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Original Research Article

Coronary angiographic abnormalities in patients of diabetes mellitus and metabolic syndrome

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ABSTRACT

Background: Diabetes mellitus and Metabolic syndrome, both are established risk factors for CAD. In our study, we tried to compare the effects of these two diseases individually as well as their combined effect.
Methods: we performed an Observational, cross-sectional, hospital-based, single center study on 240 patients presenting at our hospital with chest pain. we assessed the severity of CAD with Syntax score and divided the study population into three groups with SS of <=22, 23-32 and >=33.
Results: statistically significant difference was found in each of the first three groups of combined MS plus DM, only MS without DM, only DM without MS when compared with the fourth group of nondiabetics nonmetabolic syndrome patients. Strongest difference was found between patients with combined diabetes and metabolic syndrome with those who had none of these (<0.001). Thus, complexity of CAD is much severe in patients who have diabetes and/or metabolic syndrome.
Conclusions: Patients having diabetes mellitus and/or metabolic syndrome are found to have more severe form of coronary artery disease than those who don't have either of these. However, presence of both diabetes and metabolic syndrome has not been found to impose any significant additional risk than their isolated presence.

Keywords: Diabetes mellitus, Metabolic syndrome, Syntax score

INTRODUCTION

Metabolic syndrome is a cluster of risk factors associated with insulin resistance, subclinical inflammation, increased future risk of diabetes, and coronary artery disease (CAD). South Asians are more prone to develop Metabolic Syndrome because of their high percentage of body fat, abdominal obesity, and insulin resistance.[1,2] Most experts appear to believe that the increased cardiovascular risk seen in these subjects is probably due to the clustering of risk factors.[3]

There are reports in the literature on association of inflammatory markers and insulin resistance with severity of disease. There are very few studies showing association of metabolic syndrome and number of its components with severity of disease in India. the aims and objectives of the study was to evaluate the coronary angiographic abnormalities in patients of metabolic syndrome with or without diabetes mellitus presenting with chest pain.

METHODS

Study area

Nilratan Sircar Medical College and Hospital, AJC Bose Road, Kolkata-700014.

Study population

Adult patients of both sexes admitted in Department of Cardiology with presumed diagnosis of coronary artery disease who underwent coronary angiography for diagnostic or therapeutic purpose. Patients presented with chest pain at OPD or emergency of our hospital.

Study period

From Feb 2015 - Jan 2016.

Sample size

Two hundred and forty (240) patients presenting with chest pain.

Study design

Observational, cross-sectional, hospital-based, single centre study.

Parameters to be studied

- Detailed clinical history (risk factors like DM, HTN, smoking, family history of CAD, past h/o CAD etc.)
- Thorough clinical examination (BP, peripheral pulses etc.),
- Laboratory investigations like lipid profile, blood sugar, HbA1c, cardiac enzymes, serum creatinine etc.,
- Imaging studies e.g. CXR and Echocardiography (specially ejection fraction),
- Assessment of ankle brachial index, vi. Coronary angiography and SYNTAX score calculation by online calculator.

Inclusion criteria

Adult patients of suspected CAD who are undergoing CAG for any or diagnostic or therapeutic purpose.

Exclusion criteria

- Patients with previously diagnosed CAG abnormalities,
- Presence of severe renal, lung and liver comorbidities.

Study technique

In this cross-sectional descriptive-analytic study, 240 consecutive patients with suspected CAD were taken for study according to inclusion criteria. After history taking, examination and investigation of patients in whom coronary angiography was indicated were underwent CAG. SYNTAX score calculation was done, and analysis was performed.

RESULTS

The study included 240 patients who presented to our hospital with chest pain during the study period, either in emergency or in the OPD. The study population had 82 diabetic, 68 metabolic syndrome patients. 36 patients had both diabetic and metabolic syndrome. Mean age of presentation was 55.27 ± 10.76 years. 13.33% of the patients (32 in number) had only metabolic syndrome without diabetes mellitus. 18.33% of patients (44 in number) had only diabetes. More than 50% of the study population (53.33%, 128 in number) were free of both diabetes and metabolic syndrome. These patients had other risk factors in the form of smoking, family h/o premature CAD in the first-degree relatives etc.

Table 1: Relation between different risk factors and syntax score.

Risk factor	Present		Absent		P value
	No (%)	Syntax score	No (%)	Syntax score	
Hypertension	89 (36.97)	20.98 ± 14.17	151 (73.03)	14.09 ± 9.63	<0.0005*
Smoking	171 (71.43)	17.00 ± 11.65	69 (28.57)	14.80 ± 11.97	0.3106
Family h/o cad	83(34.45)	18.27 ± 12.71	157 (65.55)	15.79 ± 11.51	0.2095

(Mann Whitney's U test was used to check statistical significance)

Hypertensive patients constituting almost 37% study population had a Syntax score of 20.98 ± 14.17 compared to non-hypertensives whose Syntax score was 14.09 ± 9.63, having a highly significant p-value of <0.0005. So, hypertensive patients presenting with anginal chest pain are likely to have more complex coronary artery disease. Syntax score in the smoker group, constituting 71.43% of the study population, was 17.00 ± 11.65, compared to non-smokers which was 14.80 ± 11.97, but the p-value was not found to be statistically significant. So, smokers, although not statistically significant, have a trend towards more complex CAD. Patients with a family history of CAD also had a trend towards more complex CAD, although the difference was not statistically significant.

While calculating, and comparing the Syntax scores in the four groups, statistically significant difference was found in each of the first three groups of combined MS plus DM (group A), only MS without DM (group B), only DM without MS (group C) when compared with the

fourth group of nondiabetics nonmetabolic syndrome patients (group D). Strongest difference was found between patients with combined diabetes and metabolic syndrome with those who had none of these (<0.001).

Table 2: Comparison of SYNTAX scores between groups based on presence of MS & DM.

Group	Ms + DM+ (a)		MS+DM- (b)		DM+MS- (c)		DM-MS- (d)	
	No (%)	Syntax score	No (%)	Syntax score	No (%)	Syntax score	No (%)	Syntax score
	36(15)	20.97 ±9.32	32(13.33)	21.21±14.94	44(18.33)	19.72±13.52	128(53.33)	13.16±10.14

(Table 3). Thus, complexity of CAD is much severe in patients who have diabetes and/or metabolic syndrome.

TABLE 3: Difference of syntax score among the four groups and statistical significance.

Comparison	P value
MS + DM+ vs DM-MS-	<0.001
MS+DM- vs DM-MS-	<0.05
DM+MS- vs DM-MS-	<0.05

(Applying post hoc Dunn's test significant difference was found between groups.)

Presence of only DM/HTN itself also found to be significant in comparison to the group without any of them.

LDL level is significantly higher in group A (Syntax score >=33) when compared to group B (SS 23-32) and C (SS<=22). Hence it can be concluded that higher serum LDL is associated with more complex forms of CAD. Higher LDL is associated with more diffuse atherosclerosis.

Table 4: Syntax score and Hba1c.

Syntax score	>=33 Group a'		23-32 Group b'		<=22 Group c'	
	No (%)	Hba1c	No (%)	Hba1c	No (%)	Hba1c
	26(10.92)	6.88 ± 1.33	46 (19.33)	6.64 ± 1.49	168(69.75)	6.42 ± 1.77

Applying Kruskal-Wallis test, the p value found is 0.0392, so HbA1C values are significantly different between these 3 groups. Patients with Syntax score >= 33 are found to have much higher values of HbA1c than those with Syntax score of <=22. Thus, higher HbA1c value is associated with more diffuse and complex coronary artery involvement. However, the difference between group A' and B' as well as between B' and C' were not statistically significant. As shown in Table 4. Applying Kruskal-Wallis test, the p value found is 0.0126. So, FBS values are significantly different between these 3 groups. As shown in Table 6.

FBS level in SS >=33 group has been found to be significantly higher compared to the group of SS <=22. As shown in table 7. Thus, higher FBS level is associated with more complex CAD.

Table 5: Statistical significance HbA1c values among the three SS groups.

Comparison	P value
A' vs B'	>0.05
B' vs C'	>0.05
A' vs C'	<0.05

Applying post hoc Dunn's test

Table 6: Syntax score and fasting blood sugar.

Syntax score	>=33 Group a'		23-32 Group b'		<=22 Group c'	
	No (%)	FBS	No (%)	FBS	No (%)	FBS
	26 (10.92)	167.54 ± 80.95	46 (19.33)	134.30 ± 70.83	168 (69.75)	133.73 ± 96.11

Table 7: Applying post hoc Dunn's test.

Comparison	P value
A' vs B'	>0.05
B' vs C'	>0.05
A' vs C'	<0.01

Applying Kruskal-Wallis test, the p value found is <0.1313, so HDL-C values are not significantly different between these 3 groups. Serum HDL levels in the three groups are not found to be different statistically. As shown in Table 8. Applying Kruskal-Wallis test, the p value found is <0.0001. So, ABI values are significantly different between these 3 groups. As shown in Table 9.

Table 8: With HDL.

Syntax score	>=33 Group a'		23-32 Group b'		<=22 Group c'	
	No (%)	HDL-C	No (%)	HDL-C	No (%)	HDL-C
	26 (10.92)	37.31 ± 5.07	46 (19.33)	36.48 ± 4.99	168 (69.75)	38.66 ± 7.21

Table 9: With ABI.

Syntax score	>=33 Group a'		23-33 Group b'		<=22 Group c'	
	No (%)	ABI	No (%)	ABI	No (%)	ABI
	26 (10.92)	0.76 ± 0.23	46 (19.33)	0.85 ± 0.21	168 (69.75)	0.95 ± 0.13

ABI is found to be worse in patients with Syntax score of >=33. ABI is found to be significantly lower in group A and B compared to group C. This data supports the concept that atherosclerosis is a systemic disease and complex CAD is associated with more severe form of peripheral vascular disease. As shown in table 10.

Table 10: Applying post hoc Dunn's test comparison between groups.

Comparison	P value
A vs b	>0.05
B vs C	<0.001
A vs C	<0.001

DISCUSSION

The study population is divided into four groups as follows

- Group 1- Both Diabetes and Metabolic syndrome,
- Group 2- Only Diabetes without Metabolic syndrome,
- Group 3- Only Metabolic syndrome without Diabetes and
- Group 4- None of Diabetes and Metabolic syndrome.

All the patients underwent CAG and the findings are divided according to the severity and complexity of disease based on Syntax score. Syntax score divided the study population into three categories: Low score <=22, Intermediate score 23-32 and High score >=33.

Out of the 240 patients, 168 (69.75%) had low Syntax score (<=22), 46 (19.33%) had intermediate Syntax score (23-32) and 26 (10.92%) had high Syntax score of >=33. Relationship between various risk factors of CAD and Syntax score are being discussed in the following text. 15% of the study population had both diabetes and metabolic syndrome, 18.33% had only DM without MS, 13.33% had only MS without DM and the remaining 53.33% had none of DM or MS. Among the female patients with waist circumference >80 cm, the average Syntax score was 15.80 and ABI was 0.8857 and those with waist circumference <=80cm had average Syntax score of 14.75 and ABI of 0.911. Male patients with waist circumference of >90cm had average syntax score of 18.297 and ABI of 0.9001. Male patients with waist <=90cm had average Syntax score 14.8883 and ABI of 0.978. On the contrary, average waist circumference of patients with syntax score <=22 is 89.85, 23-32 is 91.64 and >=33 is 89.80.

Patients with LDL of <70mg/dl had average syntax score of 16.22 and ABI of 0.994, LDL of 70 -<100 mg/dl had average syntax score of 13.95 and ABI of 0.899 and those with LDL >=100 mg/dl had average syntax score of 17.926 and ABI of 0.895. The unexpected low average value of syntax score in the 70 -< 100 mg/dl group was due to few very low syntax scores in this group including 0 score in 4 patients among the 60. Few similar low scores are also present in the >=100 mg/dl group, but their effect on the average score was less as this group had a larger patient population of 162. However, the average syntax score of LDL>=100 mg/dl group had highest average Syntax score suggesting that LDL level of more than 100mg/dl is a risk factor for complex CAD. On the contrary, the average ABI was progressively lower with progressively increasing LDL value. This finding is in support of the literature of peripheral arterial disease where high LDL level is a known risk marker of PAD. Study on a larger number of patients is required to further clarify the findings.

Patients with TG level >150mg/dl had average syntax score of 19.76 compared to those with TG <= 150 mg/dl who had average syntax score of 16.14. Again, patients with TG > 150 mg/dl had average ABI of 0.86 and TG<= 150 mg/dl had average ABI of 0.911. Both these findings of Syntax score and ABI are in support of the concept that hypertriglyceridemia is a risk factor for atherosclerosis and is associated with more severe and complex CAD as well as PAD.

Based on BMI, the study population is divided into four groups -<23, 23-<25, 25-<30 and >=30 kg/m^2. Current literatures suggest that high BMI is a risk factor for atherosclerosis. In this study, the average syntax score in the four BMI groups were 15.7, 12.97, 16.14 and 16.55 respectively, which suggest that the severity and complexity of CAD significantly increases above BMI of 25 kg/m^2.

Average ABI in these four groups are 0.849, 0.946, 0.954 and 0.956 respectively which suggest lower BMI is associated with lower ABI suggestive of more severe PAD which is not matching with the standard literature of higher the BMI, severe the atherosclerosis, severe the PAD and hence lower the ABI. Study on a larger population is needed for further assessment of this correlation.

Approximately 37% of the study population had systemic hypertension and they had a median syntax score of 20.98 ±14.17 compared to 14.09 ± 9.63 in non-hypertensive patients (73%) with a p-value of <0.0005 which is highly significant statistically. This finding strongly indicates that hypertension is a strong risk factor for atherosclerotic coronary artery disease. This finding matches with the literature.

More than 71% of the study population were smoker and had a median syntax score of 17.00 ± 11.65 compared to non-smokers who had median syntax score of 14.80 ± 11.97 and the difference is not found to be statistically significant (p value = 0.3106). However, there is a trend towards higher syntax score among the smokers.

Patients with family h/o CAD in first degree relatives (34.45%) had a median syntax score of 18.27 ± 12.71 compared to those without this history having a median syntax score of 15.79 ± 11.51 and the difference is not statistically significant (p = 0.2095). Here also, like smoking, there is a trend towards higher syntax score although the difference is not statistically significant.

15% of the study population had combined diabetes (DM) and metabolic syndrome (MS) and this group had median syntax score of 20.97 ± 9.32. Patient group having only MS constituting 13.33% of patient pool had a median syntax score of 21.21 ± 14.94 and those having only DM (18.33%) ha d median Syntax score of 19.72 ± 13.52. The group that had none of DM or MS (53.33%) had median syntax score of 13.16 ± 10.14. The difference among these groups is statistically significant (<0.0001). So, the presence of DM and/or MS in a patient presenting with angina is a strong risk factor for more severe and complex coronary artery disease. When comparing the individual groups as group A'/B'/C' with group D', statistically significant difference has been found.

Based on syntax score, patients are divided in three groups-group A >=33, B 23 – 32 and C <=22. Group A (SS >=33) constituted 10.92% of patients and had median LDL level of 139.07 ± 32.97 mg/dl, Group B (SS 23 - 32) constituted 19.33% of patients and had median LDL level of 110.82 ± 40.68 mg/dl and Group C (SS<=22) constituted 69.75% of patients and had median LDL level of 120.06 ± 40.36. mg/dl. The p value found is 0.0108, so LDL-C values are significantly different between these 3 groups. This finding supports the concept that high LDL level is a risk factor for atherosclerotic CAD.

However, while assessing LDL in individual groups of patients of DM, MS and the non-DM non-MS, the difference is not found to be significant.

Median HbA1c value in group A is 6.88 ± 1.33, B is 6.64 ± 1.49 and C is 6.42 ± 1.77 and the p value found is 0.0392, so HbA1C values are significantly different between these 3 groups. Thus, higher HbA1c is associated with more severe and complex CAD.

Patients with SS of >=33 had a median FBS level of 167.54 ± 80.95 mg/dl, SS of 23 – 32 had median FBS of 134.30 ± 70.83 and SS <=22 had median FBS of 133.73 ± 96.11 with a p value of 0.0126 which is statistically significant. Thus, higher FBS is associated with more severe CAD.

Chronic kidney disease is an established risk factor for CAD. In our study, patients with syntax score of >=33 had a median creatinine level of 1.59 ± 0.17 mg/dl, group of syntax score of 23-32 had a median creatinine of 1.16 ± 0.37 mg/dl and those a with SS <=22 had creatinine of 1.17 ± 0.49 mg/dl. The p value found is <0.0001, so Creatinine values are significantly different between these 3 groups and hence our findings further enhances the fact that CKD is a risk factor for CAD. While comparing individual groups, group of SS >=33 found to have extremely high statistically significant difference while compared with the other two groups.

While comparing the serum HDL levels among the three groups, the difference is not found to be statistically significant. However, a significant observation is that, all the three groups had median HDL values below 40mg/dl.

When comparing PAD among the three groups, the group with most severe and complex CAD found to have median ABI of 0.76 ± 0.23 while the group with mildest form of CAD had ABI of 0.95 ± 0.13. The ABI among the three groups has significant difference (p <0.0001). while comparing the individual groups, although the

difference between group A and B was not significant, both had median ABI <0.9 while group C with SS>=22 had median ABI >0.9. Also, statistically significant difference has been found between group A and C and group B and C.

Konstantinou DM et al studied a consecutive sample of 150 patients undergoing CAG for the evaluation of chest pain.[4] Metabolic syndrome was defined according to the revised NCEP ATP III criteria, and the 10-year CAD risk was estimated by the Framingham risk score. It showed that MS is an independent determinant of significant CAD only among those individuals at low 10-year risk for future coronary events. Individual components of the syndrome, such as impaired FBS, had a stronger association with CAD than the syndrome as a whole. Aykan AC et al studied 'Is metabolic syndrome related with CAD severity and complexity: An observational study about IDF and AHA/NHLBI metabolic syndrome definitions' and found MS is associated with the presence and complexity of CAD.[5]

Rana et al also reported more CAD in DM versus non-DM individuals [SVD (19 vs. 14%), DVD (9 vs. 7%), and TVD (9 vs. 5%) (P < 0.0001 for all)].[6] Others have also observed similar findings. These results support the hypothesis of a greater severity of angiographic proven CAD in diabetic than in non-diabetic patients. Diabetics suffer from higher prevalence of diffuse and extensive coronary atherosclerosis. Contrary to our study there was no relationship between hypertension and extent of CAD. TG and VLDL was significantly high and HDL was significantly low in TVD compared with SVD. Severe CAD was present in significantly higher number of patients having Metabolic Syndrome as compared to those without Metabolic Syndrome. Kip et al reported statistically significant prevalence of severe CAD in patients with Metabolic Syndrome (47%) as compared to 25% in patients without Metabolic Syndrome.[7] Yavuz et al reported significantly higher number of patients with Metabolic Syndrome having severe CAD as compared to patients without Metabolic Syndrome (91% vs. 62%).[8] Anuurad et al in a multi-centre study also reported significantly higher prevalence of severe CAD in European American and African American patients having Metabolic Syndrome as compared to patients without Metabolic Syndrome (71% and 57% vs. 29% and 43%).[9] Cardiovascular event rates were significantly greater in those with dyslipidaemia: LDL-C>2.6 mmol/L, HDL-C ≤0.88 mmol/L and TGs ≥2.3 mmol/L, as is proved in the FIELD and ACCORD study. José Marconi Almeida de Sousa et al studied 'Comparison of coronary angiography findings in diabetic and non-diabetic women with non-ST-segment-elevation acute coronary syndrome' found that the diffuse pattern of atherosclerotic disease in diabetic patients, as well a greater deterioration of ventricular function, which may be associated to the poorer prognosis seen in this population both in the short- and long-term. In GUSTO-I study, diabetic and nondiabetic patients exhibited similar percent diameter and percent area stenosis at early angiography. Diabetic patients had a significantly smaller minimal lumen diameter in the infarct-related artery than nondiabetic patients. Reference segment diameters in all infarct-related arteries were also significantly smaller in diabetic than nondiabetic patients. This difference remained true after adjustment for multiple clinical variables, including age, gender, hypertension, hypercholesterolemia and body surface area (p = 0.0002).

CONCLUSION

This study has re-established the association of several risk factors with atherosclerotic coronary artery disease like systemic hypertension, LDL, HbA1c, fasting blood sugar (FBS) and serum creatinine. Patients having diabetes mellitus and/or metabolic syndrome are found to have more severe form of coronary artery disease than those who don't have either of these. However, presence of both diabetes and metabolic syndrome has not been found to impose any significant additional risk than their isolated presence. Serum LDL level seems to be an individual risk factor.

Patients with h/o smoking and family h/o CAD also found to have a trend towards more severe CAD although it was not found to be statistically significant. Patients with higher BMI also found to have a more severe CAD. Low serum HDL could not be isolated as an individual risk factor as the median value was low (<40mg/dl) in all the three groups without any statistically significant difference.

So, it can be concluded that, combined presence of Diabetes mellitus and Metabolic syndrome as well as presence of isolated Diabetes mellitus or isolated Metabolic syndrome is a high risk for severe and complex CAD. Also, among the individual diagnostic points of Metabolic syndrome-FBS and Hypertension-found to have significant effect on the severity of CAD. A significant association between severity of coronary artery disease and peripheral arterial disease (assessed by ABI) has been found. A much larger study is needed for further evaluation of the individual risk factors. Also, possible effect of the ethnicity and genetic factors on our study population probably played an important role which needs to be evaluated in a larger future trial.

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