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Prevalence of Microalbuminuria in Patients with Type 2 Diabetes Mellitus

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Abstract
Diabetes Mellitus has become the most prevalent endocrine disorder in recent times and associated with myriad metabolic, microvascular and macrovascular complications. India has the world's largest Diabetes population and the disease has significant morbidity and mortality. It has become one of the leading causes of acquired blindness and accounts for at-least a quarter of cases of end stage renal disease. Being a clinically silent disease, early recognition is vital to prevent visual loss. Numerous studies carried out to determine the prevalence rate of retinopathy and albuminuria in patients with type 2 diabetes have yielded different rates, thus depicting the ethnic influence. This cross-sectional study was carried out on 300 type 2 diabetic patients attending the OPD of Department of Internal Medicine in Govt T D Medical college, Allappuzha during 2012-13. In our study, prevalence of micro-albuminuria was 23% with a higher incidence in those with longer duration of diabetes, higher age and higher BMI. Further, a significant positive association was found between micro-albuminuria and retinopathy and a negative association with HDL. This study concluded that there is justification in focussing resources on early detection of microalbuminuria in order to prevent irreversible visual and renal afflictions.

Materials and Methods

This cross-sectional study was carried out on 300 patients presenting to the OPD of General Medicine in Government T D Medical College, Alappuzha, after taking clearance from the institutional ethical committee, with the diagnosis of Diabetes Type 2 during the year 2012-13 with the following objectives:

1. Estimation of prevalence of micro-albuminuria in patients with Type 2 Diabetes.
2. To study the association between micro-albuminuria and Diabetic Retinopathy in Type 2 Diabetes.

Patients with Type 2 Diabetes meeting the WHO criteria for diagnosis of Diabetes Mellitus were included in the study. These were Symptoms of diabetes plus RBS ≥ 200 mg /dl, Fasting plasma glucose ≥126 mg/dl or 2 hour plasma glucose ≥200 mg/dl.

People with pre-existant microalbuminuria, Renal Diseases, Congestive cardiac failure, urinary tract infections, Ketonuria, intake of anti-hypertensives and pregnancy were excluded from the study.

All participants underwent a detailed baseline evaluation with emphasis on history of onset of disease, familial history, treatment history, personal history, presence of hypertension and

physical indices like BMI, blood pressure and detailed fundus examination.

Fundus examination was done by the opthalmologist using direct or indirect opthalmoscope through dilated pupils. Classification of retinopathy was done using the Early Treatment Diabetic Retinopathy Study Severity system (ETDRS).

Those with no abnormalities were deemed to have no retinopathy, while those with ≥1 micro-aneurysms and intra-renal haemorrhages were labelled to have mild retinopathy. Those with more extensive haemorrhages and micro-aneurysms, cotton wool spots and venous beading were designated to have moderate NPDR. Severe NPDR included severe intra-retinal haemorrhages, micro-aneurysms, venous beading in ≥2 quadrants or prominent IRMA in ≥1 quadrants. Proliferative retinopathy was further classified into those with or without High Risk Characters. The maculopathy was classified into non-significant macular oedema, Clinically significant oedema-CSME (Focal/Diffuse), Ischemic Maculopathy (With or without CSME) and Cystoid macular oedema.

Blood samples were taken for estimation of complete Hemogram, Fasting Blood sugar, Post-prandial blood sugar, Renal Function tests (blood Urea / Serum Creatinine) and Lipid Profile.

Urine was examined for routine studies and quantitative evaluation for micro-albumin was done by Nephelometry Technology. Urinary Creatinine was estimated by modified Jaffe's method.

Normo-albuminuria was diagnosed when Urinary Albumin: Creatinine Ratio was ≤ 30 mg/gm, Micro-albuminuria when this Ratio was between 30- 300 mg/gm and Macro-albuminuria when the ratio was ≥ 300 mg /gm.

Data was expressed as frequencies and percentages as well as in mean and standard deviation. Analysis was done by Statistical Packages for Social Sciences (SPSS) version 10 software. Chi square test was used for non-parametric analysis. Mean Values were compared using Student's t Test.

One Way Anova was performed where comparison was needed between different observations on different days. For all statistical evaluations, a two-tailed probability value of < 0.05 was considered significant.

Observation:

Of the 300 patients studied in our study, maximum clustering was around age of 46-55 years and 56-65 years.

Age (years)	Frequency	Percent
36-45	46	15.3
46-55	89	29.7
56-65	93	31.0
66-75	72	24.0
Total	300	100

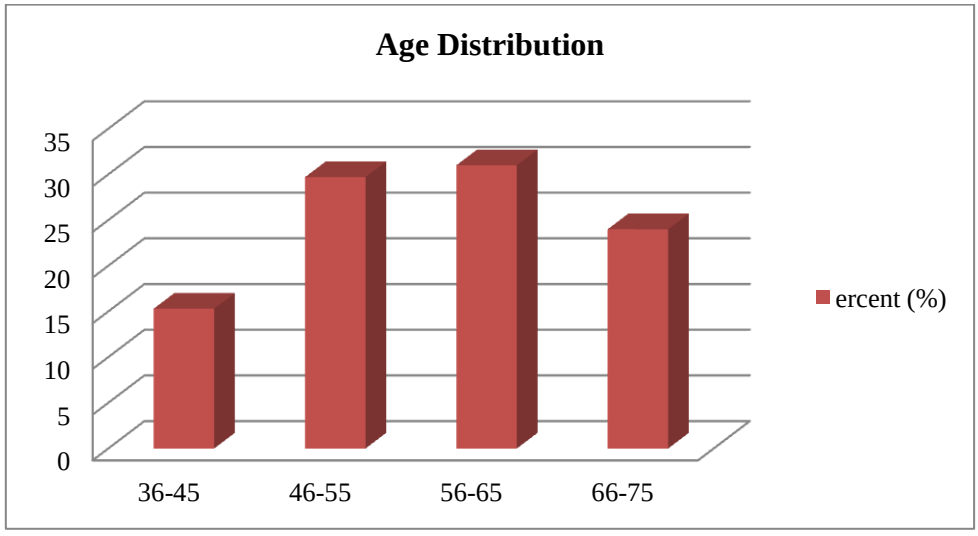

Table and Chart no 1: Percentage distribution of Age in years. (%)

Analysis regarding age and gender distribution was attempted. The mean age between male and female was not statistically significant in our study group. The mean age of male patients was 58.75 ± 10.41 and that of female patients was 55.74± 10.43 years.

Age (yrs)	Males	Females	Total
35-44	17	20	37
45-54	40	45	85
55-64	57	35	92
65-74	55	31	86
Total	169	131	300
Mean±	58.75	55.74	57.43
SD	(10.41)	(10.43)	(10.51)

Chi Square Test: 7.808; P < 0.05

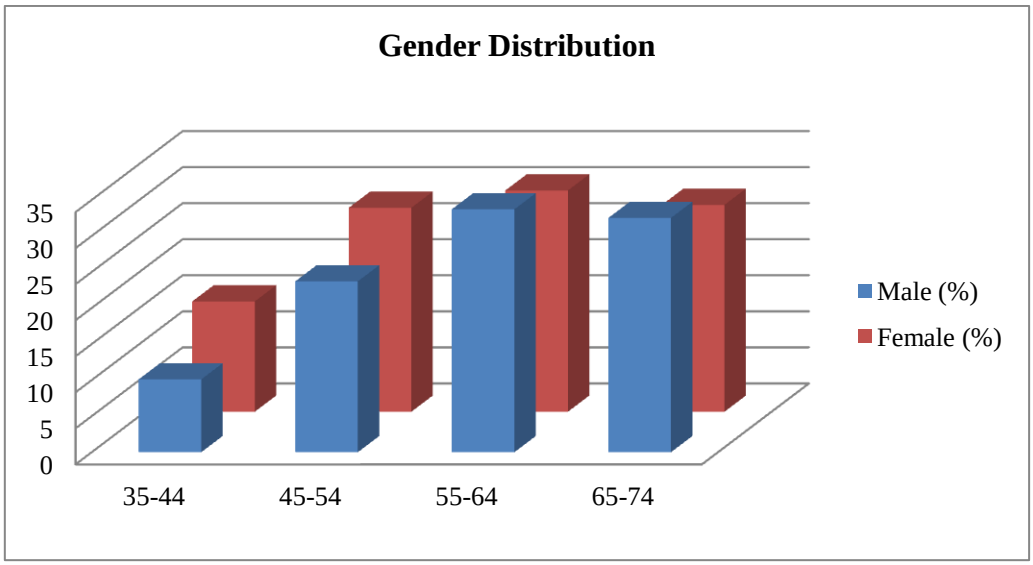

Table and Chart no 2: Gender and Age Distribution.

Analysis of duration of Diabetes in our study group did not reveal any statistically significant difference amongst either gender. 91 of our patients had diabetes duration < 5 years. 176 had diabetes for more than 5 years but less than 10 years. 28 had diabetes for more than 10 years had 5 had diabetes for more than 15 years.

Duration of DM (Yrs)	Male	Female	Total
<5	39	52	91
5-9	109	67	176
10-14	17	11	28
≥15	4	1	5
Total	169	131	300
Mean± SD	6.74 (2.99)	5.91 (2.81)	6.37 (2.93)

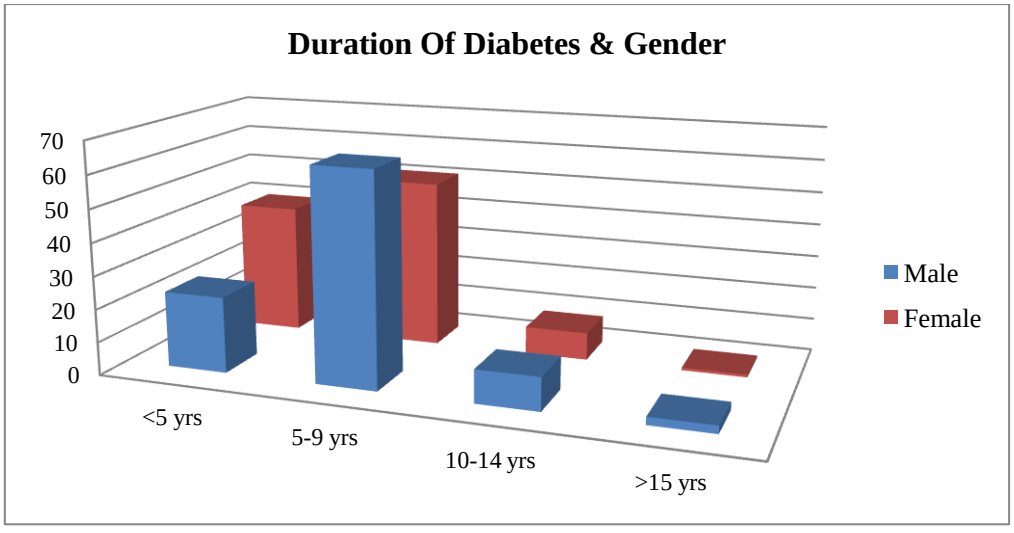

Table & Chart 3: Gender-wise Distribution of Duration of Diabetes.

Of the 300 patients studied in our group, 231 patients tested negative for microalbuminuria.

Micro-albuminuria (mg/gm)	Frequency	Percent
Normal (<30)	231	77
30-49	45	15
50-99	14	4.7
>100	10	3.3

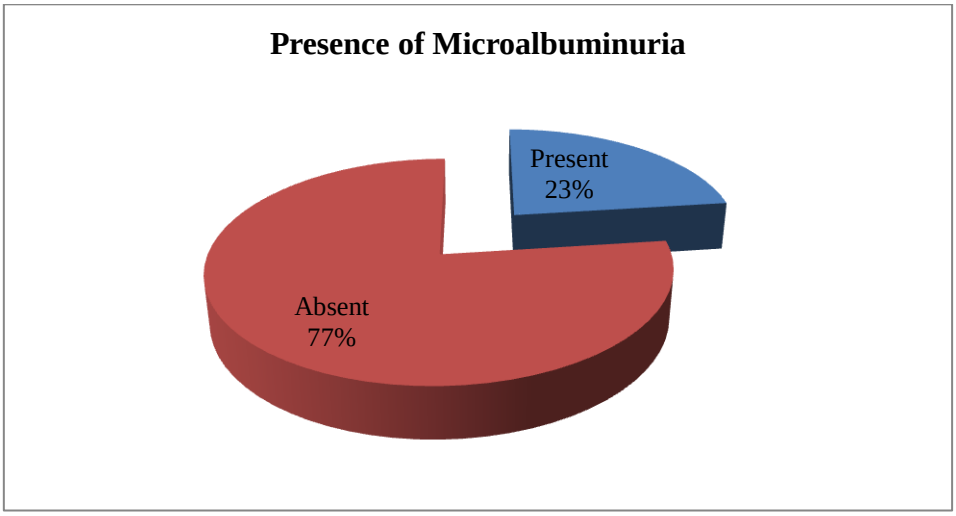

Table and Chart no 4: Distribution of Micro-albuminuria.

Analysis of treatment options in our study group revealed Insulin use in 68 patients, OHAs in 219 patients and both OHAs and Insulin in 10 patients. 3 patients were not on any treatment.

Treatment	Frequency	Percent (%)
Nil	3	1.0
Insulin	68	22.7
OHA	219	73
Both	10	3.3
Total	300	100

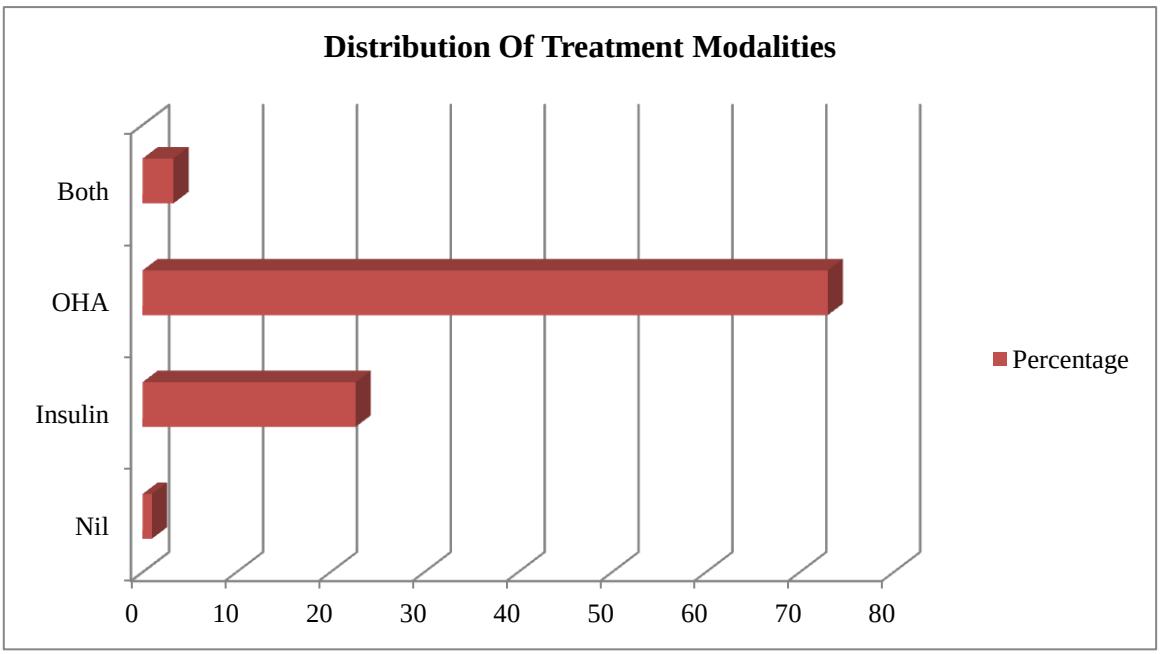

Table and Chart no 5: Distribution of Treatment Modalities for Diabetes.

Analysis of age wise distribution of occurrence of microalbuminuria showed maximum incidence in the age group of 55-64 years (92) followed by 86 in the age group of 55-64 years.

Age (yrs)	Microalbuminuria				Total
	<30 mg/gm	30-49 mg/gm	50-99 mg/gm	>100 mg/gm	
35-44	33	3	1	0	37
45-54	76	7	2	0	85
55-64	72	13	2	5	92
65-74	50	22	9	5	86

Chi Square test :32.212 ; p< 0.001

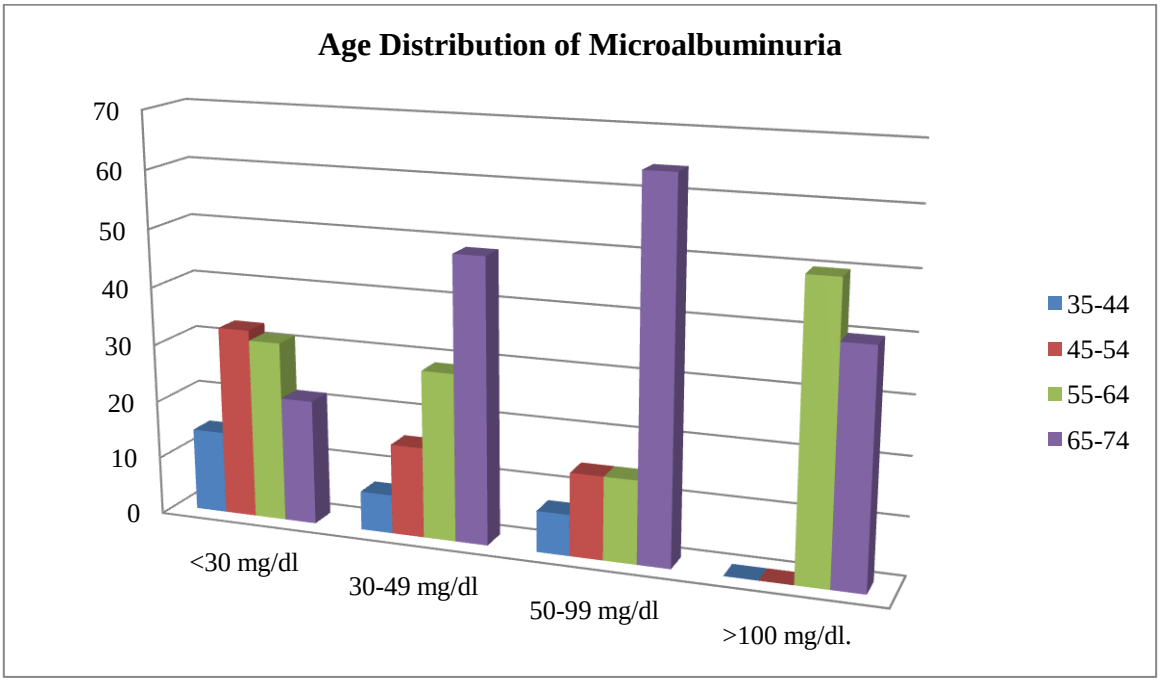

Table and Chart no 6: Age Distribution of Microalbuminuria.

The number of patients with duration of diabetes less than 5 years was 91 and 7 of these had microalbuminuria. 176 patients had diabetes duration between 5-10 years and 38 of these had microalbuminuria. 2 patients had diabetes for more than 10 years and 19 of these had microalbuminuria. All the 5 patients who had been having diabetes for more than 15 years had microalbuminuria.

Duration Of Diabetes (yrs)	Microalbuminuria				Total
	< 30 mg/gm	30-49 mg/gm	50-99 mg/gm	100 mg/gm	
<5	84	6	1	0	91
5-9	138	29	4	5	176
10-14	9	9	7	3	28
≥15	0	1	2	2	5
Total	231	45	14	10	300
Chi Square Test: 94.825; p< 0.001					

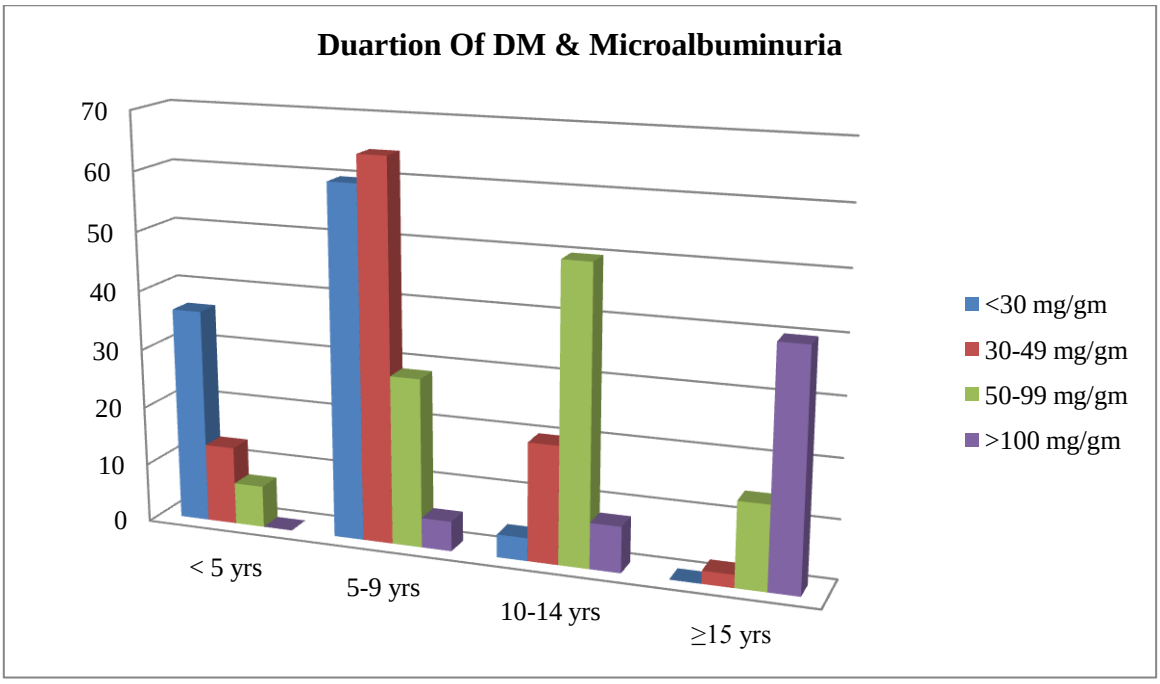

Table & Chart no 7: Duration of Diabetes and Microalbuminuria.

Analysis was also attempted between BMI and microalbuminuria. Microalbuminuria was seen in 17 of the 197 patients with BMI between 19 and 25 kg/m^2 and 52 of the 103 patients with BMI above 25 kg/m$^{2.}$ The incidence of Microalbuminuria was having a negative correlation with BMI <25 kg/m^2 and a positive correlation with BMI > 25 kg/m^2 .

BMI (kg/m^2)	Microalbuminuria				Total
	< 30 mg/gm	30-49 mg/gm	50-99 mg/gm	100 mg/gm	
19-25	180	13	4	0	197
≥ 25	51	32	10	10	103
Total	231	45	14	10	300
Chi Square Test: 70.057; p< 0.001					

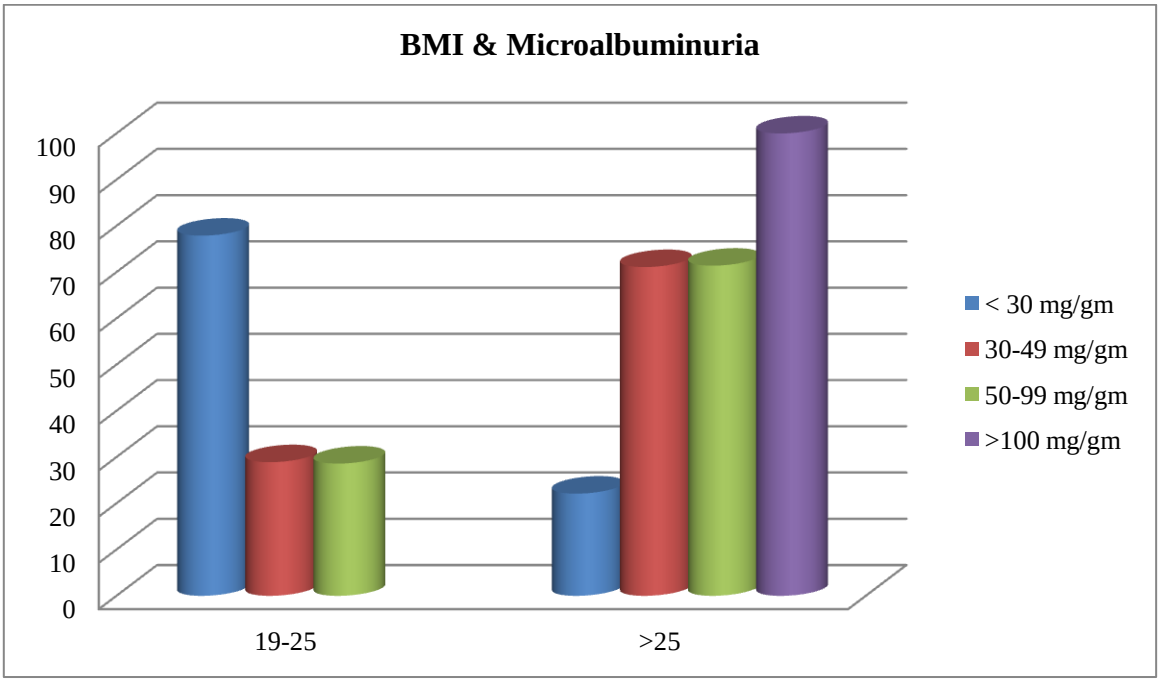

Table & Chart no 8: BMI and Microalbuminuria.

Microalbuminuria was seen in 12 of the 218 patients with Total cholesterol <200 mg/dl and 57 of the 82 patients with Total Cholesterol> 200 mg/dl. A significant association was found between abnormal Cholesterol values and microalbuminuria.

Serum Cholesterol (mg/dl)	Microalbuminuria				Total
	< 30 mg/gm	30-49 mg/gm	50-99 mg/gm	100 mg/gm	
<200	206	10	0	2	218
≥ 200	25	35	14	8	82
Total	231	45	14	10	300
Chi Square Test: 140.541; p< 0.001					

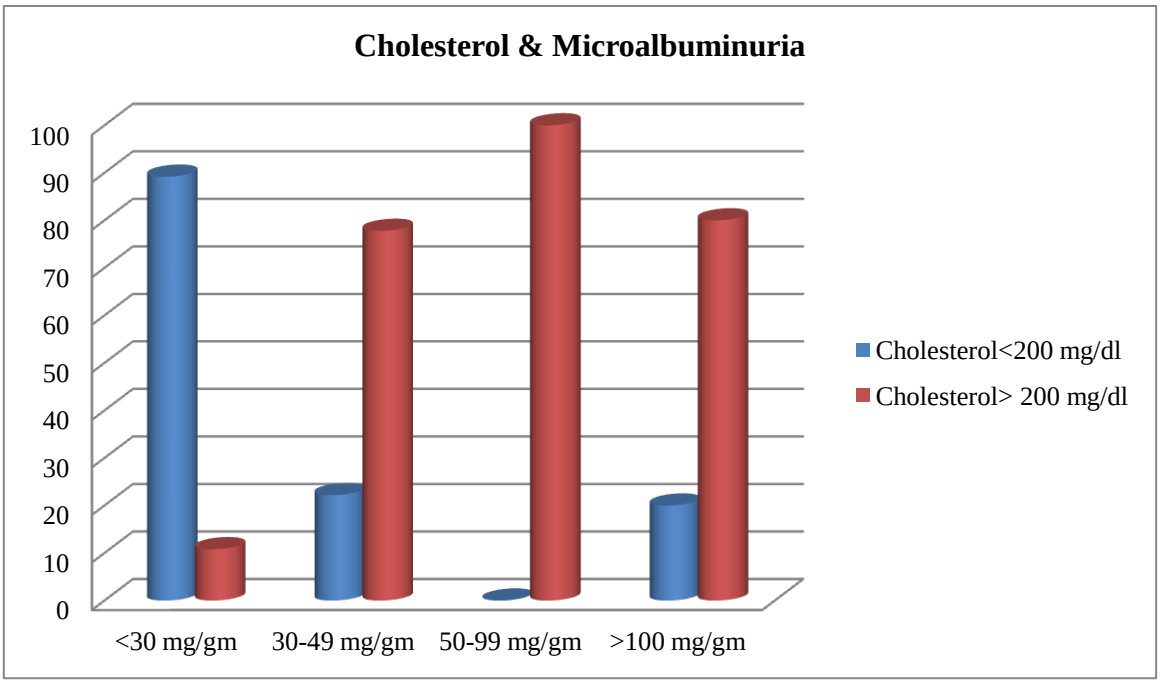

Table & Chart no 9: Serum Cholesterol and Microalbuminuria.

Microalbuminuria was seen in 19 of the 222 patients with Triglyceride levels <160 mg/dl and 50 of the 78 patients with Triglyceride levels > 160 mg/dl. A significant association was found between abnormal Triglyceride values and microalbuminuria.

Serum Triglycerides (mg/dl)	Microalbuminuria				Total
	< 30 mg/gm	30-49 mg/gm	50-99 mg/gm	100 mg/gm	
<160	203	18	0	1	222
≥ 160	28	27	14	9	78
Total	231	45	14	10	300
Chi Square Test: 111.299; p< 0.001					

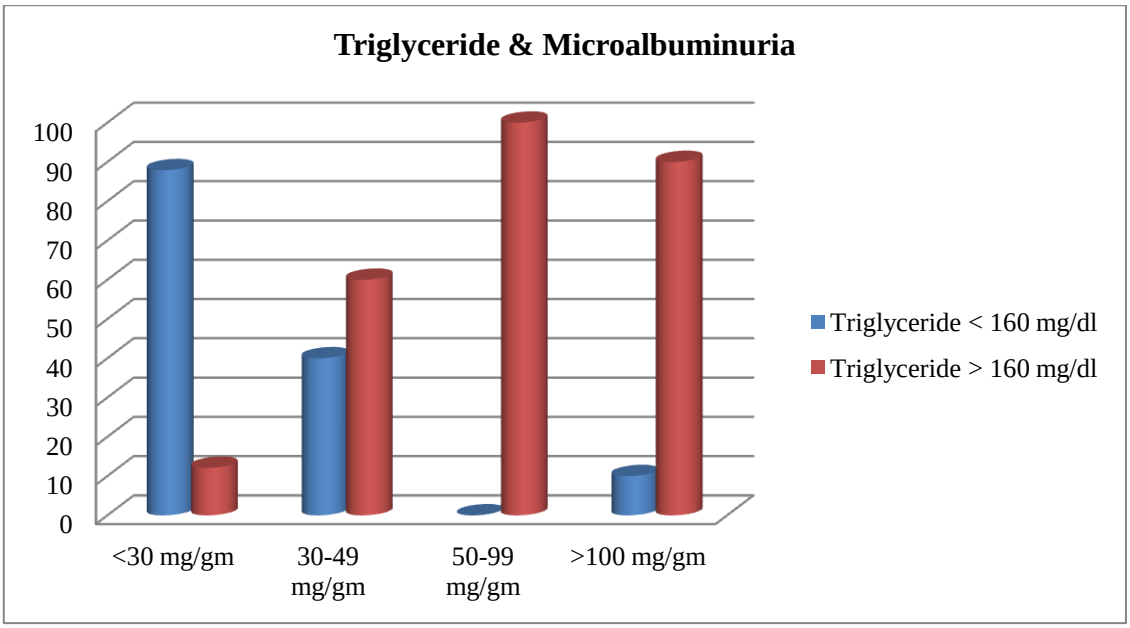

Table & Chart no 10: Serum Triglycerides and Microalbuminuria.

Microalbuminuria was seen in 1 of the 5 patients with HDL levels <30 mg/dl and 68 of the 295 patients with HDL levels > 30 mg/dl. No significant association was found between abnormal HDL values and microalbuminuria.

Serum HDL (mg/dl)	Microalbuminuria				Total
	< 30 mg/gm	30-49 mg/gm	50-99 mg/gm	100 mg/gm	
<30	4	0	1	0	5
≥ 30	227	45	13	10	295
Total	231	45	14	10	300
Chi Square Test: 3.501; p>0.05					

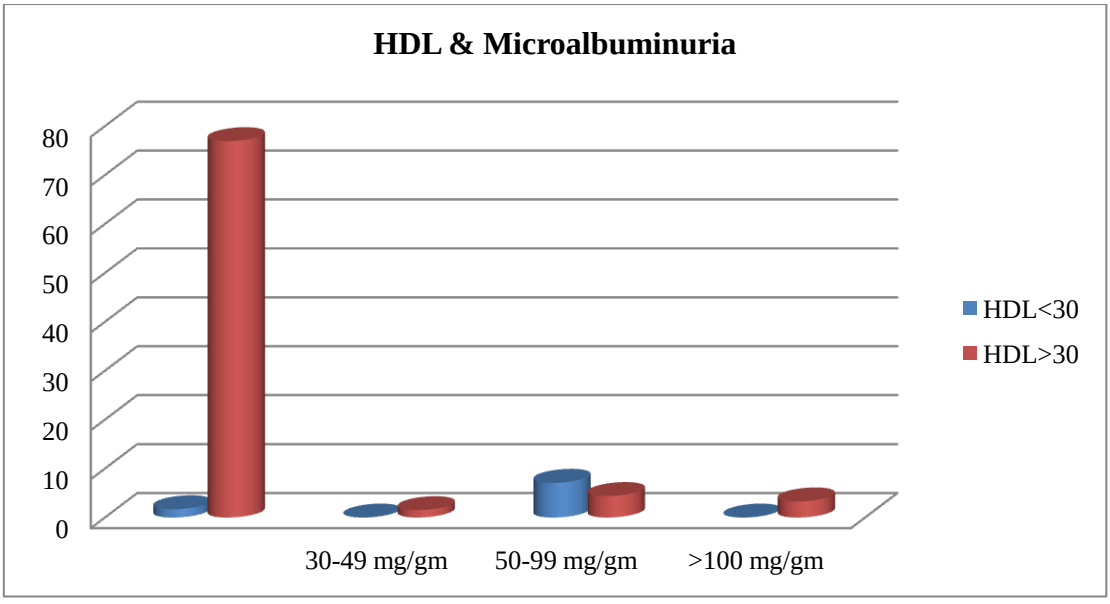

Table & Chart no 11: Serum HDL and Microalbuminuria.

Microalbuminuria was seen in 3 of the 89 patients with FBS levels <150 mg/dl and 34 of the 184 patients with FBS levels between 150 and 199 mg/dl. Of the 27 patients with FBS levels> 200 mg/dl, 8 had microalbuminuria. A significant association was found between impaired glycemic status and microalbuminuria.

Serum FBS (mg/dl)	Microalbuminuria				Total
	< 30 mg/gm	30-49 mg/gm	50-99 mg/gm	100 mg/gm	
<150	86	3	0	0	89
150-199	134	34	9	7	184
>199	11	8	5	3	27
Total	231	45	14	10	300
Chi Square Test: 46.104; p<0.001					

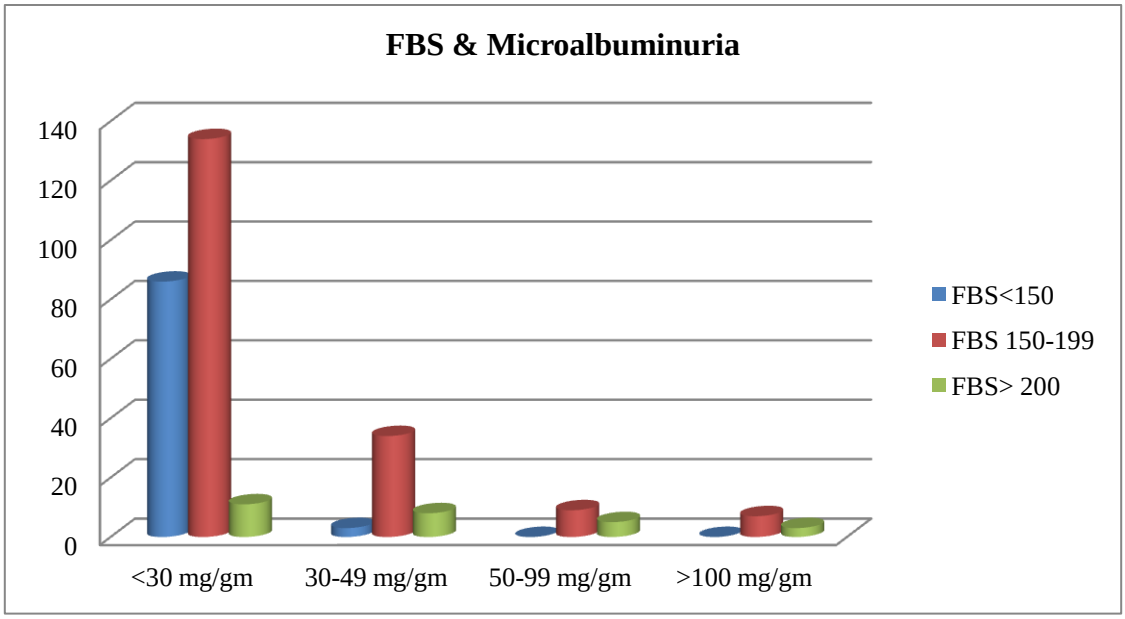

Table & Chart no 12: Glycemic Status & Microalbuminuria.

Microalbuminuria was seen in 69 of the 245 patients with PPBS > 200 mg/dl and none in the 55 patients with PPBS< 200 mg/dl. This was Statistically significant.

PPBS (mg/dl)	Microalbuminuria				Total
	< 30 mg/gm	30-49 mg/gm	50-99 mg/gm	100 mg/gm	
<200	55	0	0	0	55
≥ 200	176	45	14	10	245
Total	231	45	14	10	300
Chi Square Test: 20.117; p<0.001					

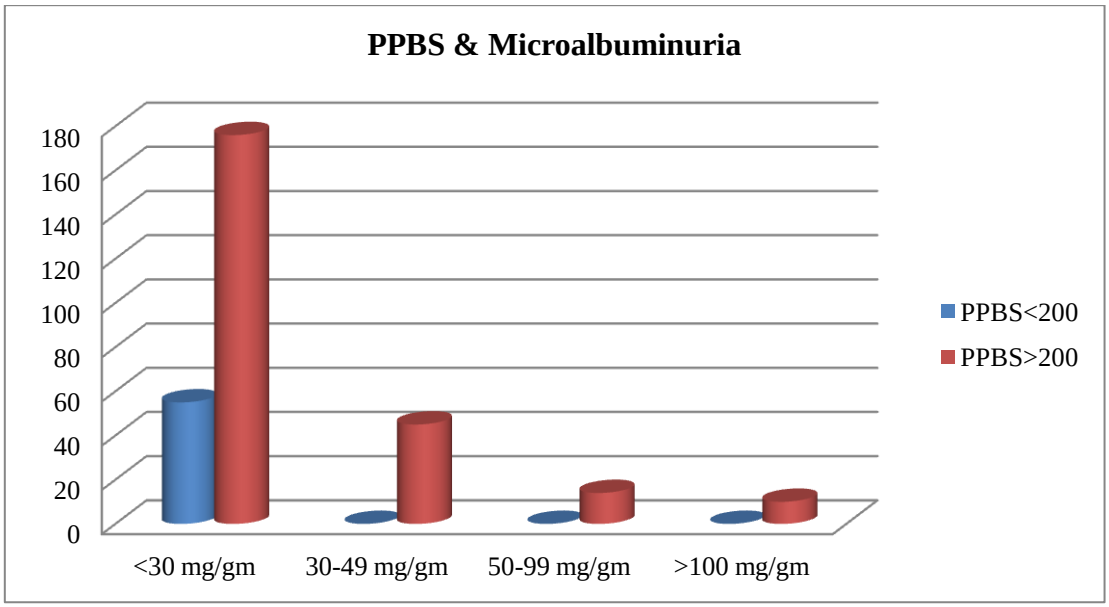

Table & Chart no 13: PPBS and Microalbuminuria.

Of the 300 patients, 34 had retinopathy. Microalbuminuria was seen in 14 of the 31 patients with Non-Proliferative Diabetic Retinopathy. Of the 3 patients with Proliferative Diabetic Retinopathy, all had microalbuminuria.

Diabetic Retinopathy	Microalbuminuria				Total
	< 30 mg/gm	30-49 mg/gm	50-99 mg/gm	100 mg/gm	
Nil	214	37	9	6	266
NPDR	17	8	5	1	31
PDR	0	0	0	3	3
Total	231	45	14	10	300
Chi Square Test: 102.607; p<0.001					

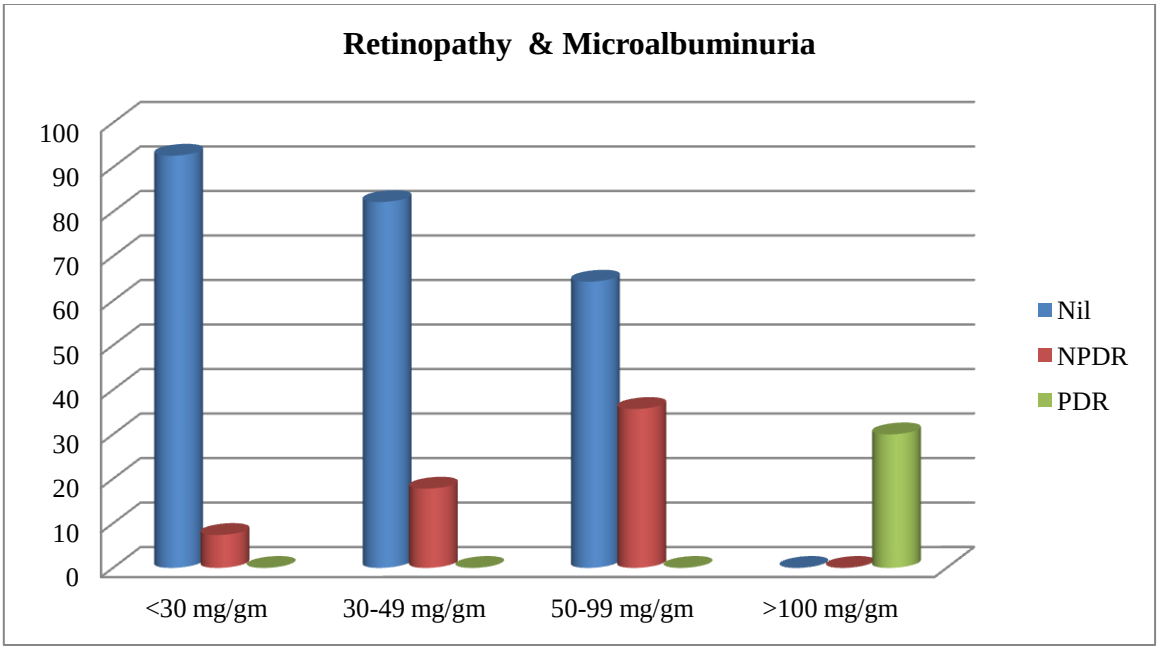

Table & Chart no 14: Retinopathy and Microalbuminuria.

Discussion

Diabetes Mellitus has become one of the most common endocrine problems with multiple complications. The prevalence of Diabetes was estimated to be around 2.8-3% in 2000. With an estimated 40.9 million people with Diabetes, India now accounts for the largest Diabetic population in the world.[1-3]

Type 2 Diabetes has now become one of the leading causes of acquired blindness as well as end stage renal disease. As most of these complications have a silent and insidious progression, early recognition of microvascular damage and prompt intervention is important[3-4].

Microalbuminuria marks the onset of endothelial dysfunction and is an early indicator of Diabetic Nephropathy. The true value of microalbuminuria lies in the fact that it indicates generalized endothelial dysfunction[5-7]. Thus, diabetes with microalbuminuria indicates ongoing progressive endothelial dysfunction manifesting as nephropathy and retinopathy. At the time of diagnosis of Type 2 Diabetes, it is important to screen for nephropathy as more than 7% of patients already would have developed microalbuminuria by that time.[6-7]

This study was attempted as an effort to understand and highlight the significance of screening for Microalbuminuria.

Analysis of literature revealed that even amongst randomly selected patients, the incidence of microalbuminuria varied extensively from 15% to 35%. Parving et al reported a prevalance rate of 22% as compared to the 15% rate reported by Lunetta et al.[7-9]

A prevalence rate of 15.7% for proteinuria was reported by Viay et al amongst patients studied in Chennai while Mohan et al reported a slightly

higher prevalence of 18% proliferative retinopathy in type 2 Diabetic patients from South India. The prevalence rate in our study was 23%. This slight increase could be probably attributed to factors like an elderly cohort of subjects, longer duration of Diabetes and a poor glycemic control.[3,6-9]

After several studies, including that by Wendy et al and Chakravarthy et al, it is now a recognised fact that microalbuminuria occurs more in diabetic patients more than 50 years old.[16,18] Similar findings were also noted in our study, with 2.54 times higher incidence in the age group above 50 years as compared to that of less than 50 years.[9-11] This could be probably explained by a concomitant decrease in β-cell mass with rising duration of diabetes.[12-18]The possible explanation could be that a higher BMI reflected a greater insulin resistance and a more severe endothelial dysfunction.

Although our study was a cross-sectional study, a blatant association was established between poor glycemic control and microalbuminuria in a rural setting. 61.30% of patients with FBS higher than 150 mg /dl and 81.70% of patients with PPBS >200 mg/dl had microalbuminuria in our study. The level of glycemic control is the strongest factor inducing microalbuminuria. Similar findings have been previously reported by Stratton Im et al[10].

This study also highlighted the strong association between microalbuminuria and BMI> 25kg/m2. Of the 103 patients with a BMI higher than 25 kg/m2 in our study group, 52 had microalbum-inuria. These were comparable to studies by Ghai R et al, Patel KL et al and Durrutty P et al.[11-14,21]

Lipid profile is essential as microalbuminuria is frequently associated with hyperlipidemia and treatment of dyslipidemia is important. Our study also brought out a correlation between lipid profile and microalbuminuria and was consistent with studies by Gaede PH et al and Seymour R et al[13-14].

60% of our patients having triglyceride values>160 mg/dl and 77.80% of patients with S Cholesterol >200 mg/dl had microalbuminuria. A 1.93 times higher incidence of microalbuminuria was found in patients with HDL<30 mg/dl in our study. Elevated serum lipid levels are associated with hard exudates in the retina and visual loss. Chakravarty B et al and Wendy PB et al had in their studies established a similar correlation between dyslipidemia and microalbuminuria.

Microalbuminuria has a strong association with Retinopathy. Early and regular ophthalmic review can help avoid blindness in diabetic patients. Masoud RM et al reported that Renal disease as manifested by microalbuminuria and proteinuria is a risk factor for developing retinopathy[17]. In our study, 11.3% patients with diabetes had Diabetic Retinopathy. Further, in our study, 50% patients with retinopathy also had microalbuminuria.

About 20% of the patients with Type 2 Diabetes might have retinopathy at time of diagnosis and most develop significant retinopathy over subsequent decades. Masoud RM et al and Taneja V et al reported an incidence of 3% and 10.2% respectively[17, 19-21].

Diabetes is becoming one of the most important health issues in a resource constrained country like ours. Many complications which put a significant emotional and monetary strain on the people as well as the health care system can be prevented by appropriate interventions. Comparable data for early recognition and influence of ethnic and social influences is however missing from community based centres where the majority of patients with Diabetes are managed. These patients might probably experience the greatest benefit from appropriate and timely interventions. This study was an attempt to analyse the associations between the various complications of microalbumnuria in a south-Indian population.

Conclusion

1) The incidence of microalbuminuria in the 300 patients studied in our group was 23%.
2) A direct correlation between increasing age of patients, and duration since

diagnosis of diabetes with prevalence of microalbumniuria was observed.

3) Severity of Diabetic retinopathy was concurrent with the duration of Diabetes.
4) There was a significant association between retinopathy, microalbuminuria and high BMI.
5) An inverse association was noted between HDL values and microalbuminuria.

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