The Association of Hypomagnesaemia, High Normal Uricaemia and Dyslipidaemia in the Patients with Diabetic Retinopathy

NAVIN S[1], KRISHNAMURTHY N[2], ASHAKIRAN S[3], C D DAYANAND[4]

ABSTRACT

Context: Diabetic retinopathy is fast becoming an important cause of a visual disability. The visual disability which results from diabetes is a significant public health problem; however, this morbidity is largely preventable and treatable. If it is managed with a timely intervention, the quality of life can be preserved.

Aims: The objective of this study was to investigate the association of serum uric acid, magnesium and the lipid profile in diabetic retinopathy with Normal subjects and Diabetes mellitus without retinopathy, among the south Indian population.

Settings and Design: The diabetic retinopathy patients were identified from the diabetic health camps which were held in rural areas, and they were compared with those with diabetes without complications and the normal subjects.

Material and Methods: The diabetic retinopathy patients were compared with the healthy subjects and with diabetes without retinopathy. Furthermore, the Diabetic retinopathy patients were grouped as proliferative and non-proliferative, based on the fundoscopic findings. Magnesium, uric acid, FPG, fructosamine and the lipid profile were measured in the above groups and they were analyzed.

Statistical Analysis: The statistical analysis was done by using the SPSS software, by applying the Student 't' test.

Results: The mean serum magnesium concentration was observed to be low in the diabetic retinopathy group (1.43mg/dl) as compared to those in the controls and the diabetic subjects. The serum Uric acid concentration was high normal (4.84mg/dl), which was associated with the dyslipidaemia in diabetic retinopathy.

Conclusion: The poor glycaemic control in diabetes is associated with hypomagnesaemia, and increased uric acid concentration with dyslipidaemia, which can be an initial picture of the ongoing biochemical changes in the complication of diabetes, which can help in predicting the onset of diabetic retinopathy in diabetes.

INTRODUCTION

Diabetic retinopathy is a major cause of blindness in the population of the working age group. It is one of the leading causes of blindness in the world, where the chances of losing the sight are about 25 times higher than that in the normal population. The prevalence of diabetic retinopathy was 18% in an urban population with diabetes mellitus in India [1]. Uric Acid (UA) is the final oxidation product of the purine catabolism. The prevalence of hyperuricaemia has been increasing around the world, which is accompanied by a rapid increase in obesity and diabetes. Kylin, in 1923, first described Hyperuricaemia as being associated with hyperglycaemia. However, the association between the serum uric acid levels and Diabetes mellitus is not clear. Some studies have reported that there is a positive association between high serum uric acid levels and diabetes [2-7], whereas other studies have reported no association [8]. Many studies have been done on the magnesium levels in diabetics, but few have been on the diabetic retinopathy in the rural population [9]. With the above background, this study was done to examine the serum levels of magnesium and uric acid in diabetic retinopathy.

MATERIAL AND METHODS

The study population

Ninty Four subjects were selected from Diabetic health camps, outpatients and the inpatients of a tertiary care setup of R. L. Jalappa Hospital and Research Centre, in the rural area of Kolar.

The following information were collected-age, sex, history about of the present illness, diabetes mellitus, hypertension, cardiovascular diseases, drug history and habits which included alcohol intake, smoking and the diet. The physical examination findings were noted.

The study group were assigned into 4 groups:

1. Thirty normal, healthy, non-diabetics, control Group (A-NDM),
2. Thirty type II Diabetic without retinopathy (B-DM).
3. Thirty four type II Diabetic with retinopathy (C-DR) thirty four

Which was further classified as:

a. Twenty one Non-proliferative (C-NPDR)
b. Thirteen Proliferative diabetic retinopathy (C –PDR)

Diabetic retinopathy was diagnosed by fundo-scopic examination by Ophthalmologist, which was further classified as Proliferative and Non-Proliferative Diabetic Retinopathy. All the subjects were examined by the same ophthalmologist, to minimizse the subjective error. The subjects were classified, based on the following findings:

Non –proliferative diabetic retinopathy (NPDR)	Any of the following: Microaneurysms >20 intraretinal hemorrhages in each of 4 quadrants Definite venous beading in 2+ quadrants

| Proliferative diabetic retinopathy (PDR) (One or more of the following) | Prominent intraretinal microvascular abnormalities in 1+ quadrant and no signs of proliferative retinopathy. Neovascular Vitreous/preretinal hemorrhage. |

The subjects with a known history of hypertension, arthritis, renal failure, angina or myocardial infarction, leukaemia, malignancy, other complications of Diabetes mellitus such as nephropathy, neuropathy or any conditions which is are known to alter the serum uric acid levels, were excluded from the study. The physical examination which revealed a "sensory loss to light touch, vibration, and temperature", a Blood pressure of more than 140/90 and a positivity for microalbuminuria were not included.

PROCEDURE

Five ml fasting sample of venous blood was drawn from the median cubital vein under aseptic precautions, after obtaining consent from the subjects. 1.5 ml of blood was transferred to a fluoride bulb for glucose analysis by the GOD-POD method immediately [8]; the remaining was centrifuged after allowing it to clot for about 15 min to obtain the serum. The serum was analyzsed for Urea by the Urease-GLDH method [10], Creatinine was estimated by the Jaffe-kinetic method [11], Total Cholesterol was estimated by the Cholesterol oxidase method [12], Triglycerides was estimated by the GPO-POD method [13], HDL was estimated by the Precipitation-Cholesterol oxidase method [14] and Uric acid was estimated by the Uricase method [15]. LDL was calculated by using Frieldwald's formula [16]. The serum fructosamine (glycated albumin) estimation was carried out by a method which was described by Johnson [17]. This is used to identify the degree of glycaemic control over an intermediate short period of time [18] where HbA1c is used for assessing the glucose levels for the preceding six weeks.

The study was approved by the Ethical committee of SDU Medical College, Kolar, India. The statistical analysis was carried out between the assigned groups by using the Student 't' test and the Mann-Whitney 'U' test

RESULTS

The study included 94 subjects, which consisted of 30 controls, 30 diabetics without retinopathy and 34 diabetics with retinopathy, after excluding 8 patients due to renal causes [Table/Fig-1]. The magnesium levels in the group C-DR were decreased as compared with to those of the groups A-NDM and B-DM. Increasing levels of serum uric acid were as observed in the group C-DR as compared to those to in the healthy controls and the group B-DM. The decreasing magnesium levels and the increasing serum uric acid levels in the group C-DR were associated with increasing fructosamine levels. Dyslipidaemia was observed in both the B-DM and the C-DR groups, which was highly significant (p<0.01) when compared with controls (A-NDM), expect the HDL levels. The observed fasting blood glucose levels in the groups B-DM and C-DR had no association with the controls (p<0.064). The C-PDR group showed low levels of magnesium and high uric acid levels as compared to the C-NPDR group [Table/Fig-2], inverse relation and significantly associated [Table/Fig-3].

DISCUSSION

In this study, magnesium was determined, because magnesium is involved on multiple levels in the insulin secretion, binding and activity. Cellular magnesium deficiency can alter the activity of the membrane bound sodium-potassium ATPase which is involved in the maintenance of the gradient of sodium, potassium and glucose transport [19]. Low levels of magnesium can reduce the secretion of insulin by the pancreas [20]. In diabetes, there is a direct relationship between the serum magnesium levels and the cellular glucose disposal, which is independent of the insulin secretion. This change in the glucose disposal has been shown to be related to the increased sensitivity of the tissues to insulin in the presence of adequate magnesium levels [21]. Magnesium activates more than 300 enzymes in the body and it is a critical co –factor of many enzymes in the carbohydrate metabolism. Observations have revealed a definite lowering of the serum magnesium levels in diabetic patients with retinopathy, especially in those with poorly controlled glucose levels [Table/Fig-1]. The patients who had proliferative retinopathy were found to have the lowest left concentrations of serum magnesium [Table/Fig-3]. Hence, hypomagnesaemia, as a possible risk factor in the development and the progress of diabetic Retinopathy, can be considered. The ex-

Group	N=94	Dur (Years)	FBS (mg/dl)	Fruc (mmol/L)	Uric acid (mg/dl)	Urea (mg/dl)	Cr (mg/dl)	Mg (mg/dl)	TC (mg/dl)	TG (mg/dl)	LDL (mg/dl)	HDL (mg/dl)
A-NDM	30		84.3±9.32	1.08±0.21	3.94±0.22	23.84±4.39	1.03±0.05	2.12±0.25	171.66±16.70	150±21.20	150±21.20	35±6.40
B-DM	30	13.7±6.02	104.43±11.68	2.06±0.47	4.27±0.47	26.34±6.33	1.24±0.12	2.10±0.26	202.93±51.00	239±33.67	99.53±18.58	44.13±8.16
C-DR (C-NDR+ C-PDR)	34 (21+13)	18.2±8.11	143.13±19.27	2.37±0.18	4.84±0.56	25.78±5.44	1.29±0.18	1.43±0.17	206.93±67.00	240±11.79	136.50±43.66	34.46±5.98

[Table/Fig-1]: Mean and Standard deviation(Mean ± SD) of duration of diabetes, fasting glucose, uric acid, creatinine, magnesium, total cholesterol, triglycerides, LDL, HDL in healthy subjects (A-NDM), diabetes without retinopathy(B-DM) and Diabetic with retinopathy(C-DR)

Groups compared	(A-NDM) + (B-DM)	(A-NDM) + (C-DR)	(B-DM)+(C-DR)
Highly significant (p<0.01)	Magnesium, Uric acid , triglycerides, LDL,	Magnesium, Uric acid, total cholesterol, LDL	Magnesium Fructosamine, uric acid, total cholesterol, triglycerides,
Significant (p<0.05)	Fructosamine, HDL, total cholesterol,	Fructosamine, triglycerides	LDL
Non-significance (p>0.05)	FBS, urea, creatinine	FBS, HDL, urea, creatinine	FBS, HDL, urea, creatinine

[Table/Fig-2]: Significance study between the groups

Group	N=34	Dur (Years)	FBS (mg/dl)	*Fruc (mmol/L)	*Uric acid (mg/dl)	Urea (mg/dl)	Cr (mg/dl)	*Mg (mg/dl)	*TC (mg/dl)	*TG (mg/dl)	LDL (mg/dl)	HDL (mg/dl)
C-NPDR	21	14.2±4.11	136.18±15.06	2.42±0.73	4.32±0.33	24.15±4.54	1.23±0.13.	1.45±0.26	206.93±67.00	237±38.34	136.50±43.66	36.65±4.54
C-PDR	13	18.43±5.11	145.17±18.86	2.33±0.13	4.64±0.56	25.78±5.44	1.28±0.15	1.33±0.16	203.93±63.	242±74.21	133.50±43.66	38.45±4.85

[Table/Fig-3]: Mean and Standard deviation (Mean ± SD) of duration of diabetes, fasting glucose, uric acid, creatinine, magnesium, total cholesterol, triglycerides, LDL, HDL in non-proliferative diabetic retinopathy (C-NPDR) and proliferative diabetic retinopathy(C-PDR)
Group C-NPDR compared with group C-PDR. *p<0.05

act cause of the hypomagnesaemia in diabetes is still unknown, but an increased urinary loss of magnesium may contribute to it. Two factors may work together in this respect,namely, the osmotic action of glucosuria and hyperglycaemia per se, the latter being known to depress the net tubular reabsorption of magnesium [22-24].

Among the diabetic retinopathy cases, it was much more evident that elevated levels of uric acid were more significant in the proliferative cases as compared to those in the non-proliferative cases. An inverse relationship between low magnesium levels and high uric acid levels in diabetic retinopathy was also observed. A plausible mechanism for the observed results, of an inverse association between the increasing serum uric acid levels and Diabetes mellitus, may be related to the inhibition of the uric acid reabsorption in the proximal tubule by the high glucose levels in diabetic individuals [25, 26].

Uric acid can act as a pro-oxidant, particularly at increased concentrations, and it may thus be a marker of oxidative stress, but it may also have a therapeutic role as an antioxidant. It is unclear whether the increased concentrations of uric acid in the diseases which are associated with oxidative stress, are a protective response or a primary cause. The strength of this study was the finding of hypomagnesaemia and high normal uric acid levels. There was a limitations of few subjects being included in this study, which was due to a difficulty in finding the cases of only retinopathy without other complications in diabetics. Further prospective studies are required to evaluate this inverse relationship between magnesium and uric acid for in the prognosis of diabetic retinopathy [27].

CONCLUSION

The patients with diabetic retinopathy had low magnesium and high normal uric acid levels. This study demonstrated an inverse relationship between the magnesium and the uric acid levels, which could be used to predict the onset of diabetic retinopathy. A large community based, prospective study in the Indian population is needed, to verify the findings.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Biochemistry, Chettinad Hospital & Research Institute, Chennai-603103, India.
2. Professor and Head, Department of Biochemistry, BGS Medical College, Bangalore, India.
3. Professor, Department of Biochemistry, Sri Devaraj Urs Medical College, Kolar, India.
4. Associate Professor, Department of Biochemistry, Sri Devaraj Urs Medical College, Kolar, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr Navin S,
A9, Staff Villa, Chettinad Health city Campus, OMR kelambakkam, Chennai-603103, India.
Phone: 9941478205, E-mail: drnavins@gmail.com

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