https://doi.org/10.30702/ujcvs/24.32(02)/IA020-4550
UDC 616.12-005.4:616.379-008.64]-073

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Determination of Correlation between Diabetes Duration and Coronary Artery Disease Severity in Patients Undergoing Coronary Angiography

Abstract

Background. Coronary artery disease (CAD) is caused by atherosclerotic process in coronary arteries. Due to extraordinary risk for atherosclerosis in diabetic patients, it is also counted as a vascular disease. Diabetes mellitus (DM) is a direct major associated risk factor in the development of cardiovascular disease with some studies from high income countries reporting correlation between duration of DM and severity of CAD. However, data from Pakistan is scarce.

The aim. To determine the correlation between duration of DM and severity of CAD in patients undergoing coronary angiography at the tertiary care cardiac center.

Materials and methods. This cross-sectional study was conducted in the Department of Cardiology, Civil Hospital Karachi, among 160 patients who were scheduled for coronary angiography with comorbid DM. Correlation between duration of DM and severity of CAD (as assessed by the modified Gensini score) was statistically measured and reported employing Pearson's correlation coefficient (r).

Results. Significant correlation between DM duration and total Gensini score was shown with r = 0.759 and p = 0.000001. With the increase in the duration of DM, the severity of CAD also increased.

Conclusion. DM duration is positively associated with the modified Gensini score and the significant determinants of CAD severity tend to be relevant.

Keywords: *atherosclerosis, modified Gensini score, cardiovascular disease, comorbidity.*

Introduction. Coronary artery disease (CAD) is caused by atherosclerotic process in coronary arteries. It is counted as the most common cause of mortality and morbidity worldwide [1]. Estimates suggests that the burden will rise to over 11 million during this decade [2]. Development of CAD has been attributed to known modifiable risk factors [3,4].

A number of factors have been reported to be associated with the severity of CAD including metabolic disorders. The association between diabetes mellitus (DM) and coronary atherosclerosis is well established and it is reported that CAD is responsible for most of the excess mortality among diabetic patients [5]. Diabetic patients have a high burden of CAD and some studies report the strong association between CAD severity and DM duration.

DM is very important issue of our society, its prevalence increases day by day. There are two types of DM: type 1 and type 2. Type 2 DM due to many common risk factors is associated with cardiovascular disease CAD. The risk factors of these two diseases are mostly the same [6,7].

With the increasing changes in the lifestyle behaviors, from more active to more sedentary, from normal eating pattern to ever increasing consumption of processed foods, the prevalence of comorbid conditions is on a steep rise. In addition, better management of chronic conditions like DM has greatly improved the longevity among those suffering from it. As a result, much greater population today is living

with DM diagnosed decades ago. In the given premise the comorbid presence of DM and its longer duration has posed many issues such as complications with other organ systems. The International Diabetic Federation most recently stated that 415 million people are currently suffering from DM. By the year 2040 the global population with DM is expected to rise to 642 million [8].

Epidemiologically the type 2 DM is a common public health issue at the present time and this disease can increase the risk of mortality and morbidity due to cardiovascular diseases [9]. The duration of DM is also linked with various aspects of CAD as its prognostic nature. DM is also an important factor for various modifiable risks factors of heart diseases [10].

DM is a metabolic disorder of carbohydrate metabolism. Due to extraordinary risk of atherosclerosis among diabetic patients, it is also counted as a vascular disease. The world prevalence of DM among adults (aged 20-79 years) was 6.4% in 2010 and will increase to 7.7% by 2030 [11].

Changes in lifestyles and eating patterns cause the disorders in metabolic activities, so these issues are increasing in developing countries like Pakistan [12].

In the United States, coronary artery atherosclerotic disease has the highest mortality rates in men and women. In this disease atherosclerotic changes occur within the wall of coronary arteries [6]. The symptoms of atherosclerosis include [13] chest pain, shortness of breath, tiredness, weakness, reduced exercise capacity, palpitations, dizziness, swelling in legs, obesity, stable angina pectoris, diaphoresis, intermittent claudication, tachycardia, abdominal angina, low and high blood pressure, S4 gallop, S3 gallop, heart murmur, tachypnea, xanthelasmas, livedo reticularis, syncope, rales.

Education related to CAD is very important; many publications and articles are available by American Heart Association that provide much information [14]. This disease can be modified through diet [15] and exercise. Education plays an important role in developing healthy dietary habits. There are many heart care centers and cholesterol centers for patient education. The primary outcome of the study is to calculate the correlation between the DM duration and CAD severity as calculated by Gensini score.

The aim. To determine the correlation between DM duration and severity of CAD using Gensini score in patients undergoing coronary angiography.

Materials and methods. This cross-sectional study was conducted at the Department of Cardiology, Dow University of Health Sciences, Civil Hospital Karachi from 1 January 2019 to 30 June 2019 via non-probability consecutive sampling technique. The sample size was calculated to be 160 patients. Both male and female patients diagnosed with CAD, with comorbid type 2 DM, scheduled for coronary angiography, aged 35 to 70 years were included in the study. Those with the history of severe CAD, percutaneous coronary intervention, coronary artery bypass grafting (CABG), valvular heart disease, congenital heart disease, cardiomyopathy, as well as smokers, individuals with obesity, hypertension, family history of CAD, were excluded. A total of 160 patients who fulfilled the inclusion criteria and provided written informed consent were included in the study and received clarification of the procedure. Principal investigator collected demographic information and clinical history of the patients. DM duration was measured in months. Patients underwent coronary angiography which was performed by expert cardiologists with an experience of at least five years. Angiography findings were examined by an operator who was unaware of patient information. CAD severity according to the modified Gensini score was determined based on the coronary angiography findings. The adjusted Gensini score was 32. The Gensini score was determined by multiplying the severity score and multiplication factor for the certain area. For each coronary stenosis, the severity score was taken with the degree of luminal narrowing, i.e. reductions of 25 percent, 50 percent, 75 percent, 90 percent, 99 percent, and full occlusion was measured with a severity score of 1, 2, 4, 8, 16, and 32. The left main coronary artery = 5. Left anterior coronary artery: proximal section equal to 2.5, middle section equal to 1.5, apical section equal to 1, the first diagonal branch equal to 1 and the second diagonal branch equal to 0.5. Left circumflex artery: proximal section equal to 3.5, distal section equal to 2 (or 1 if right coronary artery dominancy exists), the obtuse marginal branch equal to 1, posterior descending artery equal to 1, and the posterior-lateral branch equal to 0.5. Right coronary artery: proximal section, middle section and distal section remains equal to 1. Then the angiography report was analyzed and compared with the DM duration. All the data was captured. The confounding variables and biases were regulated by strict adherence to the requirements for inclusion.

The collected data was analyzed using SPSS Statistics 22. For qualitative variables, frequency distribution was calculated. The qualitative variables of our study were gender and DM. For quantitative variables, mean and standard deviation was calculated. The quantitative variables of our study were age and DM. To determine correlation between DM duration and Gensini score, the Pearson's correlation was used. A correlation coefficient of ≥0.70 was considered as very strong, between 0.4 and 0.7 as strong, between 0.2 and 0.4 as moderate, while <0.2 as weak.

Stratification was used to monitor the impact modifiers. Stratification was performed by age, gender and DM duration. Post-stratification correlation coefficient was determined and p-value ≤0.05 was taken as significant.

Results. The total sample size included 160 subjects: 106 male (66.3%) and 54 female (33.8%) patients. The

major part of the sample size was represented by male patients since men are the main earners in our society. The risks of these two diseases are also higher in men. The frequency distribution of comorbid conditions in total sample size was as follows: 144 (90 %) with comorbid condition and just 16 (10 %) without comorbid condition (Table 1). DM and heart diseases have different risk factors, so these factors increase the probability of this condition.

The patients were divided into three age groups: 35 years to 45 years, 46 to 55 years, and above 55 years. Our study revealed that proportion of the patients who were above 55 years of age was the largest (39.4%) compared to those aged 35-45 and 46-55 (32.5% and 28.1%, respectively) (Table 1). Along with DM duration, age is another non-modifiable confounding risk factor which contributes to the severity of CAD: the largest proportion of patients with CAD was above the age of 55 years.

The mean age of the patients included in our study was 51.7 (standard deviation 9.96), minimum 35 years, maximum 70 years. The level of glycosylated hemoglobin in this disease is also very important. The mean value of hemoglobin A1c (HbA1c) in our study was 8.58% with standard deviation 1.06. The minimum value of HbA1C was 6.5% and maximum value was 10.0%.The DM duration in patients was different: minimum 5 years and maximum 27 years, mean value 15.16, standard deviation 6.74. The total Gensini score is very important factor. The range of total Gensini score in our patients was from 4 to 180, mean value 79.74, standard deviation 35.37 (Table 2).

As can be seen from Table 3, patients with the longest DM duration, i.e. from 20 to 27 years, had the highest severity score ranging from 110 to 160.

In this study we also demonstrated that there exists a significantly positive linear correlation between HbA1c levels and Gensini score and, hence, the severity of CAD. This is well illustrated by the fact that increase in HbA1c level is associated with simultaneous increase in the severity score. After the data collection we summarized it in Table 4 which shows that 35 patients had multivessel disease, and their HbA1c level ranged between 8% to 10% compared to those with two-vessel or single-vessel disease who had relatively low HbA1c level. Hence, the level of HbA1c was an independent confounding risk factor influencing the severity of CAD. These values are lower than normal ranges required in people for good and proper health.

There was significant correlation between DM duration and total Gensini score: r = 0.759 with p = 0.000001. With the increase in DM duration, CAD severity also increased. The p-value is less than alpha which is level of significance, so we reject null hypothesis and conclude that there is significant linear relationship between DM duration and CAD severity and correlation coefficient significantly differs from zero (Fig. 1).

Discussion. Our study explored the association between type 2 DM duration and the severity of CAD among patients undergoing coronary angiography. In this

Table 1

Patient distribution in terms of gender, comorbid condition, and age

Distribution	Patients, n	%
Gender		
Male	106	66.3
Female	54	33.8
Comorbid condition		
Yes	144	90
No	16	10
Age group		
35-45 years	52	32.5
46-55 years	45	28.1
>55 years	63	39.4

Table 2

Patient characteristics

Variables	Minimum	Maximum	Mean ± SD
Age, years	35	70	51.7 ± 9.96
HbA1c, %	6.5	10.00	8.58 ± 1.06
DM duration, years	5	27	15.16 ± 6.74
Total Gensini score	4	180	79.74 ± 35.37

Table 3

DM duration and Gensini score

DM duration	Gensini score
5-10 years	40-100
10-15 years	60-110
15-20 years	80-130
20-27 years	100-160

Table 4

HbA1c levels and Gensini scores depending on the types of lesions

Types of lesion	Patients, n	HbA1c levels, %	Gensini score
Multivessel disease	35	8-10	120-160
Left main disease	25	7-10	100-140
Two-vessel disease	47	7-9	90-110
Single-vessel disease	53	6.5-8	40-100

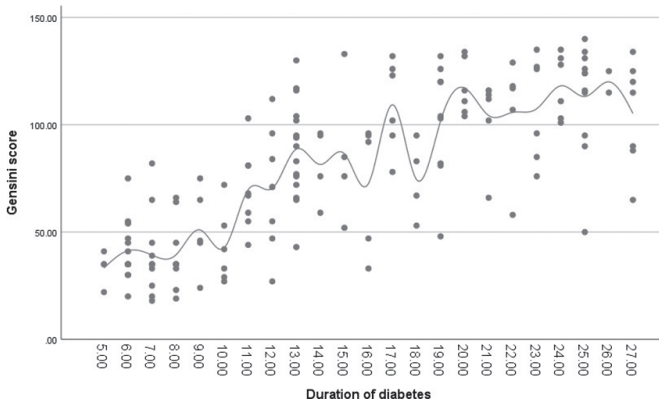

Fig. 1. *Correlation between the duration of diabetes mellitus (years) and Gensini score*

study, a total of 160 diabetic patients were enrolled, and both DM duration and corresponding Gensini score did not show statistically significant association with gender; however, the strength of association found in male patients was comparatively more than that in female patients, with males comprising 66.3% vs females 33.8%.

A relatively similar study was done by Salim et al. [16] in Peshawar in which association of glycosylated haemoglobin level with severity of CAD in diabetic patients with non-ST-elevation myocardial infarction was studied and it was found that female patients formed a very small proportion, 26.8%, which corresponds to our result.

The level of HbA1c is also an important predictor of CAD severity, and our study revealed that patients with higher level of HbA1c mostly had either multivessel involvement or left main involvement and, hence, were candidates for CABG for their ultimate treatment. This finding was very similar and correlates to the study by Malthesh et al. in which CAD severity was compared in diabetic and non-diabetic patients with acute coronary syndrome [17]. In his study, 73.1% of patients with higher HbA1c level had CABG as treatment outcome, suggesting prevalence of elevated HbA1c level in patients going for CABG. Another similar study which was carried out by Almutairi et al. [18] in the Kingdom of Saudi Arabia analyzed the association of higher HbA1c level with CAD severity. This study showed that in patients with poorly controlled DM (HbA1c >7%) the severity of CAD increased with multiple and tighter lesions. This is consistent with our findings and depicts the strong nature of evidence provided by us in establishing a linear correlation between higher level of HbA1c and severity of CAD as confirmed by the angiographic findings.

Another factor which correlated to these is the higher age of such patients. It was seen in our study that those patients who were above 55 years of age had greater severity of CAD, i.e. 39.4%, than younger patients. Our study revealed similar result with the study by Ul Amin et al. who reported that DM duration and Gensini score were found to be much higher among older patients (more than 60 years of age), and the association was found to be stronger in older patients (more than 60 years of age) with a correlation coefficient of 0.52 vs. 0.38 [2].

Majority of people being diagnosed with CAD are suffering from DM and other conditions. This has become common clinical scenario in Pakistani population as well [19]. Our study found a strong association between the duration of comorbid DM and the severity of CAD. This has serious implications on not only the treatment procedures but also the prognosis of the disease itself. Our study suggests that longer duration of DM is associated with more severe CAD among patients undergoing coronary angiography. Both these conditions negatively influence the procedure outcome [20]. It is of much importance that attention be paid to duration of DM as well when treating a CAD patient.

As diabetic patients are at higher risk of developing progressive CAD and re-stenting after the first stent implantation, much focus should be given to diabetic patients with DM lasting for more than 10 years during angiography [21]. It was observed in our study that number of patients with triple vessel disease/multivessel disease was higher with DM duration of more than 10 years. These finding correlate with other study by Fox et al. showing the risk of CAD was 1.38 times higher for each 10-year increase in the duration of DM, as cited by Hegde et al. (2014) [22]. There seem to be an urgent need of educating not only the population but also cardiac physicians so that better management can be provided for CAD patients with prolonged comorbid DM who are undergoing coronary angiography.

Limitations. The minimum age of the patients included in our study was 35 years, maximum age was 70 years. Individuals under the age of 35 were excluded from the study merely because atherosclerosis is a chronic process and it takes time for the plaque to develop, and type 2 DM is found mostly in adulthood and middle-aged people. Genetic and sedentary lifestyle are those factors which cause the plaque to build up slowly in arteries as the age progresses forward. By the time the patient grows to middle age or older, enough plaque has been built up to cause signs and symptoms. Our second limitation was that we excluded patients over 70 years of age since the interaction of DM with CAD could not be found for this cohort. Our third and one of the key limitations was cross-sectional nature of the study with a single center coverage, i.e. our center studied geographically distinct south Asian population, so our results should not be extended to another ethnic group who have high incidence of type 2 DM. Lastly it should be kept in mind that our results only correspond to the angiographic assessment of the presence, severity and extent of CAD, other imaging techniques to evaluate the presence and extent of CAD

such as intravascular ultrasound or optical coherence tomography may yield different result.

Recommendations. In our society there is need to develop a program for people to give awareness regarding these diseases, so that by getting information people could save their life from these diseases. Like other studies [23,24], we also found statistically significant correlation in DM duration and CAD severity.

Conclusion. DM duration is positively associated with the modified Gensini score and the significant determinants of CAD severity tend to be relevant. The incidence of CAD also increased, as the length of DM increased. Given this significant correlation relationship, not only the presence of DM but also its duration should be considered for the risk stratification of patients.

Conflict of Interest / Funding: The authors declare that they have no conflicts of interest, and there are no funders for this submission.

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Визначення кореляції між тривалістю цукрового діабету і тяжкістю ішемічної хвороби серця у пацієнтів, яким проводять коронарну ангіографію

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Резюме

Вступ. Ішемічну хворобу серця (ІХС) спричиняє атеросклеротичний процес у коронарних артеріях. Через підвищений ризик атеросклерозу в пацієнтів із цукровим діабетом (ЦД) його також вважають судинним захворюванням. Цукровий діабет є основним безпосереднім чинником ризику розвитку серцево-судинних захворювань, і в деяких дослідженнях, проведених у країнах з високим рівнем доходів, повідомлялося про кореляцію між тривалістю ЦД і тяжкістю ІХС. Однак даних з Пакистану обмаль.

Мета – визначити кореляцію між тривалістю ЦД і тяжкістю ІХС у пацієнтів, у яких проводили коронарну ангіографію у спеціалізованому закладі лікування серцевих захворювань.

Матеріали та методи. Це перехресне дослідження проводили у кардіологічному відділенні Громадської лікарні Карачі за участю 160 пацієнтів із супутнім ЦД, яким було призначено коронарну ангіографію. Кореляцію між тривалістю ЦД і тяжкістю ІХС (яку оцінювали за модифікованою шкалою Gensini) вимірювали за допомогою статистичних методів і описували з використанням коефіцієнта кореляції Пірсона (r).

Результати. Було продемонстровано суттєву кореляцію між тривалістю ЦД і загальним показником Gensini: r = 0,759 та p = 0,000001. Зі збільшенням тривалості ЦД тяжкість ІХС також збільшувалася.

Висновки. Тривалість ЦД прямо пропорційна показнику за модифікованою шкалою Gensini, і важливі детермінанти тяжкості ІХС зазвичай є актуальними.

Ключові слова: *атеросклероз, модифікована шкала Gensini, серцево-судинне захворювання, супутнє захворювання.*

Стаття надійшла в редакцію / Received: 13.03.2024
Після доопрацювання / Revised: 10.04.2024
Прийнято до друку / Accepted: 20.06.2024