Section: General Medicine

Original Research Article

A STUDY ON THE CORRELATION OF ADMISSION HBA1c AND EJECTION FRACTION AMONG NON-DIABETIC UNSTABLE ANGINA PATIENTS

S. Pravin Selvam[1], Namitha Narayanan[2], C. Santhi[3], S. Chandrasekar[4], N. Jayaprakash[5]

[1]Assistant Professor, Department of General Medicine, Vinayaka Missions Kirupanandha Variyar Medical College, Salem, Tamilnadu, India.
[2]Associate Professor, Department of General Medicine, Government Stanley Medical College and Hospital, Chennai, Tamilnadu, India.
[3]Senior Resident, Department of General Medicine, Government Ariyalur Medical College, Tamilnadu, India.
[4]Professor, Department of General Medicine, Government Stanley Medical College and Hospital, Chennai, Tamilnadu, India.
[5]Associate Professor, Department of General Medicine, Government Stanley Medical College and Hospital, Chennai, Tamilnadu, India.

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Corresponding Author:
Dr. N. Jayaprakash
Email: jp2012srini@gmail.com

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Abstract

Background: Elevated admission HbA1c levels correlate with adverse outcomes among Diabetic patients with Unstable Angina. There is only limited available data on the use of HbA1c levels among non-diabetic unstable angina patients.

Aim: To correlate between admission HbA1c values and Ejection Fraction in Non-Diabetic Unstable Angina patients. **Materials and Methods:** 50, non-diabetic Unstable Angina patients admitted to emergency & medical wards at Stanley medical college hospital Chennai were included in the study. Patients were subjected to clinical examination followed by relevant investigations such as HbA1c testing, ECG analysis, trans-thoracic Echo with Ejection Fraction(EF) measurement. The patients admitted to emergency wards were classified based on EF (< 50 and ≥ 50) into two groups and correlated with their respective HbA1c levels. The correlation of HbA1c and Ejection Fraction was analysed statistically. **Result:** In our study the mean age of the population was 55 years, with a predominance of male patients (62%). A correlation analysis between age and EF revealed that the age group 65-70 had the highest frequency of patients with EF < 50. The mean HbA1c of our study population was 5.9. when compared to males, females had relatively higher (HbA1c ≥ 5.7) levels. Admission HbA1c levels were higher in EF < 50% group when compared to the EF ≥ 50% group. Admission HbA1c levels of more than 5.7% were shown to be related to severe CAD (EF < 50%) in our research. **Conclusion:** Elevated admission HbA1c levels in non-diabetic individuals with Unstable Angina correlates to the severity of coronary artery disease.

INTRODUCTION

Cardiovascular disease (CVD) accounted for fewer than 10% of all fatalities globally at the turn of the twentieth century and about half of all fatalities worldwide at the beginning of the twenty-first century, making it the single most important cause of mortality worldwide and in India.[1] Angina occurs due to demand vs supply mismatch of blood flow to the heart which can even lead to cardiac arrest.[2] Unstable angina is one of the acute coronary syndromes that produce abrupt chest discomfort even during rest.[3] The advancement of CVD is more prevalent in individuals with both stable angina as well as unstable angina.

Diabetes mellitus (DM) is a major risk factor for CVD. Long-term diabetes is associated with microvascular and macrovascular problems, which cause major morbidity and death in diabetics.[4] Atherosclerotic Coronary Artery Disease (CAD) is responsible for the majority of increased mortality among people with diabetes. Several studies have convincingly proven the link between type 2 DM and acute coronary syndromes (ACS). Undetected Diabetes and pre-diabetic conditions are commonly found in people with stable or unstable CAD. Though acute hyperglycemia can be caused by pre-existing diabetes, it can also be a stress reaction to the disease condition.[5] HbA1c is a handy and well-known biomarker in clinical practice that indicates average blood glucose concentrations over the previous 2-3

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months. Acute stress has less of an effect on haemoglobin A1C (HbA1c). As a result, HbA1c readings may shed light on the relationship between chronic glucose management and patient outcomes. As a steady indication of unstressed long-term glycemic management, HbA1c level may be a more helpful predictor in ACS.[6] Several studies examining the relationship between HbA1c and ACS found conflicting results whereas certain other studies found that individuals with increased HbA1c had a higher crude death rate after controlling for various cardiovascular risk factors.[7-9] In the setting of ACS, HbA1c has been proposed as a predictor of poor outcomes.

Even in non-diabetics, stress-induced hyperglycemia is associated with increased activation of stress-responsive kinases and the onset of apoptosis and cardiac cell necrosis, leading to systolic and diastolic dysfunction. Although a link between HbA1c level and unfavourable outcomes in Diabetic individuals with Unstable Angina has been described, there are less data in non-diabetic patients with Unstable Angina. As a result, the predictive significance of HbA1c levels in non-diabetic individuals with the acute coronary syndrome is poorly understood and remains contentious.[10]

Aim

This study aimed to look at the relationship between admission HbA1c values and Ejection Fraction in non- diabetic individuals diagnosed with unstable angina.

MATERIALS AND METHODS

A Cross-sectional observational study was conducted at the Emergency & Medical wards, Department of Internal Medicine, Stanley Medical College and Hospital, Chennai, from March to September 2017 after obtaining the Institution Ethics Committee approval

Fifty non-diabetic patients with unstable angina attending the emergency ward in Government Stanley Hospital were included. Informed consent was obtained from the study participants and confidentiality maintained.

Inclusion Criteria

Non-diabetic patients diagnosed with unstable angina were included in the study. Patients with new-onset (< 2 months) angina that is severe or frequent ≥3 episodes/day or with accelerating angina, that is, those with chronic stable angina who develop angina that is distinctly more frequent, severe, prolonged or precipitated by less exertion than previously and those with angina at rest were included.

Exclusion Criteria

Patients with documented DM, ST Elevation MI(STEMI), Non-STEMI (NSTEMI), Hba1c ≥ 6.5% or lab tests indicative of DM, History of definite MI, history of congestive heart failure and chronic kidney disease in the past, patients with anaemia and pregnancy were excluded.

A detailed medical history was collected from each patient. Patients were subjected to clinical examination followed by relevant investigations such as HbA1c testing by enzymatic method and ECG. Trans thoracic Echo was also done in each patient and 3-4 cardiac cycles were analysed to get the best phase for better outcome of results. EF was calculated by the Simpsons method. Based on EF, the study participants were classified into two groups with EF <50 and EF ≥ 50. Then the correlation between HbA1c and Ejection Fraction was analysed statistically.

Descriptive statistics were done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired t-test. Categorical variables were analysed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analysed using Epi info seven and Microsoft Excel.

RESULTS

Among the study population, 62% were male (mean age 54.12), and 38% were female (mean age 57.1579). The age groups 56-60 and 65-70 had the maximum percentage of patients (20%), followed by those in groups 46 – 50 and 61-65. Only 8% of the population belonged to groups 41–45 [Table 1].

Table 1: Demographic data of patients

		Number	Frequency (%)
Gender	Male	31	62
	Female	19	38
Age distribution	< 40	6	12
	41 - 45	4	8
	46 – 50	7	14
	51 – 55	6	12
	56 - 60	10	20
	61 – 65	7	14
	65 - 70	10	20

An EF value of 45 % had the maximum frequency of 12 subjects, contributing to 24 % of the entire population. Ejection fraction values of 42, 46, 62-64 and 66 % had the least frequency (1 subject). EF<50 was recorded in 58% of the study population, and 42% accounted for EF >50. The mean EF was 51.82%, with males contributing to a higher EF (mean EF 53.22) than females (mean EF 49.52). In the study population, an HbA1c value of 6.1

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had the maximum frequency of 9 subjects (18 %), and 6.2 had the second highest frequency of 7 subjects (14 %). HbA1c value of <5.7 was recorded in 16 subjects (32%), and 68% of the population was observed with an HbA1c value of ≥5.7. The mean HbA1c of the population is 5.91, with females recording higher mean HbA1c (6.026) than males (5.838).

A correlation analysis between age and EF revealed that the age group 65-70 had the highest frequency of patients with EF < 50, and the age group less than 40 & 41-45 had the highest frequency of patients with EF ≥50 [Figure 1].

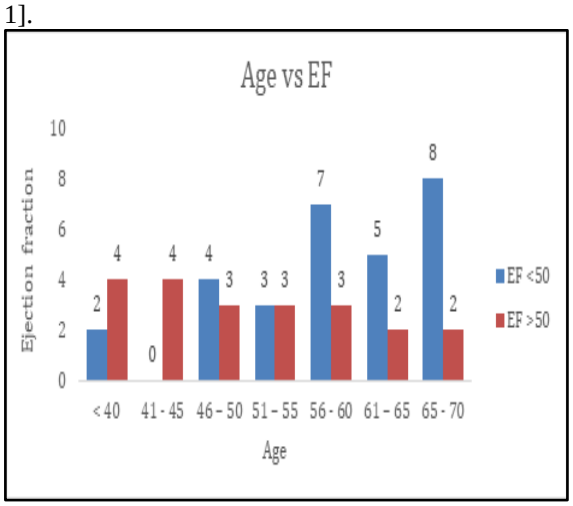

Figure 1: Correlation of age and EF

In the EF < 50 group, the maximum population were in the age group of 65-70, and the least population in 41-45. In the EF ≥ 50 group, the maximum frequency of population were in age groups less than 40 & 41-45, and the lowest frequency in the age group 61-65 years. In the assessment of age group less than 40 years, patients with EF ≥50 years had twofold increased frequency compared to patients with EF <50. In the age group 65-70 years, patients with EF<50 years have a four-fold increased frequency compared to patients with EF ≥50.

In the study population, patients with HbA1c ≥ 5.7 had a twofold increased frequency compared to patients with HbA1c < 5.7. In patients with HbA1c <5.7, the maximum population was in the age group 56-60 and the least in the age group 61-65 & 65-70. In patients with HbA1c ≥ 5.7, the maximum frequency of population was in the age groups 56-60 & 61-70, and the least in age groups 41-45.

A correlation study between age and gender revealed that the maximum frequency of males was in the age group 56-60, and the least was 41-45 & 61-65. The maximum frequency of females was in the age group 65-70, and the least was less than 40. When assessing the age group less than 40 years, males had a fivefold increased frequency compared to females. Females and males have a similar frequency when determining the age group 65-70. The significant difference in sex ratio is also seen in the age group 56- 60 years. A correlation study between HbA1c and gender revealed that in HbA1c < 5.7 group, 81 % were males, and 19% were females. Males' frequency is four folds compared to females (Figure 3). In HbA1c ≥ 5.7 group, 53 % were males, and 47% were females.

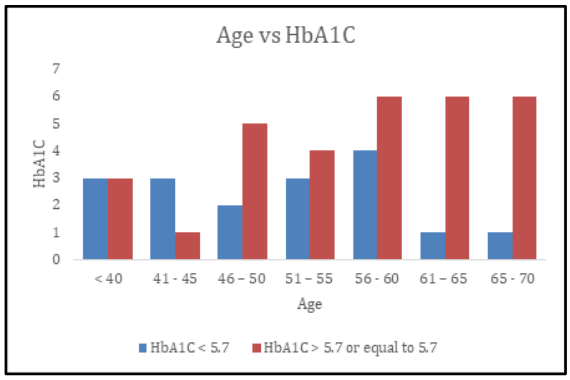

Figure 2: Correlation of age and HbA1c

In patients with HbA1c < 5.7, the maximum were in the age group 56-60, and the least in the age group 61-65 & 65 – 70. In patients with HbA1c ≥ 5.7, the maximum population in age groups 56-60 & 61-70, and the least in age groups 41-45 (Figure 2).

A correlation study between HbA1c and gender revealed that in HbA1c <than 5.7 group, 81 % were males, and 19% were females. Males' frequency is four folds compared to females (Figure 3). In HbA1c ≥5.7 group, 53 % were males, and 47% were females [Figure 3].

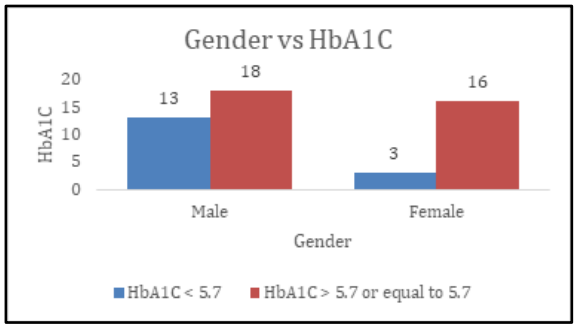

Figure 3: HbA1c Vs sex

In this study group, more than 95% of patients with EF <50 have HbA1c of more than 5.7. More than 70% of patients with EF ≥50 have HbA1c less than 5.7 when extrapolated (for 1000 patients); if EF <50, only 14 patients will have HbA1c values < 5.7.

In this study, non-diabetic unstable angina patients with EF <50 have a 25 times more chance of having HbA1c ≥ 5.7. Non-diabetic unstable angina patients with EF >50 have 25 times more chance of having HbA1c less than 5.7 [Figure 4].

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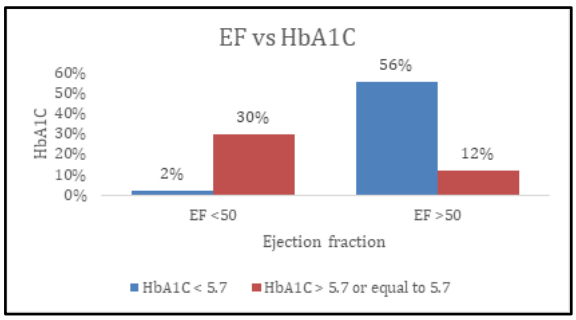

Figure 4: EF vs HbA1c

DISCUSSION

The key finding of the current study was that HbA1c level at admission is considerably related with reduced ejection fraction in diagnosed nondiabetic patients with unstable angina. Previous studies showed that increased HbA1c is related with higher cardiovascular risk in patients with and without diabetes.

In the total population of 50, males were 31, contributing 62 %, and females were 19 contributing 38 %. A similar study by Mamunuzzaman et al. also reports the increased prevalence of unstable angina among males.[13] The mean age of the population was 55 years. A similar mean age group was reported in several studies.[13,14,15] An assessment of EF fractions within the study population showed that patients within the age group 65-70 had the highest frequency of patients with lower EF (EF<50). The decline in EF rate with an increase in age has been reported earlier by Cain et al.[16]

In our study, we found that the mean admission HbA1c of our study population was 5.9 and was relatively greater in females (6.026), with a higher proportion of females with HbA1c ≥ 5.7. The fact that women of older age are prone to HFrEF with non-ischaemic aetiologies was reported in a review analysis done by Swaraj et al.[17] In a previous study; it was reported that patients with lower glycaemic variability still experienced all-cause mortality due to ACS.[18]

Also, a previous study reported that while investigating the prognostic significance of glycated haemoglobin in non-diabetic individuals with ACS, the results revealed that problems were more common in cases with HbA1c>5.7%.[19]

HbA1C levels of more than 5.7% were shown to be related to severe CAD (EF<50%) in our research. This was consistent with the findings of the investigation of Ghaffari et al.20. According to our results, HbA1c is a significant predictor of LV dysfunction in non-diabetic unstable angina patients. HbA1c levels were considerably higher in individuals with EF< 50% compared to the EF ≥50% group. These findings were also consistent with prior results published by Khaheshi et al.10. Our study successfully proved that elevated admission HbA1c levels correlated with low EF in non-diabetic unstable angina patients. Some limitations in our study included a smaller sample size, lack of sex and age-based randomization, and control group comparison.

CONCLUSION

We concluded that increased HbA1c levels in non-diabetic persons with unstable angina correlated with the severity of CAD (EF<50). In non-diabetic people, this simple HbA1c level assessment might be used as an independent predictor of CAD and its severity. Early screening may aid in maintaining an appropriate HbA1c level. Therefore, proactive treatment in the early stages of a glycometabolic condition may avoid more serious effects of coronary artery disease.

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