Prevalence of Hyperglycemia in a Pre-Surgical Population

D Roberts, T Meakem, C Dalton, D Haverstick, C Lynch III

Citation

D Roberts, T Meakem, C Dalton, D Haverstick, C Lynch III. *Prevalence of Hyperglycemia in a Pre-Surgical Population.* The Internet Journal of Anesthesiology. 2006 Volume 12 Number 1.

Abstract

Prevalence of diabetes mellitus (DM) and presumably undiagnosed DM in the US has risen at an accelerating rate.
This prospective survey studied 1,000 non-diabetic patients who were scheduled to undergo anesthesia and surgical procedures. Subjects were 57.9% female, and 85.4% Caucasian, with a mean age of 55.4 ± 14.4 years. 3.6% of the patients were hyperglycemic (FBG >125) mg/dl, while an additional 26.9% had an impaired FBG (≥100 and <125 mg/dL). Multiple logistic regression analysis indicated that age, male gender, family history, and body mass index were the independent predictors of elevated FBG.
The percent of pre-surgical patients with hyperglycemia was at or above the national population estimate, as was the fraction of patients with impaired FBG. This prevalence is important because of the variety of perioperative complications associated with hyperglycemia including increased infection rates and cost of care. This data has altered patient care patterns at our institution.

This study was funded, in part, by an unrestricted grant from Roche Diagnostics.

INTRODUCTION

The Centers for Disease Control and Prevention (CDC) estimate that 20.8 million people (7.0% of the population) have diabetes mellitus (DM), of whom nearly a third (6.2 million) are thought to be undiagnosed.[1] This increase is related to a variety of factors, including doubling of the incidence of obesity over that same time period.[2] Metabolic syndrome, the combination of hyperglycemia, central obesity, hypertension, elevated high-density lipoprotein (HDL), and hypertriglyceridemia (three or more of these five) is estimated to have an even higher prevalence of 23.7 percent of the adult population, or 47 million people.[3] Both DM and metabolic syndrome are highly significant risk factors for cardiovascular disease.[4]

Even in the absence of preexisting DM, hyperglycemia itself is associated with increased morbidity and mortality among hospital inpatient, both in medical[5] and surgical populations.[6,7,8] High blood glucose levels affect the immune system's ability to control wound infection, related to a combination of factors, including impaired vascular growth and reactivity and decreased of neutrophil activity.[9] Recent editorials have emphasized the need for assessment and control of blood glucose in the perioperative period.[8,10] Awareness of the presence of hyperglycemia is essential if comprehensive control of clinical outcomes is to be achieved in these at-risk patients. Identification of hyperglycemic patients both with and without prior formal diagnosis of DM will be crucial in achieving these care improvement objectives, yet it is not clear if routine screening is necessary or appropriate. As an initial step in addressing the problem of controlling perioperative blood glucose, we sought to determine the prevalence of hyperglycemia and undiagnosed DM among our surgical population, and its agreement with the CDC estimate. We also wanted to determine any patient characteristics that permitted identification or prediction of those patients at increased risk for hyperglycemia.

RESEARCH DESIGN AND METHODS

In a convenience sampling, 1,000 patients entering the University of Virginia Health System as outpatients to undergo surgical procedures (requiring post-procedural admission or not) were enrolled over a nine month period. The study was reviewed and approved by the Human Investigation Committee of the University of Virginia. All subjects were provided informed consent to participate, and were informed that they would receive a written copy of the test results, but that those results would not go in their medical record. Patients were excluded from participation if they had been diagnosed with DM (approximately 11% of our patients), had anything to eat or drink with sugar overnight, were pregnant or lactating, or were under 18 years of age. The few patients who refused participation (<2%) did

not represent any specific sub-population. Since fluid intake was not permitted for only the six hours preceding surgery, the study was largely restricted to patients who had fasted overnight and arrived before noon. Demographic data, vital signs, and family history of DM were recorded, and distinction was made for gender or under-represented minorities.

IDENTIFICATION OF INDIVIDUALS WITH HYPERGLYCEMIA

A blood sample was obtained either from a finger puncture or during the course of IV placement prior to the surgical procedure. Blood glucose was measured immediately following its availability using a Roche ACCU-CHEK® Inform glucose meter (Indianapolis, IN), which employs an enzyme-catalyzed (glucose dehydrogenase) reaction of glucose with molecular oxygen. In accordance with the American Diabetes Association (ADA) and CDC, a FBG level >125 mg/dL (7.0 mM) was considered to be hyperglycemia and the diabetic threshold, and a FBG of 100-125 mg/dL (5.5-7.0 mM) was considered impaired fasting glucose (IFG).[1,11] Incidence and associations of FBG ≤100 mg/dL (5.5mM) and >125 mg/dL (7.0 mM) were examined. Normal blood glucose for this study was considered as from 70-99 mg/dL (3.9-5.5 mM). During the months of the study, we also gathered for comparison data from diabetic patients, whose blood glucose levels were routinely determined.

STATISTICAL ANALYSIS

Demographic variables and family history of DM were examined as contributing toward hyperglycemia and undiagnosed DM. Age and blood glucose levels were compared using a linear regression. Various multiple logistic regression models were constructed to examine the relationship of a specific variable after controlling for other factors using fasting blood glucose as the dependent variable and gender, height, BMI, and family history of DM as well as race as the independent variables. All tests were two-tailed and a p-value of <0.05 was considered statistically significant. Data are reported as mean ±SD for continuous variables and as percentages for ordinal variables. All data were analyzed using the Statistical Package for Social Scientists for Windows (SPSS, Version 12.0, Chicago, Il). BMI was defined as mass (in kg) / height (in m)^2 and obesity was defined as BMI of ≤ 30.0.

RESULTS

Subjects were 57.9% female, 85.4% Caucasian and 12.7% African American with a mean age of 55.4 ± 14.4 years, ranging 19 to 90 years. The mean mass of the population was 80.9 ± 21.1 kg and the mean BMI was 28.4 ±7.4.

In the total surveyed population, 3.6% were above the diabetic threshold of 125 mg/dL, and 30.5% had FBG ≤ 100 mg/dL (5.5 mM). The demographic composition of the study population is shown in Table 1A. The percentage of African Americans with glucose levels over the diabetic threshold was over three times that of the Caucasians in the study (Table 1B). All variables were normally distributed except for weight and BMI, which showed a greater number of patients who weighed more and had a higher BMI ('skew right'), an observation that is consistent with the increasing prevalence of obesity in the United States' population.

Figure 1

Table 1A: Characteristics of participants.

Characteristics	Total (n=1000)	Low <70 mg/dL (n=46)	Normal 70-99 mg/dL (n=649)	FBG ≥ 100 mg/dL (n=305)	FBG >125 mg/dL (n=36)
Men	42.1%	45.7%	38.5%	49.2%	50.0%
Women	57.9%	54.3%	61.5%	50.8%	50.0%
mean age (yrs)*	55.4 ±14.4	48.9 ±15.8	54.4 ±14.5	58.7 ± 13.3	55.0 ± 12.0
mean BMI (kg/m^2)	28.4 ±7.4	25.3 ±5.5	27.9 ± 6.8	29.8 ± 8.5	30.0 ± 9.1
mean Height (in)	66.8 ±6.2	66.1 ±3.4	66.6 ± 5.1	67.3 ± 8.4	67.5 ± 5.8
mean Weight (lbs)	177.4 ±46.3	154.5 ±33.4	174.1 ± 43.5	187.3 ± 52.5	189.8 ± 55.0
family history of diabetes	47.7%	50.0%	47.3%	48.0%	55.6%

*Figures are mean ± SD

Figure 2

Table 1B: Baseline race of participants

Race	Total (n=747)	Low <70 mg/dL (<3.9 mM) (n=36)	Normal 70-99 mg/dL (3.9-5.5 mM) (n=481)	FBG ≥100 mg/dL (>5.5 mM) (n=230)	FBG >125 mg/dL (≥7.0 mM) (n=28)
Caucasian	85.4%	77.8%	86.3%	84.8%	67.9%
African American	12.7%	22.2%	11.6%	13.4%	32.1%
Other	2.1%	0%	2.1%	1.8%	0.0%

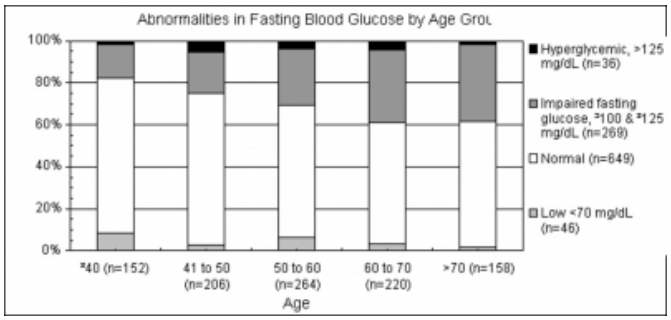
Of note, 4.6% of the patients had a FBG below 70, with an average value of 63 ±6 mg/dL (range 41-69 mg/dL), although none of the hypoglycemic patients were symptomatic. Only seven of these patients (15%) were obese, whereas 38.8% of the 305 patients with IFG or hyperglycemia were obese.

STATISTICAL RELATIONSHIP OF HYPERGLYCEMIA WITH PATIENT CHARACTERISTICS

Multiple logistic regression identified age, gender, and BMI as risk factors for IFG. Patients' FBG increased with age (linear regression, P<0.001), however, this relationship, was weak, with an R^2 of 0.02. The correlation of FBG with BMI as well as with weight was also highly significant, p<0.001. Figure 1 shows the percent of IFG and hyperglycemic patients in groups divided by age (Figure 1A) and BMI (Figure 1B). Clearly, the fraction of patients with IFG increased with age and with BMI. Our analysis showed that gender was the strongest independent predicting factor for IFG with an odds ratio for males vs. females of approximately 1.6. While men constituted 42.1% of the study population, they composed 49.3% of the population with an IFG. Although 50% of hyperglycemic patients were men (numbering 18), their number did not differ sufficiently from the number of women to make male gender a hyperglycemic risk factor. Using only the diabetic threshold of 125 mg/dL as the dependent variable, BMI was found to be the sole predictive variable (p=0.02).

Figure 4

Figure 1. Percent of patients with low (<70 mg/dL), normal (?70,<100 mg/dL), impaired fasting blood glucose (?100, ?125 mg/dL), or hyperglycemia (>125 mg/dL) divided according to (A) different age groups, or (B) grouping based on Body Mass Index (kg/m).



{image:4}

Racial information was available in only a portion of the study group (N=747), and its inclusion only affected the outcome of the model when hyperglycemia was analyzed. In this multivariate model, race was the only predictive variable with an odds ratio of 0.29; that is, the probability of having an FBG over 125 mg/dL was over three times greater for African Americans than Caucasians.

Approximately 11% of patients were not included in the study bases on a prior diagnosis of DM. During the months of the study, over 83% of the diabetic outpatients arrived with FBG ≤100 mg/dL; over 61% had a FBG >125 mg/dL, and the value exceeded 200 mg/dL in more than 20% of these patients.

DISCUSSION

We determined that over three in one hundred people who enter our hospital for surgical procedures may have hyperglycemia consistent with undiagnosed DM, and three out of every ten people have IFG as defined by the ADA. Presuming the 3.6% of patients with FBG levels >125 mg/dL represent undiagnosed diabetic patients, that fraction exceeds the CDC estimate of 2.0%, calculated based on 6.2 million undiagnosed diabetic individuals in a US population of 299 million.[1] The linear regression analyses suggest that having higher BMI or being older increases the risk of an elevated FBG, which has been documented in other studies.[2] A patient with a BMI>40 is almost twice as likely to have IFG as a patient with a BMI<25. Likewise, patients >60 years of age have twice the risk of increased FBG of those less than 40 years of age. However, for either BMI or age, the association is weak and does not permit prediction of a specific target for age or BMI above which to test glucose. Being African-American also increased the odds of IFG. While lack of regular medical care or absence of screening opportunities may contribute, the observed hyperglycemia among African Americans maybe related to the higher rate of obesity we observed: 37.9% of African Americans had a BMI >30, compared to 28.7% among Caucasians. This difference has been observed previously, although with lower rates of obesity noted in both groups (31.1% for blacks and 19.6% for whites.[2]) Although not observed in the 2003 report of prevalence, we found that being male was a significant risk factor for hyperglycemia in our patients. However, hyperglycemia in men and women differed among the various age groups. In women aged 30-69, there was a steady increase with each age decade of the fraction of patients as whose FBG was hyperglycemic, which correlates with the greater prevalence of diabetes with increasing age.[2] In men, the hyperglycemic fraction of men decreased as age exceeded 50.

Surprisingly, a family history of DM was not associated with hyperglycemia in this study when patients' other characteristics were included in the analysis. One explanation for this divergence is the relatively small size of the sample survey, where only 36 people had blood glucose levels above the diabetic threshold. Approximately 11%, of patients were excluded from the study based on their prior

diagnosis of diabetes, a fraction that is typical of our practice at present. This incidence of diagnosed diabetes is higher than the incidence of 4.9% reported by the CDC. However, since the incidence of hyperglycemia increases with age,[2] this higher prevalence probably is due in part to the greater average age of our patients (55.5 ±14.4 years) compared to the national average. If patients with previously diagnosed diabetes are included in the tabulation, 26.4% had IFG and 9.9% were hyperglycemic.

Given the association of DM with a wide variety of other chronic medical problems (heart disease, renal impairment, and neuropathy), it is important to identify previously undiagnosed patients who may be at risk for serious complications. It has been observed that patients who have not been formally diagnosed as diabetic may not receive appropriate interventions to lower glucose.[5] Unfortunately, it is highly unlikely that a glucose tolerance test can be scheduled in the timeframe of perioperative care to provide a more certain diagnosis of DM. Measurement of glycosylated hemoglobin A1c (HA1c) has been suggested to provide valuable information regarding the chronicity of the hyperglycemia. The presence of hyperglycemia or even IFG combined with other risk factors (obesity, age), may justify determination of HA1c in order to provide an indication of the duration of hyperglycemia, and likelihood of DM. Whether or not routine measurement of HA1c is done may depend on the magnitude of the surgical intervention, anticipated post-operative course, and individual patients co-morbidities. In addition to identifying patients who may need longer duration diabetic therapy, an elevated HA1c, particularly if associated with the insulin resistance of type 2 DM, may indicate that a longer period of immediate therapy or higher dose of insulin may be required for perioperative period.

While identification of undiagnosed DM is important, of equal importance may be identification of those patients with metabolic syndrome. This constellation of elevated glucose, elevated blood triglycerides (and low HDL), hypertension, and central obesity carries with it significant risk of cardiovascular disease.[4] Although the question has been raised as to whether it defines a distinct entity or rather a constellation of risk factors for cardiovascular disease,[12] IFG combined with hyperlipidemia and/or hypertension and/or central obesity does identify patients at greater risk for cardiovascular impairment.[13,14] Both type 2 DM and metabolic syndrome are associated with higher concentrations of the inflammatory mediator C-reactive protein (CRP).[15,16] Elevation of CRP is associated with coronary syndromes and other cardiovascular disease,[15,17] although its presence has also been associated with development of DM.[16]

Certainly, the microvascular changes associated with diabetes and chronic hyperglycemia would be likely to contribute to altered wound healing and resistance to infection. Although these chronic changes associated with hyperglycemia include increased risk for vascular compromise at various levels, hyperglycemia per se during the immediate perioperative period is thought to carry significant risk. Hyperglycemia alone can impair leukocyte function, increasing the risk of infection, and potentially interfere with wound healing. The relationship between blood glucose levels and surgical outcome has been most thoroughly investigated in cardiac surgery. Zerr et al. found that tight glycemic control via insulin infusion the first two days after surgery decreased infection rates from 2.4% to 1.5%.[18] Similarly, Furnary et al. found that continuous intravenous insulin infusion after surgery led to a reduction in infection rates from 2.0% to 0.8%.[19] More recent studies have also demonstrated that there are decreases in mortality, length of stay and cost when the glucose levels were well controlled.[6,9,20] An overall improvement in mortality and reduction in morbidity have also been demonstrated in intensive care units with use of insulin infusions to more carefully control blood glucose.[21,22,23,24] These improvements in quality of care have also been shown to have associated cost savings [25,26] One question that arises is whether the treatment espoused for critically ill patients (cardiac surgery,[8] intensive care[10]) should be extended to the far more numerous hyperglycemic perioperative patients. In patients hospitalized for non-surgical procedures, whether or not patients were previously diabetic, hyperglycemia by itself was associated with a significantly higher morbidity and mortality.[5,27]

In screening only participants who had engaged in an overnight fast, we presumed our patients' honesty and adequate memory. A few of the patient's caloric intake may have been slightly more recent than the eight hour fast typically utilized for a true FBG, however, most patients indicated that their last intake was prior to bed before 2300. Some diabetic patients may have denied presence of the disease for fear of canceling surgery, potentially increasing the number of ‘undiagnosed' patients. Rare patients refused to participate in the study given the perceived pain of a finger stick or not wanting to know their blood glucose level

prior to the procedure, but such self-selection bias introduced would have been minimal. Finally, while our method of measuring blood glucose using the ACCU-CHEK® Inform was fast, it is inherently less accurate than formal laboratory testing. In spite of the limitations of the study, our institution is implementing routine determination of fasting glucose in all patients scheduled for surgery to permit appropriate attempts to control blood glucose in the perioperative period.

No study has implemented strict control of post-surgical glycemic levels on a general surgical population to examine the effect on outcome, nor has any study reported the predictive capability of pre-surgical blood glucose levels on post-surgical levels. Institutionally, we are implementing testing of all patients FBG to determine the degree of elevation. IFG will indicate the need for postoperative observation, while hyperglycemia will require intraoperative glucose measurement, as well an HA1c measurement to permit the duration of the hyperglycemia to be estimated and treated as necessary to control blood glucose. While clear benefit has been demonstrated for critically ill patients, further clinical investigation of routine surgical procedures will be required to identify the benefits of rigorous perioperative control of blood glucose for hyperglycemic patients.

ACKNOWLEDGEMENTS

The authors wish to thank Katie Shepherd, Eric Diaz, Ashley Nguyen and Jiaki Zhu for assistance in conducting this study.

CORRESPONDENCE TO

David Roberts dar8n@hscmail.mcc.virginia.edu Department of Anesthesiology University of Virginia Health System Charlottesville, VA 22908-0710 USA Tel. 1-434-982-1057 Fax 1-434-982-0019

References

1. Centers for Disease Control and Prevention: National diabetes fact sheet: general information and national estimates on diabetes in the United States. Atlanta, GA, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2005
2. Mokdad AH, Ford ES, Bowman BA, Dietz WH, Vinicor F, Bales VS, et al.: Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. JAMA 2003; 289: 76-9
3. Ford ES, Giles WH, Dietz WH: Prevalence of the metabolic syndrome among US adults: findings from the third national health and nutrition examination survey. JAMA 2002; 287: 356-9
4. Resnick HE, Howard BV: Diabetes and cardiovascular disease. Annu Rev Med 2002; 53: 245-67
5. 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
6. Gandhi GY, Nuttall GA, Abel MD, Mullany CJ, Schaff HV, Williams BA, et al.: Intraoperative hyperglycemia and perioperative outcomes in cardiac surgery patients. Mayo Clin Proc 2005; 80: 862-6
7. Ouattara A, Lecomte P, Le Manach Y, Landi M, Jacqueminet S, Platonov I, et al.: Poor intraoperative blood glucose control is associated with a worsened hospital outcome after cardiac surgery in diabetic patients. Anesthesiology 2005; 103: 687-94
8. Kersten JR, Pagel PS, Warltier DC: Aggressive control of intraoperative blood glucose concentration - a shifting paradigm? Anesthesiology 2005; 103: 677-8
9. Latham R, Lancaster AD, Covington JF, Pirilo JS, Thomas CS, Jr.: The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. Infect Control Hosp Epidemiol 2001; 22: 607-12
10. Coursin DB, Prielipp RC: The new anesthesia diet plan: Keeping perioperative carbs in check. Anesth Analg 2004; 99: 316-8
11. American Diabetes Association: Diagnosis and classification of diabetes mellitus. Diabetes Care 2004; 27: S5-S10
12. Ford ES, Giles WH: A comparison of the prevalence of the metabolic syndrome using two proposed definitions. Diabetes Care 2003; 26: 575-81
13. Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, et al.: Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 2001; 24: 683-9
14. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al.: The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA 2002; 288: 2709-16
15. Ford ES: Body mass index, diabetes, and C-reactive protein among U.S. adults. Diabetes Care 1999; 22: 1971-7
16. Fröhlich M, Imhof A, Berg G, Hutchinson WL, Pepys MB, Boeing H, et al.: Association between C-reactive protein and features of the metabolic syndrome. Diabetes Care 2000; 23: 1835-9
17. Ridker PM, Wilson PW, Grundy SM: Should C-reactive protein be added to metabolic syndrome and to assessment of global cardiovascular risk? Circulation 2004; 109: 2818-25
18. Zerr KJ, Furnary AP, Grunkemeier GL, Bookin S, Kanhere V, Starr A: Glucose control lowers the risk of wound infection in diabetics after open heart operations. Ann Thorac Surg 1997; 63: 356-61
19. Furnary AP, Zerr KJ, Grunkemeier GL, Starr A: Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. Ann Thorac Surg 1999; 67: 352-60
20. Furnary AP, Gao G, Grunkemeier GL, Wu Y-X, Zerr KJ, Bookin S, et al.: Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. J Thorac Cardiovasc Surg 2003; 125: 1007-21
21. Van den Berghe G, Wouters PJ, Weekers F, Verwaest C, Bruyninckx F, Schetz M, et al.: Intensive insulin therapy in critically ill patients. N Engl J Med 2001; 345: 1359-67
22. Finney SJ, Zekveld C, Elia A, Evans TW: Glucose control and mortality in critically ill patients. JAMA 2003; 290: 2041-7

23. Krinsley JS: Effect of an intensive glucose management protocol on the mortality of critically ill adult patients. Mayo Clin Proc 2004; 79: 992-1000
24. Pittas AG, Siegel RD, Lau J: Insulin therapy for critically ill hospitalized patients - a meta-analysis of randomized controlled trials. Arch Intern Med 2005; 164: 2005-11
25. Krinsley JS, Jones RL: Cost analysis of intensive glycemic control in critically ill adult patients. Chest 2006; 129: 644-50
26. Van den Berghe G, Wouters PJ, Kesteloot K, Hilleman DE: Analysis of healthcare resource utilization with intensive insulin therapy in critically ill patients. Crit Care Med 2006; 34: 612-6
27. Capes SE, Hunt D, Malmberg K, Gerstein HC: Stress hyperglycemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. Lancet 2000; 355: 773-8

Author Information

David E. Roberts, MSE, MPH
Department of Anesthesiology, University of Virginia Health System

Timothy D. Meakem, MD
The Epsilon Group

Claudette E. Dalton, MD
Department of Anesthesiology, University of Virginia Health System

Doris M. Haverstick, Ph.D.
Department of Pathology, University of Virginia Health System

Carl Lynch III, MD, PhD
Department of Anesthesiology, University of Virginia Health System