HV et al¹⁷, Hatwal A, Gujral AS et al¹⁸.

Diabetic Neuropathy & Hypomagnesemia

Only 4 patients had neuropathy but all 4 had hypomagnesemia in our study; hypomagnesemia and presence of neuropathy were statistically correlating as shown by the p value 0.012; Rodriguez morán M et al showed a correlation between hypomagnesemia and development of neuropathy & foot ulcer in diabetic patients¹⁹.

Diabetic Nephropathy & Hypomagnesemia

Out of 100, 14 patients had diabetic nephropathy; 13 of the 40 in the hypomagnesemia group had nephropathy (32.5%) and 1 out of the 60 in the normomagnesemia group had nephropathy (1.7%). The p value too supported this association p=0.001. Studies done by Pham PC et al⁷ and Prakash DS Prabodh S et al¹⁵ support this claim; in a study by Corsanello, the explanation for this association was provided for this association; i.e as there is albuminuria in diabetes mellitus, the 30 % of the serum Mg which is protein bound might be lost more in diabetic nephropathy.

Conclusion

Low serum magnesium levels are commonly seen in diabetic patients. Hypomagnesemia patients had a higher incidence of retinopathy, nephropathy and neuropathy. A magnesium rich diet consisting of whole grains, legumes, fruits and vegetables such as spinach, okra, dry apricots may be recommended. Long term studies are needed to determine usefulness of magnesium supplementation in the management of type 2 diabetes.

References

1. Longo, Fanci, Kasper, Hanser, Jameson, Loscalzo, Harrison's principles of internal medicine 19th edition.
2. Pham PC, Pham PM, Pham SV, Miller JM, Pham PT. Hypomagnesemia in patients with type 2 diabetes. *Clin J Am Soc Nephrol*2007;2:366-73.
3. Saris NEL, Mervaala E, Karppanem H, Khawaja JA, Lewenstam A: Magnesium: An update on physiological, clinical and analytical aspects. *Clin Chem Acta* 2000; 294: 1-26.
4. Elamin A, Tuvemo T: Magnesium and insulin dependent diabetes mellitus. *Diabetes Res Clin Pract* 1990; 10: 203-209.
5. Kao WHL, Folsom AR, Nieto FJ, MO JP, Wtason RL, Brancati FL. Serumand dietary magnesium and the risk for type 2 diabetes: the atherosclerosis risk in communities' study. *Arch Intern Med* 1999; 159:2151-59.
6. Rude RK, Magnesium deficiency and diabetes mellitus- causes and effects postgrad med J. 1992;92:217-24
7. Pham pc, Pham pm, Pham pa, Pham sv, Pham Hv, miller JM, Yahagawa N, Pham PT. Lower serum magnesium levels are associated with more rapid decline of renal function in patients with diabetes mellitus type 2. *clin nephrol* 2005 jun 63(6)-429-36.

8. Nadler JC, Rude RK. Disorders of magnesium metabolism. *Endocrinol Metab Clin. North. Am.* 1995; 24: 623–41..
9. Walti MK, Zimmermann MB, Spinass GA, Hurrell RF: Low plasma magnesium in type 2 diabetes. *Swiss Med Wkly* 133:289-292, 2003.
10. Mc nair P, Christensen MS, Christiansen, Madsbad S, Transbol I: Renal hypomagnesaemia in human diabetes mellitus and its relation to glucose homeostasis. *Eur J clin Invest* 12:81-85,1982.
11. Walti MK, Zimmermann MB, Spinass GA, Hurrell RF: Low plasma magnesium in type 2 diabetes. *Swiss Med Wkly* 133:289-292, 2003.
12. Yajnick CS, Smith RF, Hockaday TDR, Ward NI. Fasting plasma magnesium concentration and glucose disposal in diabetes. *BMJ* 1984; 288:1032-4.
13. Al. Osali ME, Al - Qassabi SS, El Sayed MK, Hypomagnesium in type 2 diabetes omani patients, *Saudi Med J* 2009; 30(7) 897-901
14. Tosiello L. Hypomagnesemia and diabetes mellitus. A review of clinical implications. *Arch Intern Med.* 1996 Jun 10;156(11):1143-8.
15. Prabodh, S. Prakash, DS. Sudhakar, G. Chowdary NV, Desai V, Shekhar R Status of copper and magnesium levels in diabetic nephropathy cases: a case control study from south india, *Bio Trall Elemres* 2011; 142(1) 29-35
16. Mc Nair P, Christiansen C, Madsbad S, Lauritzen E, Faber O, Binder C et al. Hypomagnesimia - a risk factor for diabetic retinopathy - diabetics 1978;27:1075-7.
17. De Valk HW Magnesium in diabetes mellitus *Neth J Med* 1999 APR 54(4)-139-46
18. Hatwal A, Gujral A S, Bhatia DP, Agarwal JK, Bajpai HS, Association of hypomagnesemia with diabetic retinopathy - *Acta Ophthalmol (Copenh)* 1989.del: 67(6) 714-6
19. Rodriguez. Moran, M. Guerrero. Romero F, Low serum magnesium levels and foot ulcers in subject with type 2 diabetes, *Arch Med Res* 2001. Jul-Aug: 32(4): 300-3.