Relation Of Urinary Albumin Excretion And Severity of Coronary Artery Lesion In Type 2 Diabetic Patients Undergoing Coronary Angiography

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Introduction: Proteinuria has long been known as a major risk factor not only for renal disease, but also for cardiovascular disease. This has recently been confirmed in patients with type 2 diabetes and proteinuria who were followed up in a large clinical trial (**Keane et al .,2003**). However, in recent years the interest has focused on much earlier stages in renal and cardiovascular disease as established by the presence of albumin in urine both in type 1 and type 2 diabetes (**Poulsen., 2002& Mogensen., 2004**). In subjects without diabetes mellitus (DM) and hypertension, the clinical relevance of proteinuria is less clear, although several studies have been reported in the past few years with increased risk of cardiovascular disease (CVD) in non diabetic individuals with proteinuria (**Hillege et al., 2001& Damsgaard et al.,2002**). In addition, the clinical course of proteinuria has been fairly well described, although this is becoming increasingly complicated and difficult, as many patients are now being treated to accomplish optimal glycaemic (Perkins BA et al., 2005) and blood pressure control, radically changing the so-called natural history of renal and cardiovascular disease (**Parving et al., 2008& Cooper et al., 2009**).Proteinuria has long been part of a general screening programme for virtually all types of patients, but it has become equally, or perhaps even more, important as this measure makes intervention possible much earlier, usually before any decline in glomerular filtration rate (GFR) has occurred (**Sackmann et al., 2000**). Laboratory techniques for proteinuria are now simple and inexpensive (**Sackmann et al., 2000**).Regarding screening tests, several laboratories have investigated for proteinuria by measuring both albumin/creatinine concentration and an A/C ratio. This test, which offers immediate results, seems to be highly reliable and is very useful (**Mattix et al 2002& Harvey et al ., 2004**).

Aim of the work: The aim of this study is to investigate the relation between Urinary Albumin excretion and severity of coronary artery lesion by coronary angiography in type 2 diabetic patients undergoing coronary angiography at Sohag University Cath Lab Unit.

Patients and Method:

Type and location of the study: A cross sectional study, Sohag University Hospital- Cath Lab.

Patient selection: Two hundred of type 2 diabetic patients who underwent coronary angiography as a part of the clinical work-up of symptoms or signs of heart disease and documented as coronary artery disease by coronary angiography .

Exclusion criteria:

1. Patients with history of urinary tract infection.
2. Patients with history of heamaturia.
3. Patients with history of kidney disease.
4. Menstruating females.
5. Pregnant women.
6. Patients with fever.
7. Patients with congestive heart failure.
8. Associated comorbidity (ex; connective tissue disease).
9. Patients with cancers.
10. Recently diagnosed type II diabetes (less than sex monthes)

Data collection: Each patient was evaluated for the following;

1-Demographics: (sex, age, height, weight).

2-Clinical data: History of angina, myocardial infarction, Stroke. The baseline 12-lead electrocardiogram (ECG) was categorized as normal or with one of the following abnormalities: ST-T changes (including ST depression, ST elevation, T wave inversion), acute or previous myocardial infarction.

3-Echocardiography: For detection of segmental wall motion abnormalities.

4-Urine samples: (Morning urine samples) for urine analysis and for calculation of A/C ratio by using HITACHI cobas 311 analyzer.

Test principle:

Immunoturbidimetric assay, Anti-albumin antibodies react with the antigen in the sample to form antigen/ antibody complexes which, following agglutination are measured turbidimetrically.

5-Blood samples were obtained for the serum level of creatinine

6-Angiographic data: Selective coronary angiography was performed in all patients under local anesthesia via femoral artery using the Judkins technique. The severity of each lesion was assessed by quantitative coronary angiography.

The presence and total severity of CAD was assessed according to the Syntax scoring system.

The SYNTAX score calculator is available directly online at the Web site, or it can be downloaded directly to a computer.

Statistical analysis: Data was analyzed using STATA intercooled version 12.1. P value was considered significant if it was less than 0.05..

Results: The study included two hundred type 2 diabetic patients, 106 were males and 94 were females with documented CAD by coronary angiography.Patients were allocated into two groups in term of Presence of Albuminuria.Patients with ACR ≥ 30 µg albumin/mg creatinine were defined as the group with albuminuria and those with ACR < 30 µg albumin /mg creatinine are defined as the group with normal UAE. According to new terminology persistent albumin excretion between 30 µg albumin/mg creatinine and 300 µg/mg is called moderately increased albuminuria(previously called microalbuminuria).Albumin excretion above 300 µg/mg is considered severely increased albuminuria (previously called macroalbuminuria. (The severity of coronary artery lesion was calculated by SYNTAX score and classified as following:

1. Low (0-22).
2. Intermediate (23-33).
3. High (≥33).

All patients were assessed for presence of cardiovascular risk factors and ongoing medication. Urinary Albumin Excretion was measured in all patients using A/C ratio. The severity of CAD was assessed by use of SYNTAX score.Of these patients 106 patients were males and 94 were females, 90 patients had smoking history, 160 patients were dyslipidemia, 80 patients had Albuminuria, 64 patients had history of MI, one, two and three vessel disease was detected in 72, 56 and 72 patients respectively. A statistically significant difference was detected in the severity of coronary artery disease between patients with and without Albuminuria with (P value < 0.01). Based on logestic regression analysis, the increased UAE level was found to have a linear relationship with the severity of coronary heart disease with (P value < 0.02). Finding of this study confirm that UAE have an independent role in CVD.

Discussion: Few studies had assessed the relationship between UAE& severity of CAD, this study was designed to determine the relation between UAE& severity of CA lesion.

Two hundred type 2 diabetic patients underwent CA in Sohag Cath Lab were included in this study.

The main findings of this study were as following

Severity of CAD was higher in patients with albuminuria than those without albuminuria. Severity of CAD was higher in patients belonging to higher A/C ratio subgroup than patients in lower A/C ratio subgroup. In this study logistic regression analysis demonstrated that UAE was an independent risk factor for CAD.Multivariate linear regression analysis was performed to evaluate the effect of the same variable in severity of CAD as defined by SYNTAX score. According to this analysis UAE found to be an independent risk of severity of CAD in both men and women and this come in agreement with **Khan et al., 2013** who found that microalbuminuria is predictive, independent of classical risk factor of cardiovascular diseases and all causes of mortality in diabetic patients and in the general population. The presence of 1 or 2 vessel CAD showed a linear increase between the groups without microalbuminuria. Patients with microalbuminuria have more severe angiographically detected coronary artery disease than those without microalbuminuria, thus a link can be established independent of other risk factors. **Rein etal., (2011**) found that The prevalence of stenoses of ≥ 50% was significantly greater in patients with albuminuria than in those with normoalbuminuria (66% vs 51%; p <0.001). Logistic regression analysis, adjusted for age, gender, diabetes, smoking,

hypertension, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, C-reactive protein, body mass index, estimated glomerular filtration rate, and the use of angiotensin-converting enzyme inhibitors/angiotensin II antagonists, aspirin, and statins, confirmed that albuminuria was significantly associated with stenoses ≥ 50%. **Sadaka etal., (2013**) found that the patients with microalbuminuria have a greater atherosclerotic burden and a more severe coronary artery disease in the form of total number of vessels affected and total number of lesions per patient than those without microalbuminuria. Similar results were presented by **Sukhija et al., (2006**) who examined coronary angiograms for the extent of severe CAD in patients with type 2 (DM) and MA (DM+MA+ ,n= 101), patients with DM and without MA(DM+ -MA ,n= 101), patients without DM and with MA(-DM MA+ ,n= 64), and patients without DM and MA(DM-MA-,n= 64). The purpose of this study was also to document the association between MA and severe CAD. The presence of 2- or 3-vessel CAD showed a linear increase from group DM-MA-to group DM+ MA+(p< 0.001). Thus, patients with MA have more severe angiographic CAD than those without MA. This relation is independent of other risk factors and is particularly evident in patients with DM. **Parvizi et al., (2005**) had studied 228 patients with angiographically confirmed coronary atherosclerotic lesions, according to the number of diseased vessels, were di-vided into two groups: 114 patients with two diseased vessels and 114 patients with three diseased vessels. The level of albumin in all the studied patients was <300 mg/24 hour. The results showed that the urinary albumin/creatinine ratio in both groups of patients was higher than that of the control (P= 0). The ratio in the control group was markedly lower than that in the patient groups. Results of this study indicate the existence of a significant correlation between the extension of atherosclerotic lesions and the ratio of albumin/creatinine in urine. **Guo et al., (2012)** found that the incidence of coronary heart disease, the number of patients with coronary vascular disease and the Gensini scores were significantly different between the microalbuminuria group and the normal albuminuria group ($P < 0.05$). The urinary albumin excretion rate was independently correlated with the occurrence of coronary heart disease in elderly type 2 diabetes mellitus patients (odds ratio (OR) = 1.058, $P < 0.0001$, 95% confidence interval (CI): 1.036 - 1.080). Urinary albumin excretion rate and the Gensini score were independently correlated in elderly type 2 diabetes mellitus patients ($\beta = 0.476$, $P < 0.0001$). **Tong et al., (2002**) found that diabetic patients had more multivessel (48.7% versus 34.7%, P<0.01), multilesion (64.9% versus 46.1%, P<0.05), extensive (51.4% versus 7.8%, P<0.01) and small vessel disease (95.2% versus 39.8%, P<0.01) than nondiabetic patients. **Lixin et al., (2012)** found that the differences in the incidence of CHD, the number of pathological coronary vessels, the Gensini's score and LVEF% between microalbuminuria group and normal albuminuria group were statistically significant ($P < 0.05$). UAER increased significantly with an increase in the number of pathological coronary vessels. Logistic multiple regression analysis showed that UAER was independently correlated with the incidence of CHD (OR = 1.092, P = 0.000, 95% CI = 1.063–1.122. **Dhiyaa . et al.,(2009**) found that diabetic patients showed more significant stenotic lesions. Moreover the lesions in the coronary artery were more diffuse with higher incidence of multivessel involvement in comparison to non-diabetic patients. Also diabetic patients show increasing incidence of the left main stem artery involvement which carry very high mortality rate. **Andrei et al., (2001)** the number of coronary arteries with stenosis was higher in patients with than in those without diabetes (2.7±0.9 vs. 1.9±0.8 per patient, respectively, p<0.005). The mean number of stenoses (in single or multiple coronary arteries) was 3.4±1.5 and 1.9±0.8 in patients with and without diabetes, respectively (p<0.005). Furthermore, diabetic CHD patients showed an increased number of low grade stenosis (less than 50% of vessel diameter) (31.3% vs. 12.8%) and a higher Prevalence of total artery occlusion (39.4% vs. 27.3%) (p <0.05 both).

Limitations:

1. This study wasn't based the general population; selection bias might have affected the outcome of the study.
2. This study included only two hundred patients a larger number of patients could yield more significant result .
3. Analysis of this study was based on A/C ratio test which was affected by age and sex so; it was better to use age and sex adjusted A/C ratio test cut off level.
4. SYNTAX score which was dependent on angiographic interpretation by experienced cardiologist may result in over or under estimation of lesion severity and moderate inter-observer variability.

Conclusion: UAE is independent risk factor for coronary artery disease and there is linear relationship between UAE and severity of coronary artery lesion in type 2 diabetic patients.

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