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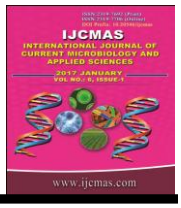

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A Study of Microalbuminuria in Coronary Artery Disease among Non-Diabetic Individuals

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A B S T R A C T

The present study was an observational cross sectional study which included sixty non diabetic subjects of both sexes with coronary artery disease admitted as inpatients in Meenakshi Medical College Hospital & Research Institute in Kanchipuram during the study period between February 2014 – September 2015. Majority of subjects were in the age group 51 to 60 yrs (40%), followed by > 60 years (30%), 41 to 50 years (20%) and < 40 years (10%). Age distribution suggests that CAD is more common after 50 years. The results showed that 66.7% of CAD subjects had positive family history of CAD; Prevalence of Microalbuminuria among CAD patients without diabetes was 88.3%; Smokers are at 10.74 time higher risk for microalbuminuria than Nonsmokers, and this observation was highly statistically significant CAD subjects with HDL <40 in Females and < 50 in males are at 2.042 times higher risk for Microalbuminuria than subjects with Normal HDL levels, but risk was not statistically significant. It is concluded that this study recommends estimating Urinary Albumin excretion for 24 hours to identify high risk individuals for Coronary Artery Disease and to add this laboratory workup as a tool for Primary Prevention of CAD.

Introduction

Cardiovascular diseases are the most prevalent serious disorders among the industrialized nations and are rapidly growing among developing nations including India. Cardiovascular disease is responsible for 12 million deaths per year globally and is the commonest cause of death (Harrison's principles of internal medicine). Previously considered a disease of rich, in the last thirty years Coronary Artery Disease (CAD) has reduced in incidence and prevalence in western nations but is increasing rapidly to become epidemic proportions in developing nations. Indians whether living in India or abroad have a higher incidence of CAD compared to other ethnic groups (API text book of medicine 10th edition).

Ischemic heart disease is a condition in which there is an inadequate supply of blood and oxygen to a portion of myocardium. It typically occurs when there is imbalance between myocardial oxygen supply and demand. The most common cause of myocardial ischemia is atherosclerotic disease of an epicardial coronary artery sufficient to

cause a regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery (API text book of medicine 10th edition).

By the year 2020, cardiovascular diseases could be the most important cause of mortality in India. The prevalence of coronary artery disease in India increased from 1% in 1960 to 9.7% in 1995 in urban populations, and in rural populations it has almost doubled in the last decade. There is an epidemiological transition from infective to degenerative diseases, increases in the prevalence of cardiovascular risk factors, and ageing of the population, which eventually leads to an increase in the absolute number of people with coronary artery disease and increased health awareness and demand for health care facilities (API text book of medicine 10th edition).

While incidence of CAD has reduced by 50% in the west, in India it has doubled in the last 25 years. The prevalence of CAD in the years 1960, 1980, 1990 and 2000 progressively increased (2%, 4% to 6%, 9.5% and 10% to 15% respectively). In rural India, the CAD prevalence increased two-fold from 2% to 4 %; in urban India the increase was three–fold from 3.45% to 9.45%. In 1990 25% deaths in India were attributable to cardiovascular disease compared to 9 % due to diarrhoeal disease, 12 % due to respiratory infections and 5% due to tuberculosis (API text book of medicine 10th edition).

There is a steep increase in prevalence of coronary artery disease in urban areas in India. Since the pioneering work of the Framingham study, many prospective and clinical studies have identified a series of independent risk factors for ischemic heart disease among which age, male gender, smoking, hypertension, and diabetes mellitus, a positive family history of premature atherosclerotic disease, hypercholesterolemia, hyper triglyceridemia and low HDL cholesterol are considered as classical risk factors.

The interest in improving cardiovascular risk assessment, resulting from a better understanding of the pathogenesis of atherosclerosis and identification of new targets for anti-atherosclerotic drug therapy has stimulated the search for novel risk factors (Hillege *et al*., 2001).

One such novel risk factor is microalbuminuria which has emerged as an independent and robust risk factor. Microalbuminuria is a well-accepted marker for micro and macro vascular damage in patients with diabetes mellitus. However more and more evidence is accumulating that microalbuminuria is an important cardiovascular risk factor even in the general population (Diercks *et al*., 2000).

The urinary protein called albumin is increasingly recognized as the earliest sign of vascular damage in both the kidney and the heart. The phenomenon of albuminuria has been recognized for more than 200 years, and its association with kidney disease dates to the epochal insights of Richard Bright in 1827. Microalbuminuria is defined as urinary albumin excretion of 30 - 300 mg / day, or 20-200 µg/min.

Microalbuminuria may be a marker of generalized vascular disease, with arterial endothelial dysfunction being involved in the pathogenesis of atherothrombotic vascular disease. The exact pathophysiology regarding how microalbuminuria contributes to or accelerates the atherosclerotic process is uncertain. The current understanding, however suggests that mechanisms of vascular injury associated with

microalbuminuria are different between those without diabetes who also have hypertension (Pedrinelli *et al*., 1994).

It is of interest that presence of microalbuminuria may even precede manifest diabetes and hypertension. Microalbuminuria may be considered one of the earliest manifestations of the insulin resistance syndrome. Indeed, it has been shown that the prevalence of microalbuminuria increases according to the number of components of the metabolic syndrome present. This raises doubt whether we should limit our screening strategies to those with known risk factors or preferably should screen the general population.

The importance of microalbuminuria as an independent predictor of progressive renal disease and cardiovascular mortality was thereafter realized in a number of prospective and epidemiological studies particularly in patients with diabetes and hypertension. In adults, the link between microalbuminuria, cardiovascular disease, and progressive renal disease is now well established in patients with systemic diseases including diabetes mellitus. Interestingly, microalbuminuria has also emerged to be an important risk factor for the development of cardiovascular disease, and all-cause mortality in the general population.

Arterial hypertension is, in some patients, associated with a subclinical increase of the albumin excretion in the urine (microalbuminuria), in spite of preserved renal function. In hypertensive patients microalbuminuria has often been related to an excess of atherosclerotic cardiovascular disease, which is more frequent in the hypertensive population, and to an increased level of atherosclerotic risk markers (Pedrinelli *et al*., 1994).

In a prospective population based study of hypertensives, that reports an independent predictive effect of microalbuminuria in the development of ischemic heart disease. Among hypertensive subjects screened within another Danish population study, the Copenhagen city heart study, we have described a cross sectional relation between urinary albumin excretion and IHD, confirming a previous report by another study done by Agrawal *et al*., Bigazzi *et al.,* analyzed data obtained from retrospectively selected hospital population of 141 hypertensives. They observed an unadjusted relative risk of 2.4 for the development of ischemic heart disease during a 7 year follow up among microalbuminuria patients.

In a study done in Danish medical research council and Danish heart foundation concluded that microalbuminuria is a marker of generalized vascular dysfunction (STENO HYPOTHESIS), elevated urinary albumin has also been demonstrated in non diabetic individuals and it has to be found associated with elevated blood pressure, dyslipidemia and high plasma insulin levels (obesity). Hypertension and dyslipidemia are both well-established risk factors for the development of cardiovascular disease.

In a study "Albuminuria and risk of cardiovascular events, death and heart failure in diabetic and non-diabetic individuals" Department of medicine, Hamilton Ontario where results indicate that any degree of albuminuria is a risk factor for cardiovascular events in individuals with or without Diabetes mellitus; The risk increases with Albumin – creatinine ratio, starting well below the cut off value of microalbuminuria. Screening for albuminuria identifies people at high risk for cardiovascular events.

Microalbuminuria is a cardinal sign and a warning to the physician about the problems

of vascular wall. It is a reversible condition so that the person by adopting control measures to reverse MAU like losing weight by increased physical activity and diet changes can be safeguarded from the dreaded complications of cardiovascular and renal diseases in future life**.**

Microalbuminuria is an important cardiovascular and mortality risk factor, irrespective of diabetes or hypertension. It increases the relative risk of major cardiovascular events, even after adjustment for other cardiovascular risk factors. Risk increases with the albumin-to-creatinine ratio, starting well below the microalbuminuria cutoff. Multivariate analysis has shown that left ventricular (LV) hypertrophy is associated with a 1.6-fold higher prevalence of microalbuminuria, independent of age, systolic or diastolic blood pressure (BP), diabetes, gender, race, serum creatinine, or smoking status (Wachtell *et al*., 2002).

Thus, microalbuminuria, an integrated marker of cardiovascular risk, may be particularly effective to identify patients at higher absolute risk in whom preventive treatment will be more beneficial than patients with a lower absolute risk. Reduction of subclinical albuminuria as such may also represent a clinically relevant end-point worth being actively pursued by pharmacological treatment. Although no evidence is available in this regard, the antiproteinuric effect of ACE inhibitors or angiotensin II receptor blockers paralleled a better renal and cardiovascular prognosis in hypertensive patients with renal failure, either diabetic or not. The issue reminds, to some extent, the debate about cardiac hypertrophy, in which earlier hypotheses were a long time being proven, although, hopefully, we will have to wait less time to get an answer about non-diabetic microalbuminuria (Knight *et al*., 2003).

It was recently suggested that smoking, in addition to its well-known cardiovascular consequences, could accelerate the progression of renal diseases. However, our understanding of the acute effects and long-term influence of smoking on renal hemodynamics and albuminuria is poor, and many questions remain unanswered. Smoking was associated with excessive urinary albumin excretion in hypertensive subjects. In fact the prevalence of microalbuminuria was two-fold higher in lean, never treated hypertensive smokers than in non-smokers. Similar results were also reported in normotensive subjects. Of note, the most important determinant of microalbuminuria is usually arterial pressure, especially when ambulatory arterial pressure is used.

Cigarette smoking causes a nicotine-induced stimulation of the sympathetic nervous system (i.e. adrenaline and nor adrenaline release) that acutely increases arterial pressure and heart rate. The implication of the sympathetic nervous system in the acute renal vasoconstriction observed following nicotine gum administration was unlikely since arterial pressure and heart rate rose in both smokers and non-smokers, whereas glomerular filtration rate and effective renal plasma flow decreased only in non-smokers. Nevertheless, the sympathetic nervous system may play a role in the chronic renal effects of smoking.

Similar to type 1 and 2 Diabetics, non-diabetic smokers, hypertensive or not, tend to excrete more albumin. The first report by Gosling *et al.*, confirmed later on by other investigators, has recently been established by the Gubbio, HOPE and PREVEND studies, all showing an association independent of coexisting diabetes and hypertension. The finding is in line with the hypothesis of microalbuminuria as an expression of diffuse endothelial dysfunction, since smoke damages endothelial function, induces a chronic

subclinical inflammatory state and promotes atherosclerotic vascular disease, and may expose to higher risk of morbid events when coexisting with elevated urinary albumin excretion (Gerstein *et al*., 2000).

Microalbuminuria seems to reflect a state of patho-physiologic vascular dysfunction that makes an individual susceptible to organ damage. High levels of albuminuria may already be found in young children and reflect a normal physiologic variation in endothelial function associated with Cardiovascular and Renal risk at later age. Intervention strategies aimed at repairing this vascular function could be very useful not only in secondary but also in primary prevention. Albumin excretion levels may represent the primary marker for success of such therapies.

The main aim and objectives of this study includes, to estimate the prevalence of Microalbuminuria in non-diabetic patients with Coronary Artery Disease (CAD). And also study the association between Microalbuminuria and other risk factors for Coronary Artery Disease.

Materials and Methods

Study Design

Observational cross sectional study

Study Subjects

Sixty non diabetic subjects of both sexes with coronary artery disease admitted as inpatients in Meenakshi Medical College Hospital & Research Institute in Kanchipuram during the study period between February 2014 – September 2015 were included.

Inclusion Criteria

- CAD patients based on Coronary Angiogram
- Both sexes
- Non-diabetic patients

Exclusion Criteria

- Diabetes Mellitus
- Congestive cardiac failure as presentation
- Female patients with vaginal discharge
- Urine showing
  - Macroalbuminuria (dipstick positive)
  - RBC`s > 50/µl
  - Leucocytes > 75/µl

Sampling Method

Non-diabetic, CAD patients were included till sample size is achieved from February 2014 - September 2015.

The patients were given a container for collection of urine over 24 hours which was sent for the estimation of Albumin level by immunoturbidimetry method.

In this study, only in patients who were diagnosed to have CAD by Coronary angiogram using Philips - Allura Xper FD10 Cardiovascular X-ray system in our Cath lab were selected.

Method of Study

After getting ethical clearance from the Institutional Ethical Committee, study was started from February 2014. Patients who fit in the inclusion and exclusion criteria were explained about the study and a written consent was obtained from those who were willing to participate in the study. All the needed information was collected using a pre tested semi structured questionnaire. Investigations were carried out in each case. Study was done with reference to risk factors like age, gender, smoking, obesity, hypertension and dyslipidemia.

Statistical Methods

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance. Continuous data was represented as mean and standard deviation. Independent t-test was used as test of significance to identify the mean difference between two groups. p-value <0.05 was considered as statistically significant.

Results and Discussion

Sixty cases of CAD without Diabetes mellitus were included in this study.

Albuminuria has been identified as a life-threatening renal and cardiovascular risk profile. This important diagnostic parameter can not only predict renal or concurrent renal and cardiovascular adverse events in high-risk patients, such as diabetics and hypertensive patients (ranging from 10 to 40%), but can also be frequently found in seemingly healthy subjects, with an overall prevalence of 5 to 7% in normal individuals.

In spite of the observed link between microalbuminuria and cardiovascular disorders, its pathophysiological mechanisms responsible for progression of cardiac dysfunction or heart failure have been largely unknown.

Majority of subjects were in the age group 51 to 60 yrs (40%), followed by > 60 years (30%), 41 to 50 years (20%) and < 40 years (10%). Age distribution suggests that CAD is more common after 50 years. There was significant difference in proportions (Table 1). In the present study, majority of subjects were males (78.3%) and 21.7% were females. This observation was statistically significant (Table 2).

Table 3 reveals that 66.7% of CAD subjects had positive family history of CAD. This observation was statistically significant. As observed from Table 4, 58.3% had history of smoking, there was no significant difference in proportions.

Table.1 Age distribution of subjects

		Frequency	%
Age	< 40 years	6	10.0%
	41 to 50 years	12	20.0%
	51 to 60 years	24	40.0%
	> 60 years	18	30.0%
	Total	60	100.0%
Mean Age		55.13 ± 9.95 years	

$\chi 2 = 12$, df = 3, p = 0.0074*

Table.2 Gender Distribution of subjects

		Frequency	%
Gender	Female	13	21.7
	Male	47	78.3
	Total	60	100.0

$\chi 2 = 18.15$, df = 1, p <0.0001*

Table.3 Family History of CAD in Subjects

		Frequency	Percent
Family H/o CAD	No	20	33.3
	Yes	40	66.7
	Total	60	100.0

χ 2 = 6.017, df = 1, p = 0.0142*

Table.4 Smoking History in subjects

		Frequency	Percent
Smoking	No	25	41.7
	Yes	35	58.3
	Total	60	100.0

χ 2 = 1.350, df = 1, p = 0.2453

Majority of CAD subjects were overweight (76.7%) and 18.3% were obese. This observation in difference in proportions among CAD subjects was statistically significant (Table 5).

The results presented in Table 6 show 61.7% of subjects with hypertension and 38.3% without hypertension. This observation was not statistically significant.

Prevalence of Microalbuminuria among CAD patients without diabetes was 88.3%. This observation was statistically significant. Mean Microalbumin levels was 56.9 ± 30.4 mg (Table 7).

Table.5 Distribution of subjects according to BMI

		Frequency	Percent
BMI	18.5 to 22.9 Normal	3	5.0
	23 to 27.5 Overweight	46	76.7
	> 27.5 Obese	11	18.3
	Total	60	100.0
Mean BMI		25.89 ± 2.24	

χ 2 = 52.3, df = 1, p <0.001*

Table.6 Distribution of Subjects according to History of Hypertension

		Frequency	Percent
HTN	No	23	38.3
	Yes	37	61.7
	Total	60	100.0

χ 2 = 2.817, df = 1, p = 0.093

Table.7 Prevalence of Micro albuminuria among CAD subjects

		Frequency	%
Micro albuminuria	Absent (<30 mg)	7	11.7%
	Present (30 to 300 mg)	53	88.3%
Mean Albumin Levels		56.9 ± 30.4	

$\chi 2 = 33.75$, df = 1, p <0.001*

Table.8 shows the various quantitative variables considered in the present study. The mean Microalbuminuria was found to be 56.9.

There was no significant association between Age and Microalbuminuria among CAD subjects in the study (Table 9). Odds ratio was 2.83, i.e. > 50 years are at 2.83 times higher risk for Microalbuminuria than < 50 years, but risk was not statistically significant. As observed from the results shown in Table 10 that there was no significant association between Gender and Microalbuminuria among CAD subjects in the study. Odds ratio was 3.225, i.e., Males are at 3.225 time higher risk for Microalbuminuria than Females, but the risk was not statistically significant (Table 10). There was no significant association between Family H/O CAD and Micro albuminuria among CAD subjects in the study (Table 11). Odds ratio was 3.083, i.e. CAD subjects with Family H/O CAD are at 3.083 time higher risk for Micro albuminuria than without Family H/O CAD, but risk was not statistically significant.

In the present study, there was a significant association between Smoking and Microalbuminuria among CAD subjects. Odds ratio was 10.74, i.e. Smokers are at 10.74 time higher risk for icroalbuminuria than Nonsmokers, and this observation was highly statistically significant (Table 12).

There was no significant association between BMI and Microalbuminuria among CAD subjects in the study (Table 13). Odds ratio was 1.19, i.e. CAD subjects with BMI >23 are at 1.19 time higher risk for Microalbuminuria than subjects with BMI < 23, but risk was not statistically significant.

Table.8 Mean and Standard Deviation of Quantitative Variables in the Study

Parameters	Mean	SD
Height	164.63	6.57
Weight	70.18	5.91
BMI (Body Mass Index)	25.90	2.24
SBP (Systolic blood pressure)	144.77	16.75
DBP (Diastolic blood pressure)	89.53	10.27
FBS (Fasting Blood Sugar)	94.27	9.19
Total Cholesterol	164.43	39.19
TG (Triglyceride)	130.28	73.61
HDL (High Density Lipoprotein)	35.82	8.32
LDL (Low density Lipoprotein)	95.82	41.19
Microalbuminuria	56.90	30.43

Table.9 Association between Microalbuminuria and Age in CAD subjects

Parameters		Microalbuminuria				P value	Odds Ratio
		Absent (<30 mg)		Present (30 to 300 mg)			
		Frequency	%	Frequency	%		
Age	< 40 years	0	0.0%	6	11.3%	0.317	2.83 (0.3158, 25.42)
	41 to 50 years	1	14.3%	11	20.8%		
	51 to 60 years	5	71.4%	19	35.8%		
	> 60 years	1	14.3%	17	32.1%		

Table.10 Association between Microalbuminuria and Gender in CAD subjects.

Parameters		Microalbuminuria				P value	Odds Ratio
		Absent (<30 mg)		Present (30 to 300 mg)			
		Frequency	%	Frequency	%		
Gender	Female	3	42.9%	10	18.9%	0.148	3.225 (0.621, 16.75)
	Male	4	57.1%	43	81.1%		

Table.11 Association between Microalbuminuria and Family H/O CAD in CAD subjects.

Parameters		Microalbuminuria				P value	Odds Ratio
		Absent (<30 mg)		Present (30 to 300 mg)			
		Frequency	%	Frequency	%		
Family H/O CAD	No	4	57.1%	16	30.2%	0.155	3.083 (0.6178, 15.39)
	Yes	3	42.9%	37	69.8%		

Table.12 Association between Microalbuminuria and Smoking in CAD subjects.

Parameters		Microalbuminuria				P value	Odds Ratio
		Absent (<30 mg)		Present (30 to 300 mg)			
		Frequency	%	Frequency	%		
Smoking	Yes	1	14.3%	34	64.2%	0.012**	10.74 * (1.202, 95.94)
	No	6	85.7%	19	35.8%		

Table.13 Association between Microalbuminuria and BMI in CAD subjects

Parameters		Microalbuminuria				P value	Odds Ratio
		Absent (<30 mg)		Present (30 to 300 mg)			
		Frequency	%	Frequency	%		
BMI	< 18.5 Underweight	0	0.0%	0	0.0%	0.759	1.19 (0.053, 26.33)
	18.5 to 22.9 Normal	0	0.0%	3	5.7%		
	23 to 27.5 Overweight	6	85.7%	40	75.5%		
	> 27.5 Obese	1	14.3%	10	18.9%		

The association between Hypertension and Microalbuminuria among CAD subjects in the study was observed to be statistically significant. Odds ratio was 32.38, i.e. Hypertensive subjects are at 32.38 time higher risk for Microalbuminuria than Non hypertensive subjects, and this observation was highly statistically significant (Table 14).

The results of the present research indicated in Table 15 reveal that there was no significant association between Total cholesterol and Microalbuminuria among CAD subjects. Odds ratio was 0.44, i.e. CAD subjects with Total cholesterol <200 mg/dl were protected from Microalbuminuria than subjects with Total cholesterol > 200mg/dl, but it was not statistically significant.

There was no significant association between Triglyceride and Microalbuminuria among CAD subjects in the study. Odds ratio was 2.83, i.e. CAD subjects with TG >150 mg/dl are at 2.83 times higher risk for Microalbuminuria than subjects with TG < 150mg/sl, but risk was not statistically significant (Table 15).

Table.14 Association between Microalbuminuria and Hypertension in CAD subjects

Parameters		Microalbuminuria				P value	Odds Ratio
		Absent (<30 mg)		Present (30 to 300 mg)			
		Frequency	%	Frequency	%		
HTN	Yes	0	0.0%	37	69.8%	<0.001*	32.38 * (1.732, 605.2)
	No	7	100.0%	16	30.2%		

Table.15 Association between Microalbuminuria and Total Cholesterol in CAD subjects

Parameters		Microalbuminuria				P value	Odds ratio
		Absent (<30 mg)		Present (30 to 300 mg)			
		Frequency	%	Frequency	%		
Total Cholesterol	<200 mg/dl	5	71.4%	45	84.9%	0.369	0.44 (0.07, 2.69)
	> 200 mg/dl	2	28.6%	8	15.1%		

Table.16 Association between Microalbuminuria and Triglyceride in CAD subjects

Parameters		Microalbuminuria				P value	Odds Ratio
		Absent (<30 mg)		Present (30 to 300 mg)			
		Frequency	%	Frequency	%		
Triglyceride	< 150 mg/dl	6	85.7%	36	67.9%	0.334	2.83 (0.31, 25.42)
	> 150 mg/dl	1	14.3%	17	32.1%		

There was no significant association between HDL and Microalbuminuria among CAD subjects in the study. Odds ratio was 2.042, i.e. CAD subjects with HDL <40 in Females and < 50 in males are at 2.042 times higher risk for Microalbuminuria than subjects with Normal HDL levels, but risk was not statistically significant (Table 17).

Table 18 shows that there was no significant association between LDL and Microalbuminuria among CAD subjects in the present study. Odds ratio was 0.76, i.e. CAD subjects with LDL > 150mg/dl are at 0.76 time higher risk for Microalbuminuria than subjects with LDL < 150mg/dl, but risk was not statistically significant.

Table.17 Association between Microalbuminuria and HDL in CAD subjects

Parameters		Microalbuminuria				P value	Odds Ratio
		Absent (<30 mg)		Present (30 to 300 mg)			
		Frequency	%	Frequency	%		
HDL	Abnormal	6	85.7%	49	92.5%	0.544	2.042 (0.19, 21.4)
	Normal	1	14.3%	4	7.5%		

Table.18 Association between Microalbuminuria and LDL in CAD subjects

Parameters		Microalbuminuria				P value	Odds Ratio
		Absent (<30 mg)		Present (30 to 300 mg)			
		Frequency	%	Frequency	%		
LDL	< 150 mg/dl	6	85.7%	47	88.7%	0.818	0.76 (0.07, 7.49)
	> 150 mg/dl	1	14.3%	6	11.3%		

Age distribution

In this study majority of subjects were in the age group 51 to 60 yrs (40%), followed by >60 years (30%), 41 to 50 years (20%) and <40 years (10%). This suggests that CAD is more common after 50 years of age. There was significant difference in proportions. The Mean age recorded in the present study was 55.13 ± 9.95 years which is very close the results of 56 ± 8, 55 ± 13 and 57 ± 10.1 years recorded by Hyo Eun Park *et al*., (2012), Diercks *et al*., (2000) and Donal *et al*., (1993) respectively.

Gender Distribution

In this study majority of subjects were males (78.3%) and rest were females (21.7%). This observation was statistically significant ($p<0.0001$). Similarly in the following studies the prevalence is more among males. Similar studies in case of males have already been reported by Hilal *et al*., (2015) (76%) Donal *et al*., (1993) (84%) The above mentioned studies also showed the higher prevalence of CAD in males.

Family history of CAD

In our study, 66.7% of CAD subjects had family history of CAD. There was no significant association between Family H/O. CAD and Microalbuminuria among CAD subjects in the study. Odds ratio was 3.083, i.e. CAD subjects with Family history of CAD are at 3.083 time higher risk for Microalbuminuria than without Family H/O CAD. This observation is statistically significant. There is a variation among similar studies. The family history of CAD was 24.3, 30.7 and 65.0% as reported by Donal *et al*., (1993), Diercks *et al*., (2000) and Vida Nesar *et al*., (2009) respectively. Donal *et al.*, obtained positive results of family history of CAD similar to present study, whereas Diercks *et al.,* and Vida Nesar *et al.,* couldn't obtain similar results.

Smoking

In this study 58.3% of subjects had history of smoking but there was no significant difference in proportions. There was significant association between Smoking and Microalbuminuria among CAD subjects in the study. Odds ratio was 10.74, i.e. Smokers are at 10.74 time higher risk for Microalbuminuria than Nonsmokers, and this observation was highly statistically significant. Klausen *et al.,* (2004) also reported very close results of 58% smoking history among subjects. However, in a similar study, Dierecks *et al.,* (2000) found lower smoking history of 47% among the subjects.

BMI

There was no significant association between BMI and Microalbuminuria among CAD subjects in the study. Odds ratio was 1.19, i.e. CAD subjects with BMI >23 are at 1.19 time higher risk for Microalbuminuria than subjects with BMI <23, but risk was not statistically significant. Similar results of BMI above 23.0 was also reported by Hyo Eun park *et al*., (2012), Klausen *et al*., (2004) and Dierecks *et al*., (2000).

Hypertension

In this study there was significant association between Hypertension and Microalbuminuria among CAD subjects in the study. 69.8% hypertensive subjects and 30.2% normotensive subjects had microalbuminuria. Odds ratio was 32.38, i.e. Hypertensive subjects are at 32.38 time higher risk for Microalbuminuria than Non hypertensive subjects, and this observation was highly statistically significant.

Similar to the present study, Damsgaard *et al.,* and Yudkin *et al.,* demonstrated significant association between Hypertension and Microalbuminuria. But studies done by Klausen *et al.,* and Hilal *et al.,* couldn't confirm the significant association between the two. This study shows 30.2% of non-diabetic, non-hypertensive patients had significant microalbuminuria.

Lipid Profile

In my study there was no significant association between Total cholesterol and Microalbuminuria among CAD subjects in the study. Odds ratio was 0.44, i.e. CAD subjects

with Total cholesterol <200 mg/dl were protected from Microalbuminuria than subjects with Total cholesterol > 200mg/dl, but it was not statistically significant.

There was no significant association between Triglyceride and Microalbuminuria among CAD subjects in the study. Odds ratio was 2.83, i.e. CAD subjects with TGL >150 mg/dl are at 2.83 times higher risk for Microalbuminuria than subjects with TGL < 150mg/dl, but risk was not statistically significant. There was no significant association between HDL and Microalbuminuria among CAD subjects in the study. Odds ratio was 2.042, i.e. CAD subjects with HDL <40 in Females and < 50 in males are at 2.042 time higher risk for Microalbuminuria than subjects with Normal HDL levels, but risk was not statistically significant.

There was no significant association between LDL and Microalbuminuria among CAD subjects in the study. Odds ratio was 0.76, i.e. CAD subjects with LDL > 150mg/dl are at 0.76 time higher risk for Microalbuminuria than subjects with LDL < 150mg/dl, but risk was not statistically significant.

In this study Total Cholesterol and all Lipid Fractions, had no statistical significanct association with microalbuminuria. Donal *et al.,* (1993) Hilal *et al.,* (2015) and Vida Nesar *et al.,* (2009) also couldn't establish significant association between Cholesterol and Microalbuminuria in their studies.

Microaluminuria and CAD

Prevalence of Microalbuminuria among CAD patients without diabetes was 88.3%. This observation was highly statistically significant ($p<0.001$). Mean Microalbumin levels was 56.9 ± 30.4 mg. A cross sectional study done by Klausen, Knut Borch-Johnson *et al.*, from the Centre of preventive medicine, Glostrup University hospital, Glostrup Department of Nephrology Herlev hospital University Herlev, Denmark have concluded that microalbuminuria is not only an independent predictor of IHD but also substantially increases the risk associated with other established risk factors for coronary artery disease. In an another study Yudkin *et al.*, in 1988 demonstrated that microalbuminuria was associated with 24 fold increased mortality in non diabetic individuals. In Danish Hospital a study done by Jensen. J.S, Feldt-Rasmusen concluded microalbuminuria as an independent risk factor for IHD among hypertensive individuals who are non diabetic.

In a study "Microalbuminuria in Non diabetic Adults and Relation of Blood Pressure, Body Mass Index, Plasma Cholesterol Levels, and Smoking":Gubbio population study for 1567 participants (677 men and 890 women) aged 45 to 64 without macroalbuminuria without diabetes, results showed blood pressure, plasma cholesterol levels, smoking and BMI significantly related to urinary albumin excretion and prevalence of microalbuminuria. The relative risk of Microalbuminuria with 18mmHg higher Systolic Blood Pressure in men and women was 2.5 and 1.62 respectively; with 40mg/dl higher plasma cholesterol was 2.25 and 2.10 respectively; with smoking was 1.99 and 1.91 respectively; with 4 kg/m^2 higher BMI was 1.83 And 1.33 respectively.

In a study Hillege HR, Jannsen WM, conducted by department of Pharmacology Groningen, Netherlands postal questionnaire and a vial to collect on morning spot urine, were sent to 85421 subjects aged between 28 to 75. Cardiovascular risk factors and morbidity were validated in a well-defined non diabetic and non-hypertensive group of 5241subjects. Microalbuminuria appears to be not only in general population but also in non-

diabetic and non-hypertensive population and is independently associated with increased cardiovascular risk factors and cardiovascular morbidity.

It is concluded that this study recommends estimating Urinary Albumin excretion for 24 hours to identify high risk individuals for Coronary Artery Disease and to add this laboratory workup as a tool for Primary Prevention of CAD.

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