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Original Research Article

Angiographic profile of coronary artery disease in patients with acute coronary syndrome in correlation to their glycaemic status

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ABSTRACT

Background: Aim of the study was to study relationship between Glycemic control and presence of coronary artery disease on clinical presentation with acute coronary syndrome (ACS). We used blood sugar levels (Fasting and post prandial) and HbA1c as parameter for evaluation of glycemic control, Gensini score was used as a parameter for evaluation of severity of coronary artery disease.
Methods: The analysis of 1200 patient's data were performed to reveal demographic characteristics, correlation of the diabetes control with severity of the ACS. A sub-set of 200 subjects that was collected with a focus to include diabetic and non-diabetic subjects in proportion 1:2 was performed.
Results: The Pearson correlation between HbA1c and Gensini score (r=0.0444) was poor the correlation between fasting blood sugar (FBS) and Gensini score (r=0.0586), and between post prandial blood sugar (PPBS) and Gensini score (r=0.0549), between random blood sugar (RBS) and Gensini score (r=0.0331) all indicative of poor correlation. Duration of diabetes and Gensini score revealed r=-0.039. The. Correlation was poor to moderate with one sided ANOVA and consistent on comparing r-sq values between, HbA1c and Gensini Score [rsq=49.62 (p<0.001)], FBS and Gensini score [rsq=32.19 (p<0.001)], PPBS and Gensini score [rsq=25.39 (<0.001)], RBS and Gensini score [rsq=42.49 (p<0.001)] and duration of diabetes and Gensini score [rsq=19.61 (p<0.001)].
Conclusions: There was no correlation evident between diabetes and Gensini dcore. The analysis was suggestive of possible strong relationship between diabetes control and IHD severity. There is no correlation between Diabetes and ACS severity. However, better diabetes control is related with better ACS profile.

Keywords: Diabetes, Gensini score, HbA1c

INTRODUCTION

Diabetes, one of the major precursors of coronary artery disease is another major global health burden, having increasing trends in overall prevalence and is anticipated to increase from 285 million in 2010 to 438 million by the year 2030.[1]

Diabetic patients when compared to non-diabetic have an increased risk of developing vascular complications and have two to the four-fold risk of developing coronary artery disease.[2] The state of chronic hyperglycemia has been now measured by HbA1c, which averages the blood sugar levels of both fasting and postprandial states.[3,4] Presenting high blood sugar levels has been considered as an independent risk factor of death in patients with or without diabetes.[5] High blood sugar levels at admission can either be diabetes or due to stress hyperglycemia or impaired glucose tolerance. Hence, it is important to study the spectrum of clinical presentation and the patterns of involvement of coronary artery disease in both diabetics and non-diabetics. While diabetes severity is based upon

the indices of blood sugar control, the severity of coronary artery involvement in diabetes, prediabetes, and non-diabetics is assessed quantitatively through Gensini score.[6] We studied relationship between blood sugar levels and presence of coronary artery disease at the time of clinical presentation. In this study, we used blood sugar levels (Fasting and post prandial) and HbA1c as a parameter for evaluation of diabetes and its control, Gensini score was used as a parameter for evaluation of coronary artery disease.

METHODS

This study was undertaken in Bharati hospital and research centre, Pune, India from January 2015 to January 2017. This Cohort study recruited 1200 patients (Retrospective data) both, diabetic and non-diabetic, and having acute coronary syndrome who were undergoing angiography.

All the subjects signed informed consent forms. Permission from the Institutional ethical committee was taken. All-female subjects in reproductive age underwent a urine pregnancy test as a hospital protocol for angiography and radiological tests. Patients who were refused angiography, or who had undergone angioplasty in the past, and patients with anaemia, renal failure or other known systemic illness were excluded from the study.

All patients were evaluated in detail as per their symptomatology, a detailed physical examination, routine blood investigations with blood sugar estimation and HbA1c, ECG and ECHO were done at admission. They were categorized into non-diabetics and diabetics according to their HbA1c levels. In addition, the diabetic patients were subcategorised according to their hbA1c levels (good control<6.5, suboptimal control=6.5-8.9, poor control >9).[2,7]

Coronary artery disease (A.M.I) is defined in the presence of minimum 2 of following[8]

Chest pain suggestive of cardiac origin or retrosternal squeezing radiating increases with exertion, not relieved by rest and nitrates and associated with sweating or trop I positive or electrocardiographic changes (one or more of the following criteria): ST-segment elevation of more than 2 mm from J point in 2 related electric fields with typical evolutionary changes, presence of new pathologic Q waves in 2 related electric fields. [for Q-M.I.], non-Q-M.I. with ST depression and T inversion on electrocardiogram.

The diabetes patients were classified into various groups on American diabetic association criteria[9]

HbA1C>6.5%. or FBS>126 mg/dl. (Fasting is defined as no food/caloric intake for at least 8 h) or 2-h plasma glucose>200 mg/dl during an OGTT, symptoms of hyperglycemia or hyperglycaemic crisis, a random plasma glucose >200 mg/dl.

Categories of increased risk for diabetes (prediabetes)[10]

Fasting blood sugar levels 100-125 mg/dl (IFG)or 2-h plasma glucose in the 75-g OGTT: 140-199 mg/dl (IGT) or HbA1C 5.7-.4%.

On completion of the primary assessment, the subjects underwent angiography and their angiography records were used for evaluation of the disease severity based upon Gensini score. The clinical outcomes were reconfirmed by clinical cardiologist. The angiographic severity of the coronary artery disease was assessed using the Gensini score.[6] Statistical analysis was planned to be assessed using Mean±standard deviation, Pearson's correlation coefficient, chi-square test and ANOVA tests using SPSS software. In the original plan for the study, there were no subsets. However, a subset analysis was introduced at the time of evaluation.

RESULTS

The statistical analysis of 1200 patients collected data was performed. To reveal demographic characteristics, correlation of the diabetes control presented by glycosylated hemoglobin with the severity of the coronary artery disease presented as Gensini score. In addition, several exploratory analyses were performed. A Sub-set of 200 subjects that were collected with a focus to include Diabetic and non-diabetic subjects in proportion 2:1 was performed.

There were in all 1200 subjects out of which 1132 (94.33%) were diabetics (Table 1). The majority (67.08%; n=805) were males, 285 (23.67%) were smokers and 497 (42.42%) had a history of hypertension. The median duration of hypertension was 1.66 years.

Table 1: Demographics of patients on clinical presentation.

Variables	N=1200
Age (Mean±SD) (years)	55.87±11.04
Males (n, %)	805 (67.08)
Females (n, %)	395 (32.92)
Gender ratio (n, %)	2.04
Smokers (n, %)	284 (23.67)
Hypertension (n, %)	497 (41.42)
Duration of hypertension (median)	1.66
Diabetes (n, %)	1132 (94.33)

All the patients had more than one symptom of cardiac disease (Table 2). In all, 1168(97.33%) had chest pain, dyspnea was presented in 214 (17.83%), sweating was a complaint in 586 (48.83%), syncope was a complaint in 3 (0.25%), giddiness was a complaint in 44 (3.67%) and abdominal pains was a complaint in 54 (4.50%). Unstable angina was a presenting condition in 108 (9.00%), STEMI in 695 (57.92%) and NSTEMI 364 (30.33%), of which 333 (27.75%) patients were thrombolized before angiography. Ejection fraction, the parameter of analysis for left

ventricular function, was 55.86±11.78%, indicating that there was a low compromise of cardiac function in most of the patients. Gensini score, the indicator of the severity of ACS was 41.995±30.74, indicating that most of the patients had a moderate disease.

Table 2: Cardiac assessment of patients on clinical presentation.

Cardiac assessment	N (%)
Chest pain	1168 (97.33)
Dyspnoea	214 (17.83)
Sweating	586 (48.83)
Syncope	3 (0.25)
Giddiness	44 (3.67)
Abdominal pains	54 (4.50)
STEMI	695 (57.92)
NSTEMI	364 (30.33)
Unstable angina	108 (9.00)
Asymptomatic	0 (0.00)
Thrombolyzed	333 (27.75)
Number of vessels 1	735 (61.25)
Number of vessels 2	222 (18.50)
Number of vessels 3	243 (20.25)
Ejection fraction (Mean±SD)	55.855±11.78
Gensini score (Mean±SD)	41.995±30.74

Out of 1132 diabetic patients, newly diagnosed were 245 (20.42%). Other 317 (26.42%) had DM<6 months, 9 (0.75%) had DM 6-12 months 110 (9.17%) had DM 12-24 months and majority of the patients [746 (62.17%)] had DM>24 months (Figure 1 and 2). The parameters of glycaemia viz. random blood sugar, fasting blood sugar, and post prandial blood sugar was 163.68±80.41 mg/dl, 127.62±51.92 mg/dl and 160.55±47.61 mg/dl respectively. Glycosylated haemoglobin, the indicator of diabetes control for 3 months was used as an indicator of diabetes control in this study with a mean of 6.84±1.93%, indicating that majority patients had good control on diabetes. The frequencies by glycosylated haemoglobin <5 (non-diabetic), 6.0-7.5 (Prediabetic/good control), 7.5-9 (Optimum control) and >9 (poor control/newly diagnosed) were 543 (45.25%), 386 (32.17%), 108 (9%) and 161(13.42%) respectively (Table 3). In all, 77.42% of people had good control of diabetes or no diabetes by HbA1c analysis. The Total Cholesterol was 178.25±75.99 mg/dl, triglycerides were 137.31±10.58 mg/dl, LDL cholesterol was 36.37±38.25 mg/dl and HDL cholesterol were 123.87±11.78 mg/dl.

The Pearson correlation between HbA1c and Gensini score revealed r=0.0444, indicative of the poor correlation. The correlation between FBS and Gensini score revealed r=0.0586, between PPBS and Gensini score, revealed r=0.0549, between random blood sugar and Gensini score, revealed r=0.0331 all indicative of the poor correlation. The duration of type 2 diabetes and Gensini score revealed r=-0.039.

The correlation was reconfirmed with one-sided ANOVA which revealed the rsq values indicative of moderate correlation for HbA1c and Gensini score [rsq=49.62 (p<0.001)], FBS and Gensini score [rsq=32.19 (p<0.001)], PPBS and Gensini score [rsq=25.39 (<0.001)], random blood sugar and Gensini score [rsq=42.49 (p<0.001)] and duration of DM and Gensini score [rsq=19.61 (p<0.001)].

Table 3: Glycaemic profile of patients on clinical presentation.

Glycaemic profile, (n, %)	N=1132
Random blood sugar (Mean±SD)	163.68±80.41
Fasting blood sugar (Mean±SD)	127.62±51.92
Post-prandial blood sugar (Mean±SD)	160.55±47.61
HbA1c (Mean±SD)	6.84±1.93
HbA1c<5	543 (45.25)
HbA1c 6-7.5	386 (32.17)
HbA1c 7.5-9	108 (9.00)
HbA1c >9	161(13.42)
Newly diagnosed DM	245 (20.42)
DM <6 month	317 (26.42)
DM 6-12 months	9 (0.75)
DM 12-24 months	110 (9.17)
DM >24 months	746 (62.17)

The analysis has a variation of calculation in different methods of correlation. Considering the goodness of fit marginal analysis (Figure 1) and further exploratory consideration, the correlation by ANOVA is considered a better relation. The data is focused around HbA1C 6% and Gensini score 30 (Figure 1). In the second set of focus was HbA1C 10% and Gensini score about 30. This error of analysis classically reveals low variety in the available population trends. The exploratory analysis was performed with various levels of Gensini score and parameters of diabetes were performed for the further in-details understanding of the effect of diabetes on severity of ACS.

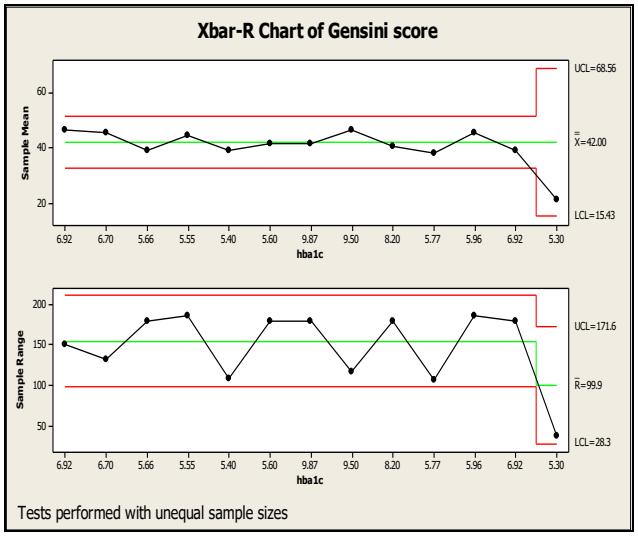

Figure 1: Xbar-R chart of Gensini score.

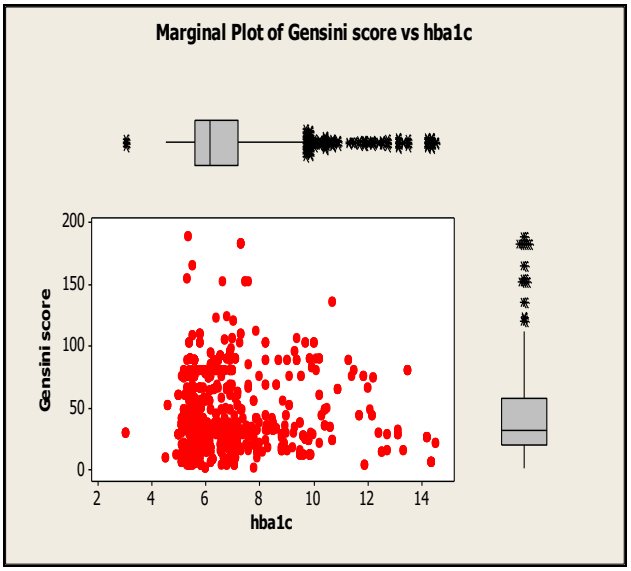

Figure 2: Marginal plot-analysis of HbA1 vs Gensini score.

The overall normal and nested analysis revealed that there was no direct correlation between the HbA1c and Gensini score, representing control over diabetes and the severity of cardiac disease respectively. However, the major limitation of the study population was skewness towards controlled diabetes and less severe disease. (Table 4 and Figure 2). Population having better control of blood sugar in DM has less severe ischemic cardiac disease.

The demographics of the subjects had a marginal propensity match. There was a total of 200 subjects of which 132 were diabetic and 68 were non-diabetic. The mean age was 56.30±11.43 years and 56.04±13.28 in the diabetic and non-diabetic group respectively with an overall mean age of 56.17. In the diabetic group, there were 109 (82.58%) males, in the non-diabetic group, there were 54 (79.41%) males totaling to be 163 of the overall. Females in the diabetic group were 23 (17%) in the non-diabetic group were 14 (20.58%) and 37 in total. This led to the gender ratios 4.74, 3.8, 4.41 in diabetic, non-diabetic and total subset respectively. The smokers in the diabetic group counted 39 (29.55%) in non-diabetic group 11 (16.18%) and 50 in total. Hypertension was reported in 47 (36%) patients in the diabetic group, 33 (48.53%) patients in the non-diabetic group, in 80 patients overall. The mean duration of hypertension was 1.39±2 years, 1.93±2.81 years in the diabetic and non-diabetic group respectively, with an overall mean of 1.66 years.

Table 4: Exploratory ANOVA of diabetes and Gensini score.

Analysis of correlation (Nested)	HbA1c<6	HbA1c 6-7.5	HbA1c 7.5-9	HbA1c>9
HbA1c and Gensini score	543	344	110	161
Gensini score mean	37.713	49.596	39.382	44.217
Gensini score SD	28.251	34.93	25.733	31.45
Pearson's R	0.0906	0.0914	-0.133	-0.204
	<90	90-117	117-140	>140
FBS and Gensini score	88	593	222	275
Gensini score mean	42.9	41.97	40.97	42
Gensini score SD	30.86	30.74	30.74	30.74
Pearson's R	0.063	0.065	0.65	0.59
	<110	110-140	140-165	>165
PPBS and Gensini score	87	394	345	369
Gensini score mean	41.61	42.07	41.99	42
Gensini score SD	30.48	30.75	30.74	30.74
Pearson's R	0.039	0.06	0.054	0.055
	<90	90-140	140-165	>165
Random blood sugar and Gensini score	51	292	281	407
Gensini score mean	42.09	41.9	42.08	42
Gensini score SD	30.791	30.67	30.74	30.74
Pearson's R	0.03	0.037	0.032	0.33
	New to 6 months	6-12 months	12-24 months	>24 months
Duration of DM and Gensini score	322	26	107	747
Gensini score mean	42.04	41.79	41.93	44.32
Pearson's R	0.25	0.22	0.26	0.25

All the patients in the subset had one or more presenting symptoms. Out of the 200 subjects, 196 (98.0%) subjects had chest pain, which was distributed as 130 (98.48%) in the diabetic group and 66 (97.06%) in the non-diabetic group. Dyspnea was present in 17 (12.88%) in the diabetic group, 47 (69.12%) in the non-diabetic group and 64 (32.0%) in an overall subset. In the diabetic group, 72 (54.55%) had sweating, in non-diabetic 30 (44.12%),

hence overall 102 (51.0%). No patient had syncope, however 6 (3%) patients, 2 (1.51%) in the diabetic group and 4 (5.88%) in the non-diabetic group and giddiness. Abdominal pains were the presenting symptoms in five (3.79%) patients in the diabetic group, 1 (1.47%) patient in the non-diabetic group with the sub-set total of the six (3%).

STEMI was the dominant presenting finding in 78(59.09%) diabetic patients, 41 (60.29%) non-diabetic patients to a subgroup total of 119 (59.5%), NSTEMI was the next major group to be present, with 43 (32.78%) in the diabetic group, 18 (26.47%) in the non-diabetic group and 61 (30.5%) overall subsets. Eight (6.06%) patients in diabetic group, 5 (7.35%) in non-diabetic group, total 13 (6.5%) had unstable angina. Total 56 (28%), 37 (28.03%) diabetic and 19 (27.94%) non-diabetic subjects were Thrombolysis and rest were planned for primary angioplasty. Overall, 132 (66%), 31 (15.5%) and 37 (18.5%) patients had single, double and triple vessel disease out of which, 86 (65.15%), 22 (16.66%), 24 (18.18%) respectively were in diabetic group and 46 (67.64%), 9 (13.24%) and 13 (19.11%) were in non-diabetic group respectively. The mean ejection fraction overall and in both groups was above 50, meaning that the cardiac function was relatively less compromised. Mean EF in the diabetic group was 55.71±11.76, in non-diabetic was 55.073±12.12 and the overall mean for the subset was 55.39±25.09. Mean Gensini score, indicative of the severity of cardiovascular disease based upon angiographic score was 38.88±30.85 in diabetic, 43.88±35.25 in non-diabetic and 41.382±5.52 of the overall subset.

Among 132 diabetic subjects in the group, the mean Random blood sugar was 131.73±52.40, fasting blood sugar was 161.60±48.24- and 2-hours post-prandial blood sugar was 176.48±47.21. The HbA1c, indicator of 3 months blood sugar control was 6.78±2.06. In this group, 65 (49.24 %) patients had HbA1c<5.35 (26.52%) had good control on diabetes, (HBa1C 6-7.5), 9 (6.82%) had moderate control in diabetes (HbA1c 7.5-9) and 18 (13.64%) had poor control on diabetes. In this group, 34 (25.76%) had newly diagnosed diabetes that was for less than 6 months. 4 (3.03%) patients had diabetes diagnosed within 1 year but not older than 6 months. Fifteen (11.36%) patients had diabetes diagnosed between 12-24 months and 79 (59.85%) had DM more than 24 months old. In the non-diabetic/prediabetic group of 68 subjects, mean random blood sugar was 93.62±9.37, mean fasting blood sugar was 128.66±25.45, mean 2-hour postprandial blood sugar was 170.79±45.25 and mean HbA1c was 5.66±0.7. In the group 63 (47.73%) patients had HbA1c<5% and 4 (3.03%) had HbA1c 6-7.5%.

The analysis of correlation (Pearson) was performed in HbA1c various levels and Gensini score. There was a poor correlation observed between the two groups. The analysis reveals that there is a poor correlation between diabetes and Gensini score (Table 5).

Table 5: Analysis of correlation (Pearson).

Variables	Diabetic	Non-diabetic	Overall
HbA1c and Gensini score	-0.05	0.02	-0.06
FBS and Gensini score	-0.07	0.12	-0.07
PPBS and Gensini score	0.02	-0.09	-0.03
Random blood sugar and Gensini score	-0.07	0.03	-0.08
Duration of DM and Gensini score	0.16	-	-

DISCUSSION

This study consists of 1200 patients divided into three groups of the prediabetic and non-diabetic population and diabetics. Diabetics were further divided into a subgroup of good control, moderate control and poor control depending on their HbA1c levels.

Out of 1200 subjects out of which 1132 (94.33%) were diabetics. The mean age of presentation was 55.87±11.04. The majority (67.08%; n=805) were males, 285 (23.67%) were smokers and 497 (42.42%) had a history of hypertension. The median duration of hypertension was 1.66 years. In the GUSTO-1 trial, it was observed that diabetic patients were older when compared to non-diabetic patients, similar results were observed in our study.[17] The female population 395 (67.08%) were mainly populated in the diabetic group rather than other pre- and non-diabetic groups. Pre-menopausal females, in general, have protection against IHD, but this cardio protection is lost in the presence of diabetes.

All the patients had more than one symptom of cardiac disease. In all, 1168(97.33%) had chest pain, ddyspnoea was presented in 214 (17.83%), sweating was a complaint in 586 (48.83%), syncope was a complaint in 3 (0.25%), giddiness was a complaint in 44 (3.67%) and abdominal pain was a complaint in 54 (4.50%). When compared with another study like the study by soler et al diabetic patients had more atypical presentations of ACS with heart failure, vomiting, collapse, confusion or CVA, which led to increased risk for them going undiagnosed and increased mortality.[18]

Glycosylated haemoglobin, the indicator of diabetes control for a span of 3 months was used as an indicator of diabetes control in this study with a mean of 6.84±1.93%, indicating that majority patients had good control on diabetes.

Diabetes is a known risk factor in cardiac conditions including ischemic heart disease. Krishnaswami et al[19] performed 1032 chest pain patients, 516 patients having

propensity matched 516 diabetic and non-diabetic patients in each arm. All subjects were examined by selective coronary arteriography was undertaken. In about 86.6% of the diabetic group, coronary artery disease was the cause of chest pain. This prevalence was directly related to the increasing age. Besides, the diabetic subjects had more frequency of multivessel disease and disease in multiple segments of the same vessel than that in non-diabetics.[19]

This above Table 6 gives the list of studies showing higher Gensini scores in the diabetic population except for one study Abadie et al which showed no difference between controlled and uncontrolled diabetic population.[27]

Table 6: The list of studies showing higher Gensini scores in diabetic population.

Principle investigator	No. of cases in study	Results
Calton et al[22]	75	Higher score, more three vessels
Natali et al[23]	2253	Higher score, greater effect on female patients
Hamby et al[24]	100	Higher score, more three vessels
Pajunen et al[25]	57 IDDM patients	More severe extensive and distal disease
Thomas et al [26]	59	More severe disease
Abadie et al[27]	36	No difference
Krishnaswami et al[28]	516	More severe disease and more multivessel disease
Moosavi et al[29]	50	More severe disease and more multivessel disease
Peppes et al[30]	115	More severe disease

In this study, the Pearson correlation between HbA1c and Gensini score revealed the poor correlation. The correlation between FBS and Gensini score, between PPBS and Gensini score, between random blood sugar and Gensini score were all indicative of the poor correlation. This correlation was reconfirmed with one sided ANOVA. The overall normal and nested analysis revealed that there was no direct correlation between the HbA1c and Gensini score, representing control over diabetes and the severity of cardiac disease respectively. However, the major limitation of the study population was skewness towards controlled diabetes and less severe disease. Population having better control of the blood sugar in diabetes mellitus has less severe ischemic cardiac disease.

CONCLUSION

The study revealed that when the diabetes is under control, the severity of cardiac disease is low. Correlation in extreme cases could not be substantiated. The statistical method of X bar R chart was used to identify the correlation of the HbA1C as a diabetic control and Gensini score, as an indicator of IHD severity. This analysis remained non-conclusive. Hence, the ANOVA method was used to analyze the negation for correlation. In this analysis, the statement "low HbA1C is related to low cardiac disease severity" was proven true. Hence, the converse that "high HbA1C is associated with high Gensini score" may correlate. The overall population was mostly distributed over the HbA1c Levels between 6 and 8 and the Gensini Score was mainly in from 20 to 70. The analysis is suggestive of a possible strong relationship between diabetes control and the severity of ischemic heart disease. To ensure the integrity of this fact a small group of patients with 2:1 random assignment was formed and tested. As a result of this analysis, at least a moderate relationship presents in the diabetes control and severity of cardiac illness. The other factor that could be seen to have a strong relationship with cardiac disease severity was the duration of diabetes.

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