

Undiagnosed and diagnosed diabetes mellitus among hospitalised acute heart failure patients in Botswana

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Abstract

Objective: The objective of this study was to determine the burden of diagnosed and undiagnosed type 2 diabetes mellitus among patients hospitalised with acute heart failure in Botswana.

Methods: The study enrolled 193 consecutive patients admitted with acute heart failure to the medical wards at Princess Marina Hospital in Gaborone. Patients were classified as previously known diabetics, undiagnosed diabetics (glycated haemoglobin $\geq 6.5\%$) or as non-diabetics (glycated haemoglobin $< 6.5\%$). Data on other comorbid conditions such as hypertension, atrial fibrillation, ischaemic heart disease, stroke, and renal failure were also collected.

Results: The mean (SD) age of the participants was 54.2 (17.1) years and 53.9% were men. The percentage of known and undiagnosed diabetes mellitus was 15.5% and 12.4%, respectively. Diabetic patients were significantly more likely to have hypertension (77.8% vs 46.0%, $p < 0.001$), ischaemic heart disease (20.4% vs 5.0%, $p < 0.001$), chronic kidney disease (51.3% vs 23.0%, $p < 0.001$), and stroke (20.4% vs 5.8%, $p < 0.01$). In addition, diabetics were older than non-diabetics (61.0 years vs 51.6 years, $p < 0.001$).

Conclusion: About 27.9% of patients admitted with acute heart failure in Botswana had diabetes, and almost half of them presented with undiagnosed diabetes. These findings indicate that all hospitalised patients should be screened for diabetes.

Keywords

Diabetes mellitus, acute heart failure, hospitalised patients, Botswana

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Introduction

Patients with diabetes mellitus have increased risk for cardiovascular morbidity and mortality.^{1,2} Compared with the general population, the risk of cardiovascular disease among diabetic versus non-diabetic patients is twofold for men and threefold for women, even when age, gender, body mass index (BMI), cholesterol, smoking, and blood pressure are taken into account.¹ The Framingham study also showed that the prevalence of heart failure is doubled in diabetic men and fivefold in diabetic women when compared with that of the age-matched control subjects.¹ Diabetes plays a role in the pathogenesis, prognosis, and response to treatment of heart failure.^{1,3–5} There has been a yearly rise in the number of cases of diabetes around the world,⁶ and according to the International Diabetes Federation, there were 415 million adults aged 20–79 years with diabetes worldwide in 2015.⁶ Because of its subclinical course, approximately 50% of

people with type 2 diabetes remain undiagnosed and are therefore at greater risk of developing cardiovascular complications.^{6,7} The highest rate of undiagnosed diabetes is in Africa, where over two-thirds (66.7%) of people with diabetes are unaware that they have the disease.⁶ There is evidence that chronic hyperglycaemia is associated with a substantially higher risk of heart failure.⁸ Furthermore, patients with

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heart failure are reported to have a high risk of developing type 2 diabetes.⁹ The later association is multifactorial and may involve increased levels of inflammatory cytokines, a hypermetabolic state, and insulin resistance.⁹ Because of the known relationship between heart failure and diabetes, plus the fact that diabetes has a negative effect on the prognosis of heart failure, screening for diabetes and prevention of progressive cardiac injury is of particular clinical importance. However, published data on the prevalence of undiagnosed diabetes mellitus in heart failure in sub-Saharan Africa are scant. The objective of this study was to determine the burden of diagnosed and undiagnosed diabetes in patients with acute heart failure in Botswana. Such information could be important for health care planning.

Patients and methods

This study formed part of a larger prospective, observational study which was conducted at the Princess Marina Hospital, a tertiary and referral hospital for 231,592 people living in Gaborone and surrounding areas.^{10,11} All acute heart failure patients ≥ 18 years of age admitted in the medical wards at Princess Marina Hospital from February 2014 to February 2015 were eligible for inclusion in the study. Heart failure was defined according to the European Society of Cardiology (ESC) criteria, and cases of both systolic and diastolic heart failure were included.¹²

At admission, each patient's diabetes status was assessed and classified as previously known diabetes, undiagnosed diabetes, or no diabetes. Patients with a pre-admission diagnosis of diabetes or a history of prior treatment with either oral antidiabetic agents or insulin were classified as known diabetics. All study patients had glycosylated haemoglobin (HbA1c) testing.

HbA1c was measured with a standardised high-performance liquid chromatography (HPLC) assay method (Abbott Architect, 2007, Germany). Depending on the HbA1c level, patients without a prior history of diabetes were classified as having undiagnosed diabetes ($\text{HbA1c} \geq 6.5\%$) or as being non-diabetics ($\text{HbA1c} < 6.5\%$).¹³ Following admission, the following tests were also performed: fasting total cholesterol, serum creatinine, urea, sodium, and potassium.

The presence of the following medical conditions was also determined through patient interviews and from review of their medical records: atrial fibrillation, hypertension, HIV infection and cerebrovascular diseases.

Ethics approval

The study was granted ethical clearance by the University of Botswana, the Ministry of Health and PMH Institutional Review Boards (PPME 13/18/1 VIII (264)). All participants provided informed consent before participation. Written informed consent was obtained from all participants or from their legal representatives in cases where the patient had no

capacity to consent. The study conformed to the principles outlined in the Declaration of Helsinki.

Statistical analysis

All data were analysed using SPSS Version 22.0 for Windows (SPSS Inc., Chicago, IL, USA), and summary statistics were calculated for all patient variables. Continuous variables with a normal distribution were presented as means $\pm$ 2 standard deviation (SD) and skewed data as medians (interquartile range (IQR): 25th–75th percentiles). For non-continuous variables, absolute and relative frequencies (%) were used. Comparisons between continuous variables were done by the Student's *t* test or the Kruskal-Wallis test. Associations between categorical variables were tested with the use of contingency tables and calculations of the Pearson's chi-square. A two-sided *p* value of < 0.05 was considered statistically significant.

Results

Table 1 describes clinical and demographic characteristics of enrolled patients. A total of 193 patients were enrolled, with the mean (SD) age of 54.2 (17.1) years and a median left ventricular ejection fraction of 38% (IQR: 27%–55%). Thirty patients (15.5%) had a previous diagnosis of diabetes. Twenty-four patients (12.4%) were assessed as having undiagnosed diabetes ($\text{HbA1c} \geq 6.5\%$) with a mean (SD) HbA1c of 7.1(0.8) %. The total percentage of diabetes mellitus was therefore 27.9%.

Overall, diabetic patients were significantly older than non-diabetics. Known and undiagnosed diabetics had a significantly higher percentage of impaired kidney function, hypertension, stroke, and ischaemic heart disease than did non-diabetics. Although undiagnosed diabetics differed from non-diabetics in terms of clinical and demographic characteristics, there were no significant differences between known and undiagnosed diabetics. A history of atrial fibrillation was most frequently found among patients with undiagnosed diabetes than known diabetics. In addition, patients with undiagnosed diabetes had significantly lower percentage of anaemia than did known diabetics and non-diabetic patients with heart failure.

Discussion

The percentage of diagnosed and undiagnosed diabetes mellitus in our patients with acute heart failure was 15.5% and 12.4%, respectively, making the total percentage 27.9%. Although the percentage of diagnosed diabetes in this study is consistent with previous studies in which 11% to 58% of patients with heart failure were reported to be diabetics, to our knowledge, no study has so far reported the prevalence of undiagnosed diabetes among heart failure patients in Africa.^{14–17} Studies have shown that about 50%–80% of diabetic subjects

Table 1. Clinical and demographic characteristics of patients admitted with heart failure by diabetes status at Princess Marina Hospital.

Characteristics	Non-diabetics (n = 139)	Known diabetics (n = 30)	Undiagnosed diabetics (n = 24)
Age (years), mean (SD)	51.6 (17.2) [†]	63.2 (13.1)	58.2 (16.7)
Male sex, n (%)	78 (56.1)	15 (50)	11 (45.8)
Weight(kg), median median (Q1, Q3)	65.0 (52.1–75.8) [†]	84.0 (62.4–90.)	64.5 (53.15–79.8)
SBP (mmHg), median median (Q1, Q3)	120 (103–132.5) [†]	129.5 (116–149)	110.5 (99.25–131.0)
Medical history, n (%)			
Hypertension	64 (46.0) [†]	28 (93.3)*	14 (58.3)
Anaemia (haemoglobin <10g/dL)	30 (21.6) [†]	13 (43.3)	2 (8.3)
Ischaemic heart disease	7 (5.0) [†]	6 (20.0)	5 (12.5) [‡]
Stroke	8 (5.8) [†]	8 (26.7)	3 (12.5)
Atrial fibrillation	12 (8.6)	2 (6.7)	5 (20.8)
HIV positive	50 (36.0)	7 (23.3)	4 (16.7)
Laboratory parameters			
Haemoglobin (g/dL), mean (SD)	12.0 (2.7) [†]	10.6 (3.7)*	13.5 (2.3) [‡]
Creatinine (μmol/L), median (Q1, Q3)	91 (67–120) [†]	175 (111–292.5)*	98.5 (68.3–128.8)
Urea (mmol/L), median (Q1, Q3)	7.1 (4.7–12.4) [†]	17.6 (10.8–30.7)*	6.6 (4.5–9.4)
eGFR (mL/min/1.73 m ²), median (Q1, Q3)	88.6 (60.4–120) [†]	41.1 (21.5–64.4)*	71.5 (51.9–110.7)
HbA1c (%), mean (SD)	5.6 (0.6) [†]	8.2 (3.2)*	7.1 (0.8) [‡]
Total cholesterol (mmol/L), mean (SD)	3.8 (1.6)	3.9 (1.2)	3.6 (1.2)

LVEF: left ventricular ejection fraction; eGFR: estimated glomerular filtration rate; IQR: interquartile range, SD: standard deviation, SBP: systolic blood pressure.

[†]Significant difference ($p < 0.05$) between non-diabetics and known diabetics; [‡]significant difference ($p < 0.05$) between non-diabetics and undiagnosed diabetic group; *significant difference ($p < 0.05$) between known diabetics and undiagnosed diabetics.

remain undiagnosed for a long period of time.^{6,7,18,19} The proportion of undiagnosed diabetes in high-income and low-income countries is 66.7% and 81.1%, respectively.⁹ In fact, patients with cardiovascular diseases are known to have a high prevalence of undiagnosed diabetes.²⁰

In our study, there was a significantly higher percentage of hypertension, impaired kidney function, stroke, and ischaemic heart diseases among diabetics than non-diabetics. Although there was an increasing trend, the proportion of the above comorbidities did not differ significantly in patients with known and undiagnosed diabetes. Nevertheless, the findings in our study underscore the fact that undiagnosed diabetes can be as harmful as known diabetes, because morbidity and mortality in undiagnosed diabetes mellitus are as high as that observed in known diabetes mellitus, and are significantly higher than in non-diabetic individuals.^{1,19} Evidence already exists for the role of diabetes in the pathogenesis, prognosis, and treatment response of heart failure.^{1,4,5} The prevalence of heart failure is twofold to fivefold higher in diabetics compared with age-matched non-diabetic subjects.¹ Diabetics with heart failure have a more than eightfold increase in mortality as compared with diabetics alone.⁵ Screening and proper management of diabetes is therefore advised for heart failure patients, as it is for any cardiovascular disease.

The high percentage of ischaemic heart disease among diabetics found in this study is not unexpected, since coronary artery disease may be the underlying cause of heart failure in up to two-thirds of diabetics.^{1,21} Because of accelerated

atherosclerosis, diabetes mellitus is commonly associated with microvascular and macrovascular complications, including coronary artery disease and stroke.²² The risk of microvascular and macrovascular complications increases with increasing HbA1c levels, and each 1% rise in HbA1c is associated with a 16% rise in the risk for heart failure.²³ There is also evidence to suggest that diabetes mellitus increases the risk of heart failure independent of underlying coronary artery disease.^{21,22} This observation may be of particular importance in Africa, where ischemia-related heart failure is less common.¹⁴ In addition, diabetes is commonly associated with multiple comorbidities that can independently lead to the development of heart failure and affect the prognosis and outcome of heart failure treatment.²⁴ Indeed, the coexistence of diabetes and hypertension (the commonest comorbidity in our study) is associated with a higher incidence of heart failure.¹⁴ Thus, early and proper management of these coexisting morbidities is important in patients with diabetes.

In our study, there were patients whose heart failure could not be explained by either coronary artery disease or associated comorbidities such as hypertension. It is likely that these patients had diabetic cardiomyopathy, a condition in which diabetes mellitus directly affects cardiac structure and function.²⁴ The pathogenesis of diabetic cardiomyopathy is complex and involves a hyperglycaemic-induced excessive generation of highly active free radicals which causes microangiopathy and consequential myocardial fibrosis, endothelial

dysfunction and derangement of calcium homeostasis.²⁴ Additionally, patients with heart failure have been reported to have marked insulin resistance with hyperinsulinemia, which can independently induce myocardial dysfunction after accounting for diabetes mellitus.^{4,9,25}

Study limitations

This was a small hospital-based study, and thus its findings may not be generalisable. Although HbA1c is a convenient and largely reliable test for diabetes, as it can be performed in a non-fasting state and at any time of the day, the high proportion of HIV infection, anaemia, and impaired kidney function among our patients may have led to either underestimation or overestimation of the HbA1c results. In addition, we enrolled patients admitted with decompensated heart failure and hence more likely to have other illnesses that may shorten red blood cell life and reduce HbA1c values.

Conclusion

There was a high percentage of diabetes mellitus among acute heart failure patients seen at Princess Marina Hospital in Botswana. About 44% of the total cases with diabetes were previously undiagnosed and could have potentially remained untreated for a considerable period of time. Given this high percentage of undiagnosed diabetes and the known poor outcome associated with diabetes, all hospitalised patients should be screened for diabetes.

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Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics approval

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Informed consent

Written informed consent was obtained from all subjects before the study or from legal representatives in cases where the patient had no capacity to consent.

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