Correlates of Microalbuminuria in Patients with Diabetes Mellitus: Automated Urine Analysis

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Abstract

Introduction: Type 2 diabetes mellitus accounts for more than 90% of all patients with diabetes worldwide. According to ADA, microalbuminuria is defined as levels of urinary protein from 30 to 300 mg/day or 20 μg/ minute, or 30 to 299 μg/ mg creatinine. *Methodology:* 250 out patients of type 2 diabetes mellitus were selected at random. Based on levels of albuminuria the patients were categorized into normoalbuminuria with <30 mg/gm of creatinine, microalbuminuria with 30- 300mg/gm of creatinine, and macroalbuminuria with >300mg/gm of creatinine. *Results:* In the present study, Serum Triglyceride was 116+43.9mg/dl, Serum Total cholesterol 154±39.mg/dl, HDL was 45.4+10.8mg/dl, and LDL was 96.3+29mg/dl and there were significant correlations of microalbuminuria with reference to duration (1-5 years since diagnosis) (p-value<0.10) and HbA1C >7%, total cholesterol >200 mg/dl, serum triglycerides >150 mg/dl, HDL <35 mg/dl and hypertension (p value<0.05). *Conclusion:* Microalbuminuria is associated with various microvascular and macrovascular co-morbidities of diabetes. Microalbuminuria in itself being a predictor of diabetic nephropathy showed positive association with diabetic neuropathy and diabetic retinopathy (microvascular complications).

Keywords: Diabetes Mellitus; Microalbuminuria; Lipid Profile; Correlates.

Introduction

Diabetes mellitus is a heterogenous chronic metabolic disorder principally characterized by persistent hyperglycemia resulting from defects in insulin action and/or insulin secretion.

Primarily diabetes evolves from interaction of genetic and environmental factors resulting in autoimmune destruction of the beta cells or progressive deterioration in â-cell capacity on the face of gross defects in insulin action [1].

Prevalence of diabetes is increasing globally and it is one of the major health problems of the 21st century. In the year 2003, it is estimated that there were 194 million adult subjects with diabetes (5.1%) and 314 million subjects with impaired glucose tolerance (IGT) (8.2%). The prevalence of diabetes and IGT are expected to increase to 6.3 and 9% respectively by 2025 [2].

India is currently experiencing an epidemic of diabetes mellitus. 25 Type 2 diabetes mellitus accounts for more than 90% of all patients with diabetes worldwide 26. Reports from different parts of India have also suggested a rising trend in the prevalence of diabetes54. In India there was an estimated 19.4 million diabetes individuals in 1995 which is projected to increase to nearly 80 million in 2030 [3].

According to ADA, microalbuminuria is defined as levels of urinary protein from 30 to 300 mg/day or 20 μg/minute, or 30 to 299 μg/ mg creatinine. Screening for microalbuminuria can be done in any of the four different methods [4]:

1. Measure the albumin to creatinine ratio in a random spot collection.

2. Collect a 24 hour urine sample and test for creatinine (assess creatinine clearance).

3. Obtain a timed (i.e. 4 hour or overnight) of urine sample.

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4. Test for microalbuminuria qualitatively on a random urine sample

Microalbuminuria is an early predictor of diabetic nephropathy and premature cardiovascular disease [5]. The earliest clinical evidence of nephropathy is the appearance of low but abnormal levels of albumin in urine referred to as microalbuminuria and patients with microalbuminuria are referred to as having incipient nephropathy [6]. Without specific interventions 80% of subjects with type I diabetes who develop sustained microalbuminuria have urinary albumin excretion increase at a rate of 10-20% per year to the stage of overt nephropathy or clinical albuminuria over a period of 10-15 years with hypertension also developing along the way. Once overt nephropathy occurs without specific interventions the GFR gradually falls over a period of several years at a rate that is highly variable from individual to individual 2- 20 ml/min/year. ESRD develops in 50% of type I diabetic individuals with overt nephropathy within 10 years and in >75% by 20 years [6].

A higher proportion of individuals with type 2 diabetes are found to have microalbuminuria and overt nephropathy shortly after the diagnosis of their diabetes because diabetes is actually present for many years before the diagnosis is made and also because the presence of albuminuria may be less specific for the presence of diabetic nephropathy as shown by the biopsy studies [6].

Methodology

250 out patients of type 2 diabetes mellitus were selected at random, Based on levels of albuminuria the patients were categorized into normoalbuminuria with <30 mg/gm of creatinine, microalbuminuria with 30- 300mg/gm of creatinine, and macroalbuminuria with >300mg/gm of creatinine.

Hypertension defined as blood pressure of >130/80 mmHg or those on antihypertensive treatment, Ischemic heart disease defined by presenting complaint or history of angina/myocardial infarction, Diabetic neuropathy defined by signs and symptoms of neuropathy and Diabetic retinopathy defined by signs of retinopathy on slit lamp biomicroscopy. Detail history, examination followed by investigations-Fasting Blood Sugar, Postprandial Blood Sugar, Glycosylated Haemoglobin, Lipid Profile, Urine analysis by dipsticks, estimation of albumin creatinine ratio and urine microscopy was done.

Inclusion Criteria

• Already diagnosed adult type 2 diabetes mellitus (NIDDM) patients.

Exclusion Criteria

• Gestational diabetes mellitus and Type 1 diabetes mellitus (IDDM) patients.

• Cases of urinary tract infection, haematuria, intake of Vit. B-complex, Jaundice, urinary antiseptic which interfere with urine strip analysis were excluded from the study.

Statistical Analysis

Univariate analysis was done for Categorical data using chi-square test**.**

Results

Among the total 250 cases 164 were normoalbuminurics 50 were microalbuminurics and 36 were macroalbuminurics. Among the Microalbuminuria cases 52% of the cases presented in the 1-5yrs duration since diagnosis of diabetes followed by 38% in the 6-10yrs duration since diagnosis, 6% in the 11-15 yrs duration and 4% in the 16-20yrs duration since diagnosis of type 2 diabetes. Among Macroalbuminuria cases 55.6%of the cases presented in the 1-5 yrs duration since diagnosis followed by 30.6% in the 6-10yrs duration.

Table 1: Duration & albuminuria groups

| Duration (years) | Alb Groups | | | | | | Total | |
| | Macro | | Micro | | Normalbum | | | |
	No.	%	No	%	No	%	No	%
1-5	20	55.60	26	52.00	97	59.10	143	57.20
11-15	4	11.10	3	6.00	7	4.30	14	5.60
16-20	1	2.80	2	4.00	0	0	3	1.20
6-10	11	30.60	19	38.00	60	36.60	90	36.00
Total	**36**	**100**	**50**	**100**	**164**	**100**	**250**	**100**

X^2=9.197,   df : 6   p=0.163(not significant)

Table 2: diet & albuminuria groups

| Diet | Alb Groups | | | | | | Total | |
| | Macro | | Micro | | Normalbum | | | |
	No.	%	No	%	No	%	No	%
Non-veg	4	11.10	6	12.00	23	14.00	33	13.20
Veg	32	88.90	44	88.00	141	86.00	217	86.80
Total	**36**	**100**	**50**	**100**	**163**	**100**	**250**	**100**

$X^2=0.297$, df : 2   p=0.862(not significant)

Among 250 cases vegetarians were largest group with 217 cases and non vegetarians were 33 cases. Percentage of microalbuminurics was 88% when compared to 12% in non-vegetarians although this association was not significant.

of the 250 cases maximum were in the category of obese (>27.5) followed by normal BMI(18.5-22.9) and then the overweight(23-27.5) BMI category. The percentage of microalbuminurics is more in the obese and the overweight BMI categories when compared to microalbuminurics in normal BMI category.

Among 250 cases 140 cases show HbA1C more than 7%.Percentage of microalbuminuria cases is more (27.1%) in HbA1C more than 7% group when compared to 10.9% in the HbA1C less than 7%group.

Table 3: Body mass index & albuminuria groups

| BMI | Alb Groups | | | | | | Total | |
| | Macro | | Micro | | Normalbum | | | |
	No.	%	No	%	No	%	No	%
Normal	14	38.90	13	26.00	66	40.20	93	37.20
Obese	19	52.80	25	50.00	64	39.00	108	43.20
Over weight	3	8.30	12	24.00	34	20.70	49	19.60
Total	**36**	**100**	**50**	**100**	**164**	**100**	**250**	**100**

$X^2=7.016$,   df : 4   p=0.135(not significant)

Table 4: Hba1c& albuminuria groups

| Blood sugar | Alb Groups | | | | | | Total | |
| | Macro | | Micro | | Normalbum | | | |
	No.	%	No	%	No	%	No	%
<7%	13	36.10	12	24.00	85	51.80	110	44.00
>7%	23	63.90	38	76.00	79	48.20	140	56.00
Total	36	100	50	100	164	100	250	100

$X^2=13.106$,   df : 2   p=0.001(significant)

Table 5: Total cholesterol& albuminuria groups

| TC | Alb Groups | | | | | | Total | |
| | Macro | | Micro | | Normalbum | | | |
	No.	%	No	%	No	%	No	%
> 200mg/dl	27	75.00	35	70.00	147	89.60	209	83.60
< 200mg/dl	9	25.00	15	30.00	17	10.40	41	16.40
Total	**36**	**100**	**50**	**100**	**164**	**100**	**250**	**100**

$X^2=13.043$,   df : 2   p=0.001(significant)

Table 6: Triglyceride& albuminuria groups

| Triglyceride | Alb Groups | | | | | | Total | |
| | Macro | | Micro | | Normalbum | | | |
	No.	%	No	%	No	%	No	%
< 150mg/dl	9	25.00	19	38.00	97	59.10	125	50.00
> 150mg/dl	27	75.00	31	62.00	67	40.90	125	50.00
Total	**36**	**100**	**50**	**100**	**164**	**100**	**250**	**100**

$X^2=17.368$,   df : 2   p=0.02(significant)

Among 250 cases 209 (83.6%) cases showed total cholesterol more than 200mg/dl and cases with total cholesterol less than 200 mg/dl were 41 (16.4%).70% of microalbuminurics belong to the total cholesterol more than 200mg/dlgroup.

Among 250 cases 125 were showing Serum Triglyceride more than 150mg/dl.

The percentage of microalbuminuria(62) and macroalbuminuria(75)is more in the more than 150mg/dl group when compared to the less than 150mg/dl

Table 7: HDL group & albuminuria groups

HDL	Alb Groups						Total	
	Macro		Micro		Normalbum			
	No.	%	No	%	No	%	No	%
>35mg/dl	4	11.10	7	14.00	36	22.00	47	18.80
<35mg/dl	32	88.90	43	86.00	128	78.00	203	81.20
Total	**36**	**100**	**50**	**100**	**164**	**100**	**250**	**100**

$X^2=3.216$,df :   2   p=0.2(not significant)

Table 8: LDL group & albuminuria group

LDL group	Alb Groups						Total	
	Macro		Micro		Normalbum			
	No.	%	No	%	No	%	No	%
<100mg/dl	21	58.90	34	68.00	111	67.60	166	96.40
> 100mg/dl	15	41.10	16	32.00	53	32.40	84	3.60
Total	**36**	**100**	**50**	**100**	**164**	**100**	**250**	**100**

$X^2=1.858$,df : 2   p=0.320 (not significant)

Table 9: Neuropathy &albuminuria groups

Neuropathy	Alb Groups						Total	
	Macro		Micro		Normalbum			
	No.	%	No	%	No	%	No	%
Present (+)	1	9.10	4	36.40	6	54.50	11	100
Absent (-)	35	14.60	46	19.20	158	66.10	239	100
Total	**36**	**14.40**	**50**	**20.00**	**164**	**65.60**	**250**	**100**

$X^2=1.980$,df : 2   p=0.372 (not significant)

Table 10: IHD & albuminria groups

IHD	Macro		Alb Groups				Total	
			Micro		Normalbum			
	No.	%	No	%	No	%	No	%
Present (+)	5	25.00	7	35.00	8	40.00	20	100
Absent (-)	31	13.50	43	18.70	156	67.80	230	100
Total	**36**	**14.40**	**50**	**20.00**	**164**	**65.60**	**250**	**100**

$X^2=6.314$,df : 2   p=0.0439(significant)

Table 11: Retinopathy &albuminuria groups

Retinopathy	Alb Groups						Total	
	Macro		Micro		Normalbum			
	No.	%	No	%	No	%	No	%
Present (+)	1	50.00	8	40.00	11	55.00	20	100
Absent (-)	35	15.20	42	18.30	153	66.50	230	100
Total	**36**	**14.40**	**50**	**20.00**	**164**	**65.60**	**250**	**100**

$X^2=6.054$,df : 2   p=0.0489(significant)

Table 12: Hypertension & albuminuria groups

Hypertension	Alb Groups						Total	
	Macro		Micro		Normalbum			
	No.	%	No	%	No	%	No	%
Present (+)	16	19.50	22	26.80	44	53.70	82	100
Absent (-)	20	11.90	28	16.70	120	71.40	168	100
Total	**36**	**14.40**	**50**	**20.00**	**164**	**65.60**	**250**	**100**

$X^2=7.713$,df : 2   p=0.021(significant)

group Among the total 250 cases 47 cases showed HDL less than 35mg/dl. The percentage of cases in the more than 35mg/dl group is 86% of microalbuminurics and 88.9% macroalbuminurics .

Among 250 cases, 84 cases had LDL more than 100 mg/dl. There is no positive association with microalbuminuria and LDL levels more than 100mg/dl.

Among 250 cases 11 cases had neuropathy. The cases with neuropathy had more percentage of microalbuminuria cases (36.4) when compared to the cases without neuropathy(19.2).

Among 250 cases 20 case had IHD. 35% of the cases with IHD were microalbuminurics cases and only 18.7% of the cases were microalbuminuric in those without IHD.

Among total 250 cases 20 cases had retinopathy. Microalbuminuria case were 40% among those with retinopathy as compared to only 18.3% of the cases in those without retinopathy

Among 250 cases hypertension was present in 82 cases and 26.8% of the cases with hypertension had microalbuminuria while only 16.7% of the cases without hypertension were microalbuminuric

Discussion

Duration of diabetes when the patient presented was divided into four categories ranging from 1-5, 6-10, 11-15, 16-20yrs. Most of the patients were detected with microalbuminuria in the first few years of the disease i.e, 1-5yr period. There was significant correlation of microalbuminuria with first 5 years since diagnosis ($p<0.10$).

Duration of Diabetes in Different Studies (mean±sd)

	Mean ± SD (years)
Present study 2013	5.5±4.4
Mohammed et al[7] 2003	8.8±5.21

The study contained both vegetarians and non-vegetarians. However no significance was found with respect to diet.

Body Mass Index was estimated and patients were categorized as Normal

BMI, Obese and Overweight. 43.2% were obese, 19.6% were overweight and 37.2% had normal BMI. Patients falling in the obese category showed maximum number of micro and macroalbuminurics.

Body Mass Index and Microalbuminuria in Different Studies

% of Microalbuminurics	BMI>23 (over weight+obese)	BMI<23 (normal)
In present study 2013	74	26
Mohammed et al 2003[7]	86.6	13.4

Based on the glycemic control they were divided into those with HbA1c less than 7 and those with HbA1c equal to or more than 7%. 63.9% of macroalbuminurics and 76% of microalbuminurics fell into the group of >7% HbA1c.

Glycosylated Haemoglobin (HBA1c) in Different Studies (mean±sd)

	HbA1c Values (Mean±SD)
Present study 2013	8.2±2.6
Steno diabetes study[8] 1984-1987	8.9±0.3

In the present study, there was significant correlation of microalbuminuria with HbA1c >7% group ($p<0.05$).

Lipid Profile (Serum Total cholesterol, Serum Triglyceride and HDL) showed positive correlation with microalbuminuria but not with high Serum LDL levels.

35 cases of microalbuminuria belonged to the total cholesterol >200mg/dl group whereas only 15 cases belonged to <200mg/dl group. 31 cases of microalbuminuria had serum triglyceride >150mg/dl whereas only19 cases were in the <150mg/dl group.HDL group with <35mg/dl had 43 cases of microalbuminuria whereas only 7 cases had HDL>35mg/dl.

Serum Cholesterol in Different Studies (mean±sd)

Study	Serum cholesterol (mean±sd)
In present study 2013	154±39.mg/dl
M.Afkhami-Ardekani[9] 2005-2007	200+44 mg/dl

In the present study, there was significant correlation of microalbuminuria with total cholesterol >200mg/dl group. ($p<0.05$)

Serum Triglyceride and Microalbuminuria in Different Studies (Mean±Sd)

Percentage of microalbuminuria	Serum Triglyceride >150mg/dl
in Present study 2013	62
Mohammed et al 2003[7]	93.7

In the present study, there was significant correlation of microalbuminuria with serum triglyceride >150 mg/dl group. ($p<0.05$)

Serum HDL and Microalbuminuria in Different Studies

Percentage of microalbuminurics	Low Serum HDL
In the present study 2013	86
Mohammed et al 2003[7]	91.3

In the present study, there was significant correlation of serum HDL <35 mg/dl with microalbuminuria ($p<0.05$).

Serum LDL and Microalbuminuria in Different Studies

Percentage of microalbuminurics	Serum LDL>100mg /dl
In the present study 2013	32
Mohammed et al 2003[7]	93.2

In a study done by Chang Sheng Sheng et al [10] the following results were got. The 1079 participants included 410 (38.0%) hypertensive patients, and 66

(6.1%) diabetic patients. The prevalence of microalbuminuria was 3.2 times higher in 167 patients with the metabolic syndrome than 912 subjects without the metabolic syndrome (12.0% *vs.* 2.9%, $P < 0.0001$). In multiple regression adjusted for sex, age, body mass index, current smoking, alcohol intake and the use of antihypertensive drugs, and mutually adjusted for the components, microalbuminuria was significantly associated with diastolic BP and fasting plasma glucose but not with waist circumference, systolic BP, or serum HDL cholesterol and triglycerides ($P > 0.10$).

In the present study, Serum Triglyceride was 116 ± 43.9mg/dl, Serum Total cholesterol $154\pm39.$mg/dl, HDL was 45.4 ± 10.8mg/dl, and LDL was 96.3 ± 29mg/dl and there were significant correlations of microalbuminuria with reference to duration (1-5 years) (p-value<0.10) and HbA1C, total holesterol, serum triglycerides, HDL and hypertension (p value<0.05).

Neuropathy and Microalbuminuria in Different Studies

% of microalbuminuria	With Neuropathy (%)
Present study 2013	36.4
Mohammed et al 2003[7]	48.8

Cases were divided into those with neuropathy and those without neuropathy in which microalbuminuria cases made upto 36.4% in with neuropathy group when compared to 19.2% in those without neuropathy.

Ischemicheart Disease and Microalbuminuria in Different Studies

% microalbumiunrics	With IHD (%)
Present study 2013	35
A Varghese et al [11] 1998	47

So also cases were grouped under those with Ischaemic Heart Disease and those without Ischaemic Heart Disease in which 35% of those with IHD were microalbuminuric when compared to only 18.7% of those without IHD were microalbuminuric.

Retinopathy and Microalbuminuria in Different Studies

% of microalbuminurics	With Retinopathy (%)
Present study 2013	40
Mohammed et al 2003[7]	48.3

After dividing the cases as to those with and without retinopathy it is observed that 40% of those with retinopathy were microalbuminuric as compared to 48.3 % in a study done by Mohammed et al [7].

Hypertension and Microalbuminuria in Different Studies

% of microalbuminurics	With hypertension (%)
Present study 2013	26.8
Mohammed et al 2003[7]	73

26.8 % of those with hypertension were microalbuminurics as compared to 16.7% of those without hypertension were microalbuminurics

Conclusion

In this study it is shown that there is significant correlation of microalbuminuria with duration since diagnosis i.e, first 1-5yrs of NIDDM; HbA1c values more than 7%, total cholesterol >200 mg/dl, serum triglycerides >150 mg/dl, HDL < 35 mg/dl and with hypertension thus proving the association of microalbuminuria with early onset in NIDDM population, with poor glycemic control, with cardiovascular risk factors like dyslipidemia and hypertension.

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