Association of Glycosylated Haemoglobin Level with the Severity of Coronary Artery Disease in NSTEMI Diabetic Patients

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Key Words : *HbA_{1C}, Coronary Artery Disease.*

Abstract:

Background: *Relation between diabetes mellitus and ischemic heart disease is well established. But the effect of HbA_{1C} on severity of coronary artery disease remains uncertain in non-ST elevation myocardial infarction and diabetic patient. Objective of our study was to know the relationship of HbA_{1C} with the severity of coronary artery disease.*

Methods: *In this cross sectional analytical study a total of 104 NSTEMI diabetic patients were enrolled by purposive sampling. They were divided into two groups according to the level of HbA_{1C}, Group-I patients having HbA_{1C}<7% and Group-II patients having HbA_{1C} ≥7%. Vessel score and Gensini score was calculated from coronary angiogram and compared between groups.*

Results: *Single vessel disease were significantly higher in group-I compared to Group-II(38.5% vs 7.7% in Group-I vs Group-II,p<0.05). Double vessel disease were higher in group-II compared to Group-I but the difference was statistically not significant (42.3% vs 48.1% in Group-I vs Group-II respectively (p>0.05). Triple vessel disease were significantly higher in group-II compared to Group-I (19.2% vs 44.4% in Group-I vs Group-II,p<0.05). Mean Vessel score was higher in Group-II compared to Group-I(1.73 ± 0.86 vs 2.50 ±0.70 in Group-I vs Group-II, p<0.05). Mean Gensini score was higher in Group-II compared to Group-I (44.6 ± 38.4 vs 76.9 ± 44.6 in Group-I vs Group-II, p<0.05). There were significant positive linear correlation between HbA1C and Vessels score and Gensini score (p<0.05).*

Conclusion: *This study may be concluded that the presence of HbA_{1C} ≥7% are associated with of severe coronary artery disease in NSTEMI with diabetes mellitus.*

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Introduction:

Cardiovascular diseases are leading cause of mortality and morbidity in industrialized countries, and they are also emerging as a prominent public health problem in developing countries.[1] between 1990 and 2020 ischaemic heart disease (IHD) mortality is expected to increase by 120 percent in women and by 137 percent in men in developing countries. It is estimated that the annual number of the deaths caused by IHD in developing countries will rise to 11.1 million in 2020.[2]

Non ST-segment elevation myocardial infarction (NSTEMI) & unstable angina are more heterogeneous in their presentation & may be poorly characterized in clinical practice, leading to greater variation in diagnosis & treatment.[3] Among patients with UA or NSTEMI, approximately 15% will die or have a reinfarction within 30 days of diagnosis.[4]

Diabetes mellitus (DM) is becoming a pandemic worldwide. The worldwide number of people with DM is expected to double in thirty years, increasing from 171 million in 2000 to 366 million in 2030. The highest percentages of increases in disease prevalence are likely to be in developing nations, with major increases in the Middle-East, Sub-Saharan Africa, South Asia, and Latin America.[5]

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WHO listed 10 countries to have the highest numbers of people with DM in 2000 and 2030. According to this report, Bangladesh has 3.2 million of diabetic subjects in 2000 and the number is expected to increase to a staggering 11.1 million by 2030 placing her among the top 10 countries with DM.[5]

In a study Rahim showed a significant increase in the prevalence of DM in rural Bangladesh from 2.3% to 6.8% over 5 years.[6] In another study Akter showed the prevalence of DM in the rural population of Bangladesh is 7.2%.[7] DM is associated with an increased risk of cardiovascular morbidity and mortality, therefore as the prevalence of DM increases there will also be a corresponding increase in morbidity and mortality from cardiovascular disease.[8]

The incidence of DM in patients hospitalized with myocardial infarction ranges between 10–20% and approximately 40% have impaired glucose levels.[9,10] Patients with DM and myocardial infarction have greater incidence of major adverse cardiovascular events, higher in-hospital and long term mortality.[9]

Diabetic patients have a higher prevalence of coronary heart disease with an increased number of fatal coronary events due to a higher incidence of plaque rupture and superimposed thrombosis in diffusely diseased coronary arteries. Diabetic patients develop complications more frequently after myocardial infarction (MI) and have double the in-hospital and six-month mortality compared to non-diabetic patients.[11]

The primary outcome of ACCORD (MI, stroke, or cardiovascular death) was lower in the intensive glycemic control group, due to a reduction in nonfatal MI, but this reduction was not statistically significant when the study was terminated.[12]

Diabetes Control and Complications Trial (DCCT) had shown that, improved glycaemic control in type 1 DM is associated with a sustained decrease in microvascular, macrovascular and neuropathic complications. HbA_{1C} is a widely used marker of chronic glycemia, reflecting average blood glucose levels over a 2- to 3-month period of time.[13] International Expert Committee, after an extensive review of both established and emerging epidemiological evidence, recommended the use of the HbA_{1C} test to diagnose DM, with a threshold of <6.5%, and American Diabetic Association affirms this decision.[14]

The UKPDS-35 demonstrated that each 1% reduction in haemoglobin HbA_{1C} was associated with a 14% decrease in risk for MI.[15] Gensini suggested a scoring system which allocates a numerical value for the degree of stenosis in a coronary artery and a multiplication factor that depends on which coronary artery is involved and where the stenosis is located in the coronary artery. This provides a detailed assessment of coronary artery disease and does not ignore even very trivial lesions in coronary arteries.[16] Among diabetic patients there was a positive significant correlation between Gensini score and HbA_{1C}. Poor control of DM, as measured by a raised percentage of HbA_{1C}, was found to be an independent predictor of severity of coronary artery disease.[17]

There was no study in our country regarding the association of the label of HbA_{1C} with the severity of coronary artery disease in NSTEMI.

Methods:

This Cross sectional, analytical study conducted in the department of Cardiology, National Heart Foundation Hospital & Research Institute, from June, 2011 to July, 2012. Objective of the study was to find out the association of HbA_{1c} with severity of IHD in NSTEMI Diabetic patients. Total 104 NSTEMI Diabetic patients were selected purposively. They were divided into two groups according to the level of HbA1c. Group-I patients having HbA1c <7% and group -II patients having HbA1c e"7% . The study protocol was approved by the ethical review board.

Angiographic pattern and severity of CAD:

After all routine investigation coronary angiogram was done during same hospital stay. Interpretations of coronary angiogram were done by visual estimation by two cardiologists to assess the severity of coronary artery disease. Severity of coronary stenosis was graded according to Vessel score and Gensini score.

A. Vessel score[18]: This is the number of vessels with a significant stenosis (for left main coronary artery 50% or greater and for others 70% or greater reduction in luminal diameter). Score ranges from

0 to 3, depending on the number of vessel involve. Left main coronary artery will be scored as single vessel disease.

Score 0 = no vessel involvement.
Score 1 = single vessel involvement.
Score 2 = double vessel involvement.
Score 3 = triple vessel involvement
B. Gensini score (Gensini, 1983)[16]:
It grades narrowing of the lumen of the coronary artery and scores it as-
1 for 1–25% narrowing,
2 for 26–50% narrowing,
4 for 51–75%,
8 for 76–90%,
16 for 91–99% and
32 - completely occluded artery.

This score is then multiplied by a factor according to the importance of the coronary artery. The multiplication factor for a left main stem (LMS) lesion is 5, it is 2.5 for proximal left anterior descending artery (LAD) and proximal circumflex artery (CX) lesions, 1.5 for a mid-LAD lesion, and 1 for distal LAD, mid / distal CX and right coronary artery lesions. The multiplication factor for any other branch is 0.5. Severity of the coronary artery disease was studied by Gensini scoring system.

Statistical Methods:
Data obtained from the study were analyzed and significance of differences was estimated by using statistical methods. Variables were analyzed by chi-square test, t-test, Mann Whitney test where applicable. Correlations were done by Pearson's correlation and Spearman's correlation where applicable. Multiple Linear regression analysis was done. P value <0.05 were considered as significant. Statistical analyses were performed with SPSS, version 17.0 (SPSS Inc).

Results:

Table-I

Distribution of the age and BMI between the Group-I and Group-II(n=104).

Variables	Group-I (n=52) Mean ± SD	Group-II (n=52) Mean ± SD	p value*
Age(years)	57.3 ±13.2	58.4 ± 10.7	.852
BMI(kg/m²)	25.5 ± 3.9	24.5 ± 2.6	.078

*t –test was done to measure the level of significance.

Table-I shows that, mean age was 57.3 ±13.2 and 58.4 ± 10.7 years in group-I and group-II respectively. The mean body mass index was 25.5± 3.9 kg/m² and 24.5 ± 2.6 kg/m² in group-I and group-II respectively. Difference was statistically not significant (p>0.05).

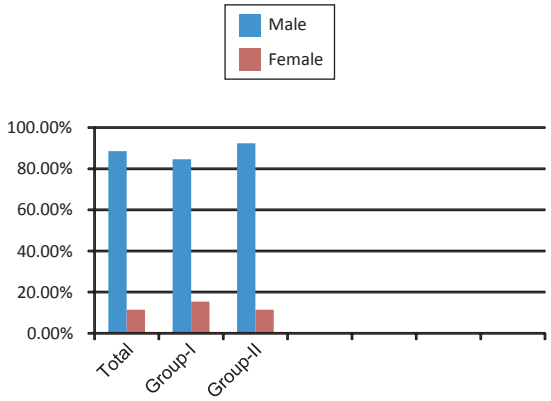

Fig -1: *Bar diagram showing the sex distribution in different groups.*

Female patients are small in number in every group. In total sample, 88.5% male and 11.5% female. In Group-I, 84.6% male and 15.4% female. In Grouop-II, 92.3% male and 11.5% female. There was no statistically significant difference between groups in terms of sex distribution (p>0.05).

Table-II

Distribution of risk factors between Group-I and Group- II (n=104)

Risk factor	Group I (n=52)		Group II (n=52)		p value*
	n	%	N	%	
Hypertension	41	78.8%	37	71,2%	.497
Tobacco use	34	65.4%	40	76.9%	.279
Dyslipidaemia	17	32.7%	21	40.4%	.542
Family H/O IHD	16	30.8%	12	23.1%	.508
Obesity	10	19.2%	3	5.8%	.072

*Chi-square test was done to measure the level of significance. Fisher's exact test was done to measure the level of significance for cell value <5.

Table II shows that hypertension was found 78.8 and 71.2% in Group-I and Group-II respectively. Tobacco user was found 65.4%, and 76.9 % respectively in Group I and Group-II. Dyslipidaemia was found 32.7% and 40.4% in Group I and Group II respectively. Family history of ischemic heart disease was found 30.8% & 23.1% in Group I and Group II respectively. Obesity was found 19.2% & 5.8 % in Group I and Group II

respectively. There was no statistically significant difference between groups in terms of risk factor distribution (p>0.05).

Table-III

Distribution of the study patients by number of coronary artery involvement between Group-I and Group-II (n=104).

Number of involved vessels	Group I (n=52)		Group II (n=52)		p value*
	n	%	N	%	
SVD	20	38.5%	4	7.7%	0.001
DVD	22	42.3%	25	48.1%	0.347
TVD	10	19.2%	23	44.2%	0.005

SVD (single vessel disease), DVD (double vessel disease), TVD (triple vessel disease).

Chi-square test was done to measure the level of significance. Fisher's exact test was done to measure the level of significance for cell value< 5.

Table-III shows that, single vessel coronary artery disease was significantly higher in Group-I compared to Group-II (38.5% and 7.7% in Group-I and Group-II respectively) (p<0.05). Double vessel coronary artery disease was higher in Group-II compared to Group-I but statistically not significant (42.3% and 48.1% in Group-I and Group-II respectively) (p>0.05). Triple vessel coronary artery disease was significantly higher in Group-II compared to Group-I(19.2% and 44.2% in Group-I and Group-II respectively). (p<0.05)

Table-IV

Distribution of Vessels score between Group-I and Group-II (n=104).

	Group-I (n=52)	Group-II (n=52)	p value
Mean ± SD	1.73±0.86	2.50±0.70	.001

* Student's t- test was done to measure the level of significance.

Table-IV shows that, Mean Vessels score was significantly higher in Group-II compared to Group-I (1.73±0.86 and 2.50±0.70 in Group-I and Group-II respectively)(p<.05).

Table-V

Distribution of Gensini score between Group-I and Group-II (n=104).

	Group-I (n=52)	Group-II (n=52)	p value
Mean±SD	44.6±38.4	76.9±44.6	.001
Median	26	73	

* Mann Whitney test was done to measure the level of significance.

Table-V shows that, Mean Gensini score was significantly higher in Group-II compared to Group-I (44.6±38.4 and 76.9±44.6 in Group-I and Group-II respectively)(p<.05). Median was also higher in Group-II compared to Group-I (26 and 73 in Group-I and Group-II respectively) (p<0.05)

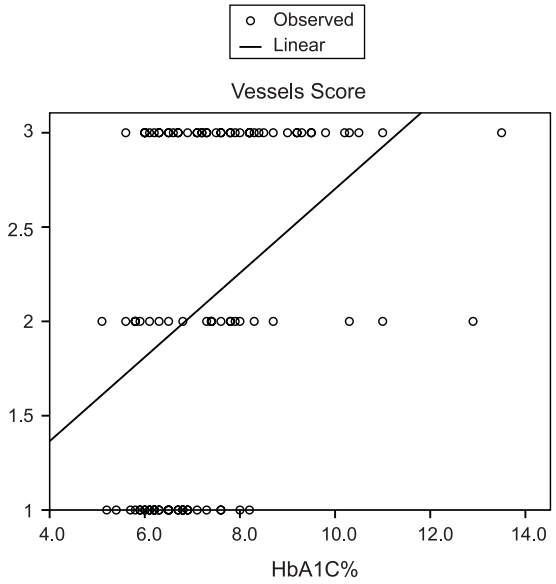

Fig.-2: *Correlation between HbA_{1C} level and Vessel score (n=104). r =.397 ,p =.001*

Figure -2 showing positive linear correlation between the level of HbA_{1C} and Vessel score. Correlation was statistically significant (p<0.05).

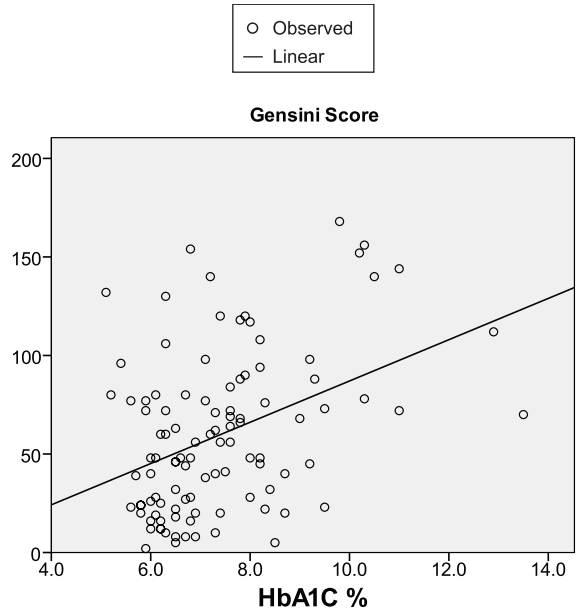

Fig 3: Correlation between HbA1C level and Gensini score (n=104). r =.350, p=.001

Figure -3 showing positive linear correlation between the level of HbA_{1C} and Gensini score. Correlation was statistically significant ($p<0.05$).

Multiple regression analysis clearly showed that HbA_{1C} was an independent factor influencing the severity of coronary artery disease.

Discussion:

In the present study, female patients formed a small percentage in every group. In Group-I only 15.4% & in Group-II only 11.4% patients were female. In Bangladesh, the various studies showed the female patients formed a small percentage (6.7% - 11.2%).[19,20] Hypertension was the commonest risk factor among the groups. The difference between the groups was not statistically significant. Hypertension was found 58.9% of patient in the study of Malik[1] and 46% of the patient in the study of Kabiruzzaman.[21] Smoking was found 65.4%, 76.9% in Group-I & Group-II. The difference between the groups was not statistically significant. Smoking was found in 81.8% of patient in the study of Malik[1] and 80% of the patient in the study of Kabiruzzaman. [21]

Single vessel coronary artery disease was significantly higher in Group-I compared to Group-II. Double vessel coronary artery disease was higher in Group-II compared to Group-I but not statistically significant. Triple vessel coronary artery disease was significantly higher in Group-II compared to Group-I. Similar result was also shown in the work of Saleem.[17]

In our study mean Vessel score was significantly higher in Group-II compared to Group-I. Mean Gensini score was significantly higher in group-II compared to group-I. Similar result was also shown in the work of Saleem.[17]

In this study, we demonstrated significantly positive linear correlation between HbA_{1C} level and Vessel score, HbA_{1C} level and Gensini score. Similar result was also shown in the work of Saleem.[17] In a multiple linear regression model was developed, it clearly showed that HbA_{1C} was an independent factor influencing the severity of coronary artery disease. Similar result was also shown in the work of Saleem.[17]

Conclusion:

From this study it may be concluded that the presence of HbA1c $\geq$7% is associated with severe coronary artery disease with multi vessel involvement in NSTEMI diabetic patients.

Conflict of Interest - None.

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