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The Utility of Screening for Pre-Diabetes and Diabetes Mellitus with Hba1c in Patients who are Admitted to the Hospital with Low or Intermediate Risk Chest Pain for Rule Out Myocardial Infraction

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Abstract

Introduction: Diabetes is considered a coronary artery disease equivalent. With its ever-increasing prevalence, early detection and management are imperative. Glycosylated Hemoglobin (HbA1c) has become the recognized marker for screening and diagnosis of diabetes.

Objective: To screen and diagnose patients for prediabetes and Diabetes Mellitus (DM), among patients admitted to the hospital with the principal diagnosis of low or intermediate risk chest pain to Rule Out Myocardial Infarction (ROMI). The study was done to emphasize the importance of diabetes screening in these patients and to include this test as part of a chest pain admission order set in our hospital.

Methods: After randomized retrospective review of 400 patients, 175 subjects with no prior diagnosis of diabetes were included. Data variables included patient demographics, Body Mass Index (BMI), TIMI® score and HbA1c results when available. BMI and HbA1c were also analyzed to previously established categories. BMI (kg/m2) was categorized as 18 to 24.9, 25 to 29.9 and 30 and above as healthy (0), overweight (1) and obese (2), respectively. HbA1c was categorized as 6.1% (normal), 6.2 to 6.4% (Impaired Glycemic Control) and 6.5% and above as DM as per our hospital criterion. Data were then summarized using descriptive statistics; chi-square and analysis of variance were performed to determine relationships between the variables.

Results: Of the 175 subjects, 18 had HbA1c greater than 6.5% (10%), 19 subjects (11%) had HbA1c greater than 6.2% (prediabetes) and 138 (79%) had HbA1c less than 6.1%. An analysis of variance comparing mean age, BMI and TIMI score by HbA1c categories revealed p-values of 0.894, 0.054 and 0.320, respectively.

Conclusion: Patients who are admitted to the hospital for low/intermediate chest pain to rule out myocardial infarction should be screened for DM using HbA1c, as we identified 18 subjects (10%) with HbA1c greater than 6.5% and 19 subjects (11%) with prediabetes as a subset of the population. We suggest that the admission order set for "Chest Pain" include HbA1c to regularly screen patients for diabetes and prediabetes and recommend close follow-up of the patients who have prediabetes with repeat HbA1c. Strong consideration should be made in screening patients with elevated BMI >30 for DM if they are admitted not just for chest pain but also for other medical ailments.

Keywords: Chest Pain;Glycosylated Haemoglobin (HbA1c); Screening of Diabetes and Diabetes Mellitus

Introduction

The volume of patients visiting Emergency Departments (ED) for evaluation of chest pain to "Rule Out Myocardial Infarction (ROMI)", is ever increasing. According to the National Centres for Health Statistics, U.S. Department of Health and Human Services, Centres for Disease Control and Prevention, the number of non-injury ED visits with chest pain as the primary reason for the visit was 5.5 million in 2007-2008 [1]. The patients admitted to Abington Memorial Hospital® for chest pain as the principle diagnosis are further risk stratified using the TIMI® score (elaborated in Table 1) for need of urgent revascularization. Based on the TIMI score, the 14-days endpoint range, based on the risk score of low to high, is 4.7% to 40.9%, respectively [2].

History Criterion	Points
Age ≥ 65	1
≥3 CAD risk factors (FH, HTN, HLD, DM, Active Smoker)	1
Known CAD (stenosis ≥50%)	1
ASA use in the past 7 days	1
Presentation Criterion	Points
Severe Angina (≥ 2 episodes in 24h)	1
Elevated cardiac biomarkers	1
EKG-ST deviation ≥ 0.5mm	1
	Total

Table 1: TIMI Score.

Abbreviations: CAD = Coronary Artery Disease, FH = Family History, HTN = Hypertension, HLD = Hyperlipidemia, DM = Diabetes Mellitus, ASA = Aspirin, EKG = Electrocardiogram, ST = Repolarization Segment on Electrocardiogram, Mm = Millimeters.

Diabetes Mellitus (DM) accounts for 1 point of the total TIMI score and hence a risk stratification criteria. The presence of DM is a significant poor prognostic factor in Coronary Artery Disease (CAD) and is considered a CAD equivalent when it comes to hyperlipidaemia management [3]. Early detection and screening are imperative for preventing multi-organ complications, which result from undiagnosed DM and poor glycaemic control.

The diagnosis of DM is primarily based on laboratory criteria which include a fasting blood glucose level ≥126 mg/dl or a random blood sugar level >200 mg/dl with symptoms of polyuria, polydipsia, fatigue and weight loss. However glycosylated HbA1C has become the recognized marker of diagnosis of DM and superior to fasting blood glucose levels or two consecutive blood sugar levels, as it does not require the patient to be in a fasting state and gives a glycaemic index of about 3 months [4,8].

As recommended by National Institute of Health and American Diabetes Association (ADA) defined HbA1C ≥6.5% as DM, HbA1C < 5.7% as normal and HbA1c 5.7-6.4% as impaired glycaemic control i.e., pre-diabetes. Within the pre-diabetes A1C range of 5.7 to 6.4%, the higher the A1C, the greater the risk of diabetes. Those with pre-diabetes are likely to develop type 2 diabetes within 10 years, but they can take steps to prevent or delay diabetes. The American Diabetes Association (ADA) recommends screening patients, who are overweight, and have high-risk race/ethnicity (e.g. Hispanic, Native-American, African-American, Pacific Islander), strong family history (first degree relative with diabetes), but also mentions that it is reasonable to screen if the clinical index of suspicion is high [5].

In 2009-2012, based on fasting blood glucose or HbA1c levels, 37% of U.S. adults aged 20 years or older had pre-diabetes (51% of those aged 65 years or older). Applying the percentage to the entire U.S. population in 2012 yields an estimated 86 million Americans aged 20 years or older with pre-diabetes. About 208,000 people younger than 20 years have DM type II or I, this represents 0.25% of all people in this age group [1].(Figure 1)

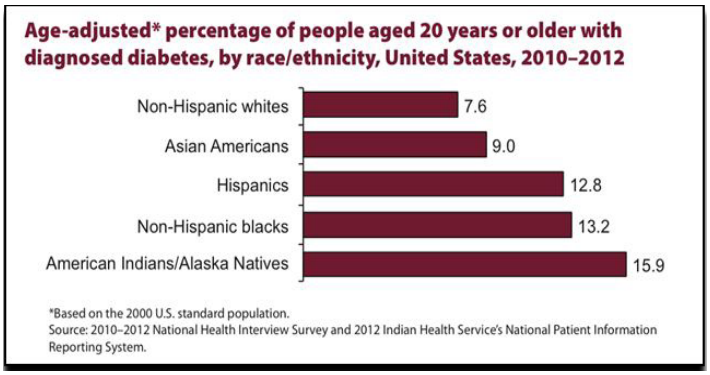

Figure 1: Age-Adjusted Percentage of People Aged 20 Years or Older with Diagnosed Diabetes, by Race/Ethnicity, United States, 2010-2012.

At Abington Memorial Hospital, our lab reports HbA1C as abnormal if ≥ 6.2% prompting physicians to institute strict glycemic control and repeat HbA1c testing in 3-4 months. Our study attempted to retrospectively "screen" patients, who had presented to the hospital with chest pain to rule out myocardial infarction, for DM and pre-diabetes using HbA1c based on risk factors included in the TIMI risk score and sex, racial ethnicity, and Body Mass Index (BMI) [6].

Methods

Study Sample

After obtaining approval from the Abington Memorial Hos-

pital® Institutional Review Board, patients who had been admitted to the ED with the principal diagnosis of chest pain between July 2013 and June 2014 were considered for the study. (Figure 2 outlines subject eligibility).

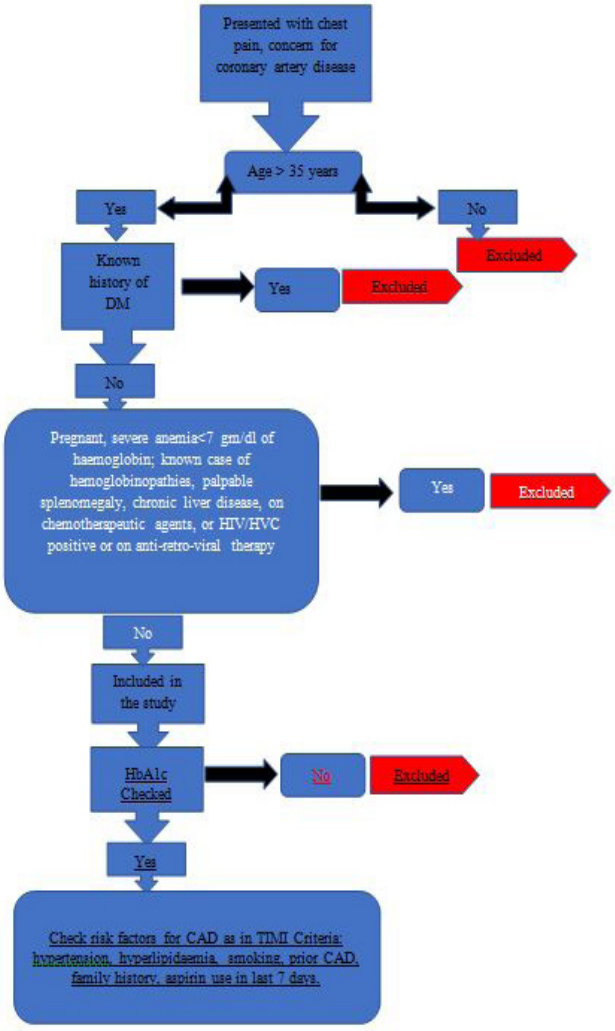

Figure 2: Selection Criteria

Protection of Subjects and Ethical Declaration

The study was per ethical standards and data collection did not pose any direct or indirect threat to the patient's management or safety. All data were recorded in a de-identified manner. All patients included in the study were assigned a unique study identification number. This study identification number cannot be linked back to identifiable information about the subject. The medical information gathered during the study was treated confidentially except as may be required by the law.

Research Design and Data Collection

This was a single-centre, retrospective cohort study looking at patients admitted to Abington Memorial Hospital with the principle diagnosis of "Rule Out Myocardial Infarction (ROMI)" from the duration of July 2013 to June 2014. About 400 charts were reviewed. Those patients who met the selection criteria outlined above were included. Data were collected and categorized as noted in the data collection form (Appendix A).

Data collection form format: Subject Number #

Data Collection Form			
1	Subject No.		
		Options	Answers
2	Age(years)	1.≥35-59years	
		2.≥ 60 years	
3	Sex	1. Male	
		0. Female	
4	Race	1 Hispanic	
		2 Native	
		3 American	
		4 African	
		American	
		5 PacificIslander	
		6 CaucasianAsian	
		7 Others_____	
5	Body Mass Index(BMI)	1. BMI ≥ 18-25(Healthy)	
		2. BMI≥ 25 -29.9(Overweight)	
		3. BMI ≥ 30(Obesity)	
6	Smoking	1. Yes	
		0. No	
		2. Ex-smoker	
7	Hypertension	0) Controlled with medicines or no hypertension	
		1) Blood pressure ≥ Systolic 140-149 or Diastolic ≥ 90-99	
		2) Blood pressure ≥ Systolic 160 or Diastolic ≥ 100	
8	Hyperlipidaemia	1) LDL ≥ 70-100	
		2) LDL ≥ 101-159	
		3) LDL≥ 160	

9	Family History of CAD	1) Yes	0) No	
10	Aspirin Use	1) Yes	0) No	
11	Prior CAD	1) Yes	0) No	
12	EKG Changes from Baseline (EKG -ST Changes ≥ 0.5mm)	1) Yes	0) No	
13	Cardiac Biomarkers:	1) Positive Troponin >= 0.10		
		0) Troponin < 0.10		
14	Angina Symptoms:	1) Yes	0) No	
15	Calculated TIMI =	1) High		
		2) Low		
		3) Intermediate (Low = 0-2, Intermediate = 3-4, High = 5-7)		
16	HbA1c:	1) HbA1c Value ≥ 6.2%		
		0) HbA1c value ≤ 6.2		

The total number of subjects eligible for the study was 175 of which 170 had complete data for all variables studied. Only 5 medical records did not have Body Mass Index (BMI) recorded after reviewing nursing profiles, height/weight recordings, or any diagnostic test, which might have had their BMI, mentioned. Hence those 5 patients were not included in the inferential statistical analyses.

Statistical Analysis

Categorical data were summarized as frequencies and percentages; continuous data as means and standard deviations. Analysis of variance was used to compare mean age, BMI, and TIMI score for subjects with HbA1c levels of ≥ 6.2% or ≤ 6.1%. Chi-square analyses were performed to determine an association between HbA1c and BMI. All data were analysed using IBM SPSS for Windows version 20.0. All p-values were two-tailed and a level of < 0.05 was considered significant. Our study is a descriptive study to determine the prevalence of diabetes and pre-diabetes in patients with ROMI and thus we did not do sample size or power calculations for this study (Table 2).

Demographic Characteristics		N (%) (N=175)
Age	≥ 35-59 ≥ 60	94 (53.7) 81(46.3)
Sex	Male Female	81(46.3) 94(53.7)
Race	Caucasian African American Hispanic Others	106(60.6) 50(28.6) 4 (2.3) 9(10.8)
Body Mass Index (BMI)	BMI ≥ 18-25 BMI ≥ 25 ≤ 29 BMI ≥ 30	53(30.3) 59(33.7) 62(35.4)
Smoking	Current Former Non-Smoker	31(17.7) 37(21.1) 107(61.1)
Hypertension	Controlled Uncontrolled	93(53.1) 82(46.9)
Hyperlipidemia	Controlled Uncontrolled	73(41.7) 102(58.3)
Family History of CAD	Positive Negative	35(20.0) 140(80.0)
Aspirin Use	Yes No	89(50.9) 86(49.1)
Prior CAD	Yes No	36(20.6) 139(79.4)
EKG Changes from Baseline	Yes No	7(4.0) 168(96.0)
Cardiac Biomarkers	Positive Negative	7(4.0) 168(96.0)
Angina Symptoms	Yes No	98(56.0) 77(44.0)
Calculated TIMI	High (5-7) Moderate (3-4) Low (0-2)	7(4.0) 48(27.4) 115(65.7)
HbA1c	≥ 6.2 % ≤ 6.1 %	37(21.1) 138(78.9)

Table 2: Descriptive Statistics for Demographic Characteristics and Other Study Variables.

Abbreviations: CAD = Coronary Artery Disease, ASA = Aspirin, TIMI = Thrombolysis in Myocardial Infarction, EKG = Electrocardiogram, BMI = Body Mass Index, N=Frequency, %= Percentage Subjects.

Results

Demographic data are presented in Table 2. Upon reviewing the subject demographics, we found that of the 175 subjects, 94 (53.7%) were females as opposed to males who traditionally have a higher risk of coronary artery disease and angina. The mean age of the subject population was observed to be 61.7±14.9 years. The other striking characteristic was that 33.7% of the subjects had BMI in the overweight range (25-29.9 kg/m2) and 35.4% were clinically obese with BMI>30 kg/m2. The mean BMI was 29.5±7.1 kg/m2 (minimum = 15, maximum =59). There was an

approximately equal distribution of typical angina pain 56%, and 44% having an atypical presentation. 65.7% of subjects had a calculated TIMI score of 0-2 (Low), 27.4% had a score of 3-4 (Moderate) and only 4% of patients had a high TIMI score (5-7). The mean TIMI score was 1.91±1.3.

The results indicate that 18 subjects had HbA1c greater than 6.5% (10%). In addition, 19 subjects (11%) had HbA1c greater than 6.2% (pre-diabetes) and 138 (79%) had HbA1c less than 6.1%. As previously mentioned, 5 patients who did not have a BMI recorded in their medical record were excluded from the inferential statistical analyses. An analysis of variance comparing mean age, BMI and TIMI score by HbA1c categories revealed a nearly significant difference in mean BMI between those subjects with HbA1c ≤6.1 % and those ≥ 6.2 % (p=0.054) (Table 3).

	HbA1c	N	Mean ± SD	95% Confidence Interval		P-value
				Lower bound	Upper bound	
Age	≤ 6.1 %	138	62.0 ± 14.9	59.3	64.3	
	≥ 6.2 %	37	61.4 ± 13.3	57	65.9	
	Total	175	61.7 ± 14.9	59.5	63.9	0.894
BMI	≤ 6.1 %	133	28.9 ± 6.9	27.8	30.2	
	≥ 6.2 %	37	31.6 ± 7.6	29.0	34.1	
	Total	170	29.5 ± 7.1	28.5	30.6	0.054
TIMI	≤ 6.1 %	138	1.8 ± 1.3	1.6	2.1	
	≥ 6.2 %	37	2.1 ± 1.3	1.7	2.5	
	Total	175	1.9 ± 1.3	1.7	2.1	0.320

Table 3: Means, Standard Deviations (SD) and 95% Confidence Intervals for Age, BMI & TIMI Score Grouped by Hba1c Categories.

Abbreviations: HbA1c = Glycosylated Haemoglobin, BMI = Body Mass Index, N = Frequency, SD= Standard Deviation, TIMI = Thrombolysis in Myocardial Infarction. Data Analysed Using Analysis of Variance.

Results of the Chi-Square Analysis to Assess the Association between BMI Categories and Hba1c Categories was Statistically Significant (P=0.038) (Table 4). For the 49 Subjects with A BMI of 18-24.9, 6 Had Hba1c ≥ 6.2% of which 4 had a Hba1c ≥ 6.5%. Of The 59 Subjects with A BMI ≥ 25 to ≤ 29.9, 9 had Hba1c more than 6.2% of which 3 had Hba1c ≥ 6.5%. From a Total of 62 Subjects having BMI ≥ 30, 22 had Hba1c > 6.2%, of which 11 had Hba1c ≥ 6.5%.

		HbA1c		Total
BMI (kg/m2)	≤ 6.1%	≥ 6.2-6.4%	≥ 6.5%	
1. (≥ 18-24.9)	39	2	4	49
2. (≥ 25-29.9)	51	6	3	59
3. (≥ 30)	43	11	11	62
Total	133	19	18	170

Table 4: Distribution of Study Subjects Among Hba1c and BMI Categories.

Abbreviations: HbA1c-Glycosylated Haemoglobin, BMI-Body Mass Index, p = 0.038 per chi-square analysis.

Discussion

As noted previously, 10% of our study population had HbA1c value ≥ 6.5% which is a little more than that of the Pennsylvania state age-adjusted rate of 8.9% in 2012 as per the CDC National Diabetes Surveillance System. In addition, 11% had pre-diabetes, i.e., HbA1c ≥ 6.2% as per the lab reference at Abington Memorial Hospital. These individuals are at 10-year risk of progression to DM and require closer follow-up and better glycaemic control.

With the staggering statistic of having approximately 69% of the subject population overweight or clinically obese and a mean BMI 29.5 kg/m2 the likelihood of these individuals progressing to DM is theoretically higher7. As evident by our results, there is a significant association between impaired glycaemic control and elevated BMI, as 35.5% (22/62) of the subject population who had BMI>30 had HbA1c ≥ 6.2%. Amongst this population, 17.7% (11/62) had HbA1c ≥ 6.5%.

Currently, at Abington Memorial Hospital we do not routinely screen patients for DM unless successive blood sugar levels are elevated, which might very well be one blood draw evaluation upon initial admission, secondary to the rapid turnover in modern medicine. There might be a considerable portion of individuals who were admitted and might not have had HbA1c testing done, who might have DM or more commonly impaired glycaemic control. Hence there should be clinical decision support for physicians built in to screen for DM. In the age of Electronic Medical Records (EMR) HbA1c should be incorporated into the admission order set for chest pain, to better screen for DM and pre-DM.

One limitation of this study was that some of the patients might have been followed on an outpatient basis by physicians who do not share the same EMR network as Abington physicians, hence we could not prognosticate if the subjects who had pre-diabetes progressed to DM, or if there was any difference in the overall outcome. The other limitation of this study is that we only included patients admitted for angina, as the subject sample population. As mentioned earlier, the ADA regards a HbA1c range from 5.7-6.4% as impaired glycaemic control. At Abington Memorial Hospital, our lab reports abnormal glycaemic control as ≥ 6.2% which is the cut-off we used for this study for impaired glycaemic

control. Hence the percentage of subjects who have true glycaemic impairment might be higher than calculated.

Conclusion

Our study results support screening patients who are admitted for low or intermediate chest pain to rule out myocardial infarction for diabetes mellitus and pre-diabetes using HbA1c. We suggest that HbA1c be included in the admission order set for "Chest Pain" to regularly screen patients for DM and pre-diabetes. Patients should receive close follow-up which should include repeat HbA1c for those who are diabetic or pre-diabetic. Based on the results of our study, we strongly recommend screening patients with BMI $\geq$ 30 for DM if they are admitted not just for chest pain but other medical ailments as well [8].

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IA, ZA and KB contributed to data collection and manuscript writing. DS contributed to manuscript review and editing. MN contributed to manuscript review, editing, and statistical analysis. The study was self-funded. The researchers have no conflicts of interest.

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