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**Original Research Article**

# Correlation between Microalbuminuria and Ischemic Heart Disease in Non-diabetic Patients

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**Abstract**

**Background**: In patients with diabetes mellitus, microalbuminuria is a recognized marker for both micro and macrovascular damage. Microalbuminuria is a significant risk factor for the onset of ischemic heart disease, according to the latest research data. The current study sought to determine whether microalbuminuria and ischemic heart disease were related in non-diabetic cases.

**Methods**: After the selection of the patient based on the inclusion criteria complete details were recorded which included the demographic profile of the patient, past history, and family history, and a complete clinical examination was done. The WHO/Rose Questionnaire was given to each one of the subjects. Those already with the diagnosis of IHD were included and ECG/TMT was done for inducible ischemia. The patients were given a container for the collection of urine over 24 hours which was then sent for estimation of microalbuminuria level by the immunoturbidimetry method. The result was reported in mg/day of albumin.

**Results:** The mean levels of serum total cholesterol in males were 179.11 ± 21.38 mg/dl and in females were 189.23± 18.95 mg/dl. Similarly, the mean serum triglyceride levels in males were 134.28 ± 15.95 mg/dl and in females was 171.23±78.26 mg/dl and serum HDL in males mean values were 41.19 ± 2.56 mg/dl and in females, it was 42.36± 5.47 mg/dl and the LDL-C levels in males mean values were 125.10± 17.36 mg/dl and in females, it was 125.67 ± 21.02 mg/dl. Out of the total n=35 males, n=27(77.14%) cases were having abnormal microalbumin levels similarly, in females n=9(81.81%) cases were having abnormal microalbumin levels.

**Conclusion**:This study concluded that in non-diabetic cases, urine microalbumin seems to be a good marker for predicting the risk of IHD. Despite the drawback of the small sample size in this study, the robust and independent relationship between higher urine microalbumin and IHD was found in our investigation and this adds more support for microalbuminuria as a biomarker of IHD in non-diabetics, even if at levels lower than those seen in the diabetic cases

**Keywords**: Microalbuminuria, Ischemic Heart Disease, Infarction, ECG, Non-diabetics

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## Introduction

Over 7.3 million people died from ischemic heart disease (IHD) in 2008 alone, making it one of the top causes of mortality in the world. Furthermore, low- and middle-income nations currently account for more than 80% of cardiovascular mortality. [1] Since over 25% of these deaths still take place in South Asia, cardiovascular disease is currently to blame for 24% of all fatalities in India. [2] The fact that an estimated 31.8 million Indians suffer from IHD makes the situation much worse; in 2020, the country's cardiovascular disease death has increased by an incredible 111 percent above 1990 levels [3], with IHD accounting for the majority of that increase. [4]According to the World Health Organization, India is responsible for one-fifth of these global deaths, particularly among the younger population. According to the findings of the Global Burden of Disease study, India has an age-standardized CVD death rate of 272 per 100,000 people, significantly higher than the global average of 235. Indians are affected by CVDs ten years earlier than people in the west. [5] Numerous studies on Diabetes Mellitus (DM) patients have identified urine microalbumin as a marker for systemic atherosclerosis. [6] Numerous studies on Diabetes Mellitus (DM) patients have identified urine microalbumin as a marker for systemic atherosclerosis. [6] A urinary albumin excretion rate of more than 30 mg/24 hours or a urine albumin creatinine ratio of more than 30 mg/g in an early morning sample is the classic definition of microalbuminuria. [7, 8] It is important to remember that these cut-off values have mostly been established for proteinuria in diabetic persons and have not yet undergone rigorous validation in non-diabetic individuals. Regarding a temporal model of biomarker associations with developing IHD, [9] A urinary albumin excretion rate of more than 30 mg/24 hours or a urine albumin creatinine ratio of more than 30 mg/g in an early morning sample is the classic definitions of microalbuminuria. [7, 8] It is important to remember that these cut-off values have mostly been established for proteinuria in diabetic persons and have not yet undergone rigorous validation in non-diabetic individuals. Regarding a temporal model of biomarker associations with developing IHD, [9] one of the important indicators of the subclinical disease is urine microalbumin which may be altered at the early stage of the disease progression. The shared pathogenetic mechanisms of endothelial dysfunction, systemic inflammation, and vascular injury readily explain the close association between microalbuminuria and coronary artery disease; [10] it is reasonable to assume that such a relationship should exist regardless of the concurrent presence or absence of diabetes. Since there a relative paucity of data on the relationship between IHD in non-diabetics and urine microalbumin led to the design of this study.

## Material and Methods

This cross-sectional study was conducted in the Department of General Medicine, Deccan College of Medical Sciences, Owaisi Hospital & Research Centre, Hyderabad, Telangana State from March 2020 to Feb 2021. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the participants of the study after explaining the nature of the study in the local language.

*Sample size calculation*: $n=4pq/d^2$

Where n=sample size, p=prevalence taken as p=8, q=92, d=absolute error taken as 8

n=4*8*92/64=46 (The sample size taken in the study was 46)

### *Inclusion criteria*

1. Adult non-diabetic subjects with ECG suggestive of IHD

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2. Those diagnosed as IHD based on 12 lead ECG examination/Exercise thread mill testing.
3. Elevated cardiac enzymes in biochemical analysis

***Exclusion criteria***

1. Known Diabetic patients
2. Congestive cardiac failure as presentation
3. Urine showing - Macroalbuminuria (dipstick-positive albuminuria)
4. Pregnant Females or those with vaginal discharge
5. Those who did not wish to participate voluntarily

After the selection of the patient complete details were recorded which included the demographic profile of the patient, past history, and family history, and a complete clinical examination was done. The WHO/Rose Questionnaire was given to each one of the subjects. [11] Those already with the diagnosis of IHD were included and ECG/TMT was done for inducible ischemia. The patients were given a container for the collection of urine over 24 hours which was then sent for estimation of microalbuminuria level by the immunoturbidimetry method. The result was reported in mg/day of albumin.

*Statistical analysis*: the available data was uploaded on an MS Excel spreadsheet and analyzed by SPSS version 22 in windows format. Quantitative variables were expressed on mean and standard deviations and qualitative variables were expressed in proportions and percentages. Fisher's exact test has been used to find the difference between two proportions.

**Results**

Out of the total n=46 cases in the study, n=35(76.08%) were males and n=11(23.09%) were females. The mean age of the study population was 52.38 ± 8.52 years. It was 51.25 ± 9.5 years for males and 58.02 ± 5.03 for females. Subjects in the age group 56-65 constituted 39.13% of the study group. The majority of females were aged above 55 years details depicted in table 1.

**Table 1: Demographic profile of the study subjects**

| *Age group (years)* | *Male* | *Female* | *Total (%)* |
|---|---|---|---|
| 21-30 | 3 | 0 | 3 (6.52) |
| 31-40 | 7 | 0 | 7 (15.21) |
| 41-50 | 10 | 2 | 12 (26.08) |
| 51-60 | 10 | 8 | 18 (39.13) |
| 61-70 | 5 | 1 | 6 (13.04) |
| Total | 35 | 11 | 46(100.0) |

Based on a family history of ischemic heart diseases in males no family history of IHD was found in n=19(54.28%) out of n=35 cases. Similarly, for females, no family history of IHD was found in n=7(63.63%) out of the total n=11 cases in the study. History of smoking revealed n=30(85.71%) out of n=35 cases males were smokers or ex-smokers in females no such case was found all the females in the study were non-smokers. Most of the males were found to be overweight (BMI > 25.1) 60.0% similarly, in females' cases 63.63% cases were in the overweight category details are given in table 2.

**Table 2: Distribution of cases based on BMI**

| *BMI ($kg/m^2$)* | *Males (n=35)* | *Female (n=11)* |
|---|---|---|
| < 23.0 | 0 | 0 |
| 23.1 – 25.0 | 9 (25.71%) | 2 (18.18%) |

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| | | |
|---|---|---|
| 25.1 - 29.9 | 21 (60.0%) | 7 (63.63%) |
| > 30.0 | 5(14.28%) | 2(18.18%) |

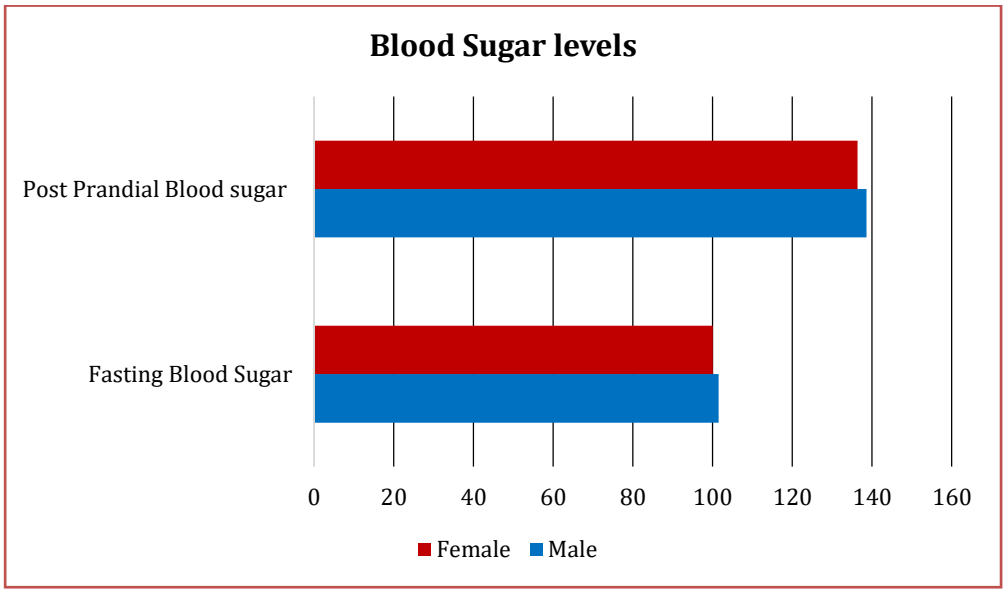


**Figure 2: Mean blood sugar levels in the cases of study**

The mean fasting blood sugar levels in males was 101.52± 7.22 mg/dl in females the mean values were 100.03±7.93 mg/dl. Similarly, the postprandial blood sugar levels in males were 138.63±12.43 mg/dl and in females, it was 136.36± 13.47 mg/dl.

**Table 3: Abnormal lipid parameters recorded in the cases of study**

| *Lipid parameters* | *Males (n=35)* | *Females (n=11)* | *Total (n=46)* |
|---|---|---|---|
| Total cholesterol (>200 mg%) | 5(14.28%) | 2(18.18%) | 7(15.21%) |
| Triglycerides (>150 mg%) | 9(25.71%) | 1(9.09%) | 10(21.74%) |
| HDL (M<40 mg% F<50 mg%) | 4(11.43%) | 4(36.36%) | 8(17.39%) |
| LDL-C (>150 mg%) | 4(11.43%) | 1(9.09%) | 5(10.87%) |

The mean levels of serum total cholesterol in males were 179.11 ± 21.38 mg/dl and in females were 189.23± 18.95 mg/dl. Similarly, the mean serum triglyceride levels in males were 134.28 ± 15.95 mg/dl and in females was 171.23±78.26 mg/dl and serum HDL in males mean values were 41.19 ± 2.56 mg/dl and in females, it was 42.36± 5.47 mg/dl and the LDL-C levels in males mean values were 125.10± 17.36 mg/dl and in females, it was 125.67 ± 21.02 mg/dl. The mean values of elevated serum lipid parameters and the distribution of the parameters have been depicted in table 3. Out of the total n=35 males, n=27(77.14%) cases were having abnormal microalbumin levels similarly, in females n=9(81.81%) cases were having abnormal microalbumin levels. The details and distribution of microalbumin levels recorded in the group have been depicted in table 4. Higher levels of microalbumin were recorded in the age group of 51- 60 years as compared to other age groups.

**Table 4: Levels of microalbuminuria (mg/day)**

| *Microalbuminuria* | *Males (n=35)* | *Females (n=11)* | *Total (n=46)* |
|---|---|---|---|
| < 30 | 08 (22.86%) | 2 (18.18%) | 10 (21.74%) |
| 30-50 | 17 (48.57%) | 6 (54.54%) | 23 (50.00%) |
| > 50 | 10 (28.57%) | 3 (27.27%) | 13 (28.26%) |

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*χ2- 11.26; p<0.000*

The relationship of microalbumin levels to the presence of hypertension, ischemia, and infarct pattern showed n=26 cases with a history of hypertension in which n=20 cases were with hypertension and microalbumin levels > 30 mg/dl. Out of these n=20 cases, n=7 cases were of ischemia and n=13 cases of infarction. The relationship between microalbumin levels with ECG pattern is given in figure 2.

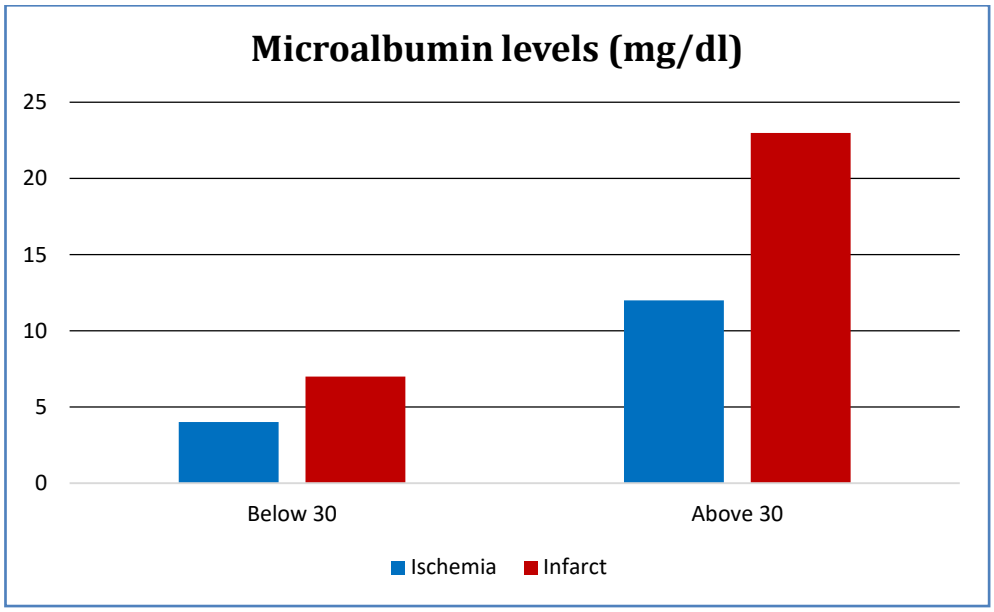


**Figure 2: Relation of microalbumin levels to the ECG pattern**

Out of the n=36 cases of microalbumin levels > 30 mg/dl n=24 cases were smokers or past smokers and n=12 were non-smokers. In the total n=7 cases of higher cholesterol levels, n=6 had urinary microalbumin levels > 30mg/dl.

**Discussion**

The prevalence of acute coronary syndrome and ST-elevation myocardial infarction is now the highest in India (MI). With 261,694 fatalities from hypertensive heart disease in 2013, it is a serious issue in India together with other CVDs (an increase of 138 percent in comparison with 1990). In India, the prevalence of rheumatic heart disease is still epidemic-level, at 1.5–2 cases per 1000 people. [12] To target preventive strategies, risk stratification of the population should be effective. There are many reports emanating from the western literature about microalbuminuria as an independent risk factor for the development of ischemic heart disease. Microalbuminuria was formerly thought to be a sign of endothelial dysfunction in diabetes mellitus, but numerous studies have demonstrated that it is also a reliable indicator of generalized vascular dysfunction in the general population, including those who do not have diabetes. This study was done to find out whether there is an association between IHD and MA in non-diabetic subjects. In the present study, the diagnosis of IHD was by ECG changes. Cassar A et al., [13]have shown that ECG can be used to determine the presence of IHD in a population at large. In this study n=35(76.08%) were males and n=11(23.09%) were females. This is in accordance with the knowledge that males are more prone to ischemic heart disease than females. The mean age of the study population was 52.38 ± 8.52 years. It was 51.25 ± 9.5 years for males and 58.02 ± 5.03 for females. The females were in the post-menopausal age group which shows that sex hormones have a protective effect as far as cardiovascular risk is concerned. [14]Out of the n=36 cases of

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microalbumin levels > 30 mg/dl n=24 cases were smokers or past smokers and n=12 were non-smokers. Umesh N Khot et al.**,** [15]found a prevalence of 41.6% in males and 29.5% in females in their study for smoking as a risk factor for ischemic heart disease. The BMI in most of the cases of the study was > 25.1 (table 2) showing a higher percentage of the study population was either overweight or obese. Nordestgaard BG et al., [16] in a study on the effect of elevated body mass index on ischemic heart disease risk found that observational estimates indicated a 26 percent increase in chances for IHD for every 4 $kg/m^2$ rise in BMI, while causal estimates indicated a 52 percent increase. These findings strengthen the case for a causal relationship between elevated BMI and an increased risk of IHD, even though the process may ultimately be due to intermediary conditions such as type 2 diabetes, hypertension, and dyslipidemia.

In this study, we found that 65.21% of all cases with abnormal lipid profiles (Table 3). Out of this 62.85% of all males and 72.72% of females were with abnormal lipid profiles. 21.74% were with hypertriglyceridemia and 17.39% were with abnormal HDL levels. Umesh N K et al., [15] in their study found that 39.6% of females and 34.1% of males had abnormal lipid parameters. In our study, n=16 cases with ischemic patterns in ECG n=30 showed infarction. Out of these ischemic cases, n=12 were also associated with microalbuminuria and out of the total infarction cases n=23 were also associated with microalbuminuria (Figure2) microalbuminuria showed a positive association with both in our study. The PREVEND study [16] showed that in a multivariate model adjusted for established cardiovascular risk factors, microalbuminuria was independently associated with infarct pattern (7.1%) (OR-1.61), and major ischemia (10.6%) (OR-1.43) and minor ischemia (15.1%) (OR-1.32). In our study 75% of ischemic heart disease cases had microalbuminuria and 76.67% had microalbuminuria in infraction cases. In the PREVEND study, [16] 32.8% of ischemic heart disease patients had microalbuminuria and in the HOPE study [17] cohort mentioned above, 20.4% of patients with cardiovascular disease had microalbuminuria compared to 76% in this study. This was probably because the present study had a cohort of IHD patients in whom microalbuminuria was estimated whereas the studies mentioned above were done on the general population. The present study showed that microalbuminuria can be used as an additional cardiovascular risk indicator even in non-diabetic patients.

**Conclusion**

Within the limitations of the current study, it can be concluded that in non-diabetic cases, urine microalbumin seems to be a good marker for predicting the risk of IHD. Despite the drawback of the small sample size in this study, the robust and independent relationship between higher urine microalbumin and IHD was found in our investigation and this adds more support for microalbuminuria as a biomarker of IHD in non-diabetics, even if at levels lower than those seen in the diabetic cases. Hence, screening for microalbuminuria in the general population may be a worthwhile public health tool for cardiovascular risk stratification and targeting preventive strategies.

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