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ORIGINAL ARTICLE

Blood glucose control for patients with acute coronary syndromes in Qatar

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Abstract *Background:* Blood glucose is known to be elevated in patients presenting with acute coronary syndromes. However a gap in knowledge exists regarding effective management strategies once admitted to acute care units. It is also unknown what factors (if any) predict elevated glucose values during initial presentation. *Objectives:* Objectives of the study were to characterize blood glucose control in patients admitted to the cardiac care unit (CCU) in Qatar and to determine predictive factors associated with high glucose levels (> 10 mmol/l) on admission to the CCU. *Setting:* All data for this study were obtained from the CCU at Heart Hospital in Doha, Qatar. *Method:* A retrospective chart review was completed for patients admitted to the CCU in Qatar from October 1st, 2012 to March 31st, 2013, of which 283 were included. Baseline characteristics (age, gender, nationality, medical history, smoking status, type of acute coronary syndrome), capillary and lab blood glucose measurements, and use of insulin were extracted. Time spent in glucose ranges of < 4, 4 to < 8, 8 to < 10, and > 10 mmol/l was calculated manually. Univariate and multivariate logistic regression were performed to assess factors associated with high glucose on admission. The primary analysis was completed with capillary data and a sensitivity analysis was completed using laboratory data. *Main outcome measure:* Blood glucose values measured on admission and throughout length of stay in the CCU. *Results:* Capillary blood glucose data showed majority of time was spent in the range of > 10 mmol/l (41.95%), followed by 4–8 mmol/l (35.44%), then 8–10 mmol/l (21.45%), and finally < 4 mmol/l (1.16%). As a sensitivity analysis, laboratory data showed very similar findings. Diabetes, hypertension, and non-smoker status

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predicted glucose values >10 mmol/l on admission ($p < 0.05$) in a univariate analysis but only diabetes remained significant in a multivariate model (OR 23.3; 95% CI, 11.5–47.3). *Conclusion:* Diabetes predicts high glucose values on hospital admission for patients with ACS and patients are not being adequately controlled throughout CCU stay.

1. Introduction

Diabetes and cardiovascular disease are highly prevalent in Western societies and are rapidly becoming major health concerns within other global regions (Wild et al., 2004). Both are associated with high rates of morbidity and place significant cost and resource burdens on healthcare systems (Zhang et al., 2010). In addition to the burden on society, these diseases greatly affect patients and their caregivers. Patients commonly develop symptoms and/or complications that negatively influence their quality of life, while increasing potential for physician visits and hospitalizations (Sudore et al., 2012; Ciechanowski et al., 2003; Nishi et al., 2014).

The relationship between Acute Coronary Syndromes (ACS) and diabetes is poorly understood, however both those with and without diabetes commonly present to the hospital with elevated glucose levels upon admission for an ACS event (Kosiborod, 2009). The mechanism for serum glucose elevation in non-those without diabetes is unclear but may be a marker of undiagnosed diabetes or impaired glucose tolerance (Norhammar et al., 2002). The effect is concerning, as hyperglycemia is associated with a higher risk of mortality and complications in patients experiencing ACS (Donahoe et al., 2007; Deedwania et al., 2008). This is true for glucose levels on admission, as well as glucose levels throughout hospitalization (Kosiborod, 2009). It is speculated that abnormal glucose metabolism may have a role in left ventricular remodeling (Hofsten et al., 2009; Nicolau et al., 2007). However, this remains yet to be confirmed.

A key area of interest is determination of the most effective management strategy for ACS patients presenting with hyperglycemia on admission to the critical care unit. There is evidence that glucose normalization upon admission to a hospital setting can reduce mortality risk, without any major increases in adverse effects (Kosiborod, 2009). Moreover, greater reduction of glucose over 24 h in those without diabetes has predicted lower mortality (Goyal et al., 2009). However, large studies in critical care settings have demonstrated increased morbidity and mortality in patients who received intensive glycemic control, likely due to hypoglycemia (Finfer et al., 2009). As such, current clinical practice guidelines recommend maintaining blood glucose in the range of 7–11 mmol/l for patients presenting with ACS (Canadian Diabetes Association Practice Guidelines Expert Committee, 2013).

In recent years, the Middle East has observed a sharp increase in the prevalence of both diabetes and cardiovascular diseases (Habibzadeh, 2012). The State of Qatar is a member state of the Gulf Cooperation Council (GCC) and is currently undergoing healthcare reform, with comprehensive strategies being implemented to develop a modernized world-class healthcare system (Supreme Council of Health, 2012). However, this system is challenged by very high rates of both diabetes and cardiovascular disease within local populations (Supreme Council of Health, 2012; Bener et al., 2009; Almahmeed et al., 2012). There is currently a gap in knowledge regarding the presentation and management of ACS patients in Qatar, and whether or not practice trends mirror that of other international centers. Specifically, it is unknown how glucose is managed upon presentation in patients with ACS and what (if any) predictive factors are associated with high glucose levels on admission.

The primary objective of this study was to characterize capillary blood glucose control in ACS patients admitted to the cardiac care unit (CCU) in Qatar. A secondary objective was to determine predictive factors associated with high glucose levels (>10 mmol/l) on admission to the CCU. Approval was received from the Institutional Review Boards at both Hamad Medical Corporation and Qatar University.

2. Methods

2.1. Design and patients

This study was a retrospective chart review of all patients admitted with a diagnosis of ACS to the CCU at Heart Hospital in Qatar, from October 1, 2012 to March 31, 2013. Inclusion criteria were patients admitted to the CCU at the Heart Hospital with a diagnosis of ST segment elevated myocardial infarction (STEMI), non-STEMI, or unstable angina that had at least one documented blood glucose measurement during CCU stay. Patients who were not admitted for ACS or who did not have a plasma glucose level taken at any time during admission to the CCU were excluded from the study.

2.2. Outcomes

The primary endpoint was characterization of blood glucose control in patients admitted to the CCU through determination of the time spent in blood glucose ranges of <4, 4 to <8, 8 to <10, and >10 mmol/l measured through capillary mechanisms. These ranges were chosen based on institution levels of hypoglycemia (<4) and hyperglycemia (>10). The threshold for initiation of sliding scale insulin at the center studied is 10 mmol/l and therefore correlates to institutional definitions of control. The secondary endpoint was the determination of factors associated with initial glucose levels >10 mmol/l on admission to the CCU.

2.3. Data collection

A standardized data extraction tool was developed for collecting patient data. Patients were identified using hospital records for all admissions to the CCU during the time period of interest. Data were collected from the patient's healthcare record in paper form. Blood glucose values measured by capillary and laboratory methods were documented. Capillary glucose data were obtained from a blood glucose monitoring form standard for all patients. Blood glucose data measured by the laboratory were obtained from printed copies in the patient's file. The baseline characteristics of age, gender, weight, nationality, co-morbidities (diabetes, hypertension, coronary artery disease), smoking status, and infarct type were documented. Based on nationalities found, categories were determined as South Asian (India, Sri Lanka, Bangladesh, Pakistan, and Nepal), East Asian (Philippines, Indonesia), North Africa (Egypt, Sudan, Ethiopia, Eritrea), Middle Eastern (Palestine, Syria, Jordan, Yemen, Iran), GCC (Qatar, Saudi Arabia, Kuwait, UAE, Bahrain, Oman), and Western (USA, UK, South Africa, Sweden).

2.4. Statistical analysis

Time spent in each pre-established glucose range was calculated manually. From the patient's first capillary measurement, it was assumed that the patient remained in the specified range until the next glucose measurement was given. For example, if a patient's glucose measured 12 mmol/l at time 0 but measured 8 mmol/l at time 4 h, it was determined that the patient spent 4 h within the range of > 10 mmol/l. A sensitivity analysis employing the same methodology but using solely laboratory values was also completed.

Results pertaining to the time spent in each glucose range were reported using descriptive statistics. Univariate logistic regression was used to assess the association between baseline characteristics and glucose levels > 10 mmol/l on admission. Baseline characteristics assessed were gender, age, weight, nationality, presence of diabetes, presence of coronary artery disease, presence of hypertension, presence of dyslipidemia, active smoking status, and type of infarction. A subgroup analysis was completed to assess the same variables in known diabetes patients. Multivariate logistic regression was used to analyze any factor deemed significant from univariate results. Results were shown as odds ratios (OR) with 95% confidence intervals (CIs), and a *p*-value of < 0.05 was considered statistically significant. All inferential analyses were completed using Statistical Package for Social Sciences (SPSS) version 21.

Table 1 Baseline characteristics of included patients (n = 283).

Characteristic	*N* (%)
Age (years)	
< 40	34 (12.0)
40–50	91 (32.2)
50–60	103 (36.4)
60–70	43 (15.2)
> 70	12 (4.2)
Gender	
Male	270 (95.4)
Female	13 (4.6)
Weight (kg) [mean, SD]	75.2 (15.3)
Nationality	
South Asia	189 (66.8)
Gulf Cooperation Council (GCC)	41 (14.5)
North Africa	22 (7.8)
Middle East (aside from GCC)	18 (6.4)
East Asia	9 (3.2)
Other	4 (1.4)
Co-morbidities	
Diabetes	125 (44.2)
Coronary Artery Disease	161 (56.9)
Hypertension	132 (46.6)
Dyslipidemia	54 (19.1)
Current smoker	163 (57.6)
Infarct type	
STEMI	225 (79.5)
NSTEMI	35 (12.4)
Unstable angina	27 (9.5)

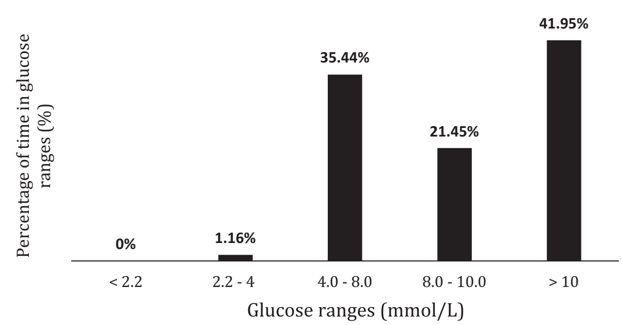

Figure 1 Time spent in glucose ranges based on capillary data.

3. Results

A total of 377 patients were identified for review for which 283 met pre-established inclusion criteria. Patients were excluded for not having a diagnosis of ACS or did not have a blood glucose level reported. Baseline characteristics are presented in Table 1. Notably, the majority of patients were of South Asian nationality (66.80%) with an average age of 51.4 years. Almost half (44.2%) had a documented diagnosis of diabetes.

The primary endpoint for capillary data showed that the majority time was spent in the blood glucose range of > 10 mmol/l (41.95% of time), followed by 4.0–8.0 mmol/l (35.44%), then 8.0–10.0 (21.45%), and finally 2.2–4.0 (1.16%). No patient spent any time below the blood glucose value of 2.2 mmol/l, as captured by data extraction (Fig. 1). When the 4.0–8.0 mmol/l and 8.0–10.0 mmol/l categories were combined, the time spent surpassed that of the > 10 mmol/l range with a value of 56.89%. The sensitivity analysis showed very similar results with the most time spent in the range of > 10 mmol/l (46.39%), then 4.0–8.0 mmol/l (36.28%), then 8.0–10.0 mmol/l (16.20%), and finally 2.2–4.0 mmol/l (1.13%). No time was documented in the range below 2.2 mmol/l.

Univariate analysis found that the presence of diabetes (OR 26.3 95% CI [13.4–51.6]) and the presence of hypertension (OR 2.884 95% CI [1.762–4.721]) to be significantly associated with initial glucose values > 10 mmol/l. Active smokers were less likely to have high values, as compared to non-smokers

(OR 0.577 95% CI [0.356–0.933]). However, only the presence of diabetes remained significant when these factors were combined in a multivariate regression model (OR 23.3 95% CI [11.5–47.3], $r^2 = 0.53$). For diabetes patients alone, no factor was significantly associated with initial glucose values > 10 mmol/l.

4. Discussion

This study characterized blood glucose control for patients with ACS in the CCU in the Heart Hospital in Qatar, and it assessed predictive factors of patients presenting with high glucose values. Findings showed that patients spent a large proportion of time (42%) within the glucose range above 10 mmol/l. Additionally, it was found that the diagnosis of diabetes was the only significant predictive factor for patients presenting with initial glucose levels above 10 mmol/l, when corrected for hypertension and smoking status. Interestingly, the majority of patients admitted to the CCU with ACS were of South Asian nationality and almost half were diabetes patients.

The findings concerning the primary outcome demonstrate a large proportion of time spent in a glucose range above 10 mmol/l. According to the pre-defined blood glucose ranges, patients spent the most time in this range. However, when the two ranges representing normal non-fasting glycemic values were combined (4–8 mmol/l and 8–10 mmol/l), more patients spent time within these ranges as compared to > 10 mmol/l (56.89% vs. 41.95%, respectively). Even with 41.95% who had values > 10 mmol/l, these findings show that a large proportion of patients are not achieving glycemic targets, according to institutional policies and international guidelines (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, 2013). The reasons for this finding are not known, however fear of hypoglycemia by healthcare professionals, ineffective insulin sliding scale regimens, and context-specific patient values and preferences may all be contributors. Observations from practice suggest that the fear of hypoglycemia and patient aversion to insulin may be primary factors, which are causing clinical staff (including physicians, nurses, and pharmacists) to not proactively advocate for optimal use of sliding scale insulin, when necessary. These considerations match previously speculated ones generated from studies that found similar results in other settings (Kosiborod, 2009).

The high blood glucose values (> 10 mmol/l) on admission were also of concern, especially for diabetes patients. While no cause and effect relationship can be determined, it is possible that physiological mechanisms during ACS result in elevated glucose levels (Opie, 2008). However, an alternative explanation may be that diabetes patients in Qatar are not being adequately controlled as outpatients, leading to higher glucose levels during times of acute stress. Diabetes has been a target disease for prevention and treatment in Qatar (Supreme Council of Health, 2012) yet it is unknown if efforts are resulting in better treatment control. The results of this study warrant further investigation to determine the degree of diabetes control in Qatar.

As described above, available evidence for therapeutic decision-making in this area is scarce and mostly consists of observational studies. This study adds to the literature regarding glucose control in ACS patients by bringing a diverse perspective from a rapidly developing healthcare system. There are very few studies published from critical care settings in the Middle East, which is unfortunate because the ethnic diversity of local populations (including large amounts of expatriates) can serve as a form of generalizability to many international settings. Our findings show that patients in Qatar are not achieving target glucose values during ACS care and call for other centers to perform similar analyses for characterization of international care. The results also confirm that diabetes is associated with high glucose levels in ACS (especially within an ethnically diverse population) and provide justification for further evaluation of inpatient and outpatient diabetes care.

This study has limitations that should be addressed. First, the retrospective observational design limits the ability to determine cause and effect for associations found. Therefore, it is mostly hypothesis generating for further studies within the GCC context and elsewhere. Secondly, due to limitations of data available (i.e. charting practices and hospital record coding), clinical outcomes were unable to be obtained. Therefore, no associations could be made regarding effects of hyperglycemia on mortality or other morbidities. Finally the method of calculating the time spent in each glucose range is prone to error based on the assumption that patients remained within a category until the subsequent measurement, however the sensitivity analysis yielded similar findings.

Blood glucose control in patients with ACS is an emerging area of interest and optimal blood glucose targets during hospital admission for these patients remain yet to be defined. This study assessed hospital practices in the only coronary care unit in Qatar and found that most patients are achieving glucose values > 10 mmol/l during CCU stay. It can be concluded from this study that diabetes predicts high blood glucose values on admission for patients with ACS and that insulin protocols are not being well adhered to. As such, prospective international trials are needed to determine the effect of blood glucose control on patient outcomes and to optimize blood glucose targets. Outpatient diabetes care should also be examined to ensure inadequate long-term control is not putting patients at risk for ACS within this setting.

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References

Almahmeed, W., Arnaout, M.S., Chettaoui, R., Ibrahim, M., Kurdi, M.I., Taher, M.A., et al, 2012. Coronary artery disease in Africa and the Middle East. Ther. Clin. Risk Manag. 8, 65–72. http://dx.doi.org/10.2147/tcrm.s26414.

Bener, A., Zirie, M., Janahi, I.M., Al-Hamaq, A.O., Musallam, M., Wareham, N.J., 2009. Prevalence of diagnosed and undiagnosed diabetes mellitus and its risk factors in a population-based study of Qatar. Diabetes Res. Clin. Pract. 84 (1), 99–106. http://dx.doi.org/10.1016/j.diabres.2009.02.003.

Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, 2013. Canadian Diabetes Association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada. Can. J. Diabetes 31 (Suppl 1), S1–S212.

Ciechanowski, P.S., Katon, W.J., Russo, J.E., Hirsch, I.B., 2003. The relationship of depressive symptoms to symptom reporting, self-care and glucose control in diabetes. Gen. Hosp. Psychiat. 25 (4), 246–252.

Deedwania, P., Kosiborod, M., Barrett, E., Ceriello, A., Isley, W., Mazzone, T., et al, 2008. Hyperglycemia and acute coronary syndrome: a scientific statement from the American Heart Association Diabetes Committee of the Council on Nutrition, Physical Activity, and Metabolism. Circulation 117 (12), 1610–1619. http://dx.doi.org/10.1161/circulationaha.107.188629.

Donahoe, S.M., Stewart, G.C., McCabe, C.H., Mohanavelu, S., Murphy, S.A., Cannon, C.P., et al, 2007. Diabetes and mortality following acute coronary syndromes. JAMA 298 (7), 765–775. http://dx.doi.org/10.1001/jama.298.7.765.

Finfer, S., Chittock, D.R., Su, S.Y., Blair, D., Foster, D., Dhingra, V., et al, 2009. Intensive versus conventional glucose control in critically ill patients. New Engl. J. Med. 360 (13), 1283–1297. http://dx.doi.org/10.1056/NEJMoa0810625.

Goyal, A., Mehta, S.R., Diaz, R., Gerstein, H.C., Afzal, R., Xavier, D., et al, 2009. Differential clinical outcomes associated with hypoglycemia and hyperglycemia in acute myocardial infarction. Circulation 120 (24), 2429–2437. http://dx.doi.org/10.1161/CIRCULATIONAHA.108.837765.

Habibzadeh, F., 2012. Diabetes in the Middle East. Lancet 380, 1.

Hofsten, D.E., Logstrup, B.B., Moller, J.E., Pellikka, P.A., Egstrup, K., 2009. Abnormal glucose metabolism in acute myocardial infarction: influence on left ventricular function and prognosis. JACC Cardiovasc. Imag. 2 (5), 592–599. http://dx.doi.org/10.1016/j.jcmg.2009.03.007.

Kosiborod, M.D.P., 2009. An overview of glycemic control in the coronary care unit. J. Diabetes Sci. Technol. 3 (6), 1342–1351.

Nicolau, J.C., Maia, L.N., Vitola, J.V., Mahaffey, K.W., Machado, M.N., Ramires, J.A., 2007. Baseline glucose and left ventricular remodeling after acute myocardial infarction. J. Diabetes Complications 21 (5), 294–299. http://dx.doi.org/10.1016/j.jdiacomp.2006.01.003.

Nishi, T., Babazono, A., Maeda, T., 2014. Risk of hospitalization for diabetic macrovascular complications and in-hospital mortality with irregular physician visits using propensity score matching. J. Diabetes Invest. 5 (4), 428–434. http://dx.doi.org/10.1111/jdi.12167.

Norhammar, A., Tenerz, A., Nilsson, G., Hamsten, A., Efendic, S., Ryden, L., et al, 2002. Glucose metabolism in patients with acute myocardial infarction and no previous diagnosis of diabetes mellitus: a prospective study. Lancet 359 (9324), 2140–2144. http://dx.doi.org/10.1016/s0140-6736(02)09089-x.

Opie, L.H., 2008. Metabolic management of acute myocardial infarction comes to the fore and extends beyond control of hyperglycemia. Circulation 117 (17), 2172–2177. http://dx.doi.org/10.1161/circulationaha.108.780999.

Sudore, R.L., Karter, A.J., Huang, E.S., Moffet, H.H., Laiteerapong, N., Schenker, Y., et al, 2012. Symptom burden of adults with type 2 diabetes across the disease course: diabetes & aging study. J. Gen. Intern. Med. 27 (12), 1674–1681. http://dx.doi.org/10.1007/s11606-012-2132-3.

Supreme Council of Health. Strategy Goals & Projects. Qatar National Health Strategy, 2012. <http://www.nhsq.info/strategy-goals-and-projects> (accessed 22.01.15).

Wild, S., Roglic, G., Green, A., Sicree, R., King, H., 2004. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 27 (5), 1047–1053.

Zhang, P., Zhang, X., Brown, J., Vistisen, D., Sicree, R., Shaw, J., et al, 2010. Global healthcare expenditure on diabetes for 2010 and 2030. Diabetes Res. Clin. Pract. 87 (3), 293–301. http://dx.doi.org/10.1016/j.diabres.2010.01.026.