



## Prevalence of Microalbuminuria and Its Association with Ischemic Heart Disease in Non Diabetics- An Interesting Prospective Study

**Dr.Manish Patil**

M.D.(Medicine), Assistant Professor, Department Of Medicine, Dr.B.R.A.M Hospital, Pt.J.N.M.Medical College, Raipur, Chhattisgarh, India

**Dr.Pradeep Beck**

M.D.(Medicine), Associate Professor, Department Of Medicine, Government Medical College, Rajnandgaon, Chhattisgarh, India

### ABSTRACT

**Introduction-** Ischemic Heart Disease (IHD) is a condition in which an inadequate supply of blood and oxygen to the portion of the myocardium; it typically occurs when there is imbalance between oxygen supply and demand. IHD causes more death and disability and incurs greater economic cost than any other illness in the developed world. 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. Microalbuminuria is a well-accepted marker for micro and macro vascular damage in patients with diabetes mellitus. It gradually became increasingly evident that microalbuminuria is associated with an increased risk of cardiovascular disease even in non diabetic patient. Parving showed that microalbuminuria occurs in benign essential hypertension. In fact microalbuminuria occurs in response to acute inflammatory conditions such as ischemia, trauma and thermal injury, surgery, pancreatitis and inflammatory bowel disease. However more and more evidence is accumulating that microalbuminuria is an important cardiovascular risk factor even in the general population.

**Material and Methods-** The study conducted in the Department of Medicine, Pt. J.N.M. Medical College and Dr. B.R.A.M. Hospital, Raipur from 2009 to 2010. 100 adult patients admitted in ICCU who were diagnosed as first time reported case of non diabetic ischemic heart disease on the basis of inclusion criteria (Age >30 years, ischemic heart disease on the basis of chest pain, Electrocardiographic changes Biochemical markers) and exclusion criteria, were included. Data was compiled in MS excel and checked for its completeness, correctness and then it was analyzed.

**Results-** In the present study, out of 100 cases, 71 male and 29 cases were female. In our study maximum number of cases in 41-50 yrs age group, constituted 30% of the study. Out of 100 patients, 86% cases had myocardial infarction while 14% cases had presentation of Unstable Angina with ischemic changes in electrocardiogram. Out of the 100 cases, 30 cases had microalbuminuria, Out of 30 cases, and 26 (35.1%) Infarct cases and 4 (33.3%) Ischemia cases had microalbuminuria, while out of 70 cases, 60 (64.8%) Infarct and 10(66.6%) Ischemia cases had normoalbuminuria.

**Conclusion:** Our study shows microalbuminuria is positively associated with Ischemic Heart Disease in non-diabetic subjects and can be regarded as an important additional risk factor for Ischemic Heart Disease.

### KEYWORDS

Microalbuminuria, Non-diabetic, Myocardial infarction, Raipur, Chhattisgarh

### INTRODUCTION

Ischemic Heart Disease (IHD) is a condition in which an inadequate supply of blood and oxygen to the portion of the myocardium; it typically occurs when there is imbalance between oxygen supply and demand. IHD causes more death and disability and incurs greater economic cost than any other illness in the developed world. With urbanization in the developing world the Prevalence of risk factors is increasing in these regions. Ischemic Heart Disease which has an estimated prevalence of 6-9% in the general population in India may become the leading cause of mortality and morbidity by the year 2015 (**Antman EM et al, 2008**). [1]

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, a positive family history of premature atherosclerotic disease, smoking, diabetes mellitus, hypertension, hypercholesterolemia, hypertriglyceridemia and low HDL cholesterol are considered as classical risk factors. (**Toto D Robert et al 2004**). [2]

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.

One such novel risk factor is microalbuminuria which has emerged as an independent and robust risk factor. Microalbuminuria (MA) 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 MA contributes to or accelerates the atherosclerotic process is uncertain.

Microalbuminuria is a well-accepted marker for micro and macro vascular damage in patients with diabetes mellitus. It gradually became increasingly evident that microalbuminuria is associated with an increased risk of cardiovascular disease even in non diabetic patient (**Haffner et al 1990**). [3]

Parving showed that microalbuminuria occurs in benign essential hypertension (**Parving H et al 1974**). In fact microalbuminuria occurs in response to acute inflammatory conditions such as ischemia, trauma and thermal injury, surgery, pancreatitis and inflammatory bowel disease (**Gosling P et al 1998**). [4, 5]

Amongst all these, the association of microalbuminuria with cardiovascular diseases is very important owing to cardiovascular morbidity and mortality. Myocardial infarction is the most important manifestation of cardiovascular diseases. Microalbuminuria is an early response to myocardial infarction. (**Gosling**

**P et al 1991).** While Berton et al showed that microalbuminuria occurs in acute myocardial infarction and predicts early mortality (**Berton et al 2001**). [5, 6]

In all these conditions the degree of microalbuminuria is proportional to the severity of the inflammatory insult, predictive of outcome and not associated with any other feature of renal impairment. (**Hartland A 1999**). [7] However more and more evidence is accumulating that microalbuminuria is an important cardiovascular risk factor even in the general population.

**MATERIAL AND METHODS**

The study conducted in the Department of Medicine, Pt. J.N.M. Medical College and Dr. B.R.A.M. Hospital, Raipur from 2009 to 2010. 100 adult patients admitted in ICCU who were diagnosed as first time reported case of non diabetic ischemic heart disease on the basis of inclusion criteria (Age >30 years, ischemic heart disease on the basis of chest pain, Electrocardiographic changes Biochemical markers) and exclusion criteria, were included.

**Inclusion criteria for study group:**

- A. Age >30 years.
- B. Criteria for diagnosis of ischemic heart disease are:
  - a) Chest pain suggestive of angina
  - b) Electrocardiographic changes
  - c) Biochemical markers.

**Exclusion criteria for study group:**

- 1. Age <30 yrs
- 2. Previous history of IHD
- 3. Diabetes (by ADA CRITERIA 2004)
- 4. Urinary tract infection
- 5. Any acute systemic illness
- 6. Surgery
- 7. Trauma
- 8. Female patient with vaginal discharge
- 9. Drugs- ACE Inhibitor , Angiotensin receptor blocker

**Test for Micro albumin:**

Morning random, mid stream urine sample collected, on third day after admission, then urine specimen was tested for micro albumin as soon as possible by Clinitek Auto Analyser. Any single-void urine specimen, when evaluated in conjunction with the albumin-to-creatinine ratio, can be used to discriminate between normal and abnormal levels of microalbuminuria. Estimation of microalbuminuria level based on dye binding using sulfonephthalein by Clinitek Auto analyser which is a semi quantitative method for detecting urine micro albumin. The result shown as Albumin x mg/l (85% accuracy), Creatinine mg/dl and Albumin /Creatinine ratio as mg/g (86%accuracy).

**EXPECTED VALUES:**

**Albumin:** Albumin is normally present in urine at concentrations of less than 20 mg/L. Microalbuminuria is indicated with results of 20–200 mg/L; results of >200 mg/L indicate clinical albuminuria. These levels have been found to be predictive of albumin excretion rates of 30–300 mg/24 hours and >300 mg/24 hours, respectively.

**Creatinine:** Creatinine is normally present in urine at concentrations of 10 to 300 mg/dL.

**Albumin-to-Creatinine Ratio:** Albumin is normally present in urine at concentrations of less than 30 mg albumin/g creatinine. Microalbuminuria is indicated at a ratio result of 30–300 mg/g.

Data was compiled in MS excel and checked for its completeness, correctness and then it was analyzed. Suitable statistical test was applied and p value <0.05 was considered as a statistical significant.

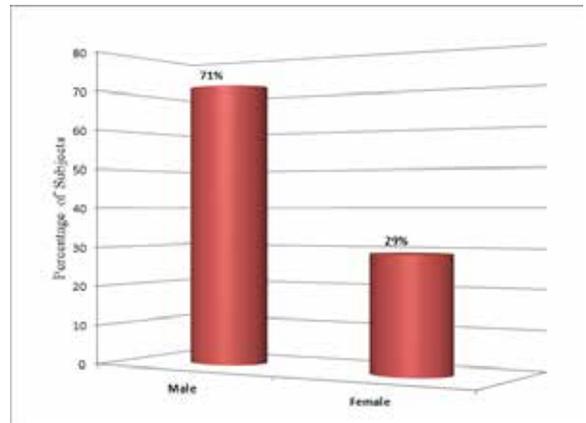
**Results-**

**Table-1. Background characteristics of study subjects**

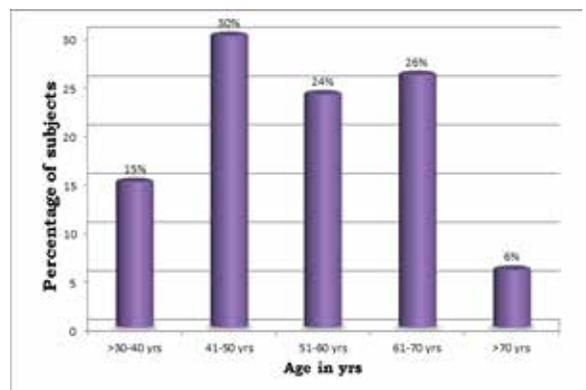
Background characteristics	No.	Percentage
<b>Sex</b>		
Male	71	71%
Female	29	29%
<b>Age in years</b>		
31-40	15	15%
41-50	30	30%
51-60	26	26%
61-70	24	24%
>70	5	5%
<b>Infarct/ Ischemia</b>		
Infarct	86	86%
Ischemia	14	14%

In the present study, out of 100 cases, 71 male and 29 cases were female. Out of 100 cases, 15 cases in >30-40 yrs age group, 30 cases in 41-50 yrs age group, 26 cases in 51-60 yrs age group, 24 cases in 61-70 yrs age group and 5 cases constituted >70 yrs age group. In our study maximum number of cases in 41-50 yrs age group, constituted 30% of the study. Out of 100 patients, 86% cases had myocardial infarction while 14% cases had presentation of Unstable Angina with ischemic changes in electrocardiogram. [Table-1, Figure-2, 3]

**Figure-1. Sex wise distribution of study subject**

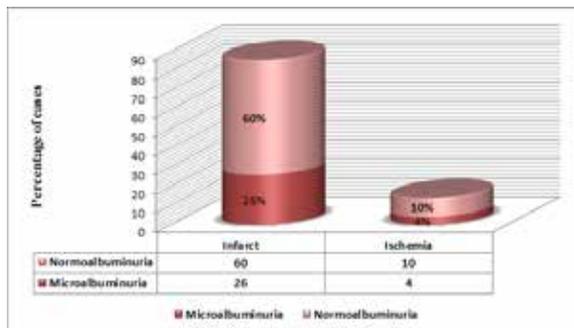


**Figure-2. Age wise distribution of study subject**



**Table-2. Association of microalbuminuria in cases with infarct/ischemia**

Microalbuminuria (>20-200mg/L)	Cases	
	Ischemia (n=14)	Infarct (n=86)
No.	04 (33.3 %)	26 (35.18%)
Mean	67.5	98.09
SD	7	28.8
P value	<0.05	

**Figure-3. Distribution of microalbuminuria in cases with infarct/ischemia**

Out of the 100 cases, 30 cases had microalbuminuria. Out of 30 cases, and 26 (35.1%) Infarct cases and 4 (33.3%) Ischemia cases had microalbuminuria, while out of 70 cases, 60 (64.8%) Infarct and 10(66.6%) Ischemia cases had normoalbuminuria. Microalbuminuria in Infarct and Ischemia cases had similar prevalence. The calculated difference for mean level of Microalbuminuria between Infarct and Ischemia cases was found to be statistically significant ( $P < 0.05$ ). [Table-2, Figure-3]

## DISCUSSION

In the present study, total number of cases was 100, out of these 71 cases were male and only 29 were female. The male-female ratio in the study was 2.44: 1. In 2007 **Jordanova-Laleva P. et al**, In their study population 78.08% were male while 21.92% were female. In 2006 **Hashim Rizwan et al**, In their study population included one hundred non diabetic IHD patients (73 were men, 27 were women). The M: F ratio was 2.7: 1. In 2006 **Lekatsasa I et al**, in their study, two hundred twenty-three patients of non-diabetic acute myocardial infarction, out of which 172 were male and 51 female. The male female ratio in the study was 3.3: 1. Thus, the male female ratio of the present study is in accordance with the above mentioned studies. This is in accordance with the knowledge that males are more prone for ischemic heart disease than females. [9, 10, 11]

In the present study, mean age of the patients in study group was  $54.24 \pm 11.44$ , with age ranging 30 - 85 yrs. Majority of the patients (56%) were in 41 to 60 year age group. The mean age of males was  $56.57 \pm 11.89$  yrs and the mean age of females was  $54.79 \pm 10.47$  yrs. **Hashim Rizwan et al**, in their study on Non Diabetic Ischemic Heart Disease, they found mean ages were  $59.1 \pm 13.7$ ,  $60.3 \pm 9.9$  and  $59.4 \pm 12.8$  years in men, women respectively. [10]

In 2007 **Jordanova-Laleva P. et al**, Had found 32.8% prevalence of microalbuminuria in AMI patients. In 2006 **Hashim et al**, they found 37% microalbuminuria in their study on Microalbuminuria: Association with Ischemic Heart Disease in Non-Di-

abetics. This is significantly higher as compared to the general population which ranges from 2.2% to 10.2%. In 2006, **Sukhija et al**, found 19.6% prevalence of microalbuminuria in non diabetic patients, in their study on Relation of Microalbuminuria with coronary artery disease patients with and without diabetes. In 2004 **Lekatsasa I et al**, studied Two hundred twenty-three (172 men and 51 women) non-diabetic patients with acute myocardial infarction and a significant proportion of patients (33.6%) had microalbuminuria. In current study. One more study was found similar results related to the current study. In 2000 **Diercks et al**, In the **PREVEND study**, they found 32.7% prevalence of Microalbuminuria in Non-Diabetic Ischemic Heart Disease patients. [12, 13, 14] In 2000 **Gerstein H C et al (HOPE study)**, Microalbuminuria was detected in 14.8% of those without Diabetes mellitus at baseline in a cohort of Heart Outcomes Prevention Evaluation Study conducted between 1994 and 1999. This showed that 20.4% of patients with microalbuminuria had a myocardial infarction, stroke or cardiovascular cause of death as compared to 13.8% of those without microalbuminuria. [15] In 2006, **Sukhija et al** had found prevalence of microalbuminuria 72% in Hypertensive non Diabetic CAD patients. Thus, result of present study was in accordance with the above mentioned studies.

In present study, mean level of microalbuminuria was 67.5 mg/L in Unstable Angina while 98 mg/L in Infarct. The mean level of microalbuminuria in Infarct cases was significantly higher compared to Unstable Angina cases. In 2007 **Díaz García et al**, found . More elevated values in acute myocardial infarction than those observed in unstable angina. microalbuminuria of  $45 \pm 38$  mg/L was present in subjects with unstable angina compared with  $147 \pm 131$  mg/L of the acute myocardial infarction group and they found difference was significant. Thus, Infarct cases had significantly higher level of microalbuminuria than Unstable Angina and result of present study was in accordance with the above mentioned study. [16]

**Conclusion:** Our study shows microalbuminuria is positively associated with Ischemic Heart Disease in non-diabetic subjects and can be regarded as an important additional risk factor for Ischemic Heart Disease. The level of significance of microalbuminuria, in our study was comparable to the conventional risk factors. In the absence of any renal insufficiency, microalbuminuria is a non-specific yet highly sensitive marker of Ischemic Heart Disease. Since microalbuminuria is a simple investigation and relatively inexpensive test we propose the use of microalbuminuria as an adjunct biochemical parameter. Hence, screening for microalbuminuria in the general population is a worthwhile public health tool for cardiovascular risk stratification and targeting preventive strategies.

## Acknowledgement

The authors are thankful to all the faculty and technical staff of department of Medicine, Pt. J. N. M. medical college, Raipur (C.G.) India, for their cooperation and support during the entire study period.

## REFERENCES

- Antman EM, Braunwald E. ST-segment elevation myocardial infarction: In: Fauci A.S., Kasper D.L., Longo D.L., Braunwald E., Hauser S.L., Jameson J.L. Editors. Harrison's Principles of Internal Medicine, 17th Edition. Mc Graw Hill Publication, 2008; p1532-1544. | 2. Toto Robert D. Microalbuminuria: Definition, Detection, and Clinical Significance, the Journal of Clinical Hypertension suppl. 3 vol. VI no. XI November 2004. | 3. Haffner SM, Stern MP, Gruber MK, Hazuda HP, Mitchell BD, Microalbuminuria. Potential marker for increased cardiovascular risk factors in nondiabetic subjects? Arteriosclerosis 1990; 10: 727-31 | 4. Parving HH, Jensen HE, Mogensen CE, Evrin PE. Increased urinary albumin excretion rate in benign essential hypertension. The Lancet 1974; 1190-92 | 5. Gosling P. Microalbuminuria and cardiovascular risk: a word of caution; Journal of Human Hypertension (1998) 12, 211-213 | 6. Gosling P, Hughes EA, Reynolds TM, Fox JP: Microalbuminuria is an early response following acute myocardial infarction. Eur Heart J 1991; 12: 508 | 7. Berton G, Cordiano R, Palmeri R, Cucchi F, De Toni R, Microalbuminuria during acute myocardial infarction; a strong predictor for 1 year mortality. Eur Heart J. 2001; 22(16):1466-75. | 8. Hartland A et al : Microalbuminuria :yet another cardiovascular risk factor? Ann clin Biochem 1999;36: 700-703 | 9. Jordanova-Laleva P, Grigorov F, Petkova V, Tisheva S. The Level of Microalbumin excretion and its short term prognosis in Acute Myocardial Infarction. Trakia Journal of Sciences, Vol. 5, No. 1, pp 6-9, 2007 | 10. Hashim Rizwan, Nisar Shazia , Khalil ur , Rehman Naeem Microalbuminuria : Association with Ischemic Heart Disease in Non-Diabetics J Ayub Med Coll Abbottabad 2006;18(1) | 11. Lekatsasa I et al Prognostic significance of microalbuminuria in non-diabetic patients with acute myocardial infarction International journal of cardiology Volume 106, Issue 2, Pages 218-223 (13 January 2006) | 12. Sukhija Rishi, MD, Aronow W S MD, Kakar Priyanka, MD, Garza Luis MD; Relation of Microalbuminuria and Coronary Artery Disease in Patients With and Without Diabetes Mellitus Am J Cardiol 2006;98: 279-281 | 13. Khot Umesh N.; Khot Monica B.; Bajzer Christopher T.; et al Prevalence of Conventional Risk Factors in Patients With Coronary Heart Disease JAMA. 2003;290(7):898-904 | 14. Diercks GF, Hillege HL, van Boven AJ, Kors JA, Crijs HJ, Grobbee DE, de Jong PE, van Gilst WH: Microalbuminuria modifies the mortality risk associated with electrocardiographic ST-T segment changes. J Am Coll Cardiol 40: 1401, 2002 | 15. Gerstein HC, Mann JF, Pogue J et al. Prevalence and determinants of microalbuminuria in high-risk diabetic and nondiabetic patients in the Heart Outcomes Prevention Evaluation Study. The HOPE Study Investigators. Diabetes Care 2000; 23 (suppl 2): B35-39. | 16. Diaz García Norma Angélica, Alberto Rubio Guerra, Leticia Rodríguez López, Ana Chávez Rivera, América López Maldonado; Determination of microalbuminuria in acute coronary syndrome patients Medicina Interna de México Volumen 23, Núm. 4, julio-agosto, 2007 |