ORIGINAL PAPER

IJCP THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

Admission blood glucose helps predict 1 year, but not 2 years, mortality in an unselected cohort of acute general medical admissions

F. Haddadin,[1] A. Clark,[2] N. Evans,[1] K. Dhatariya[1,2]

SUMMARY

Aim: We previously showed that hyperglycaemia in newly hospitalised medical inpatients is associated with longer length of hospital stay, higher 28-day readmission rates and increased 28-day mortality. We aimed to assess whether a single blood glucose measurement taken at the time of admission could help to predict 1 and 2 years mortality. **Methods:** We retrospectively reviewed data from all 1502 patients admitted to our Acute Medical Unit during February 2010. **Results:** By using a blood glucose range of 6.5–7.0 mmol/l as the comparator, an admission blood glucose between 9.1 and 20 mmol/l was associated with an increased risk of death at 1 year ($p < 0.05$). In addition, those people with admission glucose readings of < 6.5 mmol/l showed a strong trend towards a higher mortality ($p = 0.053$) at 1 year. **Conclusion:** Thus admission blood glucose can be used to help predict the risk of 1 year mortality in an unselected cohort of general medical admissions.

What's known

Hyperglycaemia is common in acutely unwell patients and is associated with poor short term outcomes. It has previously been shown that the measure of long-term glycaemic control, the glycated haemoglobin (HBA1c), is a predictor of mortality in acutely hospitalised patients. It has also been shown that a random blood glucose taken at the time of admission predicts 28-day readmission rates, length of stay and mortality

What's new

This study shows that at admission random blood glucose can predict 1 year mortality, with a glucose level of 6.5–7.0 mmol/l being associated with the lowest mortality rates. There is a statistically greater risk of death at 1 year with glucose levels > 9.1 mmol/l and a strong trend towards increased mortality with glucose levels lower than 6.5 mmol/l.

[1]Elsie Bertram Diabetes Centre, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, Norfolk, UK
[2]Norwich Medical School, University of East Anglia, Norwich, UK

Correspondence to:
Dr Ketan Dhatariya, Elsie Bertram Diabetes Centre, Norfolk and Norwich University Hospital NHS Foundation Trust, Colney Lane, Norwich, Norfolk NR4 7UY, UK
Tel.: + 01603 288170
Fax: + 01603 288438
Email: ketan.dhatariya@nnuh.nhs.uk

Disclosures
The authors declare no conflicts of interest.

Introduction

Elevated plasma glucose levels in people not previously known to have diabetes – so called 'stress hyperglycaemia' – is a common feature in the acutely ill patient (1). Hyperglycaemia of any cause in hospitalised inpatients is associated with increased short-term mortality, in-hospital complications and lower functional outcome (2–4). With the increasing prevalence of obesity and consequent insulin resistance it is likely that the incidence of stress hyperglycaemia, and subsequent complications, will rise.

We have previously shown that in a cohort of all 1502 patients admitted to our Acute Medical Unit (AMU), a random plasma glucose taken during the first few hours of admission was strongly related to length of hospital stay, 28-day readmission rate and 28-day mortality (5). What is not known, however, is if a single random admission glucose measurement can help predict outcomes over a longer period.

Methods and procedures

These have been described previously (5). Briefly, the medical records of all unselected emergency medical admissions to the AMU at the Norfolk and Norwich University Hospitals NHS Foundation Trust during February 2010 were reviewed retrospectively for short (30 days) and long-term (2 years) mortality rates. Venous blood glucose was measured on admission at the time of first assessment either in the emergency department, or in the AMU if the patient was referred directly from their general practitioner.

We wanted to determine if there was a relationship between the single admission blood glucose value and mortality at 1 and 2 years after that index admission. We subsequently did a retrospective case notes review to determine the status of those individuals who had an admission blood glucose measured to see if they were alive or, if they had died, and if so how long after their admission in February 2010

they died. We assessed overall mortality, whether in or out of hospital.

Ethical approval was not deemed necessary for this work, because this was retrospective analysis of data and no patient identifiable information was collected. It was classified as a 'service improvement exercise' by our institution.

To allow a comparison with our initial report, patients were divided into six prespecified groups based on their blood glucose on admission: < 6.5 mmol/l, 6.5–7 mmol/l, 7.1–9 mmol/l, 9.1–11 mmol/l, 11.1–20 mmol/l and > 20 mmol/l. These prespecified cut-offs were chosen to allow direct compassions with similar work presented as an abstract prior to this work being undertaken (Dr Philip Dyer, personal communication). Crude odds ratios were estimated to assess the association between mortality and blood glucose. To eliminate potential confounding with age and gender, a multivariable logistic regression model was fitted to estimate the adjusted odds ratios. Age was split into five equal groups for the regression model.

Results

During the 28 days of February 2010, 1502 patients were admitted through the AMU. Of those, 240 (16%) had an established diagnosis of type 1 or type 2 diabetes. 943 of the 1502 patients (63%) had a blood glucose measured on admission.

The results are shown in Tables 1–4. Table 1 shows the basic information of the patients admitted – how many were admitted under which speciality and how many of them had diabetes. Table 2 shows the number of individuals in each category of blood glucose and the number and percentage of those who died at 28 days, 1 and 2 years follow-up. At 28 days, there was a significantly increased odds ratio of death for those in the 11.1–20 mmol/l category compared with the <6.5 mmol/l category, which was not because of confounding by age or sex. However, the association was not present at either 1-year follow-up (p = 0.150) or 2-year follow-up (p = 0.171).

Table 1 A breakdown of total admissions under each speciality during February 2010, and what proportion of them had diabetes

Specialty	Number of patients	Number (%) with diabetes
Medicine for elderly people	577	94 (16.3)
Cardiology	221	25 (11.3)
Respiratory	200	28 (14)
Nephrology	30	9 (30)
Gastroenterology	132	18 (13.6)
Endocrinology	30	22 (73)
Neurology	77	12 (16.9)
Dermatology	1	0 (0)
Haematology	16	0 (0)
Oncology	56	4 (7.4)
General medicine	162	27 (16.7)

Table 3 shows the crude and adjusted odds ratio of death. Adjustment was made for age and gender. There was no significant relationship between admission blood glucose at admission in February 2010 and risk of death after 1 or 2 years of follow-up. The mortality in each group was in a mixture of people with and without a previous diagnosis of diabetes, that is, the deaths in each group were not limited to those with known diabetes.

Table 4 shows the crude and adjusted odds ratio of death. After adjustment for age and gender, mortality rates for each admission blood glucose range were compared with those using a baseline of 6.5–7 mmol/l. This demonstrated a significant increase in the odds ratio of death in the two groups with admission blood glucose between 9.1 and 11 mmol/l and 11.1 and 20 mmol/l at 28 days and 1 year, but not 2 years.

Discussion

We have shown that an admission blood glucose level between 9.1 and 20 mmol/l was associated with a statistically significant odds ratio for increased risk of mortality over 1 year of between 2.04 and 2.57 (p = 0.047 for glucose levels between 9.1 and 11.0 mmol/l, and p = 0.006 for glucose levels 11.1 and 20 mmol/l) when compared with an admission glucose of 6.5–7.0 mmol/l. The adjusted odds ratio for mortality at 1 year with a blood glucose < 6.5 mmol/l was 1.63 and showed a strong trend towards being statistically significant (p = 0.053).

Before publication of the Diabetes Control and Complications Trial (DCCT) in 1993, there was an enormous amount of information that showed long-term poor diabetes control was associated with poor outcomes (6). It was only after the publication of the DCCT, and subsequently the United Kingdom Prospective Diabetes Study (UKPDS) in 1998, that showed intervention in long-term glycaemic control made a difference in reducing diabetic complications (7). Inpatient diabetes care is in a similar position to that of outpatient treatment of diabetes prior to the publication of the DCCT, i.e. there is a lot of evidence to show that transient high blood glucose levels in hospitalised inpatients are associated with harm, but there is little evidence to show that

Table 2 Number of patients and the number and percentages of death by each follow-up time point

Blood glucose (mmol/l)	Number of patients	Number (%) of deaths within 28 days	Number (%) of deaths within 1 year	Number (%) of deaths within 2 years
< 6.5	488	64 (13.11)	146 (29.92)	166 (34.02)
6.5–7	122	11 (9.02)	28 (22.95)	40 (32.79)
7.1–9	152	22 (14.47)	47 (30.92)	57 (37.5)
9.1–11	64	14 (21.88)	24 (37.5)	27 (42.19)
11.1–20	76	17 (22.37)	29 (38.16)	32 (42.11)
> 20	41	4 (9.76)	12 (29.27)	14 (34.15)

intervention makes a difference (8). There are, however, data showing that hyperglycaemia in hospitalised patients with a wide range of specialities is associated with increased mortality (9,10). Our data are different, however, because we have focussed on analysing outcomes depending on a single blood glucose level taken on admission, rather than later on during the course of the inpatient stay.

Recent data have shown that there is a relationship between HbA1c and the 2-year risk of hospitalisation and mortality (11). In this respect, our data are similar in showing a relationship with a measure of glycaemic control; however, our data differ because rather than showing a relationship between a measure of overall glycaemic control over a 3-month period, we have shown a relationship between a single random blood glucose level and mortality.

The data we present make no attempt to identify the potential causes of the increased mortality, only to describe a relationship between admission blood glucose and the risk of death. It remains to be determined whether specific glucose lowering intervention will benefit these individuals – indeed, the benefits of tight glycaemic control remain hotly debated (8,12) – but the process of more frequent monitoring may be responsible for the earlier detection of potential complications (13). However, in an analysis of over 10 million hospital admissions across all English Hospitals between 2010 and 2012, the 11.2% of people recorded as having diabetes accounted for 21.5% of all deaths – and, as the authors explained, diabetes was associated with a 6.3% greater risk of dying (10). Therefore, the question of whether being labelled as having diabetes is somehow 'protective' or not in hospitalised patients, remains unanswered.

Previous work has shown that the prevalence of inpatient hypoglycaemia and hyperglycaemia are high (14). While not being statistically significant, the strong trend in our data towards a higher mortality in those with blood glucose levels < 6.5 mmol/l ($p = 0.053$) reflects the work of others to show that hypoglycaemia is associated with an increased risk of 1 year mortality (15,16). These individuals were not limited to one particular speciality, which made them more susceptible to hypoglycaemia, neither were these individuals limited to those known to have diabetes on glucose lowering drugs. Whether it is dysglycaemia per se that is responsible for the increased mortality, or whether hyper- or hypoglycaemia is a manifestation of the severity of the underlying illness ultimately associated with the premature mortality remains unanswered, and more work needs to be done in this area. Previous work looking at tight glucose control in the intensive care population (17,18), or those admitted with acute myocardial infarction (19), have been conflicting with no current consensus as to whether glucose levels should be controlled, and if so, what the target glucose range should be (20). Thus, whilst 'intuitively' it would seem sensible to treat hyperglycaemia in hospitalised patients, there remains uncertainty as to whether this is of value given the lack of convincing trial evidence to show that this is the case (8). Further work on this area, in particular which groups of hospitalised patients with hyper- or hypoglycaemia are at greatest risk of dying needs to be done. Well conducted, randomised clinical trials of treating hyperglycaemia in general medical inpatients are needed to answer this important question.

In our institution, we have a 'speciality triage system;' all patients are assessed in the AMU and then triaged to the appropriate speciality. Those with severe hyperglycaemia would typically be triaged to the endocrine team. As might be expected, many of these individuals had diabetic ketoacidosis and were often younger than many others admitted with lower (but still 'high') glucose levels. Thus, as a reflection of overall mortality in diabetic ketoacidosis, their overall mortality was not significant, although did show a trend towards increased mortality when age was adjusted for ($p = 0.07$).

Our data have a number of strengths. These patients represent an unselected cohort and were admitted under any medical speciality, thus the data

Table 3 Crude and adjusted odds ratio of death. Adjustment for was age and gender

Blood glucose (mmol/l)	For death within 28 days				For death within 1 year				For death within 2 years			
	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value
< 6.5	1		1		1		1		1		1	
6.5–7	0.66 (0.33–1.29)	0.22	0.62 (0.31–1.23)	0.174	0.7 (0.44–1.11)	0.129	0.61 (0.38–1.01)	0.053	0.95 (0.62–1.44)	0.797	0.85 (0.54–1.34)	0.482
7.1–9	1.12 (0.66–1.89)	0.668	0.95 (0.56–1.62)	0.858	1.05 (0.71–1.56)	0.814	0.8 (0.53–1.22)	0.298	1.16 (0.8–1.7)	0.431	0.89 (0.59–1.33)	0.561
9.1–11	1.86 (0.97–3.55)	0.062	1.71 (0.88–3.33)	0.112	1.41 (0.82–2.42)	0.218	1.25 (0.7–2.24)	0.45	1.42 (0.83–2.41)	0.199	1.25 (0.71–2.22)	0.437
11.1–20	1.91 (1.05–3.48)	0.035	2.01 (1.08–3.73)	0.028	1.45 (0.88–2.39)	0.15	1.58 (0.91–2.72)	0.102	1.41 (0.86–2.31)	0.171	1.53 (0.89–2.62)	0.121
> 20	0.72 (0.25–2.08)	0.539	0.88 (0.29–2.6)	0.811	0.97 (0.48–1.95)	0.93	1.38 (0.63–3)	0.418	1.01 (0.51–1.97)	0.987	1.44 (0.68–3.04)	0.343

Table 4 Crude and adjusted odds ratio of death. The figures in bold are statistically significant

Blood glucose (mmol/l)	For death within 28 days				For death within 1 year				For death within 2 years			
	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value	Crude odds ratio (95% CI)	p-value	Adjusted odds Ratio (95% CI)	p-value	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value
< 6.5	1.52 (0.78–2.99)	0.22	1.61 (0.81–3.19)	0.174	1.43 (0.9–2.28)	0.129	1.63 (0.99–2.66)	0.053	1.06 (0.69–1.61)	0.797	1.18 (0.75–1.85)	0.482
6.5–7	1		1		1		1		1		1	
7.1–9	1.71 (0.79–3.68)	0.171	1.53 (0.7–3.33)	0.281	1.5 (0.87–2.59)	0.143	1.3 (0.74–2.31)	0.366	1.23 (0.75–2.03)	0.418	1.04 (0.61–1.77)	0.875
9.1–11	2.83 (1.2–6.66)	**0.018**	2.75 (1.15–6.59)	**0.023**	2.01 (1.04–3.89)	**0.037**	2.04 (1.01–4.11)	**0.047**	1.5 (0.8–2.79)	0.206	1.48 (0.76–2.88)	0.254
11.1–20	2.91 (1.28–6.61)	**0.011**	3.23 (1.4–7.45)	**0.006**	2.07 (1.11–3.87)	**0.023**	2.57 (1.31–5.02)	**0.006**	1.49 (0.82–2.69)	0.186	1.8 (0.95–3.41)	0.071
> 20	1.09 (0.33–3.63)	0.887	1.41 (0.41–4.82)	0.585	1.39 (0.63–3.07)	0.417	2.24 (0.94–5.37)	0.07	1.06 (0.5–2.25)	0.873	1.69 (0.74–3.88)	0.214

are very generalisable. In addition, we have 2 years follow-up data on all the patients who were admitted. There are, however, limitations to our data. As previously noted only 63% of patients had their admission blood glucose levels measured, despite the widespread knowledge that hyperglycaemia is associated with poorer outcomes. Another limitation of the study was that we did not have any HbA1c measurements available to us. Thus, we were unable to know if there were many people in the cohort with previously undiagnosed diabetes, or what the overall control was like of those with known diabetes. Those without diabetes are likely to be the case in only a small number of people because in a large diabetes prevention study run in our catchment area, the prevalence of previously undiagnosed diabetes found in population screening of 'at risk adults' (i.e. over 40 years old with a body mass index over 30 kg/m^2) was approximately 2.3% (Professor Mike Sampson, Chief Investigator, Norfolk Diabetes Prevention Study, personal communication). Further limitations include no data on the severity of the underlying disease for which the patients were admitted that could have contributed to the hyperglycaemia or the hypoglycaemia. Our work was a retrospective cohort analysis and we did not look to see what the cause of death was in those individuals found to be hyperglycaemic, thus we were unable to determine whether the hyperglycaemia was directly related to the cause of death or not. However, because hyperglycaemia is common in the general population with diabetes without sequelae, we believe that it is unlikely that those with blood glucose levels of between 9.1 and 20.0 mmol/l died directly because of their hyperglycaemia, but that it was a consequence of their underlying condition. When considering the consequences of hypoglycaemia, there are data to show that very low glucose levels in hospitalised inpatients are common (21) and there is work ongoing looking at the causes of why this may be the case – for example currently recently published data suggest that hypoglycaemia is most common between 9 pm and 9 am when food availability is minimal, and carbohydrate snacks that the patient may take at home may be different (22). Indeed, there are data to show that the food available in hospital is one of the commonest causes of poor satisfaction with overall diabetes care in this population (23). However, the cause of the increased mortality seen in the acutely unwell population presenting to the emergency department with lowest glucose levels needs to be further investigated.

In summary, we have shown that a single blood glucose measurement taken at the time of acute hospital admission can help to predict 1 year mortality in an unselected cohort of general medical patients. Further work, ideally in the form of large randomised clinical trials, need to be done to see if the dysglycaemia is a cause of premature mortality or a manifestation of the underlying disease, and whether intervention and normalisation of blood glucose levels in these individuals makes a difference to short and long-term outcomes.

Acknowledgement

At the time this work was carried out, the authors were employees of the UK National Health Service (FH and KD), or the University of East Anglia (AC). No external funding was used.

Author contributions

Dr Dhatariya acts as the guarantor for the paper. KD conceived the idea. NE collected the data. FH and AC analysed the data and all of the authors contributed to the discussions surrounding the manuscript. FH wrote the original manuscript. All authors have reviewed and approved the final version.

References

1 Dungan KM, Braithwaite SS, Preiser J-C. Stress hyperglycaemia. *Lancet* 2009; **373**: 1798–807.
2 Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. *Lancet* 2000; **355**: 773–8.
3 Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab* 2002; **87**: 978–82.
4 Foo K, Cooper J, Deaner A et al. A single serum glucose measurement predicts adverse outcomes across the whole range of acute coronary syndromes. *Heart* 2003; **89**: 512–6.
5 Evans NR, Dhatariya KK. Assessing the relationship between admission glucose levels, subsequent length of hospital stay, readmission and mortality. *Clin Med* 2012; **12**: 137–9.
6 The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Eng J Med* 1993; **329**: 977–86.
7 UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; **352**: 837–53.
8 Dhatariya K. Should inpatient hyperglycaemia be treated? *BMJ* 2013; **346**: f134.
9 Bruno A, Gregori D, Caropreso A, Lazzarato F, Petrinco M, Pagano E. Normal glucose values are associated with a lower risk of mortality in hospitalized patients. *Diabetes Care* 2008; **31**: 2209–10.
10 Holman N, Hillson R, Young RJ. Excess mortality during hospital stays among patients with recorded diabetes compared with those without diabetes. *Diabetic Med* 2013; **30**: 1393–402.
11 Yu D, Simmons D. Relationship between HbA_{1c} and risk of all-cause hospital admissions among people with Type 2 diabetes. *Diabetic Med* 2013; **30**: 1407–11.
12 Van den Berghe G. What's new in glucose control in the ICU? *Intensive Care Med* 2013; **39**: 823–5.

13 Kwon S, Thompson R, Dellinger P, Yanez D, Farrohki E, Flum D. Importance of perioperative glycemic control in general surgery: a report from the surgical care and outcomes assessment program. *Ann Surg* 2013; **257**: 8–14.
14 Wexler DJ, Meigs JB, Cagliero E, Nathan DM, Grant RW. Prevalence of hyper- and hypoglycemia among inpatients with diabetes. A national survey of 44 U.S. hospitals. *Diabetes Care* 2007; **30**: 367–9.
15 Turchin A, Matheny ME, Shubina M, Scanlon JV, Greenwood B, Pendergrass ML. Hypoglycemia and clinical outcomes in patients with diabetes hospitalized in the general ward. *Diabetes Care* 2009; **32**: 1153–7.
16 Nirantharakumar K, Marshall T, Kennedy A, Hemming K, Coleman JJ. Hypoglycaemia is associated with increased length of stay and mortality in people with diabetes who are hospitalized. *Diabetic Med* 2012; **29**: e445–8.
17 Van den Berghe G, Wouters P, Weekers F et al. Intensive insulin therapy in the surgical intensive care unit. *N Eng J Med* 2001; **345**: 1359–67.
18 NICE Sugar study investigators. Hypoglycemia and risk of death in critically ill patients. *N Eng J Med* 2012; **367**: 1108–18.
19 Malmberg K, Ryden L, Efendic S et al. Randomized trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. *J Am Coll Cardiol* 1995; **26**: 57–65.
20 Umpierrez GE, Hellman R, Korytkowski MT et al. Management of hyperglycemia in hospitalized patients in non-critical care setting: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2012; **97**: 16–38.
21 Health and Social Care Information Centre. *National Diabetes Inpatient Audit (NaDIA) – 2012*. 2013. http://www.hscic.gov.uk/diabetesinpatientaudit (accessed 28 July 2014).
22 Rajendran R, Kerry C, Rayman G, on behalf of the MaGIC study group. Temporal patterns of hypoglycaemia and burden of sulfonylurea-related hypoglycaemia in UK hospitals: a retrospective multicentre audit of hospitalised patients with diabetes. *BMJ Open* 2014; **4**: e005165.
23 Rutter CL, Jones C, Dhatariya KK et al. Determining in-patient diabetes treatment satisfaction in the UK – the DIPSat study. *Diabetic Med* 2013; **30**: 731–8.

Paper received March 2014, accepted August 2014