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Levels of C-Reactive Protein and Glycated Albumin as a Risk Factor of Coronary Artery Disease in Patients with Type II Diabetes Mellitus

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ABSTRACT

Background: It has been recognized that diabetes is a significant risk factor for coronary artery disease (CAD). Raised concentrations of the C-reactive protein (CRP) and Glycated albumin in individuals having type-2 diabetes mellitus and are related to the CAD occurrence and its severity. **Objective:** To determine the clinical benefits of hs-CRP and glycated albumin levels for CAD prediction in type II diabetic patients using a logistic regression model. **Study Design:** A cross-sectional study. **Settings:** Cardiology department of Ghulam Muhammad Mahar Medical College, in close collaboration with NICVD Sukkur Pakistan. **Duration:** For a one-year period from January 2019 to January 2020. **Methods:** The valuation of hs-CRP and the glycated albumin levels, were done in relation to the lumen narrowing levels among 102 patients who were scheduled for coronary angiography. Participants in the study were classified as normal if their lumen diameter was less than 30% (Group 1), mild CAD if it was 30-50% (Group II), moderate CAD if it was 51-70% (Group III), and severe CAD if it was more than 70% (Group IV). Data was entered and analyzed using SPSS version 26. **Results:** Using ANOVA, a relationship between glycated albumin, hs-CRP levels, and narrowing lumen diameter was found to be significant in all groups ($p < 0.01$). The Tukey's test after Honest Significant Difference (HSD) also showed a significant relationship between group III and group IV, except for hs CRP ($p < 0.01$) (p 0.857). **Conclusion:** Both glycated albumin and hs-CRP tests can be used to assess CAD risk levels in patients with Type II diabetes mellitus and other associated risk factors.

Keywords: *Type-II diabetes mellitus, Coronary artery disease, Glycated albumin, Hs-CRP.*

INTRODUCTION

Diabetes is considered a significant risk factor for coronary artery disease (CAD). In patients of diabetes mellitus, the risk of death from cardiovascular causes is 2 times greater than in patients without diabetes mellitus.[1-3] Early screening and detection of coronary artery disease by simple means has become important for the diabetic population, because if myocardial ischemia develops, it can lead to unfavorable prognosis at a later stage.[4] In the pathogenesis of diabetic complications, migration and proliferation of vascular smooth muscle cells, as well as inflammatory mediators in the vascular wall, the early appearance of glycated albumin, which leads to a negative effect on the biological functions of the vessels. Glucose forms a Schiff base that circulates within amine groups in a hyperglycemic medium or reacts with blood vessel wall proteins to produce Amudori type early glycation products over weeks and hours.[5] Some Amudori products endure a complex chemical rearrangement series over weeks and months to form advanced glycation end products (AGE).[6]

Atherosclerosis and acute cardiovascular events have also been revealed to be associated with CRP in type 2 diabetic patients who have not had previous cardiovascular disease. Hs-CRP proved to be a useful biomarker for the size and severity of atherosclerotic

lesions and a predictor of later events.[7] Serum glycosylated protein and CRP have been observed as a risk factor in many studies. In South Asians, there is a higher level of inflammatory markers compared to the white population; this relationship has never been studied in the Pakistani population.[8] The purpose of this training was to determine the clinical benefits of hs-CRP and glycated albumin levels for CAD prediction in type II diabetic patients using a logistic regression model.

METHODS

This study was held in the Cardiology department of Ghulam Muhammad Mahar Medical College with close association of NICVD Sukkur, for one year duration from January 2019 to January 2020. The cross-sectional study was done in 102 patients who agreed to participate and their written consent was taken. Type II diabetic patients with additional co morbidities, such as rheumatoid arthritis or other inflammatory diseases, lung, liver or kidney disease, and steroid use were excluded. The duration of diabetes, drug history, smoking, hypertension and the presence of risk factors like CAD family history and diabetes were recorded on the designed study proforma. Five (05) ml of venous blood was taken from every patient, the serum was separated, divided into samples and stored in two aliquots at -20 ° C until analysis. One aliquot was used to identify glycosylated serum protein and the other for hs-CRP. Coronary angiography was performed by one specialist interventional cardiologist. While study participants were normally divided into two groups; normal (<30% narrowing of lumen diameter) and CAD (>30% narrowing of lumen diameter) measured by trained cardiologists, blinded to the laboratory results.

Total albumin and glycosylated albumin levels were assessed using a commercially obtainable enzyme immunoassay kit (Glycaben Exocell). The amount of glycosylated albumin was expressed as the relative percentage of total and glycated albumin in the sample. Hs-CRP levels were measured using highly sensitive kits of ELISA (USA Biocheck Laboratories) with a 0.62 to 119.3 mg / L linear range.

Assay Performance: Sample processing and test conditions were strictly followed in all processes according to the manufacturer's instructions. For testing accuracy during the test procedure, calibrated micro/multichannel pipettes from Gilson were used and washing was carried out using an automatic plate washer. Glycated Albumin and hs-CRP analysis was performed using the Softmax statistical package. To ensure diagnosis of results, all studies were conducted with 6-7 standard points and 3 quality control groups in each test batch.

Test data was analyzed using SPSS 26.0. The test results included quantitative and qualitative factors related to the relationship using the Chi square test and t test. The relationship was initially assessed between the normal group and the CAD group: however, the subgroups were tested using the ANOVA test and the Hoc Tukey's Hoc test to determine its significance.

RESULTS

Patients enrolled in the study were grouped according to the narrowing of the coronary artery lumen diameter. In all groups, the average age is similar (57.5 ± 58.5, 56.5 ± 7.1, 58.1 ± 4.93 and 57.2 ± 8.5), i.e. I-IV, respectively (p> 0.05). The narrowing of lumen diameters were virtually alike in gender distribution in relative to several groups excluding in group IV, where higher lumen narrowing was noted among females as compared to males. Though patients in this group were small in numbers in both genders and the variance may not be significant statically. The majority of study participants (Group I) had diabetes duration <5 years depending on the diameter of the lumen (<30%). However, group IV showed unusually high frequency (83.3%) with shorter duration of diabetes. The history of hypertension increased from 22.2% to 58.3%, switching to group IV form group I. The smoking history also showed the same pattern and increased from 0% to 40.0% in group I respectively compared to group IV. Family history of diabetes was 16.7% in group I, 32.1% in group II and 72.4% in group III and 40% in group IV. CAD family history was observed as 10% in group I, 14.3% in group II, 20.7% in group III and 46.7% in group IV (Table 1).

The relationship between glycosylated albumin level and light shrinkage diameter was significant between all groups (p <0.01). Correspondingly the lumen narrowing and hs- CRP levels of 4 groups was institute significant using ANOVA (p<0.01), while post HOC Tukey's test exhibited significance between the groups (p<0.01) excluding between group 3 and group 4(p 0.857) individually. An increase in the average glycosylated albumin was observed in groups I to IV from 2.6% to 6.2%, respectively. The mean hs-CRP showed a similar trend from 4.1 mg / l in group I to 15 mg / ml in group IV. A striking spur was recorded from 5.9 mg / l in group II to 13.4 mg / l in group III (Table 1 and Fig. 1). Both glycosylated albumin and hs-CRP levels between the four groups showed high levels of significance (<0.001), except for the hs-CRP group III and group IV.

Glycosylated albumin and hs-CRP levels consistently showed a positive association (r = +0.99 and +0.88, respectively). The regression value for each 13% increase in lumen narrowing was the mean unit of variation in the glycated album. For hs-CRP, the regression value was more sensitive because for every 5% increase in lumen

narrowing there was an increase in the mean unit of hs CRP narrowing. Using the ANOVA and Hoc Tukey post-hoc test, a relationship between glycosylated albumin and lumen diameter was found in all groups (p <0.01). Similarly, hs-CRP levels and mild narrowing in all four groups were significant using ANOVA (p <0.01), while they were significant in all groups except between group III and group IV (p 0.857) using Tukey's post-Hoc test (p <0.01).

Table 1: Distribution of Factors and Lumen Diameter

Lumen narrowing Diameter	Group-I (n=30) 30%		Group-II (n=28) 30–50%		Group-III (n=29) 50-70%		Group-IV (n=15) >70%	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Gender								
Males	13	43.3%	15	53.6%	16	55.2%	5	33.3%
Females	17	56.7%	13	46.4%	13	44.8%	10	66.7%
	30		28		29		15	
Duration of diabetes								
> 5 Years	6	20.0%	12	48.0%	14	53.8%	2	16.7%
≤ 5 Years	24	80.0%	13	52.0%	12	46.2%	10	83.3%
	30		25		26		12	
History of								
Smoking	-	-	3	10.7%	4	13.8%	6	40.0%
Hypertension	7	23.3%	11	39.3%	15	51.7%	8	53.3%
Family history								
Diabetes	5	16.7%	9	32.1%	21	72.4%	6	40.0%
CAD	3	10.0%	4	14.3%	6	20.7%	7	46.7%
	N	x	N	x	N	X	N	X
Mean glycated albumin %	30	2.6%	28	4.1%	29	4.5%	15	6.2%
Mean hs CRP	30	4.1%	28	5.9%	29	13.4%	15	14.2%

DISCUSSION

Coronary artery disease (CAD) is one of the chief vascular complications in type 2 diabetic patients. Various analysis have revealed that up to 30% of patients with diabetes have CAD with silent ischemia, mainly due to autonomic nervous dysfunction. This rate may be up to 60% in high-risk individuals. Therefore, prompt recognition and systematic detection of CAD with simple tools for the diabetes population is important and desirable.[9-10] Among the few predictive CAD biomarkers in diabetes, hs-CRP and glycosylated albumin appear to be useful in clinical practice. In type II diabetic patients, hs-CRP serum levels above 10mg/L are related with a 2.6-fold surge in coronary artery disease risk compared to levels of hs-CRP <10 mg / L.[11]

High hs-CRP levels reflect inflammation in diabetic patients, irrespective of glycemic control, which makes hs-CRP a self-governing biomarker in coronary artery disease assessment. Glycated albumin has been reported as an independent CAD risk factor in type II diabetic patients with a probability of 3.46 (95%, CI 1.78-6.72, p <0.001).

The aim of this analysis was to assess the clinical benefit of hs-CRP and glycosylated albumin levels to compare the narrowing diameter of the coronary artery in diabetic patients.[12] This study results showed a positive correlation between hs-CRP and glycated albumin with a narrowing of 1 = 0.99 and 0.88 coronary artery respectively. A study in China reported negative effects of glycosylated albumin in type-II diabetic patients and showed that it accelerates atherosclerosis. If the level of glycosylated albumin is >19%, it acts as an independent predictor of CAD (OR 2.9 p 21%), the risk of 2-3 fold progression to level 3 vascular diseases increased <21%, which is inhibition of glycosylated albumin in vivo shows that this is important for the prevention of CAD in patients with type 2.16 diabetes.[13]

Tobacco addiction has been reported to contribute to the development and outcome of coronary artery disease (CAD) such as acute myocardial infarction, sudden

cardiac death and heart failure. In fact, 30% of all CAD-related deaths are related to smoking.[14] Continuous smoking significantly increases the sudden cardiac death risk in patients with CAD and highlights the importance of quitting smoking in changing the risk factor in patients with improved MI and / or stable angina.[15] In this study, the incidence of smoking gradually increased (0–41%) and was more frequently observed in patients with diabetes and narrowing of the diameter of the light in >70%. In this study, factors such as hypertension, familial diabetes and CAD history also showed a gradual increase from group I to group IV. Diabetes and ischemic heart disease are an ominous clinical combination. Morbidity and mortality rates as a result of cardiovascular complications are high in patients with type 2 diabetes.

CONCLUSION

Elevated serum glycosylated albumin and hs-CRP levels are related with the severity and presence of CAD and may be valuable in screening patients with type 2 diabetes, but more extensive research is needed to get stronger recommendations.

LIMITATIONS

This study had a small sample size and several additional limitations.

SUGGESTIONS / RECOMMENDATIONS

On this topic, more large-scale studies are recommended.

CONFLICT OF INTEREST / DISCLOSURE

There was no conflict of interest

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