RESEARCH ARTICLE

A CLINICAL STUDY OF MICROALBUMINURIA IN NON-DIABETIC CORONARY ARTERY DISEASE PATIENTS IN AN INDUSTRIAL HOSPITAL.

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Manuscript Info	*Abstract*
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	Objective: The objective of our study was to study the prevalence of microalbuminuria in non-diabetic patients with Ischemic heart disease and to identify whether it can be used as an independent marker of Ischemic heart disease or as a screening test for ischemic heart disease in non- diabetic patients. **Material and methods:** This was a hospital based prospective study. All patients presenting with coronary artery disease to our hospital from May 2014 to Sep 2016 were be included. Total number of patients included in our study were 50 as most patients with IHD were diabetic as well and were excluded from the study. All these patients were subjected to detailed history and physical examination. All baseline investigations, ECG, Chest X-ray, lipid profile and urine for microalbumin by Turboux method were done on these patients. **Results: -** Total 50 patients were included in the study (39 males and 11 females). The mean age of the patients was 58.22 ± 10.15 years. Out of 50 patients, 30 (60%) had microalbuminuria. There were 24 males (61.5%) and 6 females (54.5%) with abnormal microalbuminuria levels. Most of the patients with microalbuminuria were in age range of 45-65years. There was statistically significant association of microalbuminuria with hypertension, LDL >100mg/dl and HDL<35 mg/dl whereas no association was seen between microalbuminuria and other risk factors of IHD. **Conclusion:** From our study we concluded that there is high prevalence of microalbuminuria in non-diabetic ischemic heart disease patients but the association between two is not statistically significant. At present microalbuminuria cannot be used as an independent marker of IHD nor can it be used as a screening tool for IHD in general population unless further prospective studies with large sample size and comparative analysis against normal controls are done in future.

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Introduction:-
Ischemic Heart Disease has an estimated prevalence of 6-9% in the general population. The mortality rate of acute myocardial infarction is approximately 30%. 1 in 25 patients who survives the initial hospitalization die in the first year after acute myocardial infarction (1). In India, coronary artery disease is equally important and its incidence has

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increased in the last 2 decades. Many prospective clinical studies have identified a series of independent risk factors for myocardial infarction, stroke and peripheral vascular disease, among which the pre-existence of atherosclerotic vascular disease, 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. However, there are some emerging risk factors which can be used independently. Currently there is an intense discussion whether they should be introduced into routine risk assessment. This especially concerns Lipoprotein (a), CRP, fibrinogen, homocysteine and microalbuminuria.

A consensus conference in 1995 defined microalbuminuria (MA) in individuals with diabetes as an abnormal urinary excretion rate of albumin between the range of 20-200 µg/min or 30-299 mg/day. In this disease, microalbuminuria is an early predictor of renal damage. It takes usually more than 5 years for type I diabetics to have microalbuminuria. Microalbuminuria has also been implicated as a sensitive indicator of non-renal disease (2, 3). In fact microalbuminuria occurs in response to acute inflammatory conditions such as ischemia (4)   , trauma and thermal injury (5), surgery (6), pancreatitis (7) and inflammatory bowel disease (8). 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 (9).

Amongst all these, the association of microalbuminuria with cardiovascular diseases is very important owing to the burden of cardiovascular morbidity and mortality The Prevention of Renal and Vascular End Stage Disease (PREVEND) study concluded that urinary albumin measurement may be useful in early risk profiling and prevention of cardiovascular disease as it is independently associated with increased cardiovascular risk factors and cardiovascular morbidity. Myocardial infarction is the most important manifestation of cardiovascular diseases. Microalbuminuria is an early response to myocardial infarction .It is also proportional to the infarct size (10, 11). A study by Berton et. al., showed that microalbuminuria occurs in acute myocardial infarction and predicts early mortality (12, 13) . In a cross sectional study in western India in 2002, microalbuminuria was shown to be associated with carotid intima – media thickening and coronary artery disease (13).

It has been hypothesized that microalbuminuria is an indicator of wide spread endothelial cell dysfunction leading to increased penetration of atherogenic protein in the arterial wall. In the 1st MONICA (*Moni*toring Trends and Determinants of *Ca*rdiovascular Diseases) study in Copenhagen County, individuals with persistent microalbuminuria had increased transvascular albumin leakage to a level similar to that seen among individuals with severe clinical atherosclerosis.(13)Though the underlying mechanism remains undetermined, it has been hypothesized that the magnitude of albumin excretion in urine reflects the degree of atherosclerosis. If this is so, the urinary albumin excretion should be high in patients with IHD even in non diabetics. Few studies have indicated that microalbuminuria is common in nondiabetic, nonhypertensive population and is considered to be an independent indicator of cardiovascular risk factors and cardiovascular mortality. (14, 15) In clinical practice, a spot-urine sample is collected when the patient visits either the general practitioner or the health care office, where the screening takes place.

Aim of the study:-
1. To study the prevalence of microalbuminuria in non-diabetic patients with Ischemic heart disease.
2. To identify the association of microalbuminuria and other known risk factors of Ischemic heart disease.
3. To identify whether microalbuminuria can be used as an independent marker of Ischemic heart disease.
4. To identify whether microalbuminuria can be used as a screening test for ischemic heart disease in non- diabetic patients.

Material and methods:-
This was a hospital based prospective study conducted in a tertiary care referral hospital of Northern Railways at New Delhi which caters the need of Railway beneficiaries from North India constituting about 1.5 million people. All patients presenting with coronary artery disease to our hospital from May 2014 to Sep 2016 were be included in our study. Total number of patients included in our study were 50 as most patients with IHD were diabetic as well and were excluded from the study. All these patients were subjected to detailed history and physical examination. All baseline investigations, ECG, Chest X-ray, lipid profile and urine for microalbumin by Turboux method were done on these patients.

Inclusion Criteria:-
The study will include 50 cases who present with history of:
Angina on Exertion
Unstable Angina
Acute Myocardial Infarction
Post MI patients (post-CABG, post-PTCA, Medically treated patients)

Exclusion Criteria:-
1. Known diabetics
2. CKD patients
3. Systemic infection
4. Urinary tract infection
5. Inflammatory conditions like rheumatoid arthritis

This method is based on the Principle of Liquid phase immunoprecipitation assay with nephelometric end-point detection. In this, Antiserum to albumin is diluted in buffer & added to urine sample & light scattering caused by Ag-Ab complexes is measured after incubation, which is directly proportional to albumin concentration. Precalibration of curve is defined by batch specific parameters on magnetic card. The single point calibration to check the curve during assay is made with calibrator solution. The results are expressed as conc.mg/L. The method is fast & sensitive to very low conc. of albumin. The reagent used in this method contains azide (swine).Urine albumin control is available in kit.

Sample Collection:-Spot urine sample for screening

Results:-
It was a hospital based prospective study. Total 50 patients were included in the study (39 males and 11 females). The mean age of the patients was 58.22 ± 10.15 years. Family history of IHD was present in 30% patients, while smoking history was present in 66% of patients (only one female patient had smoking history compared to 82% males). Hypertension was present in 78% of patients of which females had a higher percentage (Female to Male – 81.8% to 76.9%). 40% patients had history of previous cardiac event. 21(42%) patients had raised level of cardiac enzymes on admission. Out of 50 patients, 30 (60%) had microalbuminuria in our study. There were 24 males (61.5%) and 6 females (54.5%) with abnormal microalbuminuria levels. Most of the patients with microalbuminuria were in age range of 45-65years. (TABLE 1) There was statistically significant association of microalbuminuria with hypertension, LDL >100mg/dl and HDL<35 mg/dl whereas no association was seen between microalbuminuria and other risk factors of IHD. (TABLE2)

Discussion:-
Worldwide, ischemic heart disease is assuming an increasing role as a major cause of morbidity and mortality. IHD will become a major disease burden in India by the year 2020. From 1990 to 2020, the proportion of worldwide deaths due to cardiovascular disease including IHD is expected to increase from 28·4% to 33·7%. In terms of years of life lost, cardiovascular disease will jump from fourth to first place. For premature death and disability, cardiovascular disease will move from fifth to first place. However, despite the rising tide of this tragic disease, the physicians' ability to predict the development of a cardiovascular event is limited by the low prognostic specificity of the traditional risk factors for atherosclerosis. This justifies the ongoing search for new bio markers of atherosclerosis. To target preventive strategies, risk stratification of the population should be effective. There are many reports emanating from the literature about microalbuminuria as an independent risk factor for development of ischemic heart disease. Hitherto, microalbuminuria was considered as a marker of endothelial dysfunction in diabetes mellitus, but many studies have shown microalbuminuria is an effective marker of generalised vascular dysfunction even in non-diabetic population.

This study was done to find out the prevalence of microalbuminuria in non- diabetic patients with IHD and whether it can be used as a marker or as a screening test in these patients. All the cases in the present study had a normal renal function (Sr creatinine ≤ 1.5 mg/dl). Microalbuminuria, in these patients was therefore not related to renal dysfunction. Our study in this respect agrees with the views of Peter Gosling, who considered it to be a sensitive indicator of nonrenal disease (9). Patients with renal or urinary tract disease or diabetes mellitus were excluded from

this study, as urinary albumin excretion is elevated in these diseases for reasons other than atherosclerosis. The use of early morning urine sample was preferred to minimize the contribution of posture and exercise to urinary albumin excretion which are known to cause microalbuminuria.

Out of 50 patients in our study, 60% had microalbuminuria, which is same as that found by Naser et al. who found that prevalence of MAU was 62.9% in patients with CAD55. In the PREVEND study (16), 32.8% IHD patients had microalbuminuria while in HOPE study (17) 20.4% of patients with cardiovascular disease had microalbuminuria. Of the 30 patients with microalbuminuria, 61.5% were males and 38.5% were females. Most patients with MAU were in the age group of 46-60 years which is in accordance with the study by Menno T. Pruijma et al (18), in which most patients were in the age group of 55-64 years, though they found a slight female dominance contrary to our study.

In our study 39 patients were hypertensive, out of which 66.7% had MAU and 36.4% of normotensive patients had MAU (P<0.005). In a study by Menno T. Pruijma 7% normotensive and 24% hypertensive patients had MAU (18). In a study by Michael Bohm et al, 58.4% hypertensive patients in their study had MAU which is comparable to that seen in our study (19). In our study, out of 50 patients 33 were smokers. Out of this 63.6% had MAU whereas among non-smokers 52.9% had MAU. This showed that there was no significant association between smoking and MAU. Similar results were obtained by Menno T. Pruijma et al in their study on general population of Seychelles (18).As for smoking, no significant association was seen between MAU and family history of IHD and previous cardiac events.

Conclusion:-
From our study we concluded that there is high prevalence of microalbuminuria in non-diabetic ischemic heart disease patients but the association between two is not statistically significant. Our study also showed that there is a strong association between microalbuminuria and hypertension, high LDL cholesterol, and low HDL cholesterol, while it is not significantly associated with smoking, family history of IHD and total cholesterol.

From our study we were not able to find out whether microalbuminuria was independently associated with IHD or its high prevalence was due to the presence of other risk factors of IHD to which microalbuminuria was strongly associated. So from our study we concluded that at present microalbuminuria cannot be used as an independent marker of IHD nor can it be used as a screening tool for IHD in general population unless further prospective studies with large sample size and comparative analysis against normal controls are done in future.

Table 1:-Levels of microalbuminuria (mg/day)

Microalbuminuria	Frequency	%
<= 20	20	40
>20	30	60
Total	50	100

Table 2:-Association of microalbuminuria with other risk factors of IHD:

	TOTAL	MA<=20 n=20		MA>20 N=30		p value
		Frequency	%	Frequency	%	
H/o of Smoking	33	12	36.4%	21	63.6%	0.027
Hypertension	39	13	33.3%	26	66.7%	0.003
Family H/O IHD	15	8	53.3%	7	46.7%	0.715
Previous cardiac event	20	8	40%	12	60%	0.206
Cholesterol>150	25	9	36%	16	64%	0.048
LDL>100	19	6	31.6%	13	68.4%	0.005
Triglycerides>200	7	3	42.9%	4	57.1%	0.593
HDL<35	19	4	21.1%	15	78.9%	0.004

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