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The Value of Admission Glycated Hemoglobin and Associated Factors in Non-Diabetic Patients with Heart Failure in Aden

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Abstract

Introduction: Heart failure (HF) is a multifactorial disorder characterized by impaired cardiac function, systemic inflammation and neurohormonal activation. It is a major cause of morbidity and mortality worldwide and has significant impacts on the quality of life, cost and longevity. This study was conducted to investigate the value of admission glycated hemoglobin (HbA1c) and associated factors among non-diabetic patients with heart failure.

Methods: This is a descriptive prospective-hospital based study included 42 non-diabetic patients with HF on first occasion for admission at three major Aden hospitals for the period (January1st–December 31st, 2021). After thorough clinical history and examination, patients were investigated for random blood sugar, lipid profile, Pro Brain Natriuretic Peptide (Pro-BNP), HbA1c and followed till hospital discharge.

Results: HF in non-diabetic patients predominates in males (81.0%) with a mean age of 56.0 ±11.5 years. The main associated factors were arterial hypertension (47.6%), coronary artery disease (9.5%), Khat chewing (57.1%), smoking (31.0%), obesity (28.6%), and family history of HF (21.4%). patients presented with New York Heart Association (NYHA) class III (47.6%) and low ejection fraction of ≤40.0% (76.2%). The median Pro-BNP was 2166.0 pg/mL, the mean admission HbA1c was 5.8% and the case fatality rate was 4.8%. The mean body mass index (BMI) was increasing with increasing level of admission HbA1c. HbA1c of 6.0-6.4% was associated with mortality cases and had significant positive association with BMI and significant negative association with total cholesterol.

Conclusion: The admission HbA1c of 6.0-6.4% was associated with HF hospitalization and mortality in non-diabetic patients. This association is independent of age, gender, hypertension, hypercholesterolemia, glycemia, and clinical outcome suggesting direct effects of BMI on the development of high HbA1c level in non-diabetic patients with HF.

Keywords: Heart failure, Diabetes Mellitus, Pro-BNP, HbA1c, Aden

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قيمة خضاب الدم السكري والعوامل ذات العلاقة به عند دخول مرضى فشل القلب غير المصابين بمرض السكري في عدن

مهند جعفر الخامري و عمر أبوبكر باسلم

ملخص الدراسة

المقدمة: فشل القلب هو اضطراب متعدد العوامل يتميز بخلل في وظائف القلب والتهاب عام مع تنشيط الهرمونات العصبية وهو سبب رئيس للمضاعفات والوفيات في جميع أنحاء العالم وله آثار كبيرة على نوعية الحياة والكلفة وطول العمر. أجريت هذه الدراسة لمعرفة قيمة خضاب الدم السكري والعوامل ذات العلاقة عند دخول مرضى فشل القلب غير المصابين بالسكري المستشفى.
المنهجية: تمت هذه الدراسة بصورة وصفية مستقبلية في 3 من كبرى مستشفيات عدن و شملت 42 مريضًا يعانون من فشل القلب وغير مصابين بالسكري في المرة الأولى التي يتم دخولهم فيها للمستشفى في عدن خلال عام 2021م. وبعد أخذ التاريخ المرضي الدقيق، تم فحصهم سريرياً وأخذت الفحوصات بما في ذلك فحص البروتين الدماغي الاولي وخضاب الدم السكري وتمت متابعهم حتى الخروج من المستشفى.
النتائج: ينتشر فشل القلب لدى المرضى غير المصابين بالسكري عند الذكور (81.0٪) بمتوسط عمر 56.0 ± 11.5 سنة. كانت العوامل ذات العلاقة هي ارتفاع ضغط الدم الشرياني (47.6٪) واعتلال الشريان التاجي (9.5٪) و مضغ القات (57.1٪) و التدخين (31.0%) و السمنة (28.6٪) ووجود تاريخ عائلي لمرض فشل القلب (21.4٪). كانت الفئة حسب التصنيف الوظيفي لجمعية القلب في نيويورك (NYHA) من الدرجة الثالثة عند 47.6٪ منهم، وكان 76.2٪ لديهم انخفاض في الجزء المقذوف للبطين الأيسر لأقل أو يساوي 40.0٪. كان متوسط البروتين الدماغي الاولي 2166.0 بيكوغرام/مل، وكان متوسط خضاب الدم السكري عند الدخول 5.8٪ وكان معدل إماتة الحالات 4.8٪. ارتبط خضاب الدم السكري إيجابياً مع مؤشر كتلة الجسم و سلبياً مع إجمالي الكوليسترول.
الخلاصة: خلصت هذه الدراسة إلى أن نسبة خضاب الدم السكري 6.0-6.4٪ كانت مرتبطة بشكل أكبر بالدخول للمستشفى بسبب فشل القلب وبالوفيات لدى المرضى غير المصابين بالسكري. هذا الارتباط مستقل عن العمر والجنس وارتفاع ضغط الدم وفرط كوليسترول الدم وسكر الدم والنتائج السريرية، مما يشير إلى تأثيرات مباشرة لمؤشر كتلة الجسم على تطور مستوى خضاب الدم السكري المرتفع في مرضى فشل القلب غير المصابين بالسكري.
كلمات مفتاحية: فشل القلب، داء السكر، البروتين الدماغي الاولي، خضاب الدم السكري، عدن.

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Introduction

Heart failure (HF) is one of the main grave health concerns, defined as a heterogeneous, life threatening, clinical syndrome, with a variety of underlying pathophysiological processes, traditionally described as a state of reduced ability of the heart to pump and/or fill with blood, or as an abnormal cardiac structure or function leading to an inappropriate cardiac output or to an adequate cardiac output secondary to compensatory neurohormonal activation and increased left ventricular filling pressure [1,2]. Hypertension and type 2 diabetes mellitus (T2DM) have become the most common aetiologies of incident HF [3,4].

Activation of the sympathetic nervous system is one of major neuro-hormonal mechanism of the development or progression of HF also causes inhibition of glucose-stimulated insulin secretion via the α-receptor such a pathological stress states may induce a metabolic state similar to diabetes with hyperglycemia and poor insulin responses to glucose challenge [5,6].

Cho *et al* [7] demonstrated that admission hyperglycemia, in addition to diabetes mellitus (DM), is a simple and useful predictor of in-hospital death and 1-year death in patients with acute HF and as independent predictor of non-diabetic patients with acute HF. On the other hand, Selvin E *et al* [8] found that elevated hemoglobin A1c (HbA1c) levels are also predictive of cardiovascular diseases and mortality in patients without DM, irrespective of fasting glucose levels, indicating that the long-term disturbance in metabolism of glucose even in non-diabetic individuals is linked to cardiovascular disease risk.

Recently, HbA1c has a great role in evaluating dysglycaemia in non-diabetic patients [9,10-12]. Thus, this study was conducted to test the hypothesis *"Can HbA1c screen and thus prevent the progression to HF in non-diabetic patients?"* aiming to investigate the value of admission HbA1c and associated factors among non-diabetic patients with HF admitted at major hospitals in Aden.

Methods

Study design and setting

This is a descriptive prospective hospitals-based study conducted at 3 major hospitals in Aden (Algamhuria Modern General Hospital, Alwali Private hospital and the German Aden Hospital) for a period of one year, from January 1st to December 31st, 2021.

Inclusion criteria

The study targeted patients with diagnosis of HF, who are non-diabetic, admitted to the Intensive Care Unit, Intermediate Department or the Medical wards of major hospitals in Aden during the study period. Patients who had more than one admission for HF, during the study period, were included only on the occasion of their first admission. The study included 42 non-diabetic patients with diagnosis of HF.

Exclusion criteria

Conditions that may result in discrepancies between the HbA1C result and the patient's true mean glycemia were excluded as follows:

1. Patients with conditions that affect red blood cell turnover (hemolytic and other type of anemias).
2. Patients with recent blood transfusion.
3. Patients use drugs that stimulate erythropoiesis.
4. Patients with serum creatinine >1.3 mg/dl.
5. Pregnant patients.

Data collection

Data collected by direct interview with patients and relatives. The author took the thorough history, performed the clinical examination. Blood samples were taken for random blood sugar (RBS), lipid profile, Pro Brain Natriuretic Peptide (Pro-BNP) and HbA1c. Patients were followed during hospitalization till discharge. The measurement of HbA1c was done by the National Glycohemoglobin Standardization Program - certified PDQ Plus Ultra 2 System (Primus Diagnostics, Kansas City, MO (by boronate affinity chromatography). It was categorized using the following cutoff points: <5.0, 5.0-5.4, 5.5-5.9 and 6.0-6.4% [13].

Statistical analysis

Data collected were analyzed by the SPSS program version 24. Qualitative data were presented as frequency distribution and percentages and tested by the Chi-square test or Fisher exact as appropriate. Quantitative data were first tested for normality distribution by the Kolmogorov-Smirnov test, which revealed parametric distribution for all variables except for Pro-BNP, and accordingly data were presented as means and standard deviations, and tested by parametric tests (Paired t-test for 2 means and One Way ANOVA test for more than 2 means). The Pearson correlation test (at two tailed) was conducted to investigate the association between HbA1c with the studied quantitative variables. The multiple regression analysis was conducted using HbA1c as a dependent variable, to predict variables significantly related to admission HbA1c in non-diabetic patients with HF. All tests were applied at the 95% confidence limits and *p*-values of ≤ 0.05 were considered statistically significant.

Ethical considerations

This study was approved by the Research Ethics Committee of the Faculty of Medicine and Health Sciences, University of Aden.

Results

The baseline data showed male patients more than females (81.0% vs. 19.0%) with a mean age of 56.0±11.5 years, and the median was 55.0 years. Family history of HF was reported in 21.4%, coronary artery disease (CAD) in 9.5%, and coronary revascularization in 4.8%, Khat chewing in 57.1%, smoking in 31.0% and hypertension in 47.6% of patients as shown in Table1.

The mean body mass index (BMI) was 28.1 ± 6.8 kg/m^2 and obesity was reported among 28.6%. According to the New York Heart Association (NYHA) classes, higher percentage of patients presented with NYHA class III (47.6%), followed by NYHA class II (38.1%) and NYHA class IV (14.3%). Left ventricular ejection fraction (LVEF) ranged from 20% to 87%, with a mean of 38.7 ± 14.2%. The level of LVEF was ≤40.0% in 76.2%, 41.0-49.0% in 4.8% and ≥ 50.0% in 19.0% of patients. The mean RBS was 122.7 mg/dl, the mean serum total cholesterol, low density lipoprotein

(LDL), high density lipoprotein (HDL) and triglycerides were (154.1, 98.2, 37.4 and 127.7 mg/dl respectively). Pro-BNP ranged from 100 pg/mL to 18850 pg/mL, with a median of 2166.0 pg/mL. The admission HbA1c ranged from 5.2 to 6.4% with a mean of 5.8%. The level of HbA1c was 5.0-5.4% in 23.8%, 5.5-5.9% in 28.6%, and 6.0-6.4% in 47.6% of patients [Table1].

Table 1: Baseline Characteristics of the Studied Patients (n=42)

Characteristic	№.	%
Male gender	34	81.0
Mean age ± SD (Min.-Max.), years	56.0 ± 11.5 (18 - 75)	
Family history of HF	9	21.4
Coronary artery disease	4	9.5
Coronary revascularization	2	4.8
Khat chewing	24	57.1
Smoking	13	31.0
Hypertension	20	47.6
Obesity (BMI ≥ 30 kg/m^2)	12	28.6
Mean BMI ± SD (Min. – Max.)	28.1 ± 6.8 (18.0 – 44.0)	
Presentation according to NYHA class		
II	16	38.1
III	20	47.6
IV	6	14.3
Left Ventricular Ejection Fraction (%)		
≤ 40.0	32	76.2
41.0 - 49.0	2	4.8
≥ 50.0	8	19.0
Mean LVEF ± SD (Min. – Max.)	38.7 ± 14.2 (20 – 87)	
Random blood sugar (mg/dl)	122.7 ± 36.8 (82.0 – 234.0)	
Serum total cholesterol (mg/dl)	154.1 ± 39.7 (43.0 – 244.0)	
Serum low density lipoprotein cholesterol (mg/dl)	98.2 ± 28.9 (8.0 – 147.0)	
Serum high density lipoprotein cholesterol (mg/dl)	37.4 ± 12.7 (2.0 – 58.0)	
Serum triglycerides (mg/dl)	127.7 ± 72.4 (53.0 – 376)	
Pro- Brain Natriuretic Peptide (pg/mL) Median (Min. – Max.)	2166.0 (100 – 18850)	
Glycated hemoglobin (HbA1c) (%):		
5.0 - 5.4	10	23.8
5.5 - 5.9	12	28.6
6.0 - 6.4	20	47.6
Mean HbA1c ± SD (Min. – Max.)	5.8 ± 0.4 (5.2 – 6.4)	

The clinical outcome of the studied non-diabetic patients with HF during hospitalization revealed that the majority of them improved (40, 95.2%). Only 2 patients died (4.8%) during hospitalization, giving a case fatality rate of 4.8 per each 100 hospitalized non-diabetic patients with HF [Figure1].

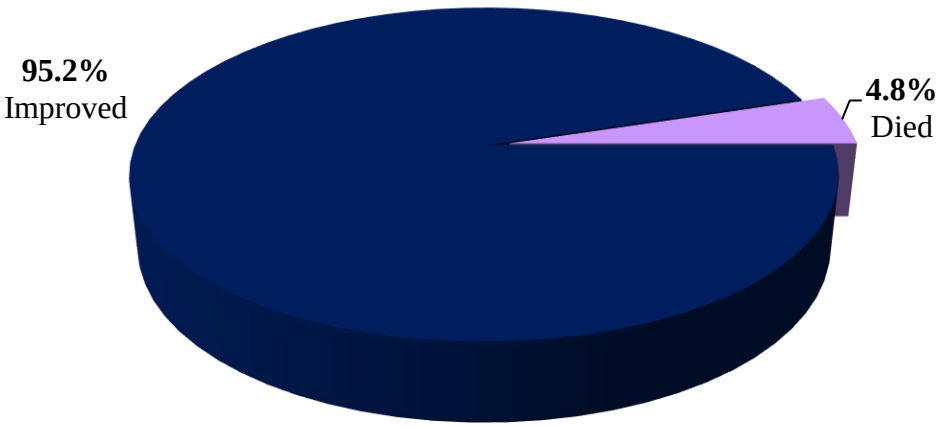

Figure 1: Clinical outcome of non-diabetic patients with heart failure

As demonstrated in Table 2 for the levels of admission HbA1c; male patients showed higher percentages in all levels than in female patients, and the mean age was not significantly differing among the various HbA1c levels (p>0.05).

The mean BMI was increasing with increasing level of admission HbA1c. It was 25.3 kg/m^2 in level of 5.0-5.4% and increasing to 25.6 kg/m^2 in level 5.5-5.9% and further increased to 31.1 kg/m^2 in level 6.0-6.4%. This trend was found statistically significant (p=0.024). On the other hand; family history of HF, hypertension, Khat chewing, smoking, hypercholesterolemia, CAD and revascularization were not significantly associated to admission HbA1c levels (p>0.05).

The median Pro-BNP was increasing with increasing level of admission HbA1c. It was 1083.5 pg/mL in level 5.0-5.4% and increased to 2272 pg/mL in level 5.5-5.9% and further increased to 2375.5 pg/mL in level 6.0-6.4%. However, this trend was not statistically significant (p>0.05). The NYHA classes and the LVEF at presentation as well the clinical outcome were not significantly associated with the level of admission HbA1c (p>0.05).

Table 2: Admission HbA1c Levels in Relation to Characteristics of Non-diabetic Patients with Heart Failure (n=42)

Characteristics		HbA1c (%) 5.0 - 5.4 (n = 10) №.	%	5.5 - 5.9 (n = 12) №.	%	6.0 - 6.4 (n = 20) №.	%	*p*
Patient demographics								
Sex of patient	Male	8	80.0	10	83.3	16	80.0	0.970
	Female	2	20.0	2	16.7	4	20.0	
Mean age ± SD (years)		53.9 ± 10.1 (40 – 70)		57.1 ± 16.9 (18 – 75)		56.5 ± 8.3 (39 – 70)		0.797
Mean BMI ± SD (kg/m^2)		25.3 ± 4.2 (19.6-31.5)		25.6 ± 5.5 (18.0-36.0)		31.1 ± 7.5 (18.5-44.0)		**0.024***
Associated factors								
Family history of heart failure		0	0.0	4	33.3	5	25.0	0.053
Arterial hypertension		5	50.0	5	41.7	10	50.0	0.887
Khat chewing		7	70.0	5	41.7	12	60.0	0.384
Smoking		3	30.0	3	25.0	7	35.0	0.837
Hypercholesterolemia		3	30.0	1	8.3	2	10.0	0.264
CAD and revascularization		0	0.0	2	16.7	4	20.0	0.786
- Median Pro-BNP (pg/mL)		1083.5 (221-5550)		2272.0 (128-18850)		2375.5 (100-7488)		0.325
NYHA class at presentation								
II		6	60.0	4	33.3	6	30.0	
III		3	30.0	7	58.3	10	50.0	0.474
IV		1	10.0	1	8.3	4	20.0	
LVEF at presentation								
≤ 40.0%		8	80.0	9	75.0	15	75.0	
41.0 - 49.0%		0	0.0	1	8.3	1	5.0	0.928
≥ 50.0%		2	20.0	2	16.7	4	20.0	
Clinical outcome								
Improved		10	100	12	100	18	90.0	0.221
Died		0	0.0	0	0.0	2	10.0	

*p-value of ≤ 0.05 is considered statistically significant.

Correlation between admission HbA1c and the various studied quantitative variables in non-diabetic patients with HF revealed that positive correlation was exist between admission HbA1c and patient's age, BMI, RBS, and the Pro-BNP. There are negative correlations between admission HbA1c and LVEF, serum total cholesterol, LDL, HDL, and serum triglycerides. Statistically, significant positive correlation was found between admission HbA1c and BMI (r: 0.424), and significant negative correlation

between admission HbA1c and total cholesterol (r:-0.341). Other correlations were not statistically significant. [Table 3, Figure 2 and 3].

Table 3: Correlation between Admission HbA1c and Various Parameters in Non-diabetic Patients with Heart Failure (n = 42)

Characteristics	r	*p*
Patient's age (years)	0.125	0.431
BMI (kg/m^2)	0.424	**0.005***
Left Ventricular Ejection Fraction (%)	-0.056	0.726
Hemoglobin concentration (g/dl)	0.112	0.481
Random blood sugar (mg/dl)	0.263	0.093
Serum total cholesterol (mg/dl)	-0.341	**0.027***
Serum low density lipoprotein cholesterol (mg/dl)	-0.259	0.098
Serum high density lipoprotein cholesterol (mg/dl)	-0.259	0.098
Serum triglycerides (mg/dl)	-0.069	0.664
Pro- Brain Natriuretic Peptide (pg/mL)	0.079	0.620

All correlations were tested (at two tailed) by the Pearson correlation test; except for Pro-BNP the Spearman correlation test was used.
r: correlation factor.
**p*-value ≤0.05 is considered statistically significant.

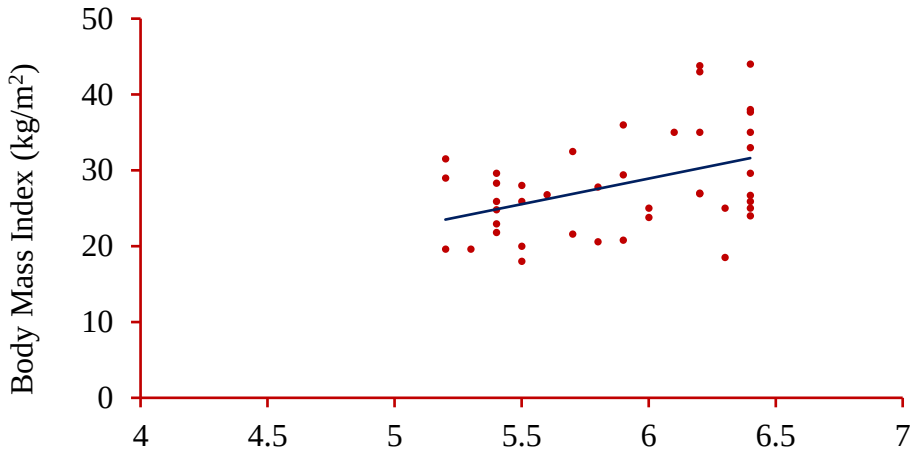

Figure 2: Glycated HbA1c (%)

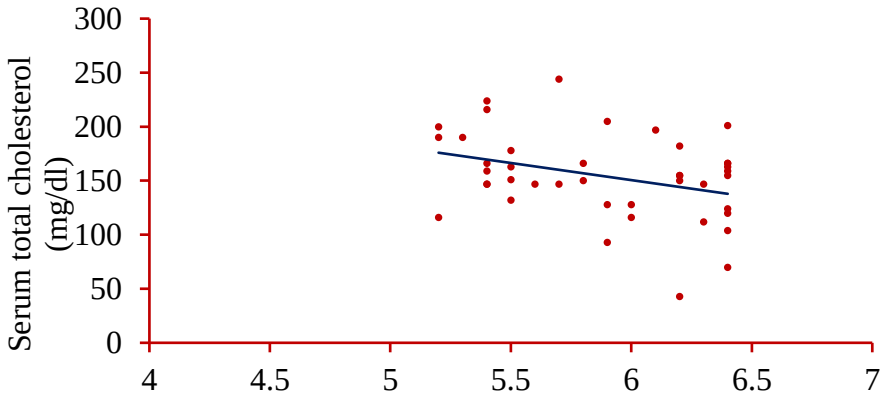

Figure 3: Glycated HbA1c (%)

The multiple regression analysis was conducted for all variables using admission HbA1c as a dependent variable to predict which variable is significantly related to admission HbA1c in non-diabetic patients with HF. It was found that the BMI showed significant positive prediction to admission HbA1c in non-diabetic patients with HF as seen in Table 4.

Table 4: Multiple Regression Analysis for Admission HbA1c Predictors in Non-diabetic Patients with Heart Failure

Parameter	(n = 42) Standardized beta coefficients	*t*	*p*
Patient's age (years)	0.150	0.710	0.485
Patient's gender	-0.106	-0.480	0.636
Body Mass Index (kg/m^2)	0.601	2.610	**0.016***
Left Ventricular Ejection Fraction (%)	0.028	0.139	0.891
Hypertension	-0.271	-0.712	0.484
Hemoglobin concentration (g/dl)	-0.032	-0.156	0.878
Total White blood cells (X10^9/L)	-0.082	-0.401	0.692
Random blood sugar (mg/dl)	0.215	1.038	0.310
Serum creatinine (mg/dl)	-0.068	-0.382	0.706
Serum total cholesterol (mg/dl)	-0.780	-1.840	0.079
Serum LDL-cholesterol (mg/dl)	0.552	1.444	0.163
Serum HDL-cholesterol (mg/dl)	-0.147	-0.727	0.475
Serum triglycerides (mg/dl)	0.250	0.939	0.358
Hypercholesterolemia	-0.067	-0.259	0.798
Pro- BNP (pg/mL)	0.073	0.330	0.744
Clinical outcome	0.047	0.235	0.817

Dependent variable: admission HbA1c.
The test performed by using the linear method (F = 1.150, p: 0.376)
Adjusted R square = 0.068
**p*-value ≤0.05 is considered statistically significant.

Discussion

Heart failure is a multifactorial disorder characterized by impaired cardiac function, systemic inflammation and neurohormonal activation. It is a major cause of morbidity and mortality worldwide and has significant impacts on the quality of life, cost and longevity [14,15].

The admission glycated hemoglobin (HbA1c) in the current study was ranging from 5.2% to 6.4% and the mean was 5.8%. This is coinciding with that reported by the study of Santos-Gallego *et al* in New York, who reported the mean HbA1c among non-diabetic patients with HF at 5.8 ± 0.3% [16] as well as the study of Tomova *et al* in California, among non-diabetic patients with HF, who reported a mean of 6.0 ± 0.6% [17].

In the current study, high percentage of patients (47.6%) showed higher level of admission HbA1c of (6.0-6.4%). This may be attributed to that HF itself is associated with insulin resistance, neurohormonal activation, and derange myocardial glucose and fatty acid metabolism [18]. Furthermore, the level of admission HbA1c in the current study was higher among male non-diabetic patients with HF (80.0%) than in female (20.0%). This finding was similar to that reported by Tomova *et al* in California where higher levels of HbA1c encountered in males (74.6%) than females (25.4%) [17].

The current study reported a significant increase in the mean BMI in association with increasing level of admission HbA1c in the studied non-diabetic patients with HF. This is coinciding with that reported by Gerstein *et a*l in Canada, who reported among diabetic and non-diabetic patients with HF an increased BMI in association with increasing level of HbA1c [19].

In relation to clinical outcome, the current study demonstrated that the two died patients had higher level of admission HbA1c (6.0-6.4%). In general, the lower sample size in the current may be the leading factor for the failure of obtaining a significant value for admission HbA1c in non-diabetic patients with HF in relation to mortality.

HbA1c level is a fundamental marker for chronic glycemia; it was studied among various cardiovascular diseases in non-diabetic patients as atherosclerosis [20], hypertension [21], acute coronary syndrome [22], acute myocardial infarction [23], cardiac perfusion [24], cardiac surgery [25], and even vascular surgery [26]. However, studies for HbA1c in non-diabetic heart failure patients are scarce. Matsushita *et al*. found an elevated HbA1C (≥5.5–6.0%) to be associated with incident HF in a middle-aged population without diabetes, suggesting that chronic hyperglycemia prior to the development of DM contributes to development of HF [27]. In patients with advanced HF; Tomova *et al*, found higher HbA1c levels to be associated with improved outcomes in patients with diabetes but not in patients without DM [17]. In a related context, Gerstein *et al* reported that in diabetic and nondiabetic patients with symptomatic chronic HF, the HbA1c level was an independent

progressive risk factor for cardiovascular death, hospitalization for HF, and total mortality [19]. Conversely, the current study did not find any significant relationship between admission HbA1c level and mortality among non-diabetic patients with HF. This may be attributed to the small sample size, while other studies included higher sample sizes of 845 in California [17], 2412 in Canada [19] and 11057 in Maryland [27].

The current study depicted statistically significant positive correlation between admission HbA1c and BMI (r: 0.424). This finding is in consistence with that reported by the study of He X *et al* in China, who reported significant positive association for HbA1c with BMI in the non-diabetic but not diabetic population [28]. Similarly, Sarnings *et al* [29] in a study in Indonesia reported positive correlation between HbA1c and BMI in young adult without diabetes mellitus (r: 0.386). This positive linear correlation may be attributed to that an increased BMI is associated with impaired adipose tissue function, inducing impaired secretion of adipokines into the circulation [30].

It was indicated that an increasing BMI is associated with excess fat cells and an increase in the process of lipolysis with free fatty acids in plasma [31]. Free fatty acids will increase gluconeogenesis resistance and then trigger insulin in the liver and muscles, as well as interfere with insulin secretion and obesity [32]. Moreover, increasing secretion of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) produced by adipocytes and monocyte derivatives, leads to more insulin resistance, resulting in high circulating blood glucose and eventually the development of increasing HbA1c [33,34].

The current study showed significant negative correlation between HbA1c and total cholesterol (r: -0.341). Previous studies proved that HbA1c can be used as a predictor of dyslipidemia in type 2 diabetes [35,36]. In non-diabetic individuals, Cicek *et al* in Turkey, showed a significant positive correlation between total cholesterol and HbA1c in young non-diabetic individuals. However, their study did not include heart failure patients [37]. The negative linear correlation in the present study may be attributed to that some of the studied patients are already using statins. Therefore, their total cholesterol level was lower than expected to obtain positive correlation to the level of admission HbA1c.

In the current study, multiple regression analysis for all variables using admission HbA1c as a dependent variable was conducted. The BMI of patients with HF without DM had significant direct relationship to the value of admission HbA1c while other variables had no significant relationship. From this analysis, it can be stated that an admission HbA1c of 6.0-6.4% was related more to HF hospitalization in non-diabetic patients and was associated with the case fatality related to HF. The association of admission HbA1C with risk factors of HF in the current study was independent of age, gender, hypertension, hypercholesterolemia, glycemia, and clinical outcome, suggesting direct effects of BMI on

the development of high HbA1c level in non-diabetic patients with HF.

Conclusion

This study concluded that the admission HbA1c of 6.0-6.4% was related more to HF hospitalization and mortality in non-diabetic patients. This association is independent of age, gender, hypertension, hypercholesterolemia, glycemia, and clinical outcome, suggesting direct effects of BMI on the development of high HbA1c level in non-diabetic patients with HF.

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