

Angiographic Severity of CAD in Patients with Acute Coronary Syndrome in Correlation to their Glycemic Status

ARZ MUHAMMAD¹, ASMA NIZAM², MUHAMMAD HANNAN YOUSUF³, HASEEB KAMRAN⁴

¹Senior Registrar Cardiology, Shaikh Zayed Hospital Lahore

²Senior Registrar Medicine, Lahore General Hospital, Lahore

³MO, Basic Health Unit Pind Makko

PGR Cardiology, Mayo Hospital Lahore

Correspondence to Dr. Asma Nizam, Email: asmanaveed-2009@yahoo.com, Ph.. 0332-2368486

ABSTRACT

Background : Atherosclerotic vascular diseases, which comprises coronary heart disease and cerebrovascular disease is a major global health burden. Diabetes is considered as an independent risk factor for coronary artery disease and cardiovascular diseases.

Aim: To assess the severity of CAD by coronary angiography in pre-diabetic, diabetic and non-diabetic patients presenting with acute coronary syndrome

Method: A total of 412 patients admitted with acute coronary syndrome in the study period who subsequently underwent coronary angiogram were included in the study that satisfied the inclusion and exclusion criteria. All patients were medically stabilised and subjected to coronary angiogram as an when it was indicated. The angiographic severity of the coronary artery disease was assessed using the Gensini score.

Results: The severity of CAD was higher in Diabetics with a mean gensini score of 47.1, followed by Pre diabetics with 41.5 and Non diabetics with comparatively lower involvement of severity of CAD with a mean gensini score of 38.5. (P value 0.049) .The severity of CAD was higher in patients with diabetes for more than 5 years. There was statistically significant correlation between the duration of diabetes and severity of CAD in diabetics

Conclusion: Diabetics had greater severity of CAD compared with pre diabetics and non diabetics although there was no significant correlation between level of glycemic control and severity of CAD

Keywords: Gensini score, coronary artery disease (CAD), Glycemic control

INTRODUCTION

Atherosclerotic vascular diseases, which comprises coronary heart disease and cerebrovascular disease is a major global health burden. They constitute 21.9 per cent of total deaths globally and are projected to increase further to 26.3 per cent by 2030¹. The prevalence of diabetes is a global health burden. The overall prevalence is expected to rise from 285 million in 2010 to 438 million by the year 2030². While diabetes poses a huge economic burden to all nations, developing countries bear the highest burden since more than 80% of cases occur in these countries. Diabetes is considered as an independent risk factor for coronary artery disease and cardiovascular diseases. As per NCEP ATP III guidelines, diabetes is considered as a coronary artery disease equivalent³. Diabetes affects the endothelium and the glycation products get denatured and accelerate the process of atherosclerosis. Diabetic patients when compared to non-diabetics have increased risk of developing vascular complications and have two to four fold risk of developing coronary artery disease (CAD)⁴. They are more likely to develop vascular complications, affecting all the major organs of body. Cardiovascular diseases constitute one of the major cause of mortality and morbidity in diabetics, accounting for nearly 65-75% of deaths^{5,6}. The results of Framingham study reveals a 2 fold risk of cardiovascular death in men and 4-5 fold risk of cardiovascular death in women with diabetes. They constitute the major cause of death in adult diabetic patients. Diabetics are likely to have low HDL levels than people without DM. Low HDL levels have been strongly associated with elevated risk for CAD². Nearly 75% to 80% of deaths in diabetic patients are due to coronary artery

disease, cerebrovascular accidents and peripheral vascular disease. Major risk factors which contribute towards cardiovascular diseases among diabetics are hypertension, dyslipidemia, hyperglycemia and obesity. There has been a direct correlation between cardiovascular complications and chronic hyperglycemia in various interventional studies^{7,8}. The state of chronic hyperglycemia has been now measured by HbA1c, which averages the blood sugar levels of both fasting and postprandial states^{9,10}. Diabetes affects both the vascular system and the myocardium of the heart. CAD is the most common cardiac manifestation in diabetic patients, followed by dilated cardiomyopathy and autonomic cardiovascular neuropathy. Women who have diabetes lose their protection against coronary artery disease¹¹. Cardiovascular disease accounted for 65% of death in women with diabetes in a western based population study¹². In OASIS study¹³ it was found that diabetes increased the mortality risk by 57.6% and in the FINISH study it was observed that men with diabetes had 28 day mortality risk of 58%¹⁴. The relation between diabetes and CAD was further supported by the INTERHEART study¹⁵. Presenting high blood sugar levels has been considered as an independent risk factor of death in patients with or without diabetes¹⁶. 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 CAD in both diabetics and non-diabetics. It has been proved in many studies that diabetes increases the mortality risk in CAD. 3 The varying patterns of involvement of CAD in patients in relation to their glycemic status was studied in detail in a point to analyse any profound differences existed in the prediabetic

group. The severity of coronary artery involvement in diabetics, prediabetics and non-diabetics were assessed quantitatively by means of GENSINI score ¹⁷ [Angiographic severity score] in our study. We have analysed the changes in patterns of CAD in patients according to their glycaemic status. The quantitative comparison of CAD and its influence by blood sugar levels and glycaemic status has been analysed in this study.

MATERIALS AND METHODS

This study was undertaken in Medical unit 01 of lahore general hospital and cardiology department mayo hospital lahore between August 2018 to February 2019. A total of 412 patients admitted with acute coronary syndrome in the study period who subsequently underwent coronary angiogram were included in the study that satisfied the following criteria.

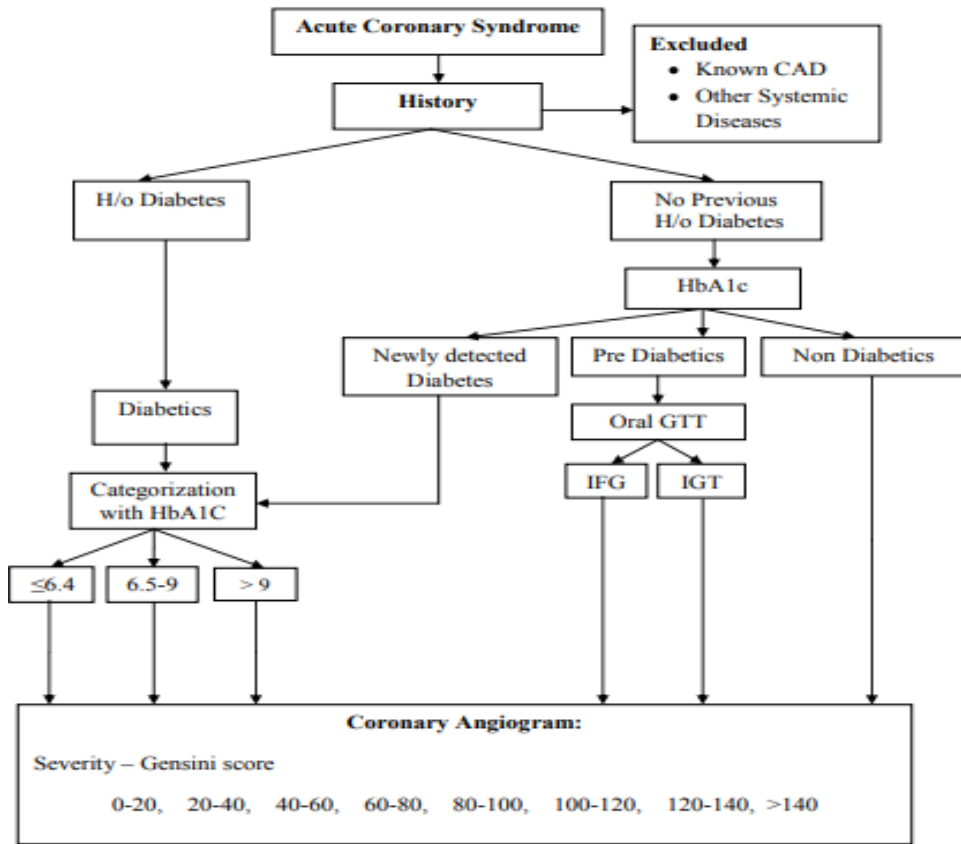
Inclusion Criteria: Patients admitted with acute coronary syndrome (STEMI, NSTEMI , Marker positive unstable angina) who underwent invasive coronary angiogram were included in the study

Exclusion Criteria:

1. Patients with known ischemic heart disease and proven CAD.
2. Patients with anaemia, renal failure or other known systemic illness.

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, diabetics and pre diabetics according to their HbA1c levels. Diabetic patients were subcategorized according to their hbA1c levels (good control = <6.5, sub optimal control = 6.5-8.9, poor control = >9). Those patients in pre-diabetic range were evaluated with FBS, PPBS, subjected to oral GTT if necessary and subcategorized into impaired fasting glucose, impaired glucose tolerance or both. All patients were medically stabilised and subjected to coronary angiogram as an when it was indicated. The angiographic severity of the coronary artery disease was assessed using the Gensini score. Proper consent was obtained from individuals enrolled into the study. Ethical clearance was obtained as per institution norms. Statistical analysis was assessed using Mean ± standard deviation, Pearson’s correlation coefficient, Chi square test and ANOVA tests using SPSS software

FLOW CHART OF THE STUDY



RESULTS

There were 412 patients with first time ACS in the study population. Of them 213 were Diabetics, 123 were non-diabetics, and 76 were pre diabetics. There was male predominance in all the study groups, with the highest noted in non-diabetics with 6.23:1. Mean Age at presentation was higher in diabetics with 56.3 years. In all the 3 groups, patients in age group between 46-60 years were mostly affected. There were no patients above 75 years in the prediabetic group. In patients above 61 years most of them were non-diabetics. There were no notable differences in the presenting symptom among the study groups. Most common symptom being chest pain and sweating in all the 3 groups. Of the ACS distribution, majority of the patients in all the 3 groups presented with ST elevation myocardial infarction. STEMI presentation was particularly higher in Non diabetics, compared to other groups. Whereas NSTEMI and unstable angina were higher in diabetic group. However it failed to prove statistical significance. Obesity was more prevalent in pre diabetics, followed by diabetics. Hypertension was more prevalent in diabetics. There was no much variation in the prevalence of smoking in the study groups. There was no much observational variation in the levels of total cholesterol in the study groups. Whereas lower levels of HDL cholesterol was noted more in Prediabetics. Very high levels of LDL cholesterol was noted in 9% of pre diabetics and 6% of Diabetics. The severity of CAD was higher in Diabetics with a mean gensini score of 47.1, followed by

Pre diabetics with 41.5 and Non diabetics with comparatively lower involvement of severity of CAD with a mean gensini score of 38.5 (P value 0.049) (Table 1). The severity of CAD was higher in patients with diabetes for more than 5 years. There was statistically significant correlation between the duration of diabetes and severity of CAD in diabetics (Fig. 1). There was no statistically significant correlation with the glycemic control as assessed by HbA1c levels to the severity of CAD (Fig. 2). Single vessel disease was found in 71.54% of non diabetics and 49.3% of diabetics. Triple vessel disease was more common in diabetics, whereas single vessel disease was more common in non-diabetic and pre-diabetics. These observations were statistically significant with a p value of <0.001 (Table 2).

Table 1: Angiographic severity of CAD in different groups

Group	Mean HBA1C	Mean Gensini Score
Diabetics	8.23±1.88	47.1±31.1
Pre-Diabetics	6.0±0.19	41.5±25.1
Non-Diabetics	5.40±0.30	38.45±33.9

P value 0.049

Table 2: Coronary artery involvement in different groups

	Single vessel	Double vessel	Triple vessel
Diabetics	105(49.3%)	46(21.6%)	62(29.1%)
Pre diabetics	51(67.1%)	14(18.4%)	11(14.5%)
Non diabetics	88(71.54%)	17(13.8%)	18(14.6%)

P value <0.001

Fig1: Correlation between duration of diabetes and gensini score in diabetics

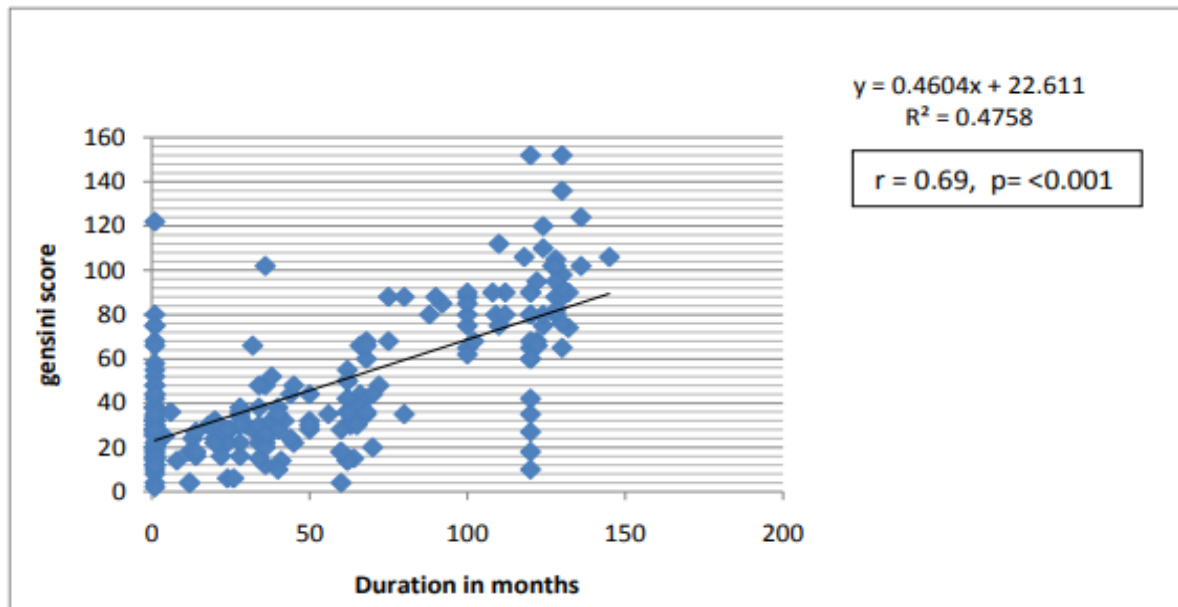
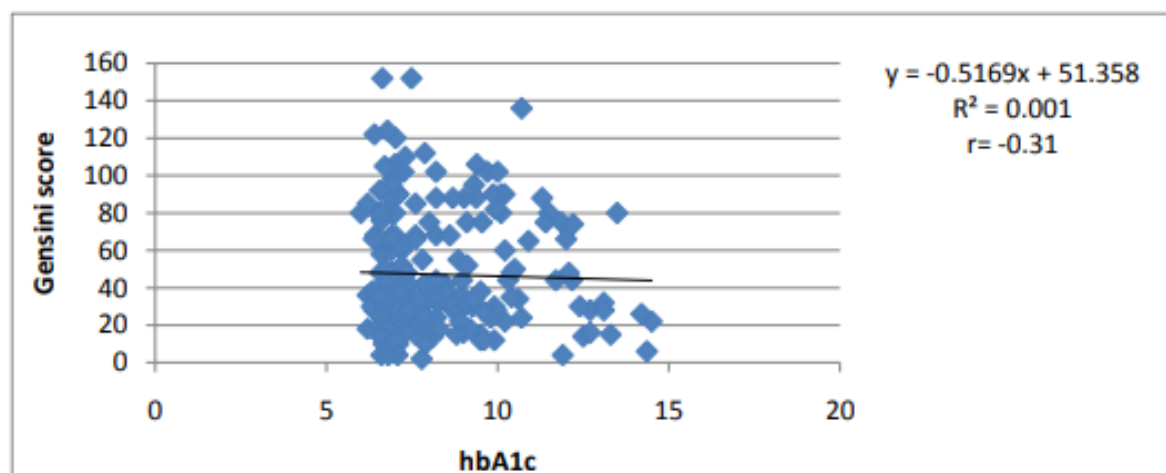


Fig 2: Correlation between HbA1c and gensini score in diabetics



DISCUSSION

A total of 412 patients admitted with first time acute coronary syndrome during the study period were analysed. Of which 213 patients were diabetics and 123 were non-diabetics and 76 were pre-diabetics. Majority of the patients were diabetics. We compared the mean age, sex, risk profile, lipid abnormalities, clinical profile, type of ACS among each group. Correlation between glycemic status according to FBS, PPBS, HbA1c levels and severity of CAD assessed by gensini score were analysed. As with other studies diabetics were the majority in our study.

In the GUSTO-1¹⁸ trial, it was observed that diabetic patients were older when compared to non diabetic patients, similar results were observed in our study. It is obvious that diabetic females had more prevalence of CAD when compared to pre-diabetics and nondiabetics. Pre-menopausal females in general have protection against IHD, but this cardio protection is lost in the presence of diabetes. A study by Soler et al¹⁹ 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. Mean HbA1c levels in diabetics was 8.23 ± 1.88 , and 6 ± 0.19 in pre-diabetic groups. We have used gensini score to estimate the severity of coronary artery disease. This gives a greater detail of assessment of CAD and does not ignore trivial lesions. Severity of CAD was higher in diabetics with a mean gensini score of 47.1 ± 31.1 , followed by pre-diabetics with a mean score of 41.5 ± 25.1 . Non diabetic patients had lesser severity of CAD with a mean score of 38.5 ± 33.9 . Our study is consistent with other studies, depicting higher severity of CAD in diabetics than in non diabetics²⁰⁻²³.

Of the 213 diabetic patients, 56 patients were newly diagnosed to have diabetes. The mean duration of diabetes was 53 months in the diabetic group. It was observed that the severity of CAD was higher in patients who had longer duration of diabetes. Patients with long standing diabetes (i.e >10 years) had more severe CAD with a mean score of 85. There was a positive linear correlation between the duration of diabetes and severity of CAD. This was

statistically significant. [Correlation coefficient $r = 0.69$, $p < 0.001$]. Studies by Tahir et al²⁴ & Syvanne et al²⁵ also found a positive linear correlation with duration of diabetes and severity of CAD. Diabetics with good glycemic control (i.e. HbA1c level <6.5) had a mean gensini score of 53.2 ± 27.8 . Patients with suboptimal control (HbA1c 6.5-8.9) and poor control (HbA1c >9) had a mean gensini score of 45.1 ± 30.9 and 50.4 ± 31.6 respectively. But this was statistically insignificant. When comparing the association between HbA1c levels to the severity of CAD in diabetic patients, there was no statistically significant correlation between them. But among pre-diabetics there was a positive linear correlation identified between the HbA1c levels and gensini score [correlation coefficient $r = 0.129$, $p < 0.01$]. Tahir²⁴ and Ayhan et al²⁶ had found positive linear correlation between HbA1c levels and severity of CAD in diabetes patients, our study did not show any relation between them.

CONCLUSION

Diabetics had greater severity of CAD compared with pre diabetics and non diabetics although there was no significant correlation between level of glycemic control and severity of CAD. A greater duration of diabetes was associated with increased severity of CAD.

REFERENCES

1. World Health Organization. World Health Statistics. Department of Measurement & Health Information Systems of the Information, Evidence and Research Cluster. Geneva: WHO Press; 2008. p. 29-31.
2. Unwin N, Whiting D, Gan D, Jacqmain O, Ghyoot G, editors. IDF Diabetes Atlas. 4th ed. Brussels: International Diabetes Federation, 2009
3. Third Report of the NCEP Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III). *Circulation*. 2002;106:3143-3421
4. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study; *JAMA* 1979; 241 : 2035-8.
5. Moss SE, Klein R, Klein BE. Cause-specific mortality in a population-based study of diabetes. *Am J Public Health* 1991; 81 : 1158-62.

6. Geiss LS, Herman WM, Smith PJ. Mortality in non-insulin-dependent diabetes. In: National Diabetes Data Group, editor. Diabetes in America, 2nd ed. Bethesda, MD: NIH & NIDDK: National Diabetes Information Clearing house; 1995. p. 233-55.
7. Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993, 329(14):977-986.
8. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR: Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000, 321(7258):405-412.
9. Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M: Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *ClinChem* 2002, 48(3):436-472.
10. Gorus F, Mathieu C, Gerlo E: How should HbA1c measurements be reported? *Diabetologia* 2006, 49(1):7-10.
11. Brezinka V, Padmos I. Coronary heart disease risk factors in women. *Eur Heart J*. 1994;15:1571–1584.
12. Geiss LS, Herman WH, Smith PJ, National Diabetes Data Group. Diabetes in America. Bethesda, Md: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 1995: 233–257
13. Malmberg K, Yusuf S, Gerstein HC, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. *Circulation*. 2000;102:1014-1019.
14. Miettinen H, Lehto S, Salomaa V, et al. Impact of diabetes on mortality after the first myocardial infarction. *Diabetes Care*. 1998;21:69-75.
15. Ceriello A, Hanefeld M, Leiter L, Monnier L, Moses A, Owens D et al. Postprandial glucose regulation and diabetic complications. *Arch Intern Med* 2004;164:2090–2095
16. Ceriello A. Acute hyperglycemia: A new risk factor during myocardial infarction; *European Heart J* 2005; 26(4): 328-31.
17. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. *Am J Cardiol* 1983;51:606.
18. Mak.K.H., Granger C.B., Miller D.P., et al — Influence of Diabetes Mellitus on Clinical Outcome in the thrombolytic era of Acute Myocardial Infarction – GUSTO – 1 Investigationsll *J.Am.Coll.Cardiol*1997; 30 : 171-179
19. Mak.K.H., Granger C.B., Miller D.P., et al — Influence of Diabetes Mellitus on Clinical Outcome in the thrombolytic era of Acute Myocardial Infarction – GUSTO – 1 Investigationsll *J.Am.Coll.Cardiol*1997; 30 : 171-179
20. Mahdi Moosavi MD, Ebrahim Nematipour MD and Maryam Mehrpooya MD Comparison of Extent of Coronary Artery Disease in Angiography of Diabetics and Non-Diabetics: *Iranian heart journal*, volume 4. 129.
21. V. Peppes, A. Panoutsopoulos, G. Rammos, N. Zakopoulos; The association of diabetes mellitus with the severity of angiographic findings in patients with newly diagnosed coronary artery disease; *Arch Hellen Med*, 28(2), March-April 2011, 245-250
22. Parvin T, Haque KS, Siddique MA, Habib SA, Rahman M, Rahman MH, Sultan MA, Hoque MH. Angiographic Severity of Coronary Artery Disease in Diabetic and Non-Diabetic Patients in a Tertiary Care Centre. *University Heart Journal*. 2014;10(1):13-7.
23. Ghaffari S, Niafar F, Separham A, Niafar M, Pourafkari L, Nader ND. Association between HbA1c levels with severity of coronary artery disease and short-term outcomes of acute ST-elevation myocardial infarction in nondiabetic patients. *Therapeutic advances in cardiovascular disease*. 2015 Oct;9(5):305-13.
24. Tahir Saleem, Kazim Hameedullah Mohammad, Moataz M Abdel-Fattah and Abdul; Association of glycosylated haemoglobin level and diabetes mellitus duration with the severity of coronary artery disease; *Diabetes and Vascular Disease Research* 2008 5: 184
25. Syväne M, Pajunen P, Taskinen MR. Determinants of severity and extent of coronary disease in type 2 diabetic nondiabetic patients (abstr). *Diabetologia* 1997;40(suppl 1):A29.
26. Ayhan SS, Tosun M, Ozturk S, Alcelik A, Ozlu MF, Erdem A, Erdem K, Erdem FH, Yazici M; Glycated haemoglobin is correlated with the severity of coronary artery disease independently of traditional risk factors in young patients; *Endokrynol Pol*. 2012;63(5):367-71.A.