Association of Glycated Hemoglobin (HbA1c) with Coronary Artery Disease In Non-Diabetic Patients: An Institutional Based Study

Mahesh Pal Khatri[1], Vijayta Modi[2]*

[1]Consultant Physician, Shri Ram Hospital, Bikaner, Rajasthan, India.
[2]*Assistant Professor, Department of Pathology, S. P. Medical College, Bikaner, Rajasthan, India.

ABSTRACT

Background: Elevated glycosylated hemoglobin A1c (HbA1c) is associated with increased risk of atherosclerosis and cardiovascular mortality in diabetic patients. In the present study, we examined the association between HbA1c and presence of angiographically proven coronary artery disease (CAD), its severity and complexity in non-diabetic subjects.

Materials & Methods: A Hospital based Observational Study done on 300 patients in Department of Medicine & Department of Pathology in S. P. Medical College & associated group of hospitals at Bikaner, Rajasthan. Assessment of the severity of coronary artery disease was done using Gensini score.

Results: Among total number of 150 screened patients as non-diabetics, 10 patients were excluded as fasting blood sugar > 126mg/dl or HbA1c more than 6.5%, 5 patients were excluded because no evidence of CAD. Among 135 patients included, male gender pre dominated (81.48%). Most of patients were overweight with mean BMI = 27.5±4.9.The most common cause of performing coronary angiography was unstable angina (45.18%). The Gensini score ranged from (1 to 168) with a mean of 33.95 ± 32.9. 100 patients were in high risk group with (HbA1c 5.7 – 6.4%) while only 35 patients were in low risk group with (HbA1c <5.7%).

Conclusion: We concluded that HbA1c level is a useful marker and has a prognostic value to predict the severity of CAD among non-diabetic patients.

Keywords: Glycated Hemoglobin, Coronary Artery Disease, Gensini Score.

*Correspondence to:

Dr. Vijayta Modi,
Assistant Professor,
Department of Pathology,
S. P. Medical College, Bikaner, Rajasthan, India.

Access this article online	
Website: www.ijmrp.com	**Quick Response code**
DOI: 10.21276/ijmrp.2018.4.3.036	

INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disorder that is caused by the raised concentration of glucose in the circulation due to the acquired and/or hereditary depict the insulin levels in blood, which were produced by pancreas.[1] According to the World Health Organization, the incidence of diabetes mellitus was 4.7% individual who have older than 18 years globally in 1980 while it increases to 8.5% in 2014. This metabolic disease was increased rapidly in lower and middle economical countries.[2]

The association between Type 2 Diabetes Mellitus and a higher incidence of coronary artery disease is well known.[3] A positive correlation has been reported between the duration of diabetes and the risk of developing CAD (coronary artery disease).[4] Studies of small sample size have shown an association between the metabolic control and duration of diabetes and the severity of coronary artery disease in subjects with diabetes.[5]

Normal fasting blood glucose level were high plus raised hemoglobin A1c (HbA1c) levels in non-diabetics patient considered as overindulgence risk factors for cardiovascular events.[6] Glycated hemoglobin values reflect two to three months average endogenous exposure to glucose including postprandial spikes in blood glucose level and have low intra-individual variability particularly in non-diabetic patients.[7] Studies suggest that coronary artery disease and HbA1c are predictors of cardiovascular mortality.[8]

Elevated glycosylated hemoglobin A1c (HbA1c) is associated with increased risk of atherosclerosis and cardiovascular mortality in diabetic patients. The association between HbA1c and cardiovascular risk is inconsistent in non-diabetic subjects. In the present study, we examined the association between HbA1c and presence of angiographically proven coronary artery disease (CAD), its severity and complexity in non-diabetic subjects.

Garg N and colleagues showed that in non-diabetics, HbA1c level has a linear incremental association with ASCVD.[9] Nonetheless, data from the Emerging Risk Factors Collaboration revealed that HbA1c merely added little incremental benefit for ASCVD risk prediction in patients without known ASCVD and diabetes.[10]

In light of previous findings, our current study was designed to evaluate whether HbA1c level was associated with the severity of coronary artery diseases (CAD) in populations without diagnostic diabetes.

MATERIALS & METHODS

A Hospital based Observational Study done on 300 patients in Department of medicine & Dept. of Pathology in S.P. Medical College & associated group of hospitals at Bikaner, Rajasthan.

Inclusion Criteria

- All non-diabetic with HbA1c < 6.5%.
- All patients with proven CAD angiographically.

Exclusion Criteria

- Patient with history of diabetes.
- HbA1c > 6.5%.
- Previous history of CAD, CABG or PTCA.
- Co-morbidities like sepsis, hemoglobinopathy or chronic kidney disease were excluded from the study.
- Patient who didn't give their consent.

METHODOLOGY

Coronary Angiogram

The diagnostic procedure was performed using Seldenger's technique, all images were recorded digitally. Assessment of the severity of coronary artery disease was done using Gensini score.[10] Gensini score grades narrowing of the lumen of the coronary artery and scores it with numerical values with the following method; score 1 for 1–25% narrowing, 2 for 26–50% narrowing, 4 for 51–75%, 8 for 76–90%, 16 for 91–99%, and 32 for a completely occluded artery. This score is then multiplied by a factor that represents the importance of the lesion's location in the coronary artery system. For the location scores, 5 points were given for the left main lesion; 2.5 for the proximal left anterior descending (LAD) or left circumflex (LCX) artery; 1.5 for the mid segment LAD and LCX; 1 for the distal segment of LAD and LCX, first diagonal branch, first obtuse marginal branch, right coronary artery, posterior descending artery, and intermediate artery; and 0.5 for the second diagonal and second obtuse marginal branches. Gensini score was expressed as the sum of the scores for all three coronary arteries to evaluate the entire extent of coronary artery disease. Appropriate statistical tests will be used to find significant association. p-value <0.05 will be considered statistically significant.

Table 1: Gensini score

% of stenosis	Score
25% stenosis	1
26-50% stenosis	2
51-75% stenosis	4
76-90% stenosis	8
91-99% stenosis	16
Totally occluded artery	32
The score is then multiplied by a factor according to the importance of the coronary artery as follows:	
Left main stem lesion	5
Proximal LAD and proximal LCX	2.5
Mid LAD lesion	1.5
Distal LAD, mid and distal LCX and RCA lesions	1
Any branch	0.5

Table 2: Demographic data of both groups

Variables	High risk(n=100)74.07%	Low risk (n=35)25.92%	p
Age	53.7±6.8	51.4±8.4	>0.05
Male	82 (82%)	28 (80%)	
Hypertension	36 (36%)	14 (40%)	
Smoking	76 (76%)	23 (65.71%)	
Family history	27 (27%)	5 (14.28%)	
BMI	27.89±4.4	27.12±5.1	

Table 3: Clinical, Laboratory Data Of Both Groups

Variables	High risk(n=100)74.07%	Low risk (n=35)25.92%	p
Unstable angina (%)	38 (38%)	23 (65.71%)	<0.05
NSTEMI (%)	26 (26%)	7 (20%)	
STEMI (%)	36 (36%)	6 (17.14%)	
FBG(mg/dl)	95.1±11.7	91.3±10.4	>0.05
TC(mg/dl)	188.7±38.9	185.6±4.5	>0.05
TGs(mg/dl)	146.2±55.1	150.3±60.4	>0.05
LDL(mg/dl)	123.2±23.7	118.7±36.2	>0.05
HDL(mg/dl)	36.1±5.7	36.4±4.3	>0.05
Creatinine(mg/dl)	1.03±0.22	1.03±0.21	>0.05

Table 4: Echocardiographic Data of Both Groups

Variables	High risk(n=100)74.07%	Low risk (n=35)25.92%	p
LVEF	55.2±7.5	57.2±9.4	>0.05
RWMSI	1.16±0.2	1.19±0.3	>0.05
Gensini score	44.5±36.1	23.4±16.8	<0.05

Table 5: Correlation between HbA1c and Gensini score, LVEF and RWMSI

		Gensini score	LVEF	RWMSI
HbA1c	**Correlation coefficient**	0.36	-0.04	-0.08
	Sig. (2-tailed)	<0.05	.>0.05	>0.05
	N	135	135	135

RESULTS

Among total number of 150 screened patients as non-diabetics, 10 patients were excluded as fasting blood sugar > 126mg/dl or HbA1c more than 6.5%, 5 patients were excluded because no evidence of CAD.

Among 135 patients included, male gender pre dominated (81.48%). Most of patients were overweight with mean BMI = 27.5 ± 4.9. The most common cause of performing coronary angiography was unstable angina (45.18%). The Gensini score ranged from (1 to 168) with a mean of 33.95 ± 32.9. 100 patients were in high risk group with (HbA1c 5.7 – 6.4%) while only 35 patients were in low risk group with (HbA1c <5.7%) (table 2, 3 & 4). Using Pearson's correlation coefficients, the level of HbA1c was strongly correlated with Gensini score (r=0.36, P<0.05) while HbA1c was weakly correlated with either RWMSI (r= -0.08, p>05) or LVEF (r= -0.04, p>0.05) (table 5).

DISCUSSION

The current study aimed to assess the correlation between HbA1c level among non- diabetics who underwent coronary angiography and the severity of CAD. We concomitantly evaluated the relationship between HbA1c level and CAD severity including clinical scenario severity and the number of coronary artery stenosis. Consistent with previous studies, our results demonstrated that Gensini score was found to be significantly higher in the high risk group. HbA1c is positively correlated with the severity of CAD (r=0.36, P<0.05). Because of increased HbA1c level could reflect more generation of advanced glycosylation end-product, which might subsequently attached to vessel wall causing endothelial dysfunction and oxidative stress promotion.[11] On the other hand, the binding of advanced glycosylation end-product might also result in inflammatory cytokines such as CRP over-production.[12] Increased CRP level has been found significantly associated with the instability of plaque.[13] Finally, increased advanced glycosylation end-product could interfere with endogenous fibrinolytic system which might result in higher risk of coronary artery stenosis.[14]

In non-diabetic patients, the predictive value of HbA1c for CAD severity was observed in previous trials since 2004. In the trial of Khaw et al, patients with HbA1c concentrations less than 5% had the lowest rates of cardiovascular disease and mortality. An increase in HbA1c of 1% was associated with a relative risk for death from any cause of 1.24 (95% CI, 1.14 to 1.34; P < 0.001).[15]

Rivera et al studied the association between increasing levels of HbA1c and coronary plaque characteristics in asymptomatic individuals who diagnosed as non-diabetics. Unadjusted analysis showed a positive association between increasing levels of HbA1c and the number of coronary segments (p<0.0001). The association persisted even when traditional risk factors were taken into account.[16]

In contrast to the results of previous trials , Ahmet G et al in 2013 showed no significant relationship between HbA1c level and CAD severity (p = 0.299) in 65 non diabetic patients with acute myocardial infarction. They concluded that the extent of CAD did not differ significantly among subjects with normal glucose tolerance, impaired fasting glucose, or impaired glucose tolerance.[17]

CONCLUSION

We concluded that HbA1c level is a useful marker and has a prognostic value to predict the severity of CAD among non-diabetic patients. It may be used as a cardiac marker in risk stratification of non-diabetic patients presenting with acute coronary syndrome and indicated for coronary angiography.

REFERENCES

1. Wang W, Guo Y, Liao Z, Zou DW, Jin ZD, Zou DJ, et al. Occurrence of and risk factors for diabetes mellitus in Chinese patients with chronic pancreatitis. Pancreas. 2011; 40: 206-12.
2. Global report on diabetes. World Health Organization, Geneva, 2016 [online database]. (accessed 18 December 2016). (http://www.who.int/mediacentre/factsheets/fs312/en/,
3. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013.GBD 2013 Mortality and Causes of Death Collaborators. Lancet. 2015;385:117.
4. Barrett-Connor E. Does hyperglycemia really cause coronary heart disease? Diabetes Care. 1997; 20: 1620-1623.
5. Castelli WP. Cardiovascular disease in women. Am J Obstet Gynecol. 1998; 158: 1553-1560, 1566-7.
6. Nasir K, Santos RD, Tufail K, Rivera J et al. High normal fasting blood glucose in non-diabetic range is associated with increased coronary arery calcium burden in asymptomatic men. Atherosclerosis, 2007; 195:e155-e160.
7. Selvin E, Crainiceanu CM, Brancati FL, Coresh J. Short-term variability in measures of glycemia and implications for the classification of diabetes. Arch Intern Med. 2007; 167:154.
8. Rossing P, Hougaard P, Borch-Johnsen K, Parving HH (1996) Predictors of mortality in insulin dependent diabetes: 10 year observational follow up study. BMJ 313: 779-784.
9. Garg N, Moorthy N, Kapoor A, Tewari S, Kumar S, Sinha A, et al. Hemoglobin A(1c) in nondiabetic patients: an independent predictor of coronary artery disease and its severity. Mayo Clin Proc. 2014;89(7):908–16.
10. Ayhan SS, Tosun M, Ozturk S, Alcelik A, Ozlu MF, Erdem A, et al. 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.
11. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism.Diabetes, 2005 ; 54:1615–1625.
12. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med, 2005; 353:2643–2653.

13. Geluk CA, Post WJ, Hillege HL, Tio RA, Tijssen JG, van Dijk RB. C-reactive protein and angiographic characteristics of stable and unstable coronary artery disease: data from the prospective PREVEND cohort. Atherosclerosis 2008; 196:372–382.

14. Dunn EJ, Philippou H et al. Molecular mechanisms involved in the resistance of fibrin to clot lysis by plasmin in subjects with type 2 diabetes mellitus. Diabetologia 2006; 49:1071–1080.

15. Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk.Ann Intern Med,2004 ;141(6):413.

16. Riveraa, Eue-Keun Choib et al. Association between increasing levels of hemoglobin A1c and coronary atherosclerosis in asymptomatic individuals without diabetes mellitus Juan J. Coronary Artery Disease2010 ; 21:157–163.

17. Ahmet Göktuğ Erte et al. Relationship between HbA1c levels and coronary artery severity in nondiabetic acute coronary syndrome patients. Arch Turk Soc Cardiol, 2013; 41:389-395.

Cite this article as: Mahesh Pal Khatri, Vijayta Modi. Association of Glycated Hemoglobin (HbA1c) with Coronary Artery Disease In Non-Diabetic Patients: An Institutional Based Study. Int J Med Res Prof. 2018 May; 4(3):169-72.
DOI:10.21276/ijmrp.2018.4.3.036