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The Role of Microalbuminuria for Assessment of Atherogenecity in Prediabetics

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Abstract:
Background: *Prediabetes is a precursor to diabetes and is considered world's fastest growing chronic disease, as aptly understood by the figures available in the literature. 285 million people are currently affected with prediabetes and the projected figure is 418 million by the year 2025. Today the evidence is undisputable that diabetes can be delayed or prevented by either intensive lifestyle modifications and/or variety of pharmacotherapies. Microalbuminuria is gaining recognition as a simple marker for determining atherogenecity. Prediabetic patients may also have predispositon for atherogenecity & hence expected to have significant microalbuminuria.*
Aim & Objective*: To find out prevalence of microalbuminuria in prediabetics, record and analyse the presence of microalbuminuria as a measure of atherogenecity in prediabetics and study the association of observed values of carotid intima media thickening (IMT) with presence of microalbuminuria in prediabetics.*
Results: *In present study the overall prevalence of microalbuminuria in prediabetics was 32.57% whereas in males, prevalence of microalbuminuria in prediabetics was 43.33% which was more than female patients [21.18%]. The Sensitivity of microalbuminuria in prediabetics was 85.29% whereas specificity was 80.19%. The observed values of microalbuminuria in prediabetics in relation to age group & BMI have been found statistically nonsignificant, however microalbuminuria outcome with dyslipidemia, smoking and alcohol were found to be statistically significant.*
Conclusion: *The prevalence of microalbuminuria was more in male prediabetic patients as compared to that of female prediabetics. Microalbuminuria seems to be a very early sensitive marker in life of the altered metabolic milieu that is associated with susceptibility of an individual to cardiovascular disease in prediabetes.*
Keywords: *Microalbuminuria, Prediabetes, Carotid Intima Media Thickeness (IMT).*

I. Introduction

Prediabetes is defined as the "gray area" between normal blood sugar and diabetic levels. According to the most recent clinical practice recommendations published in 2012 by the American Diabetes Association (ADA), prediabetes is defined.[1] Currently, prediabetes is classified into two subtypes: impaired fasting glucose and impaired glucose tolerance.

In India the estimated prevalence rates for prediabetes around 11%.[2] Prediabetes is a precursor to diabetes and is considered world's fastest growing chronic disease, as aptly understood by the figures available in the literature. 285 million people are currently affected with prediabetes and the projected figure is 418 million by the year 2025.[3] It has been termed "Americas largest healthcare epidemic", affecting more than 57 million americans.[4]

Today the evidence is undisputable that diabetes can be delayed or prevented by either intensive lifestyle modifications and/or variety of pharmacotherapies. There are many debates on the details of management of prediabetes, however controversies do not exist for addressing and treating prediabetes. Preventing diabetes is the only way of decreasing the immense of future burden of diabetes and its complications and finance.

Microalbuminuria is gaining recognition as a simple marker for determining atherogenecity. Prospective and epidemiologic studies have found that microalbuminuria is predictive, of all causes of cardiovascular mortality and CVD events, independent of traditional risk factors. The pathophysiologic mechanism underlying the association between albumin excretion and CVD is not fully defined. Microalbuminuria may be a marker of CVD because it reflects subclinical vascular damage in the kidneys and other vascular beds. It may also signify systemic endothelial dysfunction that predisposes to future cardiovascular events. Positive microalbuminuria is considered not only a marker of renal damage, rather presence of albumin in urine denotes systemic vascular damage since the kidney is the only vascularized organ that communicates with the exterior through fluid, filtered through its microvasculature. This enables renal disease to be used as a tracer disease, the diagnosis of which reveals other diseases that have vascular damage in

common[5]. Microalbuminuria not only predicts the course of CKD, but also of cardiovascular and cerebrovascular disease.[6] Considerable attention has been paid in recent at the wall of thickeness of carotid arteries, recognizing IMT as mark of atherosclerotic reflection. Microalbuminuria also has been projected as early marker of atherosclerotic reflection & hence presence of microalbuminuria especially in prediabetics is considered as an independent risk factor for cardiovascular events.

Aims and Objectives

- To record and analyse the presence of microalbuminuria as a measure of atherogenecity in prediabetics.
- To associate the observed values of carotid intima media thickening with presence of micro albuminuria in prediabetics.
- To study the associated risk factors of microalbuminuria in prediabetics.

II. Material And Methods

It is an open non randomized prospective, observational study of correlation between increased albuminuria and intima media thickening for assessment of atherogenecity in prediabetic cases. Analysis will be carried out with Chi–square values and multiple variate analysis for analysing correlation ship of microalbuminuria with carotid intima media thickening.
No. of cases: 175

Case definition: Prediabetics as per ADA Criteria 2012. Elevated urinary albumin excretion (UAE) > 30ug/mg. Intima media thickeness greater than 0.9mm is almost certainly indicative of atherosclerosis.[7]

Inclusion Criteria: All cases diagnosed as prediabetes as per criteria by American Diabetes Association (ADA) 2012 will be taken up for the study.

Exclusion Criteria: Cases of diabetes mellitus, hypertension and ischemic heart diseases with or without medications

Study Groups:
Group – A Microalbuminuria Positive Cases (> 30µg/mg).
Group – B. Microalbuminuria Negative Cases (< 30µg/mg).
A verbal informed consent of all the participants was taken as per standard protocol. Information regarding daily alcohol consumption & smoking status recorded in all acute and chronic cases.

Investigations:

1. Detection of urinary albumin-to-creatinine ratio (Albumin Creatinine Ratio) was performed by Siemens diagnostic kit (using a early morning spot urine sample). The Microalbumin (MALB) method is based on a Particle Enhanced Turbidmetric Inhibition Immunoassay (PETINIA).
2. Carotid intima media thickeness for assessment of atherogenecity determined by Carotid Doppler. (11mHZ)
3. Plasma glucose level- Fasting and 2hour OGTT
4. Glycosylated haemoglobin (HbA1c)
5. Lipid profile: Total cholesterol, HDL, Triglyceride by enzymatic colorimetric assay.

III. Results

Table 1: Association of Different parameters with Micro-Albuminuria:

		Micro-Albuminuria Positive (Group A) (n=57)	Micro-Albuminuria Negative (Group B) (n=118)	Total no. of patients, ( ) = %	p-value
Gender	Male	39(68.42%)	51(43.22%)	90 (51.42%)	P=0.025 S
	Female	18(31.58%)	67(56.78)	85 (48.58%)	
Age-Group	30-40	08 (14.03%)	24 (20.33%)	32 (18.29%)	P=0.290 NS
	41-50	18(31.58%)	41 (34.74%)	59 (33.71%)	
	51-60	19(33.33%)	26 (22.03%)	45(25.71%)	
	61-70	11 (19.29%)	19 (16.10%)	30 (17.14%)	
	71-80	01 (1.76%)	08 (6.78%)	09 (5.14%)	

Out of 175 prediabetic cases, 90(51.42%) were male and 85 (48.58%) were females. The male predominance was more in Group A than in Group B, 68.42% v/s 43.22% respectively. The prevalence of microalbuminuria in male prediabetics was more than females. The microalbuminuria was predominently found in the age group of 51-60 years. The Age-group, & Microalbuminuria outcome were not statistically significantly associated.

Table 2: Association between Risk factors with Micro-Albuminuria:

Features studied in Pre-diabetics	Categories of patients with no of patients ( )	Micro-Albuminuria Positive (Group A) (n=57)	Micro-Albuminuria Negative (Group B) (n=118)	p-value
Lipid abnormality	Dyslipidemia (39)	24 (61.53%)	15 (38.47%)	P=0.000
	Normal (136)	33 (24.26 %)	103 (75.74%)	S
Smoking	Smoker (38)	29 (76.32%)	09 (23.68%)	P=0.000
	Non-Smoker (137)	28 (20.44%)	109 (79.56%)	S
Alcohol	Alcoholic (29)	24 (82.76%)	05 (17.24%)	P=0.000
	Non-alcoholic (146)	33 (22.60%)	113 (77.40%)	S
BMI	≤25 (70)	20 (28.57%)	50 (71.43%)	P=0.357
	>25 (105)	37 (35.24%)	68 (64.76%)	NS
Coronary Atherogenecity IMT)	Positive (34)	29(85.29%)	05 (14.71%)	P=0.000
	Negative (141)	28(19.86%)	113 (80.14%)	S

Dyslipidemia, smoking and alcohol were associated significantly with microalbuminuria. The BMI & Microalbuminuria outcome was not significantly associated. Smoking increases the risk of microalbuminuria in prediabetics.

Table 3: Prevalence of microalbuminuria in prediabetics:

Gender	Total Patients	Microalbuminuria positive	
		No. of patients	Prevalence of Micro.
Male	90	39	43.33%
Female	85	18	21.18%
Overall	175	57	32.57%

In present study the overall prevalence of microalbuminuria in prediabetics was 32.57%. The male prevalence of microalbuminuria in prediabetics was 43.33% which was more as compared to female patients [21.18%].

Table 4: Sensitivity & Specificity microalbuminuria in prediabetics:

Microalbuminuria	Percentage
Sensitivity	85.29%
Specificity	80.19%

The Sensitivity microalbuminuria in prediabetics with IMT was 85.29%, where as Specificity was 80.19%.

Table 5: Negative Predictive value & Positive Predictive value microalbuminuria in prediabetics:

Microalbuminuria	Percentage
Positive Predictive Value	50.85%
Negative Predictive Value	95.76%

The Positive Predictive value & Negative Predictive value were 50.85% & 95.76% respectively.

IV. Discussion

A growing body of evidence links microalbuminuria with abnormalities in the cardiovascular system. Microalbuminuria reflects generalized endothelial dysfunction which is a key factor for coronary heart disease. Increased carotid intima media thickeness a risk factor for atherosclerosis, was observed with microalbuminuria in atherosclerotic heart diseases, hyperlipidemia, smokers, diabetes mellitus. Presence of microalbuminuria as a marker of coronary heart disease especially in prediabetics are not widely studied. Correlation has been reported by Adele Bahar et al.[8]

The present study reveals majority of patients (33.33%) having microalbuminuria in the age group of 51-60 years. Even in the study subgroups microalbuminuria prevalence rates were higher in male subjects compared to female subjects. Various studies conducted across the globe revealed that advancing age and male gender are associated with higher prevalence rates of microalbuminuria. The observations made in this study are in accordance with those studies [9,10,11].

Microalbuminuria is seen more commonly in prediabetes as compared to general population[12,13]. In a recent study Okada et al proposed that glomerular hyper filtration is responsible for Microalbuminuria in prediabetes and it is proportional to the glucose levels [14]. M. Sriharibabu et al also found significant associations between microalbuminuria and prediabetes[11].

In the present study analysis,out of 175 prediabetic cases, 90(51.42%) were male and 85 (48.58%) were females. Microalbuminuria positive (group A) reveals male predominance 68.42% v/s 43.22% group B (Table 1). The microalbuminuria was predominently found in the age group of 51-60 years. However observation is statistically significantly associated. Dyslipidemia, smoking and alcohol were associated significantly with microalbuminuria. The BMI & Microalbuminuria outcome was not significantly associated. Smoking increases

the risk of microalbuminuria in prediabetics. In the present study, group A comprised prediabetics who are smokers (n=38), while group B comprised prediabetics and non smokers (n=137). Microalbuminuria was significantly positive in smoker group 29/38(76.31%) than non smoker group. Microalbuminuria was positive in 28/137 patients (20.43%). This observation reveals that non smoker with prediabetics do have microalbuminuria is observed significantly (20.43%). This observation emphasizes that mere presence of prediabetics could lead to significant microalbuminuria. Smoking and prediabetes make the case worse for patients with positive microalbuminuria for coronary atherogenecity as assessed by IMT (Table 2). The prevalence of microalbuminuria in normal individuals (normotensive, normoglycemic) microalbuminuria was found to be 2.8 to 5% in various studies.[15,16] In a pilot study carried out in our institute, out of 25 healthy, microalbuminuria was found in none. Similar observation was made by S Jalal et al, from India.[17]

V. Conclusion

The prevalence of Microalbuminuria was more in male prediabetic patients as compared to female prediabetics. Microalbuminuria seems to be a very early sensitive marker of the altered metabolic milieu that is associated with susceptibility of an individual to coronary heart disease in prediabetes. Detection of micro-albuminuria may be considered a vital independent risk parameter of atherogenecity & coronary heart disease in prediabetics.

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