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Glucose as a risk predictor in acute medical emergency admissions

Nigel Glynn [a], Lisa Owens [b], Kathleen Bennett [c], Marie Louise Healy [b], Bernard Silke [a,*]

[a] Division of Internal Medicine, St. James's Hospital, Dublin 8, Ireland
[b] Division of Endocrinology, St. James's Hospital, Dublin 8, Ireland
[c] Department of Pharmacology and Therapeutics, Trinity Centre for Health Sciences, St. James's Hospital, Dublin 8, Ireland

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ABSTRACT

Aims: The aims of this study were to examine the relationship between admission blood glucose and mortality in a large, unselected cohort of acutely ill medical patients and to assess the impact of diabetes on this relationship.

Methods: We studied the broad pattern of acute medical admissions over an eight year period and the impact of admission serum glucose on in-hospital mortality. Significant predictors of outcome, including acute illness severity and co-morbidity, were entered into a multivariate regression model, adjusting the univariate estimates of the glycaemic status on mortality.

Results: There were 45,068 consecutive acute medical emergency admissions between 2005 and 2012. The normoglycaemic (>4.0 ≤7.0 mmol/l) cohort (86%) had a 3.9% in-hospital mortality. Both hypoglycaemia (OR: 3.23: 95% CI: 2.59–4.04; $p < 0.001$) and hyperglycaemia (OR: 2.1; 95% CI: 1.9–2.4; $p < 0.001$) predicted an increased risk of an in-hospital death. Neither of these increased risks were fully adjusted nor explained by a highly predictive outcome model, using multiple acute illness parameters. Hyperglycaemia did not carry similar adverse prognostic implications for patients with diabetes.

Conclusion: In patients without diabetes, an abnormal serum glucose is independently predictive of an increased mortality among the broad cohort of acute emergency medical patients. Similar disturbances of glucose homeostasis for patients with diabetes do not confer equivalent adverse prognostic implications.

1. Introduction

The growing number and complexity of emergency medical admissions has focused attention on the ability to predict the likely outcome of patients admitted to hospital. The identification of sicker patients earlier in the course of admission may help to direct the use of hospital resources such as acute medical admission units and critical care facilities. There is now a considerable body of literature on the development of early warning clinical scores to identify these at-risk patients by using physiological data such as blood pressure and pulse rate [1,2]. In addition certain routinely collected laboratory measurements have been shown to be closely associated with

* *Corresponding author at*: Division of Internal Medicine, GEMS Directorate, St James's Hospital, James's Street, Dublin 8, Ireland. Tel.: +353 87 7789773; fax: +353 1 453 9033.
E-mail address: bernardsilke@physicians.ie (B. Silke).
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mortality risk among hospitalised patients, including serum sodium, albumin and white blood cell count [3–6].

Disturbance of blood glucose regulation is a frequent occurrence among hospitalised patients. Hyperglycaemia is common, even in the absence of a pre-morbid diagnosis of diabetes mellitus. The prevalence of previously diagnosed diabetes among hospitalised patients varies between 7 and 25% according to ethnicity, age and case-mix [7,8]. However, the true prevalence is probably higher considering that 30–40% of patients with diabetes are undiagnosed [9,10]. Hypoglycaemia is less common and may be iatrogenic or a consequence of an underlying illness such as sepsis or liver failure.

Elevated serum glucose is associated with adverse outcomes in certain sub-groups of acute medical patients, e.g. those with stroke [11], myocardial infarction [12], pneumonia [13] and critical illness [14]. However, there is equivocal evidence that tight glycaemic control may improve outcomes for these patients [15–17]. In the critical care setting, Van Den Berghe et al. demonstrated a reduction in morbidity among medical patients who received tight glycaemic control. An improvement in mortality was also observed among patients who stayed longer than three days in the intensive care unit [18]. Nevertheless, abnormal serum glucose is not clearly established as an independent predictor of morbidity or mortality in all acute general medical patients and is therefore not a consistent component of clinical risk scores for this cohort. In the era of a diabetes pandemic, the value of blood glucose as a risk estimator among this broad patient population warrants further investigation.

The aim of this study was to examine the relationship between admission serum glucose and mortality in a large unselected cohort of acutely ill medical patients. Specifically, we sought to investigate whether an abnormal admission serum glucose contributed independently to an in-hospital death or merely indicated a more severe illness and consequent stress response.

2. Subjects

A dedicated anonymised patient database was created to link the computerised patient administration system (PAS) to the hospital in-patient enquiry (HIPE) scheme. HIPE is a national database of coded discharge summaries from acute public hospitals in Ireland, run by the Economic and Social Research Institute. Ireland uses the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) for both diagnosis and procedure coding [19]. We utilised the Clinical Classifications Software for ICD-10-CM, a diagnosis and procedure categorisation scheme, to collapse the ICD's multitude of codes (>14,000 diagnosis codes) into a smaller number of clinically meaningful categories [20]. This facilitates statistical analysis and reporting with mortality data. Major disease categories (MDC) analysed included diseases of the lungs, heart, nervous and gastro-intestinal systems, as they encompass the commonest illness among acutely ill medical patients.

Linking the HIPE dataset with the PAS database permits interrogation of routinely collected data for the purposes of research, planning and quality control. Data held on PAS includes the unique identifier, admitting consultant, date of birth, gender, area of residence by county, principal diagnosis, up to nine additional secondary diagnoses, procedures (principal and up to nine additional secondary procedures) as well as admission and discharge dates. Additional information can be accessed from a 'data warehouse' cross-linked and matched for each patient that includes physiological, haematological and biochemical measurements.

The Department of Endocrinology maintains a prospective, electronic database of all patients with diabetes who attend the out-patient clinic. These patients reside within St. James's Hospital (SJH) catchment area which serves a predominantly urban, inner city population. Most patients with diabetes attend the hospital clinic exclusively or as part of shared care agreement with their family doctor. Admitted patients who had a pre-existing diagnosis of diabetes (or impaired glucose tolerance (IGT)) were then isolated by cross-referencing the diabetes database with the aforementioned dataset using the unique patient identifier. The cross-matched patients were almost exclusively recorded as having diabetes, with less than 1% identified as IGT. Data were related to all emergency general medical patients admitted to SJH between 1 January 2005 and 31 December 2012.

3. Materials and methods

We divided admission serum glucose levels into five categories: ≤4.0 mmol/l, >4.0 ≤7.0 mmol/l, >7.0 ≤10.0 mmol/l, >10.0 ≤13.0 mmol/l and finally >13.0 mmol/l. These levels were chosen to allow easy comparison with recent, landmark studies in this area [13,21–23]. Admission glucose refers to the first serum glucose measured during admission. Serum glucose was measured in fluoride tubes by the hexokinase method. The relationship between the serum glucose measurement and fasting/meals was not recorded. Mortality was defined as any in-hospital death – we analysed the mortality rate at different time points following admission but present the data as any in-hospital death by day 30.

Derangement of haemodynamic and physiological admission parameters may be utilised to predict in-hospital mortality [24,25]. We have previously derived an Acute Illness Severity Score (AISS) that predicts clinical outcomes based on modelling of laboratory data collected at the time of hospital admission – parameters include serum sodium, potassium, urea, haematocrit or red cell distribution width, serum albumin and white blood cell count [3,4,6,26,27]. The underlying principle is that deviation beyond the boundaries of 'normal homeostasis' is an estimate of risk, although the relationship is non-linear and different for each variable or lab value. We used the method described by Royston and Sauerbrei to model the relationship between mortality and several outcome predictors [28]. Continuous variables are kept continuous and non-linear relationships are identified and modelled appropriately. Using multivariable fractional polynomial (MFP) logistic regression modelling, that makes no assumptions regarding the nature of the relationship between a variable and outcome, we demonstrated, in an 80% random derivation sample, at 30 days the area under the receiver–operator curve (AUROC) for this laboratory model to be 0.86