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Serum Uric Acid in Diabetic Retinopathy: A Case Control Study

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ABSTRACT: INTRODUCTION: Diabetic retinopathy (DR) is a highly specific vascular complication of diabetes and one of the leading causes of vision loss in the world. Uric acid (UA) is the final metabolic product of purine metabolism in humans, and is excreted in urine.It has a role in endothelial dysfunction, inflammation and vascular disease. Uric acid also has an effect on Vascular endothelial growth factor (VEGF) which is an important factor in development of DR. DR progresses in an orderly fashion from mild to severe stages when there is no appropriate intervention. It is important to recognize the stages when treatment may be most beneficial. Uric acid levels are associated with inflammation of vascular smooth muscles. It may have a role in pathogenesis of retinal vascular involvement in DR.Patients with type 2 diabetes mellitus often have coexisting microvascular complications when the diagnosis of diabetes mellitus is made. Therefore, identifying a clinical surrogate for the severity of diabetic microvascular complications is needed. Studies suggested that in clinical practice, the Serum Uric Acid level obtained from diabetic patients may reflect the severity of the current microvascular complications in patients with type 2 DM. Regular measurements of Serum Uric Acid level as a potential marker for the severity of microvascular diseases may be beneficial for patients with diabetes.

OBJECTIVES: To study the relationship between Serum Uric Acid and Diabetic Retinopathy in type 2 Diabetes Mellitus and to correlate the grades of Diabetic retinopathy with Serum Uric Acid in type 2 Diabetes Mellitus.

MATERIALS AND METHODS: The study was done over a period of 18 months and 120 patients were included in the study who attended outpatient and inpatient clinical services of a tertiary teaching Hospital in South India fulfilling the inclusion and exclusion criteria. All the subjects underwent dilated fundus examination bedside by direct ophthalmoscope. The findings were confirmed by Ophthalmologist in Ophthalmology OPD. Diabetic retinopathy was staged as Non Proliferative Diabetic Retinopathy and Proliferative Diabetic Retinopathy. Serum Uric Acid was estimated using Enzymatic Uricase method by Hitachi Cobas 6000 apparatus.

RESULTS: The Age distribution was between 35 to 82 years.Females contributed majority of study population. Majority of the patients had increased HbA1c which was statistically significant. There was statistically significant relationship between Grades of Diabetic Retinopathy and serum uric acid.

CONCLUSION: The present study was to correlate Diabetic Retinopathy with serum Uric Acid levels. There was statistically significant association between Diabetic Retinopathy and serum uric acid levels. Limitation of this study was that, there were only few patients with proliferative Diabetic Retinopathy.

Key words: Diabetic retinopathy; Uric Acid

I. INTRODUCTION

Diabetes is an important public health problem. There is a steady increase in the number of cases and prevalence of diabetes over the past few decades in low and middle-income countries than in high income countries.[1]The global prevalence has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population.[1]Diabetic retinopathy (DR) is a highly specific vascular complication of diabetes and one of the leading causes of vision loss in the world.[2] Blindness caused by diabetes mellitus currently affects approximately 150 million people worldwide, and according to estimates of World Health Organization (WHO) it will double by 2025.[2]

Uric acid (UA) is the final metabolic product of purine metabolism in humans, and is excreted in urine.[3] It has a role in endothelial dysfunction, inflammation and vascular disease.[4] Uric acid also has an effect on Vascular endothelial growth factor (VEGF) which is an important factor in development of DR.[4] Uric acid can also directly exert proinflammatory effects on vascular smooth muscle cell which has a role in development of DR . [5] DR progresses in an orderly fashion from mild to severe stages when there is no appropriate

intervention. It is important to recognize the stages when treatment may be most beneficial. Uric acid levels are associated with inflammation of vascular smooth muscles. It may have a role in pathogenesis of retinal vascular involvement in DR.Patients with type 2 diabetes mellitus often have coexisting microvascular complications when the diagnosis of diabetes mellitus is made. Therefore, identifying a clinical surrogate for the severity of diabetic microvascular complications is needed. Previous studies suggested that in clinical practice, the serum uric acid level obtained from diabetic patients may reflect the severity of the current microvascular complications in patients with type 2 DM. Regular measurements of Serum Uric Acid level as a potential marker for the severity of microvascular diseases may be beneficial for patients with diabetes.Diabetes is one of the leading cause of blindness.[6] A drastic rise in diabetes mellitus is predicted with an estimation of 592 million by 2035. [7] It affects the microcirculation of the eyes leading to a significant alteration in the retinal microvasculature before the patient undergoes ophthalmologic examination and intervention.

A study among 173 patients with diabetes in Turkey showed that Uric acid was an independent risk factor for DR. Also, Uric Acid levels were significantly higher in patients with DR when compared to those without DR.[2]Another study among 385 Taiwanese patients with Diabetes in Taiwan showed that serum Uric Acid levels were higher in patients with DR and it significantly correlated with severity of DR.[8]A Study conducted among 57 patients in Haryana suggested that low level of Uric Acid was found in diabetic subjects without Retinopathy and higher level of Uric Acid in patients with DR.[9]Another study done among 749 patients showed that increase in severity of DR was positively associated with serum uric acid concentration. Analysis also showed that patients with Serum Uric Acid levels in the third (5.9-6.9 mg/dL) and fourth (≥ 7.0 mg/dL) quartiles had increased hazard ratios for DR when compared with patients with Serum Uric Acid in the first quartile (< 4.9 mg/dL).[10]

A study done among 114 patients in China showed that there was significant increase in level of Serum Uric Acid in patients with DR compared to patients with Diabetes Mellitus.[11]A study was done by Kuwata H et al among Japanese patients with Type 2 Diabetes patients. Assessment was done by prospectively associating between baseline serum uric acid levels and consequent risk of developing diabetic retinopathy. Newly developed diabetic retinopathy was recognized in 188 patients (10.2%) during the observation period of 2 years. Higher serum uric acid levels were associated with increased risk of developing diabetic retinopathy in male patients with type 2 diabetes, but not in female patients. Serum uric acid may be a useful biomarker for predicting the future risk of developing diabetic retinopathy in male patients with type 2 diabetes.[12]A study done by Zhu DD et al reported that high uric acid can promote the inflammation of the retina and increase the activity of Notch signalling pathway on the basis of high glucose. Hyperuricemia promotes the development of diabetic retinopathy by increasing the activity of Notch signalling pathway. Notch signalling pathway is a potential therapeutic target for diabetic retinopathy.[13]A nationwide, cross-sectional study was conducted at Brazil by Melo LGN et al between August 2010 and August 2014. The study included 1760 patients with diabetes. In total, 1644 patients were studied. 35.7% presented diabetic retinopathy and 12% presented vision-threatening diabetic retinopathy. Three risk factors associated with diabetic retinopathy were in common to both groups: longer diabetes duration, higher levels of HbA1c and higher levels of serum uric acid. The higher rate of vision-threatening retinopathy was found in the study. In addition to traditional risk factors, they found an association between serum uric acid levels and diabetic retinopathy.[14]

The presence of diabetic retinopathy (DR) is associated with visceral fat accumulation and insulin resistance in T2DM patients.[15] An earlier report found no significant difference in uric acid levels between patients with or without retinopathy,[16] but several recent studies showed a significant increase of uric acid-related metabolites levels in DR compared to T2DM.[11] Serum Uric Acid concentration was shown to be associated with an increased severity of DR over a three-year period in patients with T2DM.[10]Furthermore, vitreous Uric Acid and glucose concentrations were higher in proliferative than in non-proliferative DR. Focal Uric Acid production in the vitreous is thought to be involved in the pathogenesis and progression of DR.[17]

The incidence of hyperuricemia has been on the increase since decades. The condition seems to be associated with increased insulin resistance and onset and progression of diabetic complications. Uric acid might thus be suitable marker for both risk evaluation and intervention.A study done by Yili Xu et al summarizes the available evidence on the relationship between Serum Uric Acid and the development of vascular complications and mortality in T2DM, which

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provided a meta- analysis of 9 relevant studies ,involving a total of more than 20,981 sample size. The overall findings suggested a significantly positive correlation with each 0.1 mmol/l increase in serum uric acid leads to a 28% increase for the risk of vascular complications in T2DM and a 9% increase for the risk of mortality. The relationship between serum uric acid and vascular complications remained significantly positive irrespective of mean age, adjustment for metabolic variables and medications.[18]It has been established that serum uric acid level increase is positively related with the progression of retinopathy in cross-sectional studies.[19,20]However, after using logistic regression analysis, Cai et al. showed that serum uric acid wasn't independent risk factor of diabetic retinopathy in elderly T2DM patients.[21]Furthermore, Felderman et al. followed 95 consecutive diabetes clinic patients for 15 years, which indicated higher serum uric acid levels were not related to diabetic retinopathy in a prospective study.[16]Overall, in the strata analysis of retinopathy in our study, no statistical significance was present.However, not many studies had been done on Indian population, hence the intended study.

II. METHODOLOGY

SOURCE OF DATA:

Patients with diabetes mellitus attending outpatient and inpatient clinical services of a tertiary teaching Hospital in South Indiafulfilling the inclusion and exclusion criteria were included in the study.

METHOD OF COLLECTION OF DATA:

Study type: Case Control study

The study was done over a period of 18 months from October 2019 to April 2021 and 120 patients were included in the study of which, 60 patients were with DR and remaining 60 patients were without DR.

Patients with diabetes mellitus attending outpatient and inpatient department of a tertiary teaching Hospital in South Indiafulfilling the inclusion and exclusion criteria were included in the study.

All the subjects underwent dilated fundus examination bedside by direct ophthalmoscope, Welch Allyn REF11720. The findings were confirmed by Ophthalmologist in Opthalmology OPD. Diabetic retinopathy was staged as Non Proliferative Diabetic Retinopathy and Proliferative Diabetic Retinopathy.

Serum Uric Acid was estimated using Enzymatic Uricase method by Hitachi Cobas 6000 apparatus. Normal range of serum uric acid being; Female: 2.4- 5.7mg/dl, Males: 3.4-7 mg/dl.

The clinical examination findings and laboratory investigation reports were documented on a preformatted data sheet, and further transferred to an excel sheet for analysis.

Weight, height, blood pressure, body mass index, investigations such as electrocardiogram, fasting blood sugar , post prandial blood sugar, glycated hemoglobin, urine protein, blood urea, serum creatinine, serum potassium, was done on every patient included in the study.

INCLUSION CRITERIA

- Patients with type 2 diabetes mellitus above age of 30 years

EXCLUSION CRITERIA

- Documented history of gout
- Patients on drugs altering serum uric acid levels; levodopa, cyclosporine, diuretics, pyrazinamide, ethambutol
- Hypertension
- Malignancy

III. DATA ANALYSIS

Collected data will be analyzed by percentages, frequency, mean, standard deviation, Chi square test and Karl-Pearson's correlation coefficient.

IV. RESULTS

the present study, 120 patients attending a tertiary teaching Hospital in South India fulfilling the inclusion and exclusion criteria were included.

GRADES OF DIABETIC RETINOPATHY (DR)

Among 120 diabetic patients ; 60 patients (50.0%) had DR and remaining 60 patients (50.0%) did not have DR. Among 60 subjects with DR; 56 patients (46.7%) had NPDR and remaining 4 patients (3.3%) had PDR. (Table 1)

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Table 1 : Grades of diabetic retinopathy

GRADES OF DIABETIC RETINOPATHY	NUMBER OF PATIENTS	PERCENTAGE
NO DR*	60	50.0%
NPDR**	56	46.7%
PDR***	4	3.3%
TOTAL	120	100%

*NO DIABETIC RETINOPATHY, ** NON PROLIFERATIVE DIABETIC RETINOPATHY, *** PROLIFERATIVE DIABETIC RETINOPATHY

AGE DISTRIBUTION

The mean age of patients without DR was 56.10±11.47 years (60 subjects)and 64.48±10.17 years among patients with DR (60 subjects); p 0.009. Age distribution was between 35 to 82 years as shown in Table 2.

Table 2: Age distribution

AGE	NUMBER OF PATIENTS	PERCENTAGE
35-50	25	20.8%
51-60	40	33.3%
61-70	30	25.0%
ABOVE 70	25	20.8%
TOTAL	120	100%

SEX DISTIBUTION

Among 120 subjects 79 patients were female (65.8%) and 41 patients were male (34.2%) (Figure 1). Sex distribution among patients with DR and without DR is given below. (Table 3)

Figure 1: Sex Distribution

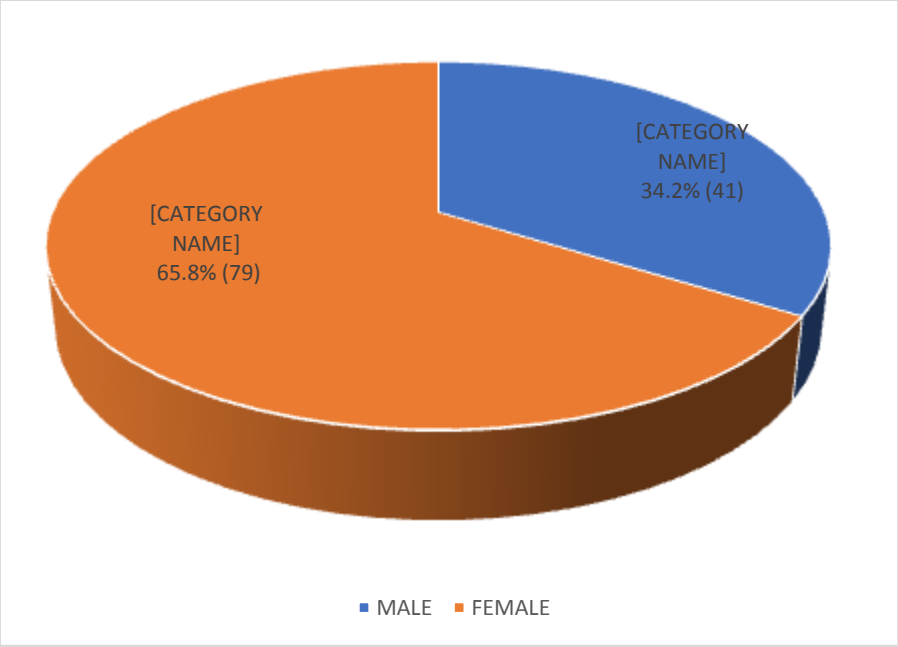

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Table 3: Sex Distribution among patients without diabetic retinopathy and with diabetic retinopathy.

SEX DISTRIBUTION	GRADES OF DIABETIC RETINOPATHY			
	NO DIABETIC RETINOPATHY		WITH DIABETIC RETINOPATHY	
	COUNT	%	COUNT	%
FEMALE	36	60	43	71.7
MALE	24	40	17	28.3
TOTAL	60	100	60	100

BODY MASS INDEX (BMI)

Among patients without DR (60 patients) ; mean BMI was 25.50±3.22, 46.7 % subjects had BMI <25, 46.7% subjects had BMI 25-30 and remaining 6.7% subjects had BMI above 30. Majority of patients among NPDR (57.1%) had BMI 25- 30 (Mean 26.96±3.41) whereas 100% of subjects with PDR had BMI <25(p= 0.076) . The BMI of patients among various grades of DR is given below (Table 4)

Table 4: BMI among various grades of diabetic retinopathy

BMI	GRADES OF DIABETIC RETINOPATHY					
	NO DR*		NPDR**		PDR***	
	COUNT	%	COUNT	%	COUNT	%
<25	28	46.7	18	32.1	4	100
25-30	28	46.7	32	57.1	0	0.0
ABOVE 30	4	6.7	6	10.7	0	0.0
TOTAL	60	100	56	100	4	100

*NO DIABETIC RETINOPATHY, ** NON PROLIFERATIVE DIABETIC RETINOPATHY, *** PROLIFERATIVE DIABETIC RETINOPATHY

DURATION OF DM

Duration of DM in subjects without DR ranged from 1 to 35 years; with 45% subjects having duration of 1-5 years, 41.7% with 6-10 years, 10% with 11- 20 years and remaining 3.3% having more than 20 years.

Patients without NPDR had a duration of 6-10 years among 37.5% subjects, 1-5 years among 23.2%, 11-20 years among 33.9% and remaining 5.4% had a duration more than 20 years.

Patients with PDR had a duration of 1-5 years among 25%, 6-10 years among 25%, 11-20 years among 25% and remaining 25% subjects had more than 20 years of DM. (p= 0.016) Table showing the data of duration of DM among various grades of DR is given below.(Table 5)

Table 5: Duration of DM

DURATION OF DM	GRADES OF DR					
	NO DR		NPDR		PDR	
	COUNT	%	COUNT	%	COUNT	%
1-5 YEARS	27	45.0	13	23.2	1	25.0
6-10 YEARS	25	41.7	21	37.5	1	25.0
11- 20 YEARS	6	10.0	19	33.9	1	25.0
ABOVE 20 YEARS	2	3.3	3	5.4	1	25.0
TOTAL	60	100	56	100	4	100

*NO DIABETIC RETINOPATHY, ** NON PROLIFERATIVE DIABETIC RETINOPATHY, *** PROLIFERATIVE DIABETIC RETINOPATHY

Glycated Hemoglobin (HbA1c)

Among 120 patients with DM; mean HbA1C was 8.25±1.81, 104 patients (86.7%) had increased HbA1c and remaining 16 patients (13.3%) had normal HbA1c. Among 60 patients without DR , Mean HbA1C was 7.72±1.20 ; 50 subjects (83.3%) had increased HbA1c and 10 subjects (16.7%) had normal HbA1c. Remaining 60 subjects with DR mean HbA1c was 8.78±2.15, 54 patients (90.0%) with increased HbA1c and 6 patients (10.0%) with normal HbA1c (p=0.008). Odds ratio was 2.662 (CI 0.673-10.532). The HbA1c among patients without DR, with NPDR and PDR is given below. (Table 6)

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Table 6: HbA1c and Grades of diabetic retinopathy

HbA1c	GRADES OF DR					
	NO DR*		NPDR**		PDR***	
	COUNT	%	COUNT	%	COUNT	%
Increased	50	83.3	50	89.3	4	100
Normal	10	16.7	6	10.7	0	0
Total	60	100	56	100	4	100

*NO DIABETIC RETINOPATHY, ** NON PROLIFERATIVE DIABETIC RETINOPATHY, *** PROLIFERATIVE DIABETIC RETINOPATHY

URIC ACID

Twenty patients (16.7%) among 120 subjects had increased uric acid levels; whereas 100 patients (83.3%) had normal uric acid. Mean uric acid level was 4.78 ± 1.34, mean uric acid among males and females was 5.12±1.32 and 4.6±1.33 respectively. In patients with no DR mean uric acid was 4.19±0.92, with NPDR mean uric acid was 5.35±1.45 and with PDR mean uric acid was 5.57±1.49. Among 60 patients without DR only 2 patients had increased uric acid (3.3%). Among 60 patients with DR, 18 patients (30.0%) had increased uric acidwith p value being significant , p=0.000. Odds ratio was 17.711 (CI 3.337-94.009). The uric acid levels in different grades of DR is given below. (Tables 7,8) (Figure 2)

Table 7: Mean Uric Acid and Grades of DR

	NO DR*	NPDR**	PDR***
URIC ACID (MEAN VALUES)	4.19±0.92	5.35±1.45	5.57±1.49

*NO DIABETIC RETINOPATHY, ** NON PROLIFERATIVE DIABETIC RETINOPATHY, *** PROLIFERATIVE DIABETIC RETINOPATHY

Table 8: Uric Acid and Grades of DR

URIC ACID	GRADES OF DR					
	NO DR*		NPDR**		PDR***	
	COUNT	%	COUNT	%	COUNT	%
Increased	2	3.3	16	28.6	2	50.0
Normal	58	96.7	40	71.4	2	50.0
Total	60	100	56	100	4	100

*NO DIABETIC RETINOPATHY, ** NON PROLIFERATIVE DIABETIC RETINOPATHY, *** PROLIFERATIVE DIABETIC RETINOPATHY

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Figure 2: Grades of DR among patients with increased uric acid

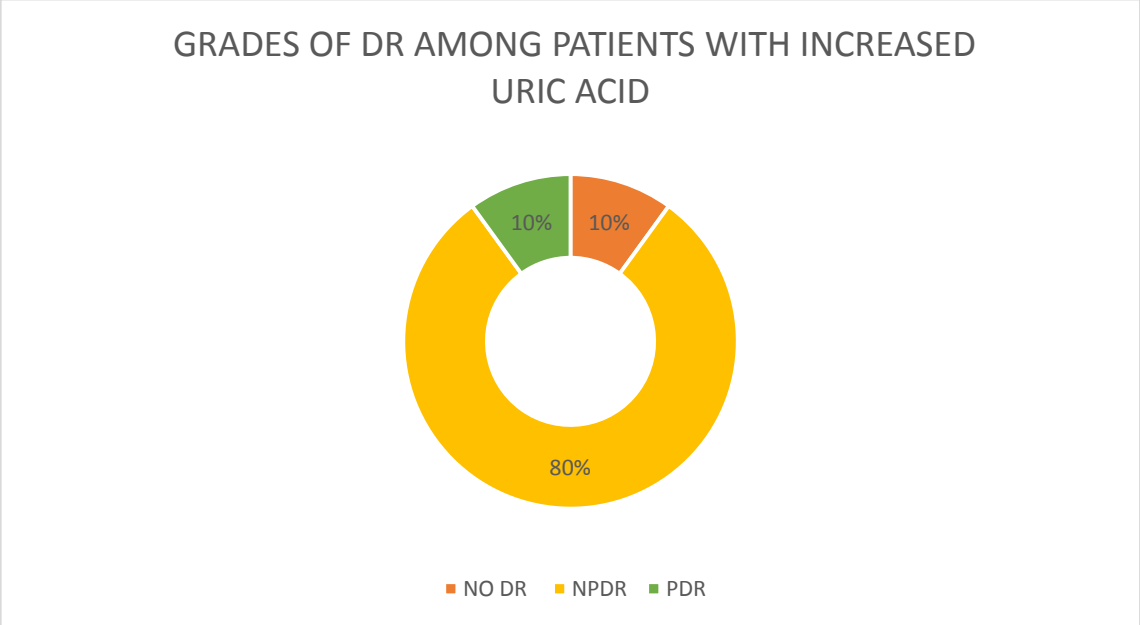
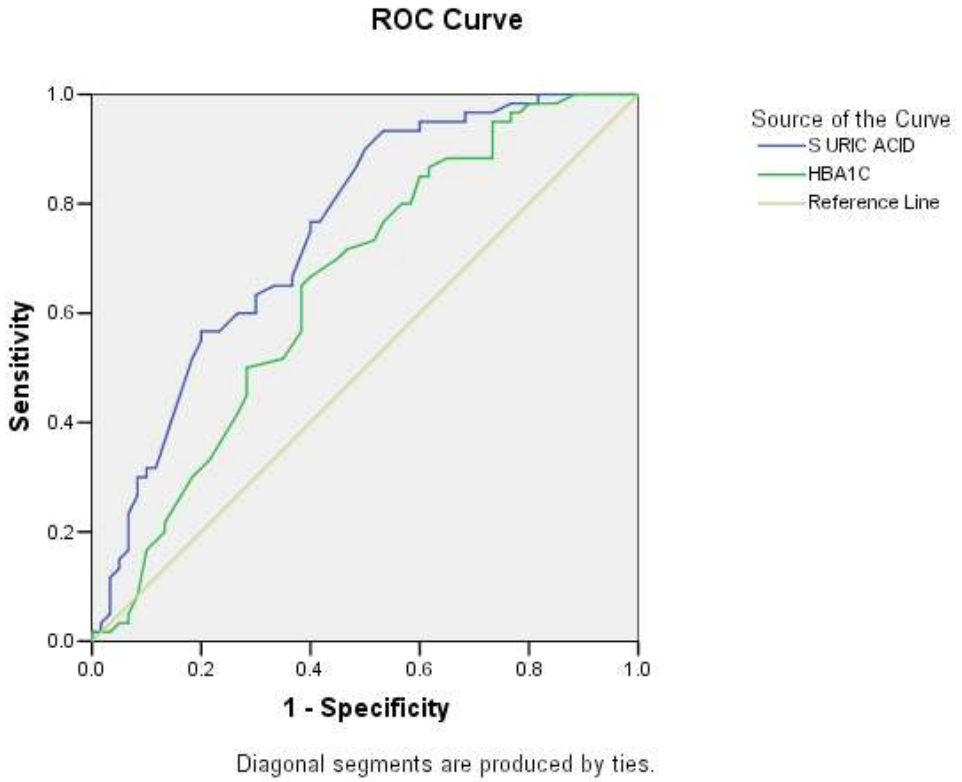


Figure 3 : Gradesof diabetic retinopathy: No diabetic retinopathy and diabetic retinopathy



The area under the curve for serum uric acidwas 0.749 (CI 0.662 - 0.836).Receiver Operator Characteristic(ROC) curve analysis showed that grades of DR increased with values of serum uric acidgreater than 4.86 with sensitivity 75% and specificity 60 %. The area under the curve for HbA1c is 0.651 (CI 0.552- 0.750) , HbA1c > 8.1 having increase in grades of DR with sensitivity 70% and specificity 55%.

V. DISCUSSION

The prevalence of diabetes is increasing all over the world; the aim of the study was tostudy the relationship between serum uric acid and diabetic retinopathy in type 2 diabetes mellitus and to correlate the grades of diabetic retinopathy with serum uric acid. This study included120 patients attending a tertiary teaching Hospital in South Indiafulfilling the inclusion and exclusion criteria. Among 120 diabetic patients ; 60 patients (50.0%) had DR and remaining 60 patients (50.0%) did not have DR. Among 60 subjects with DR, 56 patients (46.7%) had NPDR and remaining 4 patients (3.3%) had PDR. (Table 1)

In this study, minimum age was 35 years and maximum age was 82 years. The mean age of patients without DR was 56.10±11.47 years (60 subjects) and 64.48±10.17 years among patients with DR (60 subjects) which was statistically significant (p 0.009). Most of the patients with DR were above 50 years of age. According to a study by Zhang X et al [22] , among individuals with diabetes, no significant difference was found in the prevalence of DR between those aged 40 to 64 years and those aged 65 years and older (28.0%; 95% CI, 23.0%–33.6%; vs 29.5%; 95% CI, 25.4%–33.9%; p=0.64). In study done by Deniz A et al[2]mean age was 56.74±9.54 years among patients without DR, while it was 58.26±8.70 years in DR group; difference was not statistically significant (p<0.066). There was no statistical significance between age and DR in above studies which is not in concordance with this study which could have been due to a smaller sample size.

Duration of DM (Table 5) in subjects without DR ranged from 1 to 35 years; with 45% subjects having duration of 1-5 years, 41.7% with 6-10 years, 10% with 11- 20 years and remaining 3.3% having more than 20 years. Patients without NPDR had a duration of 6-10 years among 37.5% subjects, 1-5 years among 23.2%, 11-20 years among 33.9% and remaining 5.4% had a duration more than 20 years. Patients with PDR had a duration of 1-5 years among 25%, 6-10 years among 25%, 11-20 years among 25% and remaining 25% subjects had more than 20 years of DM. There was statistical significance between duration of diabetes and grades of DR in the current study; with the increase in duration of DM, the number of patients with DR increased (p=0.016). In a study done by Deniz A et al [2] median DM duration of DR group was higher than the control group without DR. It was 6.0 (2.0 -11.0) years in control group and 13.0 (7.0-20.0) years in DR group. The difference was statistically significant (p<0.001). According to a population based study named Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), in younger age group (before 30 years of age) retinopathy was present in 13% of patients who had diabetes for less than 5 years, whereas patients who had diabetes for 10 to 15 years had over 90% retinopathy.[23]The rate at which the vision is lost increased with time and grade of retinopathy according to WESDR.[23]The current study showed significant correlation with duration and grades of DR, similar to the above studies.

Among 120 subjects 79 patients were female (65.8%) and 41 patients were male (34.2%) (Figure 1). Among 79 female patients 45.6% did not have DR, 53.2% had NPDR and 1.3% had PDR. Among 41 male patients 58.5% had no DR, 34.1% had NPDR and 7.3% had PDR. In our study majority of the subjects were females and there was no significant difference between sex and grades of DR (p=0.051), which was similar to study done by Deniz A et al [2] wherethere was no significant difference between patients with and without DR regarding gender factor (p=0.290).But according to study by Zhang X et al [22] DR was slightly more prevalent among men than women with diabetes (31.6%; 95% CI, 26.8%-36.8%; vs 25.7%; 95% CI, 21.7%-30.1%; P = .04) and male sex was independently associated with the presence of DR (odds ratio [OR], 2.07; 95% CI, 1.39-3.10).

In our study, majority of the subjects were having BMI 25 to 30 but there was no statistical significance between BMI and grades of DR (p= 0.076). This was similar to a study done by Deniz A et al [2]where, BMI among non retinopathic diabetics (n=90) was 27.33 to 34.42 (29.90) and BMI among patients with diabetic retinopathy (n=73) was 29.75 to 33.89 (32.39) which was also not statistically significant (p=0.229). In a study done by Lee JJ et al[10], there was no statistical significance between the BMI and worsening in severity of DR with BMI 25.8±3.8 in patients without worsening in severity of DR (n=646) and 26.1±3.6 with worsening in severity of DR (n=103) and p=0.534.[10]

In our study majority of the patients had increased HbA1c which was statistically significant

(p=0.008). According to study done by Deniz A et al[2]the mean HbA1c was slightly higher among patients with DR when compared to the ones without DR (7.84±2.93) versus (8.59±2.67) , but it was not statistically significant (p=0.610). The main factor for the development and progression of diabetic retinopathy is blood sugar levels. The Diabetes Control and Complications Trial (DCCT), a randomized controlled study of 1441 diabetics showed decreased risk of DR with good blood glucose control by about 76%.[24]In diabetics with retinopathy, good glucose control slowed progression of retinopathy by 54%. Another study of HbA1C levels showed a 10% reduction in HbA1C resulted in a 35% to 40% decrease in the progression of retinopathy.[6] With well controlled glucose levels, a 25% decrease in microvascular complications and decrease in need for diabetic retinal laser therapy was found in the United Kingdom Prospective Diabetes Study (UKPDS).[6]

Twenty patients (16.7%) among 120 subjects had increased uric acid levels. Among 60 patients without DR only 2 patients had increased uric acid (3.3%). But among 60 patients with DR 18 patients (30.0%) had increased uric acid. The relation between serum uric acid and grades of DR was statistically significant (p=0.000) (odds ratio [OR], 17.7; 95% CI, 3.34-94.01). This is consistent with the finding of NavinS et al[25]where they have suspected the pro-oxidant role of uric acid in causation of oxidative stress leading to diabetic complication like DR, though they could not clearly state that the hyperuricemia in DR is either a protective response (due to its antioxidant role) or a primary cause of it (due to its pro-oxidant role).[25]A study done among 173 patients with diabetes in Turkey by Deniz A et al [2] showed that uric acid was an independent risk factor for DR. Also, uric acid levels were significantly higher in patients with DR when compared to those without DR. [2]The mean serum uric acid level was 3.85 ± 0.91 mg/dl in the group without DR whereas it was 5.15 ± 1.12 mg/dl in the DR group. The levels were found to be statistically significant (p<0.001) . Another study done by Liang CC et al [8]among 385 Taiwanese patients with Diabetes in Taiwan showed that serum uric acid levels were higher in patients with DR and it significantly correlated with severity of DR.[8]Agrawal P et al[9] conducted study among 57 patients in Haryana suggested that low level of uric acidwas found in diabetic subjects without Retinopathy and higher level of uric acid in patients with DR.[9]Another study done among 749 patients by Lee JJ et al[10] showed that increase in severity of DR was positively associated with serum uric acid concentration. Analysis also showed that patients with serum uric acid levels in the third (5.9-6.9 mg/dL) and fourth (≥ 7.0 mg/dL) quartiles had increased hazard ratios for DR when compared with patients with serum uric acid in the first quartile (< 4.9 mg/dL).[10] A study done by Xia J et al[11] among 114 patients in China showed that there was significant increase in level of serum uric acid in patients with DR compared to patients with Diabetes Mellitus.[11]A study was done by Kuwata H et al[12]among Japanese patients with Type 2 Diabetes patients. Assessment was done by prospectively associating between baseline serum uric acid levels and consequent risk of developing diabetic retinopathy. Newly developed DR was recognized in 188 patients (10.2%) during the observation period of 2 years. Higher serum uric acid levels were associated with increased risk of developing DR in male patients with type 2 diabetes, but not in female patients. Serumuric acid may be a useful biomarker for predicting the future risk of developing DR in male patients with type 2 diabetes.[12]A study done by Qin X et al[13]reported that high uric acid can promote the inflammation of the retina and increase the activity of Notch signalling pathway on the basis of high glucose. Hyperuricemia promotes the development of DR by increasing the activity of Notch signalling pathway. Notch signalling pathway is a potential therapeutic target for diabetic retinopathy.[13] A nationwide, cross-sectional study was conducted at Brazil by Melo LGN et al[14] between August 2010 and August 2014. The study included 1760 patients with diabetes. In total, 1644 patients were studied. 35.7% presented diabetic retinopathy and 12% presented vision-threatening diabetic retinopathy. Three risk factors associated with DR were in common to both groups: longer diabetes duration, higher levels of HbA1c and higher levels of serum uric acid. The higher rate of vision-threatening retinopathy was found in the study. In addition to traditional risk factors, they found an association between serum uric acid levels and DR.[14] The presence of DR is associated with visceral fat accumulation and insulin resistance in T2DM patients.[15]An earlier report found no significant difference in uric acid levels between patients with or without retinopathy,[16] but several recent studies showed a significant increase of uric acid-related metabolites levels in DR compared to T2DM.[11]Serum uric acid concentration was shown to be associated with an increased severity of DR over a three-year period in patients with T2DM.[10]Furthermore, vitreous uric acid and glucose concentrations were higher in proliferative than in non-proliferative DR. Focal uric acid production in the vitreous is thought to be involved

in the pathogenesis and progression of DR.[17]The incidence of hyperuricemia has been on the increase since decades. The condition seems to be associated with increased insulin resistance and onset and progression of diabetic complications. Serum uric acid might thus be suitable marker for both risk evaluation and intervention. A study done by Yili Xu et al[18]summarises the available evidence on the relationship between serum uric acid and the development of vascular complications and mortality in T2DM, which provided a meta-analysis of 9 relevant studies ,involving a total of more than 20,981 sample size. The overall findings suggested a significantly positive correlation with each 0.1 mmol/l increase in serum uric acid leads to a 28% increase for the risk of vascular complications in T2DM and a 9% increase for the risk of mortality. The relationship between serum uric acid and vascular complications remained significantly positive irrespective of mean age, adjustment for metabolic variables and medications.[18]

VI. CONCLUSION

The present study was conducted to correlate diabetic retinopathy with serum uric acid levels. There was statistically significant association between diabetic retinopathy and serum uric acid levels.

VII. SUMMARY

- The study was done to correlate serum uric acid and diabetic retinopathy in type 2 Diabetes Mellitus.
- The age distribution was between 35 to 82 years.
- Females contributedmajority of study population
- Majority of the patients had increased HbA1c which was statistically significant.
- There was statistically significant relationship between grades of diabetic retinopathy and serum uric acid.

LIMITATIONS

The limitations of the study were as follows:-

- The sample size was small
- Patients with proliferative diabetic retinopathy were only few.

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