IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 1 Ver. IV (Jan. 2016), PP 21-28
www.iosrjournals.org

A Study of cardiovascular risk factors correlation with the angiographic severity of coronary artery disease using Syntax score

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Abstract :
Background : *Traditional cardiovascular risk factors (CVRF's) including smoking, hypertension, diabetes mellitus, dyslipidaemia, obesity and family history of coronary artery disease (CAD) are well recognised for their association with atherosclerotic CAD. However the correlation between CVRF's and severity of atherosclerotic burden assessed angiographically is not well established, with studies reporting variable and inconsistent results .*
Aims and objective of the study: *This study was undertaken to see if traditional cardiovascular risk factors are also associated with angiographic severity of coronary artery disease, in patients with coronary angiography (CAG) showing triple vessel disease (TVD), with the help of syntax score.*
Materials and Methods : *Data of 102 patients having TVD on CAG over a two year period were analysed to look for an association between CVRF's and severity of CAD as assessed by SYNTAX score .The study population was divided into 3 groups on the basis of syntax score (group I <22, group II: 22-32, group III >32). Statistical analysis was done to compare the differences among the three groups and to determine the factors predicting the presence, severity and complexity of coronary artery disease.*
Results: *Diabetes was present in 33% of the study population and a significant association was seen between diabetes and the angiographic severity of CAD (P=0.003) with a significant linear correlation between the HbA1c levels and the syntax score ((p-0.001, r-0.376) in both diabetics as well as non diabetics. No significant association was seen between smoking, hypertension, dyslipidemia, obesity and family history of CAD with the severity of CAD. A significant linear correlation was also noted between increasing age and the syntax score.(p-0.001, r-0.441).*
Conclusion: *Diabetes Mellitus is found to have a significant correlation with angiographic complexity of CAD, again supporting the importance of good glycemic management and early cardiovascular screening of diabetic patients.*
Keywords: *Cardiovascular risk factors, Coronary artery disease severity, Coronary angiography, Syntax score, Diabetes Mellitus, Glycosylated haemoglobin*

I. Introduction

Coronary artery disease is a frequent and important disease, for which a number of risk factors have been identified. Coronary angiography allows a direct evaluation of coronary anatomy. The study of the magnitude of coronary artery disease in patients with confirmed disease may be of help in elucidating mechanisms underlying growth of coronary atherosclerosis lesions.

Cardiovascular risk factors (CVRFs) such as advancing age, diabetes mellitus, hypertension, dyslipidemia, smoking, obesity, and family history of CAD are well recognized for their association with clinical events and acute coronary syndromes however, the correlation between CVRFs and atherosclerotic burden, assessed angiographically, is not as well established, with studies reporting variable and inconsistent results.

An estimate of coronary artery disease burden can be obtained by analyzing each lesion with the help of syntax score found at angiography, and this was the method used in the present investigation.
In the present study we tried to explore the relationship between cardiovascular risk factors and the angiographic severity of coronary artery disease in patients with triple vessel coronary artery disease.

II. Material And Methods

Place of study: The study has been conducted in the department of cardiology, Gauhati Medical College & Hospital, located in Guwahati, Assam, India.
Duration of study: One year (From December 2012 to November 2013).
Inclusion criteria: In this study we included all patients admitted in our hospital with a confirmed diagnosis of triple vessel disease on coronary angiography over one year period.
Exclusion criteria : Patients who had undergone previous coronary artery stenting or coronary artery bypass surgery.
Study design: Following data were collected prospectively for 102 consecutive patients of triple vessel disease. Clinical and demographic characteristics including age; sex; diabetes mellitus as per American Diabetic Association (ADA) criteria; dyslipidemia as per National Cholesterol Education Program (NCEP) criteria; hypertension as per the Seventh Report of the Joint National Committee on Prevention, Detection Evaluation, and Treatment of High Blood Pressure Joint National Committee (JNC 7) criteria; current and past history of cigarette smoking; and family history of premature CAD were abstracted through retrospective cross-sectional survey of patients. In addition, the use of antihypertensive, antidiabetic, or lipid-lowering medications were used as criteria for hyper-tension, diabetes, and dyslipidemia, respectively .Obesity was defined as body mass index (BMI) >25 kg⁄m2 (WHO criteria). In addition to routine investigations, all patients had their HbA1C measured on admission, and BMI .

Coronary angiography data were obtained from the Phillips software system database that includes detailed angiographic findings of all 102 patients. Obstructive CAD burden was assessed with the help of syntax score . Each coronary lesion producing 50% diameter stenosis in vessels diameter more than 1.5 mm was scored separately and added together to provide the overall Syntax score, which was calculated prospectively using the Syntax score algorithm .The Syntax score was calculated to all 102 patients with CAD. For comparative analysis the study population was divided into 3 groups on the basis of syntax score (group I score <22, group II: score 22-32, group III score >32).
Statistical analysis: Statistical analysis was performed using the SPSS 17.0 software package. Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables were expressed as percentage. Differences in three group means or proportions were assessed using independent Pearson chi-square test as appropriate. Analysis was done to compare the differences among the three groups and to determine the factors predicting the presence, severity and complexity of coronary artery score. A 2-tailed P value <0.05 was considered statistically significant for all analysis.To ascertain the independent contribution to changes in the syntax score attributable to age, HbA1C and BMI, we constructed a multiple linear regression model with changes in syntax score as the dependent variable. A P value less than 0.05 was considered significant.

III. Results

The study cohort consists of 102 patients of triple vessel disease. For comparative analysis the study population was divided into 3 groups on the basis of syntax score (group I score <22, group II: score 22-32, group III score >32).
Demographic analysis (Table 1): Group I- 34 patients, Group II -35 patients, Group III- 33 patients**.** Their ages ranged between 39 to 70 years (mean age 57+/- 8.7 years). They included 78 males (76%), 24 females (24%) with a male to female ratio of 3.25:1 .Group I 26 males, 8 females ,Group II 26 males 9 females ,Group III 26 males 7 females.
Risk factors for Coronary Artery Disease (Table 1): In our study out of 102 patients Diabetes was present in 34(33%) patients, hypertension was present in 61(60%) patients, dyslipidemia in 40(39%), obesity in 22(21%), family history of IHD was present in 17(16%) and 34 (33%) patients were smokers.
Diagnosis of the patients in the study cohort (indication for coronary angiography) (Table 2): Number of patients with Anterior wall MI was 17 (16.6%), Inferior wall MI in 14(13.7%), Stable angina in 38 (37.2%), Unstable angina in 19(18.6%) , Non ST elevation MI in14(13.7%) patients. Stable angina was most common indication; all the stable angina patients had positive stress test.
Association Between Syntax Score And Diabetes Mellitus (Table 3; Figure 1) : Table 3 and figure 2 showing the impact of Diabetes mellitus on the syntax score. With the increasing syntax score there is increasing no of patients with diabetes mellitus, group I 18%, group II 32 %, group III 52 % .The p value between the three groups for diabetes mellitus found to be significant p –0.003 indicating it is an angiographic predictor of severity of CAD
Correlation Between Hba1c Levels And Syntax Score (Figure 2, Figure 3) : From the figure we can make out that there is gradual increase in mean HbA1C levels from group 1 to group 3 with statistical significance of p value less than 0.001,indicating that the angiographic severity of coronary artery disease increases (indicated by syntax score) with increasing levels of the diabetic severity that is increasing HbA1c levels.

Association Between Syntax Score And Hypertension (Table 4) : Table 4 showing the impact of Hypertension on the syntax score, The p value between the groups for hypertension found to be not significant p 0.0372, indicating that the hypertension is not a predictor of angiographic severity of CAD.
Association Between Syntax Score And Dyslipidemia (Table 5) : Table 5 showing the impact of Dyslipidemia on the syntax score, The p value between the groups for dyslipidaemia found to be not significant p – 0.111,indicating that the dyslipidemia is not a predictor of angiographic severity of CAD
Association Between Syntax Score And Obesity (Table 6) : Table 6 showing the impact of obesity on the syntax score. With the increasing syntax score the percentage of people with obesity increased, but the p value between the groups for obesity found to be not significant p 0.213, indicating that the obesity is not a predictor of angiographic severity of CAD.
Correlation Between Bmi And Syntax Score (Figure 4, Figure 5) : From the figure we can make out that there is gradual increase in mean BMI levels from group 1to group 3,but it did not meet the statistical significance p value 0.256,indicating that there is no correlation between the angiographic severity of CAD indicated by syntax score with the BMI levels.
Association Between Syntax Score And Family History (Table 7) : Table 7 showing the impact of Family history on the syntax score, with the increasing syntax score the percentage of people with positive family history increased but the p value between the groups for family history found to be not significant p 0.705, indicating that the family history is not a predictor of angiographic severity of CAD.
Association Between Syntax Score And Smoking (Table 8) : Table 8 showing the impact of smoking on the syntax score, with the increasing syntax score the percentage of people with the smoking history increased, but the p value between the groups for smoking found to be not significant p 0.390, indicating that the smoking is not a predictor of angiographic severity of CAD.
Correlation Between Age And Syntax Score (Figure 6, Figure 7) : From the figure we can make out that there is gradual increase in mean age of the patient's levels from group 1 to group 3,which met the statistical significance with p value 0.007,indicating that there is correlation between the angiographic severity of coronary artery disease and age.

IV. Figures and Tables

Table 1 : Clinical and demographic characteristics of the study cohort

BASELINE CHARACTERS	GROUPS ACCORDING TO SYNTAX SCORE			
	1)SCORE <22	2)SCORE 22-33	3)SCORE >33	OTAL
NO OF PATIENTS	34	35	33	102
MEAN AGE Std.deviation	53 6.98	58 9.11	60 8.14	57.3 8.7
SEX MALE FEMALE	26 8	26 9	26 7	78 24
DIABETES MELLITUS	6 (18%)	11 (32%)	17 (52%)	34 (33%)
ESSENTIAL HYPERTENSION	17 (50%)	24 (68.5%)	20 (60.7%)	61 (60%)
OBESITY	5 (14.8%)	8 (22.9%)	9 (27.3%)	22 (21%)
DYSLIPIDEMIA	8 (23.6%)	18 (51.5%)	14 (42.5%)	40 (39%)
FAMILY HISTORY	5 (14.7%)	6 (17%)	6 (18%)	17 (16%)
SMOKING	10 (29.5%)	11 (31.5%)	13 (39.4%)	34 (33%)
MEAN HbA1c LEVELS Std.deviation	4.8 0 .71	5.5 0.74	6.3 1.24	5.5 1.09
MEAN BMI Std.deviation	23.3 2.11	23.9 2.57	24 3.03	23.7 2.59

Table 2 : Shows indication for coronary angiography.

TABLE NO – 2		GROUPS * TYPE OF PRESENTATION					
SYNTAX SCORE		TYPE OF PRESENTATION					Total
		ANTERIOR WALL MI	INFERIOR WALL MI	STABLE ANGINA	UNSTABLE ANGINA	NON ST ELEVATION MI	
GROUPS	1) SCORE <22	6 (17.6%)	3 (8.8%)	14 (41.1%)	6 (41%)	5 (14.7%)	34
	2) SCORE 23-33	4 (11.4%)	8 (22.8%)	12 (34.2%)	7 (20%)	4 (11.4%)	35
	3) SCORE >33	7 (21.2%)	3 (9%)	12 (36.3%)	6 (18%)	5 (15.5%)	33
Total		17 (16.6%)	14 (13.7%)	38 (37.2%)	19 (18.6%)	14 (13.7%)	102

Table 3 : Association between syntax score and diabetes mellitus

TABLE NO - 3	GROUPS V/S DIABETES MELLITUS			P VALUE
SYNTAX SCORES		DIABETES MELLITUS		Total	
		ABSENT	PRESENT		
GROUPS	1) SCORE <22	28 (82%)	6 (18%)	34 (33.3%)	0
	2) SCORE 23-33	24 (68%)	11 (32%)	35 (34.4%)	.003
	3) SCORE>33	16 (48%)	17 (52%)	33 (32.3%)	
Total		68 (67%)	34 (33%)	102	

Figure 1 : Bar chart showing the distribution of diabetes mellitus patients in three groups

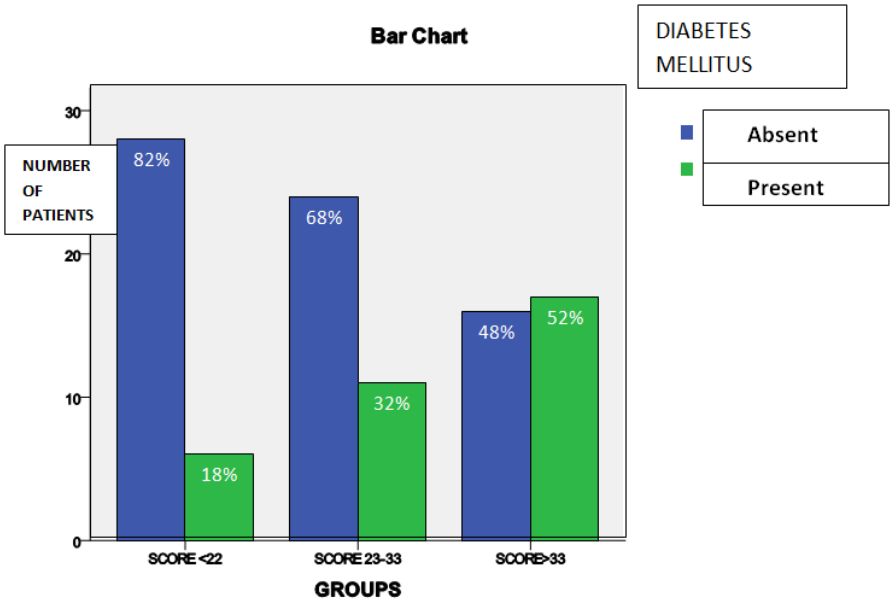


Figure 2 : Graph showing mean HbA1c levels in three groups

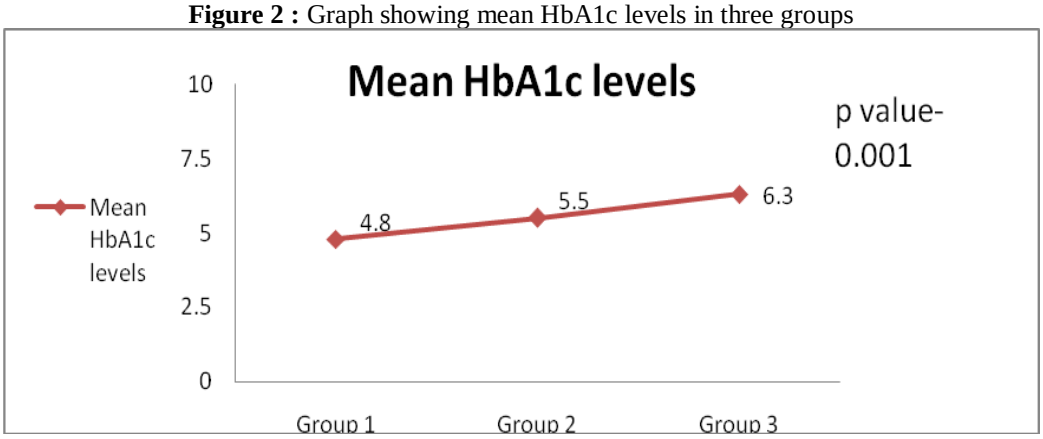


Figure 3 : Correlation analysis between syntax score and HbA1c levels

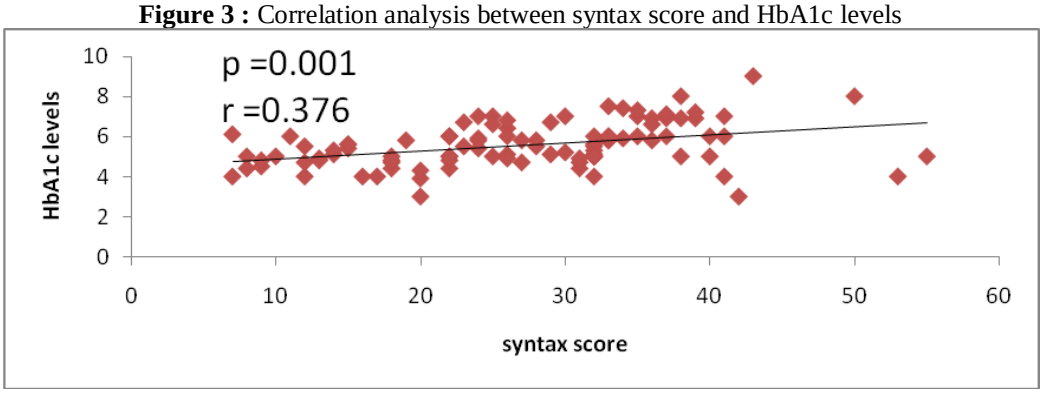


Table 4 : Showing the impact of Hypertension on the syntax score

TABLE NO- 4		GROUPS V/S HYPERTENSION			
SYNTAX SCORES		HYPERTENSION		Total	P VALUE
		ABSENT	PRESENT		
GROUPS	1) SCORE <22	17 (50%)	17 (50%)	34 (33.3%)	0.372
	2) SCORE 23-33	11 (32.5%)	24 (68.5%)	35 (34.4%)	
	3) SCORE>33	13 (39.3%)	20 (60.7%)	33 (32.3%)	
Total		41 (40%)	61 (60%)	102	

Table 5 : Showing impact of dyslipidemia on Syntax score

TABLE NO- 5		GROUPS V/S DSLIPIDEMIA			P VALUE
SYNTAX SCORES		DYSLIPIDEMIA		Total	
		ABSENT	PRESENT		
GROUPS	1) SCORE <22	26 (76.4%)	8 (23.6%)	34 (33.3%)	0.111
	2) SCORE 23-33	17 (48.5%)	18 (51.5%)	35 (34.4%)	
	3) SCORE>33	19 (57.5%)	14 (42.5%)	33 (32.3%)	
Total		62 (60.7%)	40 (39.3%)	102	

Table 6 : Showing the impact of obesity on Syntax score

TABLE NO – 6		GROUPS V/S OBESITY			
SYNTAX SCORES		OBESITY		Total	P VALUE
		ABSENT	PRESENT		
GROUPS	1) SCORE <22	29 (85.2%)	5 (14.8%)	34 (33.3%)	0.213
	2) SCORE 23-33	27 (77.1%)	8 (22.9%)	35 (34.4%)	
	3) SCORE>33	24 (72.7%)	9 (27.3%)	33 (32.3%)	
Total		80 (78.4%)	22 (21.6%)	102	

Figure 4 : Showing mean BMI levels in three groups

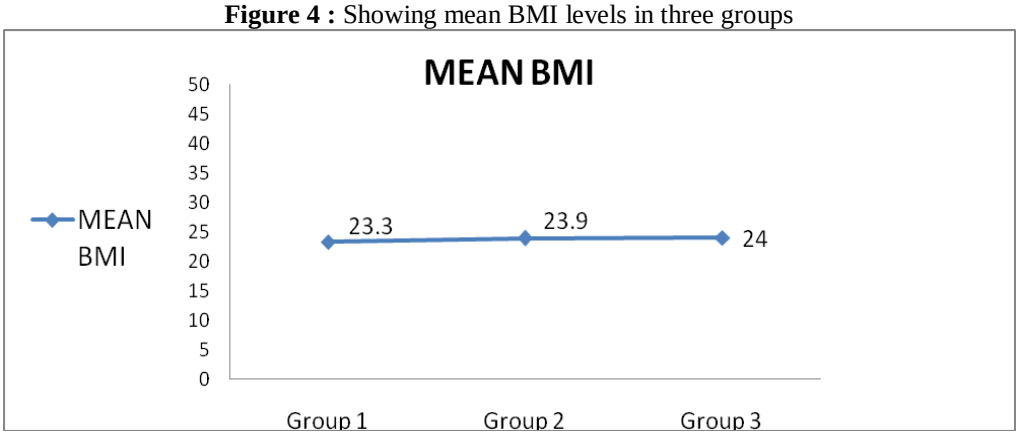


Figure 5 : Correlation analysis between syntax score and BMI

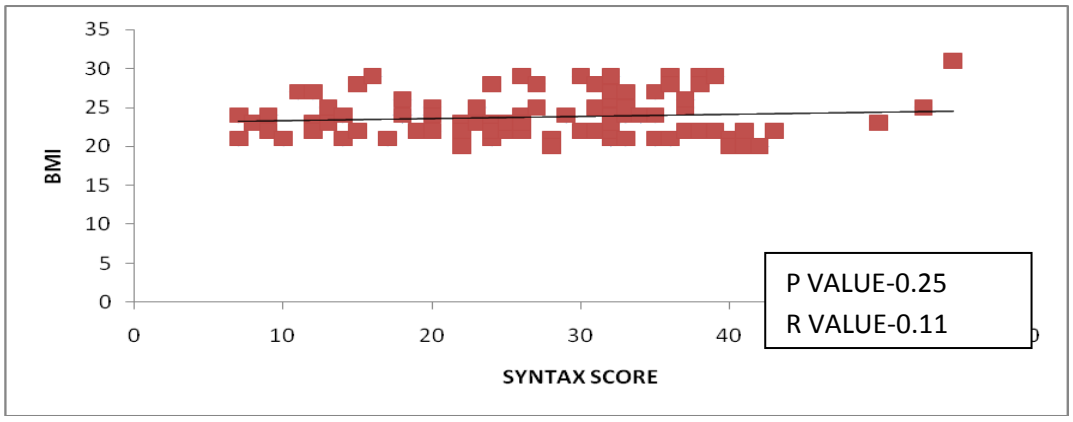


Table 7 : Impact of Family history on Syntax score

TABLE NO - 7		GROUP V/S FAMILY HISTORY			
SYNTAX SCORES		FAMILY HISTORY		Total	P VALUE
		ABSENT	PRESENT		
GROUPS	1) SCORE <22	29 (85.3%)	5 (14.7%)	34 (33.3%)	0.705
	2) SCORE 23-33	29 (83%)	6 (17%)	35 (34.4%)	
	3) SCORE>33	27 (82%)	6 (18%)	33 (32.3%)	
Total		85 (83.4%)	17 (16.6%)	102	

Table 8 : Impact of smoking on Syntax score

TABLE NO -8		GROUPS V/S SMOKING			
SYNTAX SCORES		SMOKING		Total	P VALUE
		ABSENT	PRESENT		
GROUPS	1) SCORE <22	24 (70.5%)	10 (29.5%)	34 (33.3%)	0.390
	2) SCORE 23-33	24 (68.5%)	11 (31.5%)	35 (34.4%)	
	3) SCORE>33	20 (60.6%)	13 (39.4%)	33 (32.3%)	
Total		68 (66.6%)	34 (33.4%)	102	

Figure 6 : Mean age levels in three groups

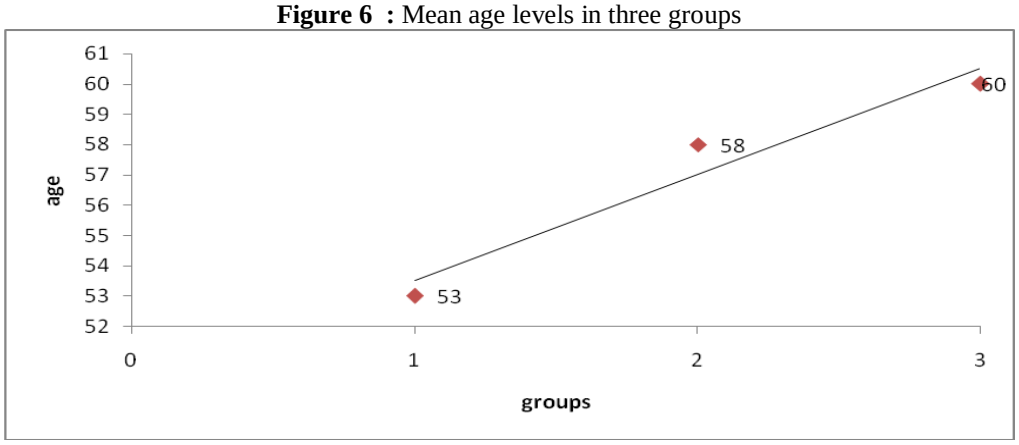
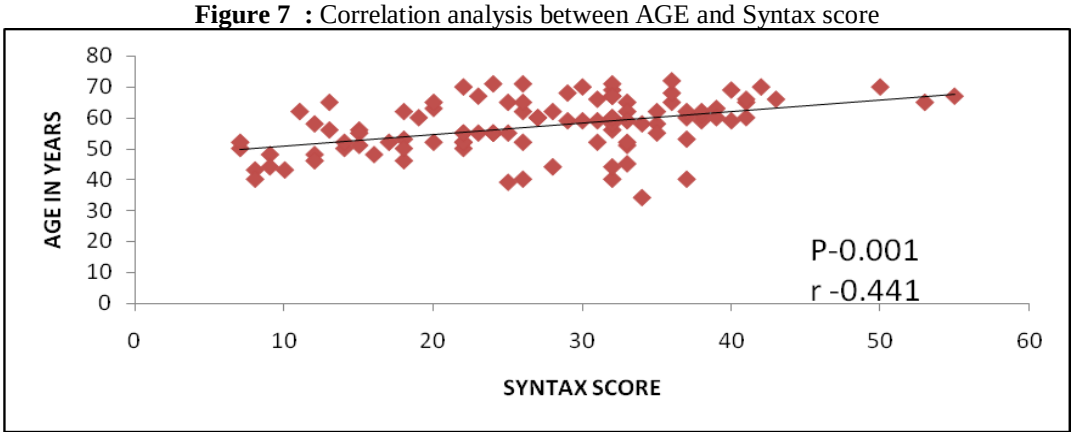


Figure 7 : Correlation analysis between AGE and Syntax score



V. Discussion

Our study was carried out to find out whether the traditional CAD risk factors in patients with triple vessel coronary artery disease– like Diabetes mellitus, Hypertension, smoking, advancing age, Dyslipidemia, obesity, family history of coronary artery disease, correlate with the severity of coronary atherosclerosis detected by coronary angiography, as they are well recognized for their association with clinical events and acute coronary syndromes.

A number of scores have been described in the past for grading the severity of coronary artery disease on angiography like Genisini score [1], Jenkins score [2] , syntax score and Friesingers score [3] . We used the syntax scoring system for assessing the coronary atherosclerotic disease burden. We chose this because of its simplicity and syntax score is widely accepted as a CAD burden marker and its prognostic value has been demonstrated in different clinical situations.

We included patients of only triple vessel disease and divided the study cohort into three groups depending upon the syntax score, group I <22, group II: 22-32, group III >32 .The same three tertiles were used as used in syntax trial which also included triple vessel disease patients to assess the coronary artery disease atherosclerotic burden and complexity for guiding management strategies and prognosis.

In our study out of 102 patients Diabetes was present in 34(33%) patients, hypertension was present in 61(60%) patients, dyslipidaemia in 40(39%), obesity in 22(21%), family history of IHD was present in 17(16%) and 34 (33%) patients were smokers.

a) Correlation between severity of CAD and Diabetes Mellitus

Our findings suggest that in patients of triple vessel disease, from among the traditional CVRFs evaluated, only diabetes emerged as an independent predictor of the extent of obstructive CAD burden. Prior studies of angiographic progression of CAD using serial quantitative angiography to define predictors of severity or progression of disease burden including CASS registry [4], [5] have also consistently identified diabetes as an independent predictor of severity or disease progression . Among these, the study by Abrahams [4] and colleagues is closest to our results, reporting that in 176 patients (age range, 27–66 years); diabetes mellitus was related to CAD severity. Atherosclerosis affects the coronary arteries of diabetic patients more severely and diffusely than those of non-diabetics. Berry et al [6] found that fasting blood glucose, HbA 1c, and presence of diabetes were associated with the severity and progression of coronary atherosclerosis. They concluded that better glycaemic control favorably influences CAD in patients with abnormal glucose tolerance or diabetes.

b) Correlation between severity of CAD and HbA1c

In this study, we further investigated the relationship between HbA1c levels and the severity of CAD in all triple vessel disease patients whether they are diabetic or non diabetic. When all the results were collected and a multiple linear regression model was developed, it clearly showed that HbA1C was an independent factor influencing the severity of coronary artery disease as demonstrated by coronary angiography. Severity of coronary artery disease was correlated with the duration of DM and with poor control of diabetes as shown by higher levels of HbA1C. This finding was comparable to many other similar studies in the past. Ravipati et al. showed that the HbA1c level increased significantly with the number of arteries involved with CAD in diabetics[7].

Gong [8] studied the association of glycaemic variability and the presence and severity of CAD in 252 patients with type 2 diabetes and reported that CAD severity (with the help of Gensini score) closely correlated with HbA1c level ($p = 0.022$) and because of this the effects of glycaemic excursions on vascular complications should not be neglected in diabetes.

Similarly, we found that HbA 1c levels were correlated with the severity of coronary atherosclerosis assessed with syntax score in both diabetic and non-diabetic patients. All these studies including ours results could be explained by the pathobiological attribution of hyperglycemia to CVD risk, although this remains poorly understood; but given the clear associations between severity of hyperglycemia and CVD risk in both type 1 and type 2 diabetes (sharing hyperglycemia as the common pathophysiologic disturbance), hyperglycemia is likely to directly influence atherosclerosis development, progression, and instability. The principal vascular perturbations linked to hyperglycemia include endothelial dysfunction, vascular effects of advanced glycation end products, adverse effects of circulating free fatty acids, and increased systemic inflammation prevalent in these people. However serial assessment of HbA1c for a longer duration of time in a diabetic will probably be a better indicator of glycaemic control to influence CAD than a single reading.

Linear positive correlation between syntax score and HbA1c in non diabetic cannot be explained on the basis of metabolic derangement present in diabetics. This needs further study to establish any correlation of CAD with HbA1c levels in non diabetic.

c) Correlation between severity of CAD and other risk factors

More notably, the presence of other risk factors like hypertension, smoking, dyslipidaemia, obesity, advancing age, family history did not correlate with angiographically assessed obstructive CAD.

Our findings support the results of the a fairly large trial by Nicholas [9] et al involving younger 654 patients (mean age, 56 years) to determine the relationship between CVRFs and the extent of ‘‘anatomic’’ coronary artery disease, none of the risk factors except for diabetes correlated with intravascular ultrasonography (IVUS)–measured coronary atheroma burden, suggesting that different mechanisms drive stenosis development and atheroma accumulation.

Another similar study by v. veeranna et al [10] supporting our study retrospectively examined the relationship between traditional cardiovascular risk factors and atherosclerotic coronary artery disease burden in a cohort of 631 elderly patients undergoing angiography. Age and male sex but not hypertension or dyslipidemia

were predictors of presence of obstructive coronary artery disease. Only diabetes mellitus emerged as an independent predictor of obstructive coronary artery disease burden.

d) Correlation between severity of CAD and age of patients:

In our study we found a statistically significant positive correlation between age & SYTAX scores (P value 0.007), SYNTAX score is higher in older patients. This relation was also demonstrated by by Zhouet al. [11] who studied 415 diabetic and pre diabetic patients who were scheduled for coronary angiography for suspected myocardial ischemia using the Gensini scoring system and reported that there is a positive correlation between age and Gensini score.

The increase of severity of CAD with aging could be explained by increasing incidence of atherosclerosis in older people in addition of increasing incidence of the other risk factors of IHD. Age-related changes are due to increases in fibrinogen, coagulation factors (V, VIII and IX, XIIa), and Von-Willebrand factor. Also, platelet phospholipid content is altered and platelet activity is increased with increased binding of platelet-derived growth factor to the arterial wall in older compared with younger individuals. Increased levels of plasminogen activator inhibitor (PAI-1) are seen with aging, especially during stress, resulting in impaired fibrinolysis. Circulating prothrombotic inflammatory cytokines, especially interleukin-6, also increases with age and may play a role in the pathogenesis of ACS. All these changes also potentiate development of atherosclerosis [12]. Presence of a risk factor for a longer duration to produce adverse effects in an elderly may be another contributing factor.

In total our findings suggest that among traditional risk factors that predict case fatality may be different from those that predict incident disease except for diabetes mellitus and advancing age.

Study limitations : Some limitations of this study should be mentioned. First, the study population is relatively small and further Studies are needed to verify our results. Second, this study was observational non-randomized and might be subjected to selection bias. Third, the mean age in our study population was 53±10years, suggesting possible exclusion of elderly patients. Fourth, we analyzed only the presence or absence of risk factors in calculating the atherosclerotic burden but not considered the duration of the risk factors present prior to the angiography which might have significant impact on findings.

VI. Conclusion

We demonstrated a significant correlation between syntax score and Diabetes mellitus. Among diabetics, poor control of DM (HbA1c level) is found to be important. This factor has a positive linear relation with the syntax score, suggesting that as the HbA1c level increases, the severity of coronary artery disease will increase with multiple and complex lesions. This correlation persisted even in non diabetic's i.e even in patients with HbA1c levels in the upper limit of normal range (pre diabetics) they will have high syntax score.

Other factors, including dyslipidemia, obesity, family history and smoking, found to be no association with severity of coronary artery disease in this study. One more important significant correlation was seen between the advancing age and severity of coronary artery disease as assessed by syntax score.

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