ORIGINAL RESEARCH

Prevalence and Clinical Outcome of Inpatient Hyperglycemia in a Community Pediatric Hospital

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BACKGROUND: Inpatient hyperglycemia in adult patients with and without a history of diabetes is a predictor of poor clinical outcome. No previous studies, however, have examined the association of hyperglycemia and clinical outcome in children admitted to a community pediatric hospital.

METHODS: The study was a retrospective observational cohort of pediatric patients admitted to a community children's hospital from January 2004 to August 2004. Medical records of 903 consecutive children admitted to critical and non–critical care areas were reviewed. Of them, 342 patients (38%) had no blood glucose measurements during their hospital stay. In the remaining patients, we determined the prevalence of hyperglycemia and examined the association of hyperglycemia with clinical outcome.

RESULTS: A total of 406 patients (75%) had an admission blood glucose ≤ 120 mg/dL (mean $\pm$ SEM 98 $\pm$ 1 mg/dL), 103 children (19%) had an admission blood glucose level of 121–179 mg/dL (mean 143 $\pm$ 2 mg/dL), and 32 patients (5.9%) had a blood glucose level ≥ 180 mg/dL (mean 260 $\pm$ 18 mg/dL). Seventeen patients (13%) had a known history of diabetes prior to admission. Children with hyperglycemia were more likely to be admitted to the ICU ($P < .001$) and had a longer length of ICU stay ($P < .001$), but admission hyperglycemia was not associated with longer hospital stay or higher hospital mortality.

CONCLUSIONS: Hyperglycemia is present in one-fourth of children admitted to the hospital, most of them without a history of diabetes prior to admission. Hyperglycemia was associated with a greater need for ICU care and longer ICU stay but not with increased in-hospital mortality. *Journal of Hospital Medicine* **2008;3:212–217.** © *2008 Society of Hospital Medicine.*

KEYWORDS: Pediatrics, hyperglycemia, hospital length of stay, morbidity, mortality.

Diabetes is one of the most common diagnoses in hospitalized patients.[1,2] Hyperglycemia is present in 38% of adults admitted to the hospital, one third of whom had no history of diabetes before admission.[3] The impact of inpatient hyperglycemia on clinical outcome in adult patients has been increasingly appreciated. Extensive evidence from observational studies indicates that hyperglycemia in patients with or without a history of diabetes is an important marker of poor clinical outcome.[3–12] Several prospective randomized trials in patients with critical illness have shown that aggressive glycemic control improves short- and long-term mortality, multiorgan failure and systemic infection, and length of hospitalization.[13–17] The importance of glucose control also applies to adult patients admitted to general surgical and medical wards.[3,6,18] In such patients, we recently reported that the presence of hyperglycemia is associated with prolonged hospital stay, infection, disability after hospital

discharge, and death.[3,6,18] Despite the extensive data in adult patients, there is little information on the impact of inpatient hyperglycemia in pediatric patients. The few observational studies in critically ill children admitted to the pediatric ICU with severe brain injury or extensive burn injuries have shown a positive association between inpatient hyperglycemia and increased length of hospital and ICU stay and a higher risk of complication and mortality rates.[19–23] No previous studies, however, have examined the association of hyperglycemia and clinical outcome in children admitted to a general community pediatric hospital. Therefore, in this study we determined the prevalence of inpatient hyperglycemia and examined the impact of hyperglycemia on morbidity and mortality in children admitted to Hughes Spalding Children's Hospital, a large community hospital serving the inner city and indigent pediatric population in Atlanta, Georgia.

MATERIALS AND METHODS

This was a retrospective observational cohort of pediatric patients consecutively admitted to Hughes Spalding Children's Hospital in Atlanta from January 2004 to August 2004. This general community pediatric hospital is part of the Grady Health System in Atlanta, a large health care organization that operates under the auspices of the Fulton-Dekalb Hospital Authority—the major counties in metropolitan Atlanta—to deliver care to their uninsured and underserved populations. Ninety percent of the organization's inpatient cases are either uninsured or dependent on Medicaid. This is a broad-based pediatric hospital without cardiac surgery, burn, or dedicated inpatient hematology-oncology units. Patients are managed by members of the pediatric residency program and supervised by faculty members from Emory University School of Medicine. The Institutional Review Board of Emory University and Grady Health System Oversight Research Committee approved the methods for data collection and analysis used in the study and waived the need for informed consent.

The medical records of 903 consecutive pediatric patients admitted to both critical and noncritical care areas were reviewed. For the analysis, patients were divided according to a known history of diabetes prior to admission and according to admission blood glucose concentration. A normoglycemic group included patients with normal plasma glucose and without a history of diabetes. Serum or plasma glucose measured in the laboratory was assumed to be equivalent to blood glucose measured by finger stick at bedside using a glucose meter. Hyperglycemia was defined as an admission or in-hospital blood glucose level >120 mg/dL. High blood glucose was subsequently divided into those with blood glucose of 120–179 mg/dL and those with blood glucose ≥180 mg/dL. Patient information was collected regarding demographic characteristics, blood glucose level on admission and during hospital stay, concurrent medical diagnoses, medical treatment, and hospital outcome (including mortality and disposition at discharge).

The primary objectives of this study were to determine the prevalence of in-hospital hyperglycemia and to examine the association of hyperglycemia and mortality in children with critical and noncritical illness in a community pediatric hospital. Secondary end points included length of hospital stay, requirement of intensive care, and treatment of hyperglycemia. In addition to blood glucose level, prognostic variables included sex, age, body mass index, admission diagnosis, presence of comorbidities, and intensive care unit admission.

Statistical Analysis

To compare demographics and clinical characteristics between groups, the independent t test and ANOVA with Sheffé's method were used for continuous variables. Levine's test for homogeneity of variances and log transformations were used when necessary. For categorical variables, χ^2 analysis was used. $P < .05$ was considered significant. SPSS version 12.0 (SPSS, Inc., Chicago, IL), was the statistical software used for the analysis.

RESULTS

Of the 903 admitted patients, 342 patients (38%) had no blood glucose measurement during the hospital stay and were excluded from the analysis. Three patients with a length of stay greater than 6 months were excluded. In addition, 16 patients admitted with diabetic ketoacidosis (DKA) and 1 subject with hyperglycemic hyperosmolar syndrome were also excluded from the analysis. The remaining 542 patients constituted the study population. Most of these, 406 patients (75%), had
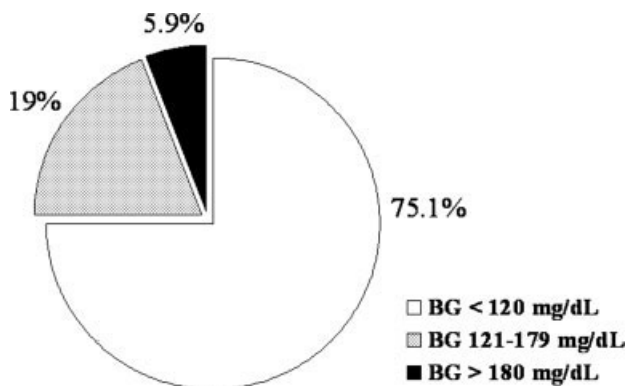
FIGURE 1. Hyperglycemia: a common comorbidity in medical-surgical patients admitted to a community pediatric hospital. A total of 24.9% of the children admitted to a community children's hospital were found to have high blood glucose on admission. Hyperglycemia was defined as an admission blood glucose level >120 mg/dL and subsequently divided into those with blood glucose between 120 and 179 mg/dL and those with blood glucose ≥180 mg/dL.

TABLE 1
Patient Characteristics on Admission

	BG <120 mg/dL	BG 121–179 mg/dL	BG ≥180 mg/dL
No. of patients (%)	406 (75%)	103 (19%)	32 (6%)
Mean age (years)	7.0 ± .4	6.8 ± .6	7.8 ± 1.1
Sex (M/F)	50/50	57/43	50/50
Race			
White	4%	8%	9%
Black	80%	80%	84%
Hispanic	15%	10%	6%
Other	1%	2%	1%
Weight on admission (kg)	29 ± 2	26 ± 3	32 ± 6
Height on admission (cm)	79 ± 4	94 ± 9	74 ± 19
Body mass index (kg/m^2)	17 ± 5	18 ± 4	37 ± 16[†]
Mean admission BG	92 ± 1	143 ± 2[‡]	260 ± 18[‡]
Mean inpatient BG	96 ± 3	109 ± 5	159 ± 13[‡]
Mean length of hospital stay	3.8 ± 0.2	5.4 ± 1.0	5.7 ± 1.8
Mean length of ICU stay	0.6 ± 0.1	1.1 ± .4[a]	3.6 ± 1.9[‡]
Admission service (%)			
Pediatrics	79.6%	58.8%	72.4%
Surgery	20.4%	41.2%	27.6%

Results are ± SEM.
Patients with d diabetic ketoacidosis (DKA) patients (n = 16) were excluded from analyses.
[†] $P < .05$ versus. normoglycemia.
[‡] $P < .001$ versus. normoglycemia.

an admission blood glucose concentration ≤120 mg/dL (mean ± SEM 98 ± 1 mg/dL, median 93 mg/dL). A total of 103 children (19%) had an admission blood glucose level of 121–179 mg/dL (mean 143 ± 2 mg/dL, median 140 mg/dL), and 32 patients (5.9%) had an admission blood glucose level >180 mg/dL (mean 260 ± 18 mg/dL, median 211 mg/dL; Fig. 1).

The clinical characteristics of study patients are shown in Table 1. Most patients in this study were from minority ethnic groups—82% were black, 12% were Hispanic, 2% were from other minority groups, and 4.2% were white. There were no significant differences in mean age, sex, racial distribution, or body mass index among the 3 groups. A total of 409 patients (75.5%) were admitted to general pediatric wards and 133 patients (24.5%) were admitted to the surgical unit. There were no differences in the admission blood glucose between patients admitted to general pediatric wards (112.2 mg/dL) and those admitted to surgical areas (115.7 mg/dL, $P > .05$). The most common diagnoses in the severe hyperglycemia group were trauma/surgery (25%), pulmonary disease (18.8%), metabolic disorders (12.5%), and infection (6.3%). Most children admitted with hyperglycemia had no history of diabetes prior to admission. Among the 135 children with admission hyperglycemia (blood glucose >120 mg/dL), 17 patients (13%) had a known history of diabetes or were receiving therapy prior to admission. The mean admission blood glucose was 162.4 mg/dL (range 121–480 mg/dL) in children with new hyperglycemia and 369.8 mg/dL (range 145–678 mg/dL) in those children with a known history of diabetes ($P < .01$). Among children without a history of diabetes, 33 of 118 children (28%) with admission hyperglycemia had 1 or more glucose values >120 mg/dL during their hospitalizations. Twenty-five children had a blood glucose of 121–179 mg/dL (mean 109 ± 5 mg/dL), and 8 children had a blood glucose ≥180 mg/dL (mean 159 ± 13 mg/dL). Most patients with a history of diabetes were admitted with significant hyperglycemia. One patient (1%) had a glucose level in the 121–179 mg/dL category, and 16 patients (50%) had a glucose level >180 mg/dL.

The presence of hyperglycemia on admission in pediatric patients was not associated with increased mortality or with increased length of hospital stay. There was only 1 death reported during the study period, which occurred in a patient with respiratory failure because of bronchiolitis who was admitted with an admission blood glucose of 151 mg/dL. The mean length of stay for patients with normoglycemia was 3.83 ± 0.2 days,

which increased to 5.36 ± 1.0 and 5.68 ± 1.8 days for children with blood glucose of 120–179 and ≥180 mg/dL, respectively ($P > .05$).

Children with hyperglycemia were more likely to be admitted to the ICU and had a longer length of ICU stay. Admission to the ICU was needed by 10% of children with an admission blood glucose <120 mg/dL, 18% of children with a blood glucose of 120–179 mg/dL, and 40% of children with an admission blood ≥180 mg/dL ($P < .01$). In addition, length of ICU stay was significantly longer for hyperglycemic children, particularly those with a glucose level ≥180 mg/dL ($P < .001$). The mean length of ICU stay (ICU) was 0.56 ± 0.1 days for patients with normoglycemia, and 1.1 ± 0.4 days and 3.6 ± 1.9 days for patients with a blood glucose of 120–179 and ≥180 mg/dL, respectively ($P < .01$).

Newly diagnosed hyperglycemia was frequently left untreated. Only 3 children without a history of diabetes but with hyperglycemia recorded during the hospital stay received insulin therapy. New hyperglycemia patients received regular insulin per a sliding scale as the main insulin regimen in the hospital. In contrast, all patients with a previous history of diabetes were treated with insulin during their hospital stay.

DISCUSSION

Diabetes mellitus represents a significant public health burden on the basis of increased morbidity, mortality, and economic costs. Increasing evidence from observational and prospective interventional studies has shown that inpatient hyperglycemia is a predictor of poor clinical outcome of adult subjects.[3–13,16,17] Admission hyperglycemia has been associated with increased morbidity and mortality in patients with critical illness, as well as in non–critically ill adult subjects admitted to general surgical and medical wards.[3,6,18] In this study we also found that hyperglycemia is a common finding in children admitted with critical and noncritical illnesses and that most children had no history of diabetes before admission. One-fourth of the children admitted to the hospital had hyperglycemia on admission. Children with hyperglycemia were more likely to be admitted to the ICU and had a longer length of ICU stay; however, inpatient hyperglycemia was not associated with higher hospital mortality or longer hospital stay than was inpatient normoglycemia. Our findings suggest

that recognition of inpatient hyperglycemia can be improved because screening for hyperglycemia was not performed in more than one third of patients (38%) during the hospital stay.

The prevalence of inpatient hyperglycemia in children varies according to the severity of the illness and the study population. Ruiz Magro et al.[21] reported that 50% of 353 critically ill children without diabetes mellitus had initial glucose values >120 mg/dL. In a study of 942 nondiabetic patients, Faustino et al.[20] found that within 24 hours of admission to the ICU, hyperglycemia was prevalent in 70.4% of patients with a glucose value >120 mg/dL, 44.5% of patients with a glucose value >150 mg/dL, and 22.3% of patients with a glucose value >200 mg/dL. The prevalence of hyperglycemia in non-critically ill children seen in the emergency department was much lower, ranging from 3.8% to 5.0% (based on an initial blood glucose >150 mg/dL).[19,24] In agreement with these studies, we found inpatient hyperglycemia to be a common finding among hospitalized children. Approximately 75% of our patients had a normal blood glucose on admission, 19% had an admission blood glucose of 121–179 mg/dL (mean 143 ± 2 mg/dL), and 5.9% of children had an admission blood glucose ≥180 mg/dL (mean 260 ± 18 mg/dL). Only 13% of our patients had a known history of diabetes prior to admission, suggesting that the hyperglycemia was a result of the stress of the medical illness or the surgery. Stress hyperglycemia, defined as a transient increase in blood glucose level during acute physiological stress, has been reported to occur in 4% of children with an acute non-critical illness and in more than 50% of children in the ICU.

A few studies have reported on the impact of inpatient hyperglycemia in children with acute critical illness.[10–15] Three retrospective studies have demonstrated that admission hyperglycemia is also a predictor of adverse outcomes in the pediatric intensive care unit.[20,22] Srinivasan and colleagues[22] demonstrated that 86% of patients in their pediatric intensive care unit had a glucose value >126 mg/dL at some point during their stay. In addition, they showed that duration of the hyperglycemia and peak glucose were also associated with mortality. Faustino and Apkon[20] demonstrated that hyperglycemia occurs frequently among critically-ill nondiabetic children and is correlated with a greater in-hospital mortality rate and longer length of stay in the ICU. They reported a 2.5-fold increased risk of dying if the

maximum glucose obtained within 24 hours of admission to the ICU was >150 mg/dL. More recently, Yates et al.[25] reported that hyperglycemia in the postoperative period was associated with increased morbidity and mortality in postoperative pediatric cardiac patients. Other studies in children with traumatic brain or head injury have also shown an association between poor neurological outcome and elevated admission blood glucose.[24,26–28] Brain trauma patients with permanent neurological deficits and in a vegetative state were found to have significantly higher admission blood glucose concentrations than children with good neurological recovery or minimal deficits. In addition, the development of inpatient hyperglycemia in children with extensive burn injuries, covering more than 60% of total body surface area, was found to increase the risk of bacteremia and fungemia, reduce skin graft adhesion, and increase the mortality rate.[29] These data show an association of initial glucose, peak glucose, and duration of hyperglycemia with increased incidence of morbidity and mortality in children with acute critical illness. We found no association between initial blood glucose and risk of death. This is in contrast to our previous results in adult patients, in whom inpatient hyperglycemia was found to represent an important marker of increased morbidity and mortality among both those critically ill and not critically ill.[3] It is important to note that the overall mortality rate reported in children with hyperglycemia relates to severity of illness and is significantly lower than that of adults.[30] In most critically ill pediatric series, hospital mortality ranges from 2% to 5.3% and is higher in patients with severe trauma and those who underwent major cardiac surgery.[23,31] The mortality in children without critical illness admitted to general pediatric wards is significantly lower.[30]

In agreement with the increasing rate of obesity among children with diabetes,[32,33] especially in minority populations, we found that hospitalized children with a history of diabetes and glucose >180 mg/dL had a higher body mass index than those with normoglycemia ($P < .001$). Obesity in children has been associated with the presence of several comorbidities and an increased risk of hospital complications.[34,35] There is also increasing evidence among patients admitted to the intensive care unit that obesity contributes to increased morbidity and to a prolonged length of stay.[35] Because they have a higher rate of hyper-

glycemia, diabetes, and hospital complications, we believe that obese children should be screened for hyperglycemia and diabetes.

We acknowledge the following limitations of this study. The main limitation was its retrospective nature. The method of blood glucose collection and analysis was not standardized; thus, it prevented uniformity in the determination of serum glucose values of individual patients. We arbitrarily used 3 glucose cutoff values in this study (<120, 120–179, and >180 mg/dL). Although similar values have been used in inpatient diabetes studies,[20–22] there is no uniform definition of hyperglycemia in hospitalized patients, and the clinical significance of these cutoff values in pediatric population has not been determined. The study was conducted in a single institution in Atlanta, whose population and disease spectrum might be different from those at other pediatric institutions. Our study did not address the question of whether treatment of hyperglycemia might improve the outcome of length of hospital stay of patients with hyperglycemia. We believe that newly diagnosed hyperglycemia is usually considered a transient finding in response to acute illness not requiring medical intervention, as indicated by the fact that more than half of these patients did not receive antidiabetic therapy. Another limitation of our study is that we were not able to determine the percentage of patients with latent or unrecognized diabetes because of the lack of hemoglobin A1C testing and follow-up after discharge. A prospective, randomized trial of strict glycemic control is certainly needed to address these issues.

In summary, inpatient hyperglycemia is a common finding in children with and without critical illness. One-fourth of the children admitted to the hospital had hyperglycemia, most of them without a history of diabetes prior to admission. Although we found a higher need for ICU admission and a longer length of ICU stay, hyperglycemia in pediatric patients was not associated with higher hospital mortality compared with that in children with normoglycemia. Several observational studies have reported an association of hyperglycemia with poor clinical outcome in critically ill children; however, no prospective controlled studies have assessed the effect of tight glucose control in pediatric populations. These studies need to be prospective, randomized multicenter trials of sufficient magnitude to provide a well-powered analysis to enable multiple observ-

ations and evaluation of subsets of critically and non-critically ill pediatric patients.

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