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Risk Factors of Recurrent Hospital Admission for Young Adults Presenting with Hyperglycemic Emergencies at an Inner City Hospital

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Abstract

Risk Factors of Recurrent Hospital Admission for Young Adults Presenting with Hyperglycemic Emergencies at an Inner City Hospital

By Mary Katherine Findley

Background: Over 150,000 hyperglycemic emergencies occur in the United States each year. Hyperglycemic emergencies are associated with morbidity, mortality, and increased healthcare costs. Young adults under the age of 35 have disproportionally high rates of hyperglycemic emergency hospital admissions. The purpose of this study was to characterize the young adult admitted to an inner-city hospital for a hyperglycemic emergency and identify risk factors for recurrent hyperglycemic emergencies.

Methods: Electronic health records were used to extract data from 273 young adult patients (18-35 years) admitted to an inner city hospital over a five-year period. Independent t-tests, Chi-Square tests, and ANOVA were used to explore differences in diabetes type, glycemic control, and recurrent admissions. Univariate binomial logistic regression was used to calculate unadjusted odds ratios and multivariable logistic regression was used to model risk factors associated with hyperglycemic emergencies.

Results: Patients were characterized as individuals in their mid-twenties, Black and non-Hispanic, with limited access to care, Type 1 Diabetes, poor glycemic control, and a high rate of chronic diabetes complications and psychiatric co-morbidities. Multiple hyperglycemic emergency admissions occurred in 43.6% of the sample. Risk factors significantly associated with recurrent hospitalization compared to a single admission included non-Hispanic ethnicity (98.2% vs. 91.6%, p=0.05), race (Black 90.8% vs 77.9%, p=0.017), lower household income (\$39,048±14,421 vs \$44,107±15,633, p=0.007), high utilization of health care services (emergency department 70.6% vs 22.1%, p<0.05; and hospitalization 68.9% vs 13.6%, p<0.05), Type 1 Diabetes (82.4% vs 66.2%, p=0.003), lower age at diagnosis (16.95±7.40 vs 19.41±8.51, p=0.039), lower BMI (25.96±8.07 vs 29.17±9.20, p=0.005), presence of chronic diabetes complications (53.8% vs 37.7%, p=0.01), and psychiatric co-morbidities (any mental health history 58.0% vs 25.0%, p<0.001; depression: 26.9% vs 5.8%, p<0.001; substance use 26.9% vs 16.9%, p=0.02).

Conclusion: There are two significant gaps in young adult diabetes care: young adult diabetes primary care and the integration of mental healthcare into primary diabetes care. Developing interventions to address gaps could have a high upfront cost, but if the intervention prevented hyperglycemic emergencies and recurrent admissions these programs could lead to decreased morbidity, mortality, and diabetes associated healthcare costs.

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Specific Aims

Hyperglycemic emergencies such as diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar syndrome (HHS) are serious acute complications in both type 1 diabetes mellitus (T1D) and type 2 diabetes mellitus (T2D). In the last three decades there has been a 226% increase in hospitalizations for DKA and HHS (Centers for Disease Control and Prevention, 2017). DKA and HHS are associated with high healthcare costs as well as substantial morbidity and mortality. In the United Sates the estimated total annual hospital cost for treating diabetic emergencies is over $2.4 billion (Kitabchi, Umpierrez, Miles, & Fisher, 2009). The overall diabetic emergency mortality recorded in the United Sates is less than 1% (Kitabchi et al., 2009); however, recent research indicates that short-term mortality rates are associated with the frequency of hyperglycemic emergency hospital admissions in a life time (Gibb, Teoh, Graham, & Lockman, 2016). A single hyperglycemic emergency is associated with a 10.6% mortality rate within five years and greater than four hyperglycemic emergency admissions are associated with almost a 30% short term mortality rate (Gibb et al., 2016).

Recurrent hyperglycemic emergencies are common, with readmission rates up to 55% (Randall et al., 2011) in five years. The rate of readmission within a year of hospitalization is over 20% (Berry et al., 2011; Malik et al., 2016; Tieder et al., 2013). Young adults under the age of 35 are at higher risk of recurrent hyperglycemic emergencies (Bradford, Crider, Xu, & Naqvi, 2017; Randall et al., 2011). As young adults transition from pediatric to adult care, glycemic control is known to decrease significantly (Bryden et al., 2001; Insabella, Grey, Knafl, & Tamborlane, 2007). These young adults often have gaps in care and significant changes in self-management (Findley, Cha, Wong, & Faulkner, 2015) that can lead to poor glycemic control and diabetic emergencies that impact long-term morbidity and mortality. Studies focusing on this vulnerable population are needed in order to determine risk factors that are associated with hyperglycemic emergencies and targets for interventions to prevent recurrent hospital admissions.

An observational study using chart reviews of 18 to 35 year old patients admitted to Grady Memorial Hospital for a hyperglycemic emergency between the years of 2010 to 2015 were used to determine risk factors of hyperglycemic emergencies in a predominantly African American young adult population. This sample included 703 hospital admissions representing 326 individual patients. Electronic health records of each patient were reviewed for demographic factors, access to care, diabetes and hospitalization characteristics, and chronic complications and co-morbidities. This information was compiled and used to address the following specific aims:

Aim 1: Characterize the young adult (18-35 year old) population admitted to an inner city hospital for a hyperglycemic emergency over a five-year period.

Aim 2: Determine factors that are associated with recurrent hyperglycemic emergencies within a five year period.

Aim 3: Determine factors that are associated with high rates of readmission (more than four admissions within five years) and frequent readmissions (less than one year between readmissions) for hyperglycemic emergencies.

These aims helped to identify young adults at risk for hyperglycemic emergencies and determined modifiable risk factors to target for interventions within this population. By reducing hyperglycemic emergencies in young adults, patient outcomes will improve and the economic burden of diabetes will decrease.

Background and Significance

Diabetes

Diabetes is a complex, chronic disease that is increasing in prevalence worldwide (Patterson et al., 2012; Vehik & Dabelea, 2011). In 2017, 30.3 million Americans or 9.4% of the population have diabetes (Centers for Diseae Control and Prevention, 2017). The incidence rate of type 1 diabetes (T1D) is rising by an average of approximately 3-4% per year (Patterson et al., 2012), and the prevalence of T1D in youth is predicted to rise 70% by 2020 (Patterson, Dahlquist, Gyurus, Green, & Soltesz, 2009). The prevalence of type 2 diabetes (T2D) is also increasing in adults and youth. Between 2001 and 2009 the prevalence for T2D increased by 30.5% in youth (Hamman et al., 2014). As the prevalence of diabetes in youth increases, more adults will be affected by the disease and its complications and require healthcare treatment.

Pathophysiology

Diabetes mellitus is an abnormality in blood glucose regulation and nutrient storage related to an absolute deficiency in insulin or resistance to the action of insulin. Blood glucose control is primarily regulated by the insulin secreting beta-cells within the islets of Langerhans in the endocrine pancreas (Porth, 2011). The release of insulin from the pancreatic beta-cells is regulated by blood glucose levels. Diabetes may result from dysregulation or deficiency in sensing of blood glucose levels or defects in insulin release or synthesis (Porth, 2011).

Insulin secreted by the beta cells enters the portal circulation and travels directly to the liver where it is bound to peripheral tissues (Porth, 2011). Insulin binds to a membrane receptor consisting of four subunits. Two larger subunits extend outside the cell membrane and are involved in insulin binding, and two smaller subunits are located inside the cell membrane and contain a kinase enzyme that becomes activated during insulin binding. Activation of the kinase enzyme results in autophosphorylation of the internal membrane receptor subunits that direct the intracellular effects of insulin on glucose, fat, and protein metabolism (Porth, 2011).

Cell membranes are impermeable to glucose and require a glucose transporter to move glucose from the blood into the cell. GLUT-4 is the insulin dependent glucose transporter for skeletal muscle and adipose tissue. It is unable to function as a glucose transporter until a signal from insulin facilitates glucose entry into the skeletal muscle and adipose tissue (Porth, 2011). With uptake of glucose by skeletal muscle and adipose tissue blood glucose levels decrease and the body is able to use glucose as a fuel source.

Type 1 diabetes mellitus (T1D) is characterized by destruction of the pancreatic beta-cells thus affecting the secretion of insulin resulting in high blood glucose levels and the inability to use glucose as a fuel source (Porth, 2011). T1D accounts for 5-10% of diabetes (American Diabetes Association, 2017b). Type 2 diabetes mellitus (T2D) is characterized by a relative, rather than absolute, insulin deficiency including insulin resistance, unbalanced secretion of insulin by the pancreatic beta-cells, and increased glucose production by the liver (Porth, 2011). Insulin resistance is the failure of target tissues to respond to insulin, leading to decreased uptake of glucose in muscle, increased glucose production in the liver, and elevated blood glucose levels (Porth, 2011). T2D accounts for 90-95% of all diabetes (American Diabetes Association, 2017b).

Diagnosis

Classification of T1D or T2D is important for determining diabetes therapy and management; however, some individuals cannot be clearly classified as having T1D or T2D at the time of diagnosis. Once hyperglycemia occurs, patients with all forms of diabetes are at risk for developing the same complications (American Diabetes Association, 2017b). Diabetes can be diagnosed based on fasting plasma glucose (≥126 mg/dL), two-hour plasma glucose after a glucose tolerance test (≥200mg/dL), or hemoglobin A1c (HbA1c) (≥6.5%) (American Diabetes Association, 2017b). T1D is defined as the presence of one or more autoimmune markers including islet cell autoantibodies and autoantibodies to GAD, insulin, or tyrosine phosphatases in the setting of hyperglycemia (American Diabetes Association, 2017b).

Management

All people with diabetes should participate in diabetes self-management education in order to increase knowledge and skills necessary for diabetes self-care. Effective self-management improves clinical outcomes, health status, quality of life, and reduces costs (American Diabetes Association, 2017e). Self-management education and support should be patient centered, responding to patient preferences, needs, and values (American Diabetes Association, 2017e).

Most people with T1D should be treated with prandial insulin and basal insulin or continuous subcutaneous insulin infusion (American Diabetes Association, 2017h; "Mortality in Type 1 Diabetes in the DCCT/EDIC Versus the General Population," 2016; Nathan et al., 2005; Nathan et al., 1993). Education is necessary on matching prandial insulin doses to carbohydrate intake, pre-meal blood glucose levels, and anticipated physical activity (American Diabetes Association, 2017h; K. J. Bell et al., 2015; K. J. Bell, Toschi, Steil, & Wolpert, 2016; Wolpert, Atakov-Castillo, Smith, & Steil, 2013). Obesity management is beneficial in the treatment of T2D. Weight loss improves glycemic control and reduces the need for glucose-lowering medications. Diet, physical activity and behavioral therapy that are designed to reduce weight by greater than 5% should be prescribed for overweight and obese patients with T2D (American Diabetes Association, 2017g; Goldstein, 1992; Lim et al., 2011; Pastors, Warshaw, Daly, Franz, & Kulkarni, 2002; "UK Prospective Diabetes Study 7: response of fasting plasma glucose to diet therapy in newly presenting type II diabetic patients, UKPDS Group," 1990). Metformin is the preferred initial pharmacologic agent for the treatment of T2D (American Diabetes Association, 2017h; Palmer et al., 2016). If noninsulin monotherapy at the maximum tolerated dose does not achieve or maintain the HbA1c target after 3 months a new class of non-insulin agent or basal insulin can be added to the initial therapy to lower HbA1c. (American Diabetes Association, 2017h; Bennett et al., 2011; Berry et al., 2011).

Glycemic Control

HbA1c indicates glycemic control. Outcome studies show that HbA1c is the primary predictor of complications (American Diabetes Association, 2017d). Numerous aspects should be considered when setting glycemic targets and should be individualized to the needs of each patient and their disease factors (American Diabetes Association, 2017d). The recommended glycemic target for most adults is <7.0% (American Diabetes Association, 2017d); however less stringent HbA1c goals can be used based on risks associated with hypoglycemia, disease duration, life expectancy, co-morbidities, vascular complications, patient attitude, and resources and support systems (American Diabetes Association, 2017d; Inzucchi et al., 2015). HbA1c greater than 9% indicates poor glycemic control ("Comprehensive Diabetes Care: HEDIS Measure," 2016; Health Resources and Services Administration, 2012).

Chronic Complications and Comorbidities

The leading cause of morbidity and mortality and the largest contributor to the cost of diabetes is cardiovascular disease (American Diabetes Association, 2017a). Cardiovascular disease includes acute coronary syndromes, myocardial infarction, angina, coronary revascularization, stroke, transient ischemic attack, and peripheral arterial disease. Hypertension and dyslipidemia are common conditions that co-exist with T2D and are risk factors for cardiovascular disease, but diabetes itself is an independent risk factor (American Diabetes Association, 2017a). Addressing individual cardiovascular risk factors or multiple risk factors can prevent or slow cardiovascular disease. With improved screening, diagnosis, and treatment of cardiovascular risk factors the risk of coronary heart disease has improved over the past ten years and cardiovascular disease morbidity and mortality has decreased (Ali et al., 2013; American Diabetes Association, 2017a; Buse et al., 2007; Gaede, Lund-Andersen, Parving, & Pedersen, 2008). Intensive glycemic control shows a cardiovascular benefit in T1D and T2D (Nathan et al., 2005; Nathan et al., 2009; Orchard et al., 2015).

Chronic kidney disease, diabetic retinopathy, and neuropathy are chronic microvascular co-morbidities (American Diabetes Association, 2017f). Chronic kidney disease attributed to diabetes occurs in 20-40% of patients with diabetes and is the leading cause of end-stage renal disease (American Diabetes Association, 2017f; Tuttle et al., 2014). Diabetic retinopathy is a microvascular complication of both T1D and T2D with prevalence related to duration of diabetes and the level of glycemic control. Diabetic retinopathy is the most frequent cause of new cases of blindness among adults 20-74 years of age (American Diabetes Association, 2017f). The diabetic neuropathies have diverse clinical manifestations including peripheral neuropathy, autonomic neuropathy, cardiac autonomic neuropathy, gastrointestinal neuropathies, genitourinary disturbances, neuropathic pain, gastroparesis, and erectile dysfunction (Insabella et al., 2007). Better glycemic control is associated with significantly decreased rates of development and progression of microvascular complications (American Diabetes Association, 2017d; Lachin et al., 2015; Nathan et al., 1993)

Emotional wellbeing is important to diabetes care and self-management. Psychological problems can impair an individual's ability to manage their diabetes and can compromise their health status (American Diabetes Association, 2017e). Anxiety symptoms and diagnosable anxiety comorbidities effect approximately 20% diabetes patients (American Diabetes Association, 2017c; Li et al., 2008; Smith et al., 2013). Depressive symptoms effect one in four diabetes patients (American Diabetes Association, 2017c; Anderson, Freedland, Clouse, & Lustman, 2001). Chronic hyperglycemia is associated with changes in brain structure and development that have been postulated to have an effect on cognition and mood (Ho, Sommers, & Lucki, 2013; McEwen, Magarinos, & Reagan, 2002; Perantie et al., 2007). Diabetes is also associated with changes in some of the same key cellular signaling molecules in the brain, the HPA axis, and inflammation as psychiatric conditions (Champaneri, Wand, Malhotra, Casagrande, & Golden, 2010; Dantzer, O'Connor, Freund, Johnson, & Kelley, 2008; Duman & Monteggia, 2006; Haroon, Raison, & Miller, 2012; Ising et al., 2007; Korczak, Pereira, Koulajian, Matejcek, & Giacca, 2011; Musselman, Betan, Larsen, & Phillips, 2003; Osborn & Olefsky, 2012; Stuart & Baune, 2012). These overlaps indicate that some neurological pathways may be disrupted in diabetes patients, establishing a predisposition to depression and other psychiatric conditions.

There is an association between substance use and recurrent hyperglycemic emergencies (Isidro & Jorge, 2013; E. A. Nyenwe et al., 2007). Drug use is also associated with longer ICU and hospital stays, higher hospital costs, more diabetes complications, and higher mortality (Saunders, Democratis, Martin, & Macfarlane, 2004); however, previous studies show that psychosocial interventions and incorporating mental health care into diabetes treatment can improve HbA1c and mental health outcomes (American Diabetes

Association, 2017e; Anderson et al., 2001; Anderson et al., 2002; Delahanty et al., 2007; Katon et al., 2010).

Acute Complications

Diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state (HHS), and hypoglycemia are acute complications in patients with T1D and T2D. DKA, HHS, and hypoglycemia are associated with morbidity and mortality. Worldwide, DKA accounts for approximately 50% of deaths in children and young adults with T1D (Basu et al., 1993; Umpierrez & Korytkowski, 2016). Death occurs in 10-20% of patients with HHS (Pasquel & Umpierrez, 2014), and hypoglycemia is associated with a two to three-fold increase in mortality (McCoy et al., 2012; Umpierrez & Korytkowski, 2016). Treatment of these diabetic emergencies are associated with high healthcare costs and creates a substantial economic burden .

Hyperglycemic Emergencies

Hyperglycemic emergencies such as DKA and HHS are serious acute complications that can be seen in T1D and T2D. In the last three decades there has been a 226% increase in these hospitalizations (Centers for Disease Control and Prevention, 2017). In the United States in 2011 there were 175,000 emergency room visits for hyperglycemic crises (Centers for Diseae Control and Prevention, 2014). In 2010, hyperglycemic crises caused 2,361 deaths in adults (Centers for Diseae Control and Prevention, 2014). Treatment of diabetes emergencies has a substantial economic burden. The average cost of managing a hyperglycemic emergency in the United States is $17,500 per patient admission, and it is estimated that the total annual hospital cost of hyperglycemic emergency management is $2.4 billion (Kitabchi et al., 2009).

Hyperglycemic emergencies were fatal until the discovery of insulin in the 1920s; since then, the related mortality has reduced to less than 1% in the United States (Kitabchi et al., 2009). Despite this greatly reduced mortality rate during a hyperglycemic emergency, there is still a substantial short-term (within 5 years) risk of death associated with hyperglycemic emergency hospitalizations. Mortality rates are significantly associated with the number of hyperglycemic emergency hospital admissions (Gibb et al., 2016). In patients admitted to the hospital for a single diabetic emergency there is a 10.6% mortality rate in the next six years (Gibb et al., 2016). Mortality rates are the highest in those with high rates of readmission. Those patients with more than four admissions within five years have a mortality rate of almost 30% (Gibb et al., 2016). The increase in hyperglycemic emergency hospitalizations and the associated short-term risk of mortality underlies the importance of hyperglycemic emergency prevention in improving patient outcomes.

Diabetic Ketoacidosis

DKA is the effect of insulin deficiency and increased counter-regulatory hormones (Porth, 2011). Insulin deficiency in skeletal muscle decreases glucose uptake resulting in the rapid breakdown of the energy stores from the muscle and leads to amino acids being converted to glucose through gluconeogenesis. Insulin deficiency also leads to lipolysis and glycerol being used for gluconeogenesis and fatty acids being converted to ketones (Porth, 2011). The increased glucose from lack of uptake by muscles and increased gluconeogenesis results in hyperglycemia, osmotic diuresis, water and electrolyte loss, dehydration, and eventually circulatory failure (Porth, 2011). The increase of ketones from fatty acids results in metabolic acidosis. Metabolic acidosis is caused by the excess of ketoacids that require buffering by bicarbonate ions leading to a decrease in serum bicarbonate levels and can lead to CNS depression (Porth, 2011). DKA is diagnosed by hyperglycemia (blood glucose levels

>250mg/dL), low serum bicarbonate, low arterial pH, and positive urine and serum ketones (Porth, 2011). DKA is more common in patients with T1D but can occur in T2D and is more prevalent in Black and Hispanic patients (Umpierrez, Smiley, & Kitabchi, 2006; Wang, Kihl-Selstam, & Eriksson, 2008). Omission of insulin therapy, inadequate dosing of insulin, and infection are the most common precipitating factors of DKA (Kitabchi & Nyenwe, 2006). The goals in treating DKA are to improve circulatory volume and tissue perfusion, decrease blood glucose, and correct the acidosis and electrolyte imbalances (Porth, 2011).

Hyperosmolar Hyperglycemic State

HHS is characterized by hyperglycemia (blood glucose >600mg/dL), hyperosmolarity (plasma osmolarity > 320mOsm/L, dehydration, and the absence of ketoacidosis (Porth, 2011). HHS is seen most frequently in patients with T2D. Partial or relative insulin deficiency initiates HHS by reducing glucose utilization while inducing hyperglucagonemia and increasing hepatic glucose output (Porth, 2011). Glycosuria results and water loss occurs. If the patient is unable to maintain adequate fluid intake, dehydration develops, the plasma volume contracts, renal insufficiency develops, and leads to increasingly higher blood glucose levels and severity of the hyperosmolar state (Porth, 2011). The most common precipitating factor of HHS is infection followed by an initial presentation of diabetes and omission of insulin or other antidiabetic medications (Umpierrez & Korytkowski, 2016). The treatment goals of HHS are similar to DKA and include restoration of circulatory volume and tissue perfusion, correction of electrolyte imbalances and hyperosmolarity, and resolution of hyperglycemia (Umpierrez & Korytkowski, 2016).

Recurrent Hyperglycemic Emergencies

The mortality related to a DKA hyperglycemic emergency is less than one percent in adult populations; however, retrospective analysis shows that even with no inpatient mortality 14% of DKA patients die within five years (Gibb et al., 2016). Mortality is higher in those with multiple hyperglycemic emergency admissions (Gibb et al., 2016; Mays et al., 2016). Patients with greater than four admissions within a five year period have a mortality rate of almost 30% (Gibb et al., 2016). Recurrent hyperglycemic emergencies are common with readmission rates up to 55% (Randall et al., 2011). Many readmissions are within one year of the initial hyperglycemic emergency. The rate of readmission for DKA or HHS within a year of hospitalization is over 20% (Berry et al., 2011; Malik et al., 2016; Tieder et al., 2013).

In the United States, the average length of stay for a DKA/HHS admission is 3.4 days (Nyenwe & Kitabchi, 2016). The cost of managing each hospitalization is approximately $17,500 (Kitabchi et al., 2009). DKA hospital admissions are responsible for a half a million hospital days per year (Nyenwe & Kitabchi, 2016), with a total annual cost of $2.4 billion (Kitabchi et al., 2009). Hyperglycemic emergencies represent more than $1 of every $4 spent on direct medical care for adult patients with diabetes, and $1 for every $2 in those patients that have recurrent hyperglycemic emergencies (Javor et al., 1997). Because of the high rates of readmission, risk associated with these recurrent hyperglycemic emergencies, and the economic costs incurred by these readmissions it is imperative to address risk factors that can prevent multiple DKA/HHS admissions.

Young Adults

In children and adolescents in the United States between 2001 and 2009, the prevalence of T1D increased by 21%. The prevalence for T2D increased during this period by 30.5% (Hamman et al., 2014). The increased rates of diabetes in adolescents places a greater demand on the pediatric health system as well as the adult health system as these adolescents transition to adult care.

Thirty-four percent of young adults report a gap between pediatric and adult diabetes care (Garvey et al., 2012). Once a patient is established within adult diabetes care, staffing and resources are often very different than what is available in pediatric care. Pediatric care multidisciplinary teams consisting of a doctor, nurse, dietician, and psychologist meet with patients and families to development care plans. This individualized holistic care model is not frequently seen in the adult care setting (Allen, Channon, Lowes, Atwell, & Lane, 2011; Hilliard et al., 2014; Kime, 2013; Lundin, Ohrn, & Danielson, 2008).

Glycemic control during young adulthood decreases significantly (Ali et al., 2013; Bryden et al., 2001; Insabella et al., 2007). Optimal glycemic control during this time of life reduces the likelihood of serious long-term health complications later in life. Specifically, tight glycemic control during young adulthood decreases risk for both microvascular and macrovascular diabetes complications (Blonde, 2012; Silverstein et al., 2005). Young adults are also at the highest risk for recurrent hospital admission for hyperglycemic emergencies (Bradford et al., 2017; Randall et al., 2011). The frequency of recurrent hospitalizations for DKA/HHS will increase as the prevalence of T1D and T2D increases in youth populations and youth transition from the pediatric to adult healthcare systems. This has the potential to greatly affect morbidity and mortality in the young adult population as well as substantially increase healthcare costs.

Disparities in Care

In order to achieve optimal diabetes outcomes, care must be individualized for each patient. The American Diabetes Association advocates for patient-centered care that is respectful and responsive to an individual's preferences, needs, and values (American Diabetes Association, 2017i). However, the healthcare system is often fragmented and is poorly designed for the coordinated care that is needed for the optimal treatment of diabetes

(American Diabetes Association, 2017i; Hill et al., 2013). In addition there are health inequalities that are related to social determinants such as economic, environmental, political and social conditions. Health disparities are complex and include societal issues such as institutional racism, discrimination, socioeconomic status, poor access to health care, education, and lack of health insurance (American Diabetes Association, 2017i; Hill et al., 2013). Ethnic, cultural, and socioeconomic differences affect diabetes prevalence and outcomes and compound the vulnerability of the inner-city low resource young adult diabetes population, Despite advances in medical knowledge and diabetes management, socioeconomic, ethnic, and racial inequalities exist in access to healthcare and these individuals have a higher risk of complications and poorer glycemic control (American Diabetes Association, 2017i; Campbell, Walker, Smalls, & Egede, 2012; H. Y. Lee et al., 2015; Ricci-Cabello, Ruiz-Perez, Olry de Labry-Lima, & Marquez-Calderon, 2010). In order for all patients to receive optimal care there needs to be substantial system level improvements that address social determinants of health that influence the prevention and management of diabetes. .

Theoretical Model

Diabetes is increasing and has a significant impact on health and the health care economy. Recurrent acute hyperglycemic emergencies increase these impacts. Young adults have a greater risk of recurrent hyperglycemic emergencies and the related hospital admissions, chronic health conditions, and economic burden will increase as greater rates of young adults with diabetes transition from the pediatric to adult healthcare systems. Health disparities associated with social determinants and barriers in the healthcare system compound these impacts. Past studies have looked at factors related to recurrent hyperglycemic emergencies but have not focused on the young adult population.

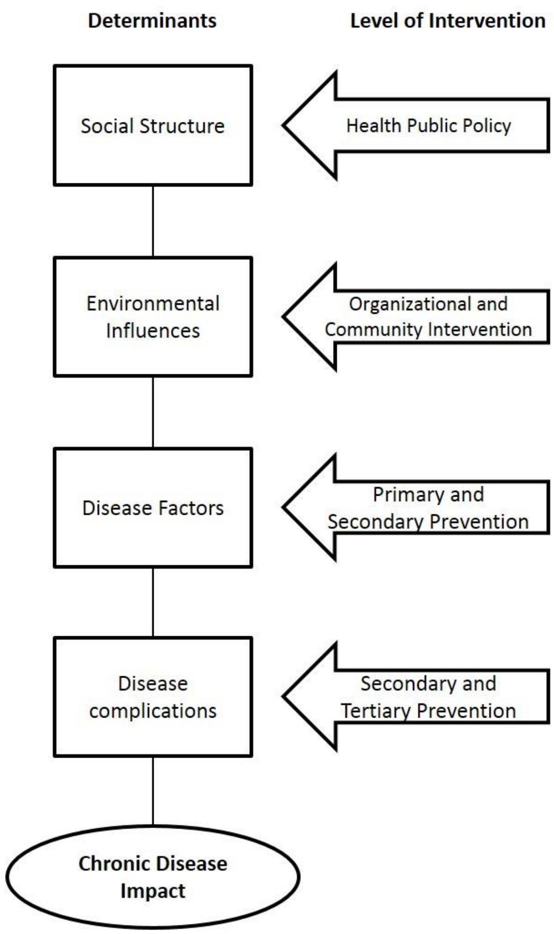

Figure 1: The WHO STEPS Model and Corresponding Levels of Intervention: a multidimentional view of disease determinants that groups risk factors along a scale of levels of intervention from public health policy to primary, secondary, and tertiary prevention. (Adapted from Noncommunicable Diseases and Mental Health World Health Organization, 2003).

The theoretical framework for the current study was adapted from the World Health Organization (WHO) Stepwise Approach to Surveillance of Non-Communicable diseases (STEPS) framework of non-communicable diseases (Noncommunicable Diseases and Mental Health World Health Organization, 2003) . The STEPS framework is a multidimensional view of disease determinants focusing on risk factors along a scale of levels of intervention from public health policy to primary, secondary, and tertiary prevention. The risk factors outlined in this framework are social structure, environmental influences, disease factors, and disease complications. Together, these four factors contribute to the impact of noncommunicable chronic diseases. The model also outlines the type of intervention for each factor (Figure 1). For this study the STEPS framework was modified to reflect risk factors related to recurrent hyperglycemic emergencies. The scope of this study does not address interventions; however, future studies could incorporate types of intervention into the theoretical model.

Through review of previous studies, risk factors related to hyperglycemic emergencies can be divided into four categories related to the initial STEPS framework category. Social structure is denoted as demographic factors that are similar to those

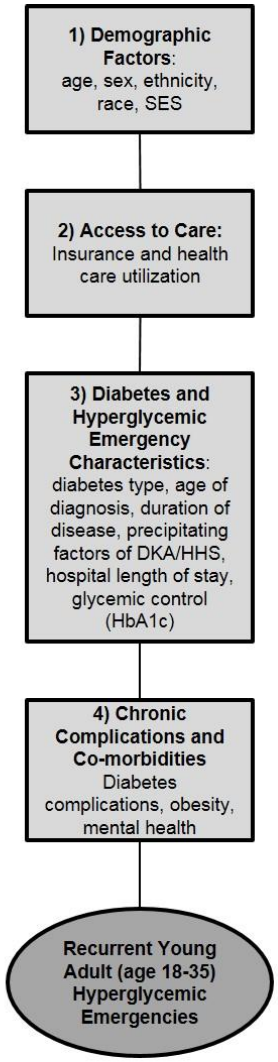

Figure 2: **Four Category Theoretical Model for Characterization and Identification of Young Adults at Risk for Hyperglycemic Emergencies.** Theoretical model based on the WHO STEPS framework of non-communicable diseases. Distributes risk factors into four categories that are the framework for characterization and identification of young adults at risk DKA/HHS hospital admissions.

described in the original framework. Environmental influences are represented by the access to care variables. Disease characteristics are represented by diabetes and hyperglycemic emergency characteristics. Finally, disease complications correspond to chronic diabetes complications and co-morbidities. The theoretical model of the current study analyzes the association of each category of risk factors with DKA/HHS and does not focus on the causal scale of risk factors (Figure 2). The non-modifiable and modifiable risk factors in the theoretical model will generate a profile to identify young adults with increased risk of recurrent hyperglycemic emergencies and identify potential targets for future intervention.

Demographic Factors

Demographic factors are non-modifiable factors such as age, sex, ethnicity, race, and socioeconomic status (SES). Younger age at the time of the initial hyperglycemic emergency has consistently been associated with risk of recurrence (Bradford et al., 2017; Kim, Ross, Melkus, Zhao, & Boockvar, 2010; Liu et al., 2010). Sex of the patient is a potential risk factor, but varies across studies. One study found readmitted adult patients are more often male than female (Steenkamp, Alexanian, & McDonnell, 2013), but another study indicated young adult readmissions were more likely female (Randall et al., 2011). Minority populations have a higher likelihood of readmission for hyperglycemic emergencies with Hispanic and non-Hispanic Black patients having a particularly high risk (Kitabchi, Umpierrez, Fisher, Murphy, & Stentz, 2008; Rewers et al., 2002). Low SES is also associated with a greater risk for readmission (Kitabchi & Nyenwe, 2006; Musey et al., 1995; E. Nyenwe et al., 2007; Randall et al., 2011)

Access to Care

Access to care includes factors that have an effect on the patient physically accessing and paying for care. Many of these factors are associated with SES but are specifically linked to access to care, including insurance and healthcare utilization. Underinsurance and patients with publicly funded health insurance have a higher risk of readmission (Bradford et al., 2017; Isidro & Jorge, 2013; E. Nyenwe et al., 2007; Randall et al., 2011). Clinic non-attendance is also related to multiple readmissions for hyperglycemic emergencies (Maldonado, Chong, Oehl, & Balasubramanyam, 2003; Musey et al., 1995; Randall et al., 2011; Umpierrez, Kelly, Navarrete, Casals, & Kitabchi, 1997).

Diabetes and Hyperglycemic emergency Characteristics

Diabetes characteristics include both non-modifiable and modifiable factors relating to the patient's diabetes and hyperglycemic emergency. Non-modifiable factors include diabetes type, the age of onset of diabetes, how long the patient has had diabetes, and length of stay at the hospital during the hyperglycemic emergency. The age of onset of diabetes, as well as the duration of the disease, is associated with recurrent hyperglycemic emergencies (Randall et al., 2011). Glycemic control indicated by HbA1c is considered a modifiable factor. Poor glycemic control indicated by elevated HbA1c has been associated with recurrent hyperglycemic emergencies (Cooper, Tekiteki, Khanolkar, & Braatvedt, 2016; Liu et al., 2010; E. Nyenwe et al., 2007). Increased mortality rate is associated with higher rates of readmission as well as intensive care admission and longer length of stay in the hospital (Gibb et al., 2016).

Chronic Complications and Co-morbidities

Co-morbidities include chronic complications of diabetes including microvascular and macrovascular complications such as cardiovascular disease, nephropathy, neuropathy and retinopathy. Obesity, as indicated by BMI, as a co-morbidity with diabetes is associated with higher risk of recurrent hyperglycemic emergencies (Randall et al., 2011). Co-morbidities also include mental health concerns and substance abuse. Patients with recurrent hyperglycemic emergencies are more likely to have a history of depression than those with a single episode. (Bradford et al., 2017; Kim et al., 2010; Randall et al., 2011) Drug and alcohol abuse, particularly cocaine use, is also associated with readmission for hyperglycemic emergencies (Balla, Malnick, & Schattner, 2008; Barski et al., 2012; Govan et al., 2011; Kim et al., 2010; Randall et al., 2011; Rewers et al., 2002).

Study Aims

The purpose of this study was to examine the four categories of risk factors in the theoretical model and their association with hyperglycemic emergencies in young adults ages 18-35 admitted to an inner-city hospital over a five year period. This analysis provided the characteristics of this vulnerable population for the hyperglycemic emergency admission and rate of recurrence **(Aim 1)**. Patients with a single admission for a hyperglycemic emergency were compared to patients with multiple admissions in a five year period. Comparison of these two groups determined factors that can be the target for future interventions to reduce recurrent hyperglycemic emergencies in this population **(Aim 2).** Patients with high rates of hyperglycemic emergencies (over four admissions in five years) and those with frequent hyperglycemic emergencies (less than one year between admissions) have the highest increased risk of mortality. Patients with high rates of readmission were compared with patients who have 2-4 admissions in five years, and those patients with only one hyperglycemic emergency in a five year period. Patients who have been readmitted within one year of hospitalization were compared to those who had a longer length of time between readmissions (up to five years). This provided characteristics to create a profile of the young adult who is at the highest risk for multiple recurrent hyperglycemic emergencies so that they can be targeted for potential interventions **(Aim 3)**.

Innovation

Although young adults are at the highest risk for recurrent hyperglycemic emergencies, this population has not been individually studied to determine who is at highest risk of recurrence and which factors to target in trying to prevent recurrence. This will be one of the first studies to focus on young adults with diabetes in an urban, inner-city hospital where the patient population is predominantly black. This population is particularly vulnerable to recurrence and the associated risks of morbidity and mortality. This work will support the creation of innovative multi-disciplinary interventions for young adults with diabetes that will decrease hyperglycemic emergencies leading to lower healthcare costs and decreased morbidity and mortality.

Approach

Electronic health records (EHR) (Epic Systems Corporation, Veronia, WI) from the Grady Health System in Atlanta, Georgia were used as the data source for this retrospective study. Grady Memorial Hospital is a 953 bed academic county hospital that serves inner city patients. International Classification of Diseases (ICD)-9 codes indicating DKA or HHS were used to identify cases from a list of patients admitted to Grady between January 2010 and November 2015. All patients 18 to 35 years old at the time of admission for

DKA/HHS were included in the study. Cases were excluded if the patient was younger than 18 or older than 35 years at the time of admission for DKA/HHS, if the patient was only seen in the emergency department or clinic and not admitted to the hospital, if there was no evidence in the EHR of a hyperglycemic emergency, or if the patient did not have a diagnosis of T1D or T2D (gestational diabetes and other diabetes types were excluded).

IRB approval was obtained from Emory University and the study was authorized by the Grady Hospital Research Oversight Committee. All analyses and study procedures complied with HIPAA regulations and federal regulations for the protection of human research subjects and inclusion of women and minorities.

Data Collection

A list was created with all patients grouped by medical record number (MRN) to determine how many unique patients were in the sample and the age range of all admitted patients with DKA or HHS. Young adults 18 to 35 years old were identified using the indicated birthdate.

Data were collected from the EHR using retrospective chart reviews completed between December 2015 and December 2016. An extraction sheet was created indicating each variable, coding for each variable's possible results, and how to denote missing information. The first ten cases were reviewed by all extractors to ensure minimal reviewer variability and consensus in coding for each variable.

The first hyperglycemic emergency that occurred between 2010 and 2015 in which the patient was greater than or equal to 18 years old but less than 35 years old was identified as the primary DKA/HHS admission. Data was extracted relating to the primary admission; however, all EHR documentation was examined in order to gather patient history and information about previous and subsequent encounters and hospital admissions. For this study all demographic variables, access to care data, diabetes and hyperglycemic emergency characteristics, and chronic complications and co-morbidities were extracted from the EHR including the patient's encounter log, lab results and documentation from physicians, nurses, social workers, dietitians, diabetes educators and other healthcare providers (Table 1)

1) Demographic variables for this study included age at admission, sex, race, ethnicity, and socio-economic status (SES). Patient's age at admission was calculated by subtracting the primary admission date from the date of birth indicated in the EHR. Sex was recorded as designated in the EHR. Race and ethnicity were extracted from the clinicians' documentation of the history and physical (H&P) at admission and other clinical notes. Race was recorded as Caucasian, Black, Asian, or other. For the purpose of analysis, race was converted into a dichotomous variable (Black/Non-Black). Ethnicity was recorded as Hispanic or non-Hispanic. SES was derived from the zip code at the time of the primary admission and associated with the median household income for that zip code as indicated by the 2011-2015 American Community Survey 5-Year Estimates collected by the U.S. Census Bureau (2011-2015 American Community Survey 5-Year Estimates, 2017).

2) Access to care was indicated by insurance status at the primary admission and utilization of the Grady Health System within one year of the primary admission. Insurance information for the primary admission was extracted from the H&P at admission, social worker and healthcare provider notes, and discharge summaries. Insurance was categorized as private insurance, public insurance (Medicare or Medicaid), or no insurance. In addition to analysis of each type of insurance, insurance was also converted to a dichotomous variable (private or public insurance/ no insurance). The EHR encounter log was analyzed to

Table 1: Variables within the Four Category Theoretical Model of Risk Factors Associated with Hyperglycemic Emergencies

Risk Factor	Definition	Data Source
Demographic Variables		
Age at admission	Age at primary DKA/HHS admission	Calculated by subtracting the primary admission date from the date of birth indicated in the EMR
Sex	Male or Female	As designated in the EMR
Race	Caucasian, Black, Asian, or Other (also converted into a dichotomous variable for analysis-- Black/Non-Black)	Extracted from the H&P or other clinical notes
Ethnicity	Hispanic or Non-Hispanic	Extracted from the H&P or other clinical notes
SES	Household median income (also converted to a dichotomous variable for analysis--</> $35k)	Derived from the zip code at the time of primary admission and associated with the median household income for that zip code as indicated by the 2011-2015 American Community Survey 5-Year Estimates collected by the U.S. Census Bureau.
Access to Care		
Insurance Status	Insurance status at the time of primary admission categorized as private insurance, public insurance (Medicare or Medicaid), or no insurance (converted to a dichotmous variable for analysis-- private or public insurance/ no insurance)	Extracted from the H&P, healthcare provider notes, and discharge summary
Hospital Utilization	Emergency room utilization and other hospitalizations for any reason in the year following the primary DKA/HHS admission	Extracted from the EMR encounter log.
Utilization of the Grady Diabetes Clinic	Attendance of appointment at the Grady Diabetes Clinic in the year previous to the primary admission.	Extracted from the EMR encounter log
Diabetes and Hyperglycemic Emergency Characteristics		
Diabetes Type	Type 1 Diabetes or Type 2 Diabetes	Extracted from the H&P , clinical notes, or labs indicating autoantibody screening
Age at diagnosis	Age when diabets was first diagnosed	Extracted from the H&P or other clinical notes
Duration of disease	Duration of diabetes at primary DKA/HHS admission	Calculated by subtracting the age at diagnosis from the age at primary admission
Precipitating Factors for the primary DKA/HHS admission	Categorized as medication non-adherence, infections, untreated new diabetes diagnoses, and other factors	Extracted from the H&P or other clinical notes
Length of stay	Total length of hospital stay for the primary DKA/HHS admission	Determined by the DKA/HHS primary admission encounter date and discharge date
ICU Length of stay	Length of stay in the ICU (also converted to a dichotomous variable for analysis-- ICU admission/ no ICU admission)	Extracted from emergency department summaries indicating admission to the hospital and nurses' notes on admissions to the ICU unit and discharges to step-down or other units
Glycemic Control	HbA1c upon primary admission and previous HbA1c most recent to primary admission	Extracted from primary admission and previous lab values
Chronic Complications and Co-morbidities		
Chronic Diabetes Complications	Categorized as microvascular complications (retinopathy, nephropathy, and neuropathy), macrovascular complications (cardiovascular disease), and other complications (including but not limited to hypoglycemia unawareness, gastroparesis, non-healing skin infections, recurrent urinary tract infections, and vaginal infections). (Also converted to a dichotmous variable for analysis--Complication/ no complications)	Extracted from the H&P, healthcare provider notes, discharge summary, and lab values.
Obesity	BMI (stratified by the CDC classification for underweight, normal/healthy weight, overweight, and obese)	Calculated from the patient's height and weight recorded at the time of primary admission
Mental Health	Categorized as history of depression, history of substance use, or any psychiatric condition including depression and substance use	Extracted from the H&P, healthcare provider notes, discharge summary, and lab values.

determine if the patient was seen at Grady's Diabetes Center within the year previous to their primary DKA/HHS admission. Hospital utilization was also captured by collecting information from the encounter log on emergency room utilization and other hospitalizations for any reason in the year following the primary DKA/HHS admission.

3) Diabetes and hyperglycemic emergency characteristics for this study include diabetes type, age at diagnosis, duration of the disease, precipitating factors of DKA/HHS, length of hospital stay for the primary admission, admission to the intensive care unit (ICU), ICU length of stay, and glycemic control. Diabetes type and age at diagnosis were extracted from the H&P. Duration of the disease was calculated by subtracting the age at diagnosis from the age at primary admission. Precipitating factors for the primary DKA/HHS admission were also recorded as indicated in the healthcare provider notes, H&P, and discharge summary. These factors were categorized as medication non-adherence (including not being able to get medications, discontinuing medication, and changing medications without consulting a healthcare provider), infections (non-communicable and communicable), new onset diabetes diagnoses, and other factors. Length of stay for the primary admission was determined by the DKA/HHS admission encounter and discharge dates. Emergency Department summaries and nurses' notes on admissions to the unit and discharges to step-down or other units were used to determine if the patient was admitted the ICU and the length of stay in the ICU. HbA1c upon admission was recorded as the first HbA1c in the laboratory values during the primary admission, and previous HbA1c was recorded as the most recent laboratory HbA1c prior to the primary admission.

4) Chronic Complications and Co-morbidities for this study include chronic diabetes complications, obesity as indicated by body mass index (BMI), and co-morbid psychiatric conditions. Diabetes complications and psychiatric history were extracted from the H&P at admission, discharge summary, and lab values. For the purpose of analysis diabetes complications were converted to a dichotomous variable (present/ not present), but also separated by microvascular (retinopathy, nephropathy, and neuropathy), macrovascular (cardiovascular disease), and other complications (including but not limited to hypoglycemia unawareness, gastroparesis, non-healing skin infections, recurrent urinary tract infections, and vaginal infections). BMI was calculated from the patient's height and weight recorded at the time of the primary admission and stratified by the Centers for Disease Control (CDC) classification for underweight, normal/healthy weight, overweight, and obese (Centers for Diseae Control and Prevention, 2015). A history of any psychiatric co-morbidities was analyzed as a dichotomous variable (present/ not present) as well as exploring depression and substance use as separate variables.

Extractors compiled all information from each case into a shared spreadsheet. All data compiled in the spreadsheet was de-identified. After the initial identification of the patient using the MRN, study numbers were assigned to indicate unique patients. Additionally, birthdates were removed after determining age of admission, and zip codes were deleted after determining the associated median income.

Statistical Analysis

Extracted data from the patients who met the inclusion/exclusion criteria were uploaded to SPSS software for all analyses (SPSS Version 22, Armonk, NY). All data were reviewed for implausible values. Missing data was assumed to be at random and complete case analysis was used for all analyses

Aim 1: Characterize the young adult (18-35 year old) population admitted to an inner city hospital for a hyperglycemic emergency over a five-year period.

Descriptive statistics were analyzed for each study variable within the four categories of risk factors. Differences in T1D versus T2D were analyzed using independent t-tests for continuous measures. Chi-square tests of independence were used to determine association between categorical variables. Glycemic control was stratified by less than 9%, 9% to less than 12%, and greater than or equal to 12%. 9% was chosen based on the Health Resources and Service Administration (HRSA) and the Healthcare Effectiveness and Data Information Set (HEDIS) cut point of an HbA1c greater than 9% indicating poor glycemic control ("Comprehensive Diabetes Care: HEDIS Measure," 2016; Health Resources and Services Administration, 2012). The second cut-point of 12% was based on the average HbA1c of the sample. Analysis of variance (ANOVA) was used for continuous outcomes, and Chi- square tests of independence were used to determine association between glycemic control and categorical outcomes. To adjust for multiple comparisons between groups, Bonferroni correction was utilized. The significance level was set at 0.05 for all analyses.

Aim 2: Determine factors that are associated with recurrent of hyperglycemic emergencies within 5 years.

Single admissions were compared to multiple admissions for each study variable within the four categories of risk factors. Independent t-tests were used for continuous measures, and Chi-square tests of independence were used to determine association between categorical variables with z-tests to compare stratified groups and *p*-values adjusted by Bonferroni correction.

Univariate logistic regression was used to calculate unadjusted odds ratios for risk factors that had a significant difference between one DKA/HHS admission and multiple admissions. For this analysis, more than one DKA/HHS admission was treated as the primary outcome of interest while the demographic, diabetes characteristics, co-morbidities, and access to care variables were the exposures. Multiple logistic regression was used to model all variables associated with multiple DKA/HHS readmissions. A parsimonious model was chosen using forward conditional stepwise selection. The significance level for entry into the model was set at 0.05. The Nagelkerke R^2 value was used to estimate variation in DKA/HHS recurrence explained by the model. The Hosmer and Lemeshow Goodness of Fit Test was used to evaluate the model's fit. The significance level was set at 0.05 for all analyses.

Aim 3: Determine factors that are associated with high rates of readmission (more than four admissions within five years) and frequent readmissions (less than one year between readmissions) for hyperglycemic emergencies.

Single admissions were compared to 2-4 admissions and greater than four admissions for each study variable. Analysis of variance (ANOVA) was used for continuous measures, and Chi- square tests of independence were used to determine association between categorical variables. In order to compare the stratified groups, z-tests with *p*-values adjusted by Bonferroni correction were utilized. Patients who were readmitted within one year of their primary admission were compared to patients who were readmitted 1-5 years after the primary admission. Independent t-tests were used for continuous measures, and Chi-square tests of independence were again used to determine association between categorical variables. Alpha was set at 0.05 for all analyses.

Univariate binomial logistic regression was used to calculate unadjusted odds ratios for risk factors that had a significant difference among the comparison groups. For this analysis, the risk factors were treated as exposures and more than four admissions and admissions within one year were considered the primary outcomes of interest. Multiple logistic regression was used to model the probability of the primary outcomes based on the exposure variables. The Nagelkerke R^2 value was used to estimate how much variation in the outcome could be explained by the model. Based on the study model, each of the categories of risk factors was added in a stepwise manner to determine the added variance for each category and the overall variance explained by the model.

Limitations

The data collected in this study were limited to information in the EHR. Much of the data extracted were found in provider notes which are a subjective source of information and can lead to missing or incorrect data. Some study variables were not always recorded for every patient which could lead to misinterpretation. There is bias in the data towards patients who have high utilization rates of the Grady Health System as there are more encounters in the chart from which to pull data. There may be an additional bias towards T1D classification in this sample because diabetes type was primarily extracted from emergency department notes due to limited utilization of the diabetes clinic. In the emergency department patients are often not classified by autoantibody screening which is the ADA standard of diagnosis (American Diabetes Association, 2017b).

The Grady Health System EHR did not capture information from the patient's utilization of other hospital systems at the time of this data extraction. Additionally, patients did not have a consistent five year follow-up time in this study due to primary admissions spanning the entire study period (3.24±1.30 years). The readmission rates in this population may be even higher than the study results suggest since not all hospital utilization was captured and not all patients were followed for a full five years.

Despite limitations, this study is the foundational work to reduce the recurrence and frequency of hyperglycemic emergencies in young adults. The study helps to identify young adult patients at risk for recurrent hyperglycemic emergencies and provides information on risk factors associated with recurrent hyperglycemic emergencies that can be used to develop multi-disciplinary interventions in hopes of reducing hospital costs for treating diabetic emergencies and improving patient outcomes.

Paper 1: Hospital Admissions for Hyperglycemic Emergencies in Young Adults at an Inner-City Hospital

Authors: MK Findley, J Sonya Haw, Sudeshna Paul, Melissa Spezia Faulkner, Eun Seok Cha, Farah Khan, Sara Markley, Anastasia-Stefania Alexopoulos, David A Alpha, Mohammed K Ali

Abstract

Background: There are over 150,000 hyperglycemic emergencies in the U.S. each year. Hyperglycemic emergencies are associated with complications, mortality, and increased healthcare costs. Young adults have disproportionally high rates of hyperglycemic emergency hospital admissions. The purpose of this study was to characterize the young adult admitted to an inner city hospital for a hyperglycemic emergency.

Methods: Electronic health records were used to extract data from 273 young adult patients (18-35yrs) admitted to an inner city hospital over a 5 year period. Independent t-tests, Chi-Square tests, and ANOVA were used to explore differences in T1D vs T2D and glycemic control (HbA1c < 9%, 9% ≤ HbA1c < 12.%, HbA1c ≥ 12%).

Results: There was a significantly higher percentage of Black patients with uncontrolled diabetes (HbA1c ≥ 9%: 84.8% vs HbA1c<9%: 65.0%, $p<0.05$). Significantly more of those with T1D were insured (T1D-35.0% vs T2D-19.17%, $p<0.05$). Only 3.7% utilized the diabetes clinic in the past year. Mean HbA1c at admission was 12.38% and 90.5% had HbA1c ≥9%. T2D had higher HbA1c (T2D-13.07% vs T1D-12.11%, $p<0.05$). Diabetes complications were present in 44.7%, and 47.3% were overweight or obese (mean BMI 27.76kg/m^2 ± 8.85). Psychiatric co-morbidities were present in 35.5%.

Conclusion: Results of this study characterize young adults hospitalized for hyperglycemic emergencies in an urban inner-city hospital. These patients tend to be Black, have poorly controlled diabetes, with lack of routine follow-up care. A substantial percentage also have psychiatric co-morbidities and diabetic complications, which may contribute both to uncontrolled diabetes and hospitalizations for hyperglycemic emergencies.

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Paper 1: Hospital Admissions for Hyperglycemic Emergencies in Young Adults at an Inner-City Hospital

Introduction

Diabetes is a complex, chronic disease that is increasing in prevalence worldwide (Patterson et al., 2012; Vehik & Dabelea, 2011). The incidence rate of type 1 diabetes (T1D) is rising approximately 3-4% per year (Patterson et al., 2012). The prevalence of type 2 diabetes (T2D) is also increasing in youth and adults. Between 2001 and 2009 the prevalence for T2D increased by 30.5% in youth (Hamman et al., 2014). As the prevalence of diabetes in youth increases, more adults will be affected by the disease, develop diabetes complications, and seek healthcare treatment.

Hyperglycemic emergencies such as diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar syndrome (HHS) are serious acute complications that affect individuals with T1D or T2D. In the last three decades there has been a 226% increase in DKA/HHS hospitalizations (Centers for Disease Control and Prevention, 2017). Treatment of diabetes emergencies has a substantial economic burden. The average cost of one hospital admission for a hyperglycemic emergency in the United States is $17,500 per patient, and it is estimated that the total annual hospital cost of hyperglycemic emergency management is $2.4 billion (Kitabchi et al., 2009).

Studies have identified that young adults less than 35 years have disproportionally high rates of diabetic emergencies and hospital utilization (Bradford et al., 2017; Randall et al., 2011; Rewers et al., 2002). As young adults transition from pediatric to adult care, optimal diabetes control is significantly more difficult to achieve (Bryden et al., 2001; Insabella et al., 2007). These young adults often have gaps in care and significant changes in self-management (Findley et al., 2015). The American Diabetes Association (ADA) recommendations for glycemic control as indicated by hemoglobin A1c (HbA1c) for adults with diabetes over the age of 18 is less than 7% (American Diabetes Association, 2017d), however, less stringent HbA1c goals (<8%) may be suggested for young adults who are transitioning from pediatric to adult care and subsequently have fewer resources, changing support systems, and alterations to self-management and self-care (American Diabetes Association, 2017d). Young adult diabetic emergencies and hospital utilization will continue to increase as the prevalence of T1D and T2D increases in youth and young adults.

Uncontrolled diabetes (HbA1c ≥ 9.0%) ("Comprehensive Diabetes Care: HEDIS Measure," 2016; Health Resources and Services Administration, 2012) and multiple hyperglycemic emergencies during young adulthood have the potential to greatly affect morbidity and mortality throughout adult life (American Diabetes Association, 2017d) as well as substantially increase healthcare costs now and as this population ages. Despite this vulnerability of the young adult population, most studies focus on either pediatric patients under the age of 18 or consolidate all adult patients over the age of 18.

This retrospective study provides a descriptive analysis unique to young adults at an inner city hospital. Ethnic, cultural, and socioeconomic differences affect diabetes prevalence and outcomes and compound the risks of hospitalizations and diabetic complications of the low resource inner-city young adult diabetes population. Despite advances in medical knowledge and diabetes management, socioeconomic, ethnic, and racial inequalities exist in access to healthcare resulting in a higher risk of complications and poorer glycemic control for the disadvantaged (American Diabetes Association, 2017i; Campbell et al., 2012; H. Y. Lee et al., 2015; Ricci-Cabello et al., 2010).

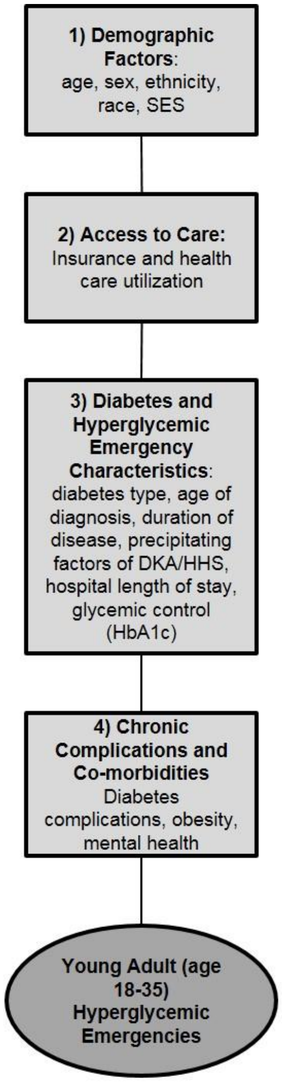

Figure 1: Four Category Theoretical Model for Characterization and Identification of Young Adults at Risk for Hyperglycemic Emergencies. Theoretical model based on the WHO STEPS framework of non-communicable diseases. Distributes risk factors into four categories that are the framework for characterization and identification of young adults at risk DKA/HHS hospital admissions.

Risk factors associated with hyperglycemic emergencies that have been previously identified by studies using pediatric and adult populations were analyzed in this study. The theoretical framework was based on the World Health Organization (WHO) STEPwise Approach to Surveillance of Non-Communicable Public Diseases (STEPS) framework for non-communicable diseases (Noncommunicable Diseases and Mental Health World Health Organization, 2003). This adapted framework distributes risk factors among four categories (Figure 1) *demographic factors* including age, sex, ethnicity, race, and SES (Bradford et al., 2017; Kim et al., 2010; Kitabchi & Nyenwe, 2006; Kitabchi et al., 2008; Liu et al., 2010; Musey et al., 1995; E. Nyenwe et al., 2007; Randall et al., 2011; Rewers et al., 2002; Steenkamp et al., 2013); 2) *access to care* indicated by insurance status and healthcare utilization ; 3) *diabetes and hyperglycemic emergency characteristics* relating to the patient's disease history and current hyperglycemic emergency (Centers for Disease Control and Prevention, 2017; Cooper et al., 2016; Liu et al., 2010; E. Nyenwe et al., 2007; Randall et al., 2011); and 4) *chronic complications and co-morbidities* including microvascular and macrovascular complications, obesity, and mental health (Balla et al., 2008; Barski et al., 2012; Bradford et al., 2017; Govan et al., 2011; Kim et al., 2010;

Randall et al., 2011); The purpose of this study was to describe the young adult patient population with a diagnosis of diabetes admitted to an inner city hospital for a hyperglycemic emergency based on the four categories of risk factors. This characterization can be used to identify target populations for future interventions to prevent young adult hospital admissions for hyperglycemic emergencies.

Methods

Population and data sources

Electronic health records (EHR) (Epic Systems Corporation, Veronia, WI) from the Grady Health System in Atlanta, Georgia were used as the data source for this study. Grady Memorial Hospital is a 953 bed academic county hospital that serves low resource inner city patients. International Classification of Diseases (ICD)-9 codes indicating DKA or HHS were used to identify patients admitted to Grady between January 2010 and November 2015. All patients 18 to 35 years old at the time of admission for DKA/HHS were included in the study. Cases were excluded if the patient was younger than 18 or older than 35 years at the time of admission for DKA/HHS, if the patient was only seen in the emergency department or clinic and not admitted to the hospital, if there was no evidence in the EHR of a hyperglycemic emergency, or if the patient did not have a diagnosis of T1D or T2D (gestational diabetes and other diabetes types were excluded).

IRB approval was obtained from Emory University and the study was authorized by the Grady Hospital Research Oversight Committee. All analyses and study procedures complied with HIPAA regulations and federal regulations for the protection of human research subjects and inclusion of women and minorities.

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Data were collected from the EHR using retrospective chart reviews completed between December 2015 and December 2016. An extraction sheet was created indicating each variable, coding for each variable's possible results, and how to denote missing information. The first ten cases were reviewed by all extractors to ensure minimal reviewer variability and consensus in coding for each variable.

The first hyperglycemic emergency that occurred between 2010 and 2015 in which the patient was greater than or equal to 18 years old but less than 35 years old was identified as the primary DKA/HHS admission. Data was extracted relating to the primary admission; however, all EHR documentation was examined in order to gather patient history and information about previous and subsequent encounters and hospital admissions. For this study all demographic variables, diabetes characteristics, co-morbidities, and access to care data were extracted from the EHR including the patient's encounter log, lab results and documentation from physicians, nurses, social workers, dietitians, diabetes educators and other healthcare providers (Paper 1-Table 1).

1) Demographic variables for this study included age at admission, sex, race, ethnicity, and socio-economic status (SES). Patient's age at admission was calculated by subtracting the primary admission date from the date of birth indicated in the EHR. Sex was recorded as designated in the EHR. Race and ethnicity were extracted from the history and physical (H&P) at admission and other clinical notes. Race was recorded as Caucasian, Black, Asian, or other. For the purpose of analysis, race was converted into a dichotomous variable (Black/Non-Black). Ethnicity was recorded as Hispanic or non-Hispanic. SES was derived from the zip code at the time of the primary admission and associated with the median household income for that zip code as indicated by the 2011-2015 American Community Survey 5-Year Estimates collected by the U.S. Census Bureau (2011-2015 American Community Survey 5-Year Estimates, 2017).

2) Access to care was indicated by insurance status at the primary admission and utilization of the Grady Health System within the one year of the primary admission. Insurance information for the primary admission was extracted from the H&P at admission, social worker and healthcare provider notes, and discharge summaries. Insurance was categorized as private insurance, public insurance (Medicare or Medicaid), or no insurance. In addition to analysis of each type of insurance, insurance was also converted to a dichotomous variable (private or public insurance/ no insurance). The EHR encounter log was analyzed to determine if the patient utilized the Grady Diabetes Center within the year previous to their primary DKA/HHS admission. Hospital utilization was also captured by collecting information from the encounter log on emergency room utilization and other hospitalizations for any reason in the year following the primary DKA/HHS admission.

3) Diabetes and hyperglycemic emergency characteristics for this study include diabetes type, age at diagnosis, duration of the disease, precipitating factors of DKA/HHS admission, length of hospital stay for the primary admission, admission to the intensive care unit (ICU), ICU length of stay, and glycemic control. Diabetes type and age at diagnosis were extracted from the H&P. Duration of the disease was calculated by subtracting the age at diagnosis from the age at primary admission. Precipitating factors for the primary DKA/HHS admission were also recorded as indicated in the healthcare provider notes, H&P, and discharge summary. These factors were categorized as medication non-adherence (including not being able to get medications, discontinuing medication, and changing medications without consulting a healthcare provider), infections (non-communicable and communicable), new onset diabetes diagnoses, and other factors. Length of stay for the primary admission was determined by the DKA/HHS admission encounter and discharge dates. Emergency Department summaries and nurses' notes on admissions to the unit and discharges to step-down or other units were used to determine if the patient was admitted the ICU and the length of stay in the ICU. HbA1c upon admission was recorded as the first HbA1c in the laboratory values during the primary admission, and previous HbA1c was recorded as the most recent laboratory HbA1c prior to the primary admission.

4) Chronic Complications and Co-morbidities for this study include diabetes complications, obesity as indicated by body mass index (BMI), and co-morbid psychiatric conditions. Diabetes complications and psychiatric history were extracted from the H&P at admission, discharge summary, and lab values. For the purpose of analysis diabetes complications were converted to a dichotomous variable (present/ not present), but also separated by microvascular (retinopathy, nephropathy, and neuropathy), macrovascular (cardiovascular disease), and other complications (including but not limited to hypoglycemia unawareness, gastroparesis, non-healing skin infections, recurrent urinary tract infections, and vaginal infections). BMI was calculated from the patient's height and weight recorded at the time of the primary admission and stratified by the Centers for Disease Control (CDC) classification for underweight, normal/healthy weight, overweight, and obese (Centers for Diseae Control and Prevention, 2015). Psychiatric co-morbidities were analyzed as a dichotomous variable (present/ not present) as well as exploring depression and substance use as separate variables.

Table 1: Variables within the Four Category Theoretical Model of Risk Factors Associated with Hyperglycemic Emergencies

Risk Factor	Definition	Data Source
Demographic Variables		
Age at admission	Age at primary DKA/HHS admission	Calculated by subtracting the primary admission date from the date of birth indicated in the EMR
Sex	Male or Female	As designated in the EMR
Race	Caucasian, Black, Asian, or Other (also converted into a dichotomous variable for analysis-- Black/Non-Black)	Extracted from the H&P or other clinical notes
Ethnicity	Hispanic or Non-Hispanic	Extracted from the H&P or other clinical notes
SES	Household median income (also converted to a dichotomous variable for analysis--</> $35k)	Derived from the zip code at the time of primary admission and associated with the median household income for that zip code as indicated by the 2011-2015 American Community Survey 5-Year Estimates collected by the U.S. Census Bureau.
Access to Care		
Insurance Status	Insurance status at the time of primary admission categorized as private insurance, public insurance (Medicare or Medicaid), or no insurance (converted to a dichotmous variable for analysis-- private or public insurance/ no insurance)	Extracted from the H&P, healthcare provider notes, and discharge summary
Hospital Utilization	Emergency room utilization and other hospitalizations for any reason in the year following the primary DKA/HHS admission	Extracted from the EMR encounter log.
Utilization of the Grady Diabetes Clinic	Attendance of appointment at the Grady Diabetes Clinic in the year previous to the primary admission.	Extracted from the EMR encounter log
Diabetes and Hyperglycemic Emergency Characteristics		
Diabetes Type	Type 1 Diabetes or Type 2 Diabetes	Extracted from the H&P , clinical notes, or labs indicating autoantibody screening
Age at diagnosis	Age when diabets was first diagnosed	Extracted from the H&P or other clinical notes
Duration of disease	Duration of diabetes at primary DKA/HHS admission	Calculated by subtracting the age at diagnosis from the age at primary admission
Precipitating Factors for the primary DKA/HHS admission	Categorized as medication non-adherence, infections, untreated new diabetes diagnoses, and other factors	Extracted from the H&P or other clinical notes
Length of stay	Total length of hospital stay for the primary DKA/HHS admission	Determined by the DKA/HHS primary admission encounter date and discharge date
ICU Length of stay	Length of stay in the ICU (also converted to a dichotomous variable for analysis-- ICU admission/ no ICU admission)	Extracted from emergency department summaries indicating admission to the hospital and nurses' notes on admissions to the ICU unit and discharges to step-down or other units
Glycemic Control	HbA1c upon primary admission and previous HbA1c most recent to primary admission	Extracted from primary admission and previous lab values
Chronic Complications and Co-morbidities		
Chronic Diabetes Complications	Categorized as microvascular complications (retinopathy, nephropathy, and neuropathy), macrovascular complications (cardiovascular disease), and other complications (including but not limited to hypoglycemia unawareness, gastroparesis, non-healing skin infections, recurrent urinary tract infections, and vaginal infections). (Also converted to a dichotmous variable for analysis--Complication/ no complications)	Extracted from the H&P, healthcare provider notes, discharge summary, and lab values.
Obesity	BMI (stratified by the CDC classification for underweight, normal/healthy weight, overweight, and obese)	Calculated from the patient's height and weight recorded at the time of primary admission
Mental Health	Categorized as history of depression, history of substance use, or any psychiatric condition including depression and substance use	Extracted from the H&P, healthcare provider notes, discharge summary, and lab values.

Extractors compiled all information from each case into a shared spreadsheet. All data compiled in the spreadsheet was de-identified. After the initial identification of the patient using the MRN, study numbers were assigned to indicate unique patients. Additionally, birthdates were removed after determining age of admission, and zip codes were deleted after determining the associated median income

Data Analysis

All data were reviewed for implausible values. Missing data was assumed to be at random and complete case analysis was used for all analyses. Descriptive statistics were analyzed for each study variable within the four categories of risk factors. Differences in T1D versus T2D were analyzed using independent t-tests for continuous measures. Chi-square tests of independence were used to determine association between categorical variables. Glycemic control was stratified by less than 9%, 9% to less than 12%, and greater than or equal to 12%. Poor glycemic control as indicated by a HbA1c of 9% was chosen as the first cut-point based on the Health Resources and Service Administration (HRSA) and the Healthcare Effectiveness and Data Information Set (HEDIS) ("Comprehensive Diabetes Care: HEDIS Measure," 2016; Health Resources and Services Administration, 2012). The second cut-point of 12% was based on the average HbA1c of the sample. Analysis of variance (ANOVA) was used for continuous outcomes, and Chi- square tests of independence were used to determine association between glycemic control and categorical outcomes. To adjust for multiple comparisons between groups, the Bonferroni correction method was utilized. The significance level was set at 0.05 for all analyses. All analyses were performed in SPSS (SPSS Version 22, Armonk, NY) .

Results

During the study period, Grady admitted 2,427 cases with an ICD-9 classification indicating DKA or HHS. There were a total of 703 (29%) young adult cases (18-35 years) during this period with 326 unique MRN's. Inclusion/exclusion criteria removed 53 patients leaving 273 in the study sample. Data was extracted from the EHR of 273 unique young adult patients. These 273 young adults accounted for a total of 636 DKA/HHS admissions during the five-year study period.

Demographic variables are presented in Table 2. The average age at admission was 26.0± 4.5 years with T2D patients having a significantly higher age than T1D patients (28.5 years vs 25.1 years, $p < 0.001$). The study sample predominantly identified as Black (83.5%), and there were significantly more Black patients with an HbA1c greater than or equal to 12% compared to an HbA1c of less than 9% (92.2% vs 65.0%, $p < 0.05$).

Table 2: Admitted Young Adult Demographic Characteristics

Characteristic	All admissions (n=273) Mean (SD) or %	T1D (n=200) Mean (SD) or %	T2D (n=73) Mean (SD) or %	HbA1c<9.0% (n=20) Mean (SD) or %	9.0%≤HbA1c<12.0 % (n =75) Mean (SD) or %	HbA1c≥12.0% (n=116) Mean (SD) or %
Age at primary admission, years (n=273)	26.02 (4.52)	25.12 (4.25)	28.48 (4.36)**	27.50 (4.60)	26.82 (4.35)	25.44 (4.54)*
Sex (n= 273)						
Male	52.7	52.0	48.0	45.0	54.7	54.3
Female	47.3	48.0	52.0	55.0	45.4	45.7
Ethnicity (n=273)						
Non-Hispanic	94.9	96.0	91.8	100.0	92.0	96.6
Hispanic	5.1	4.0	8.2	0.0	8.0	3.4
Race (n=271)						
Black	83.5	84.0	82.2	65.0	73.3	92.2*[a]
Non-Black	16.5	16.0	17.8	35.0	24.0	7.8
Median Household Income, $10k (n= 271)	41.89 (15.29)	42.12 (15.89)	41.25 (13.61)	46.09 (20.38)	44.17 (16.91)	40.16 (12.60)

*significant at alpha p<0.05
**significant at alpha *p*<0.001
[a] significant difference between HbA1c <9.0% and HbA1c >=12.0% at alpha p<0.001

Variables indicative of access to care are presented in Table 3. Only 31% of patients admitted to GMH for DKA/HHS had insurance. Significantly more patients with T1D

Table 3: Admitted Young Adult Access to Care

Characteristic	All admissions (n=273) Mean (SD) or %	T1D (n=200) Mean (SD) or %	T2D (n=73) Mean (SD) or %	HbA1c<9.0% (n=20) Mean (SD) or %	9.0%≤HbA1c<12.0% (n =75) Mean (SD) or %	HbA1c≥12.0% (n=116) Mean (SD) or %
Insurance (n=166)						
Any Insurance	30.8	35.0	19.2*	60.0	37.4	21.6*[a]
Private Insurance	11.4	13.0	6.8	20.0	9.3	11.2
Public Insurance	19.4	22.0	12.3	40.0	28.0	10.3*[a]
No Insurance	49.4	65.0	80.8*	40.0	62.6	78.4
Healthcare Utilization (n=271)						
Emergency Visits	43.2	44.5	39.7	40.0	45.4	40.5
Hospitalization	37.7	42.5	24.7*	45.0	44.0	31.0
Diabetes Clinic Attendance	3.7	4.5	1.4	0.0	4.0	0.9

*significant at alpha *p*<0.05
[a] significant difference between HbA1c <9.0% and HbA1c >=12.0% at alpha p<0.05

have insurance than patients with T2D (35.0% vs 19.12%, p=0.01). Significantly fewer patients with HbA1c greater than 12% have insurance, specifically public insurance, compared to those with an HbA1c of less than 9% (any insurance: 21.6% vs 60.0%, $p<0.05$; public insurance: 10.3% vs 40.0%, $p<0.05$). Only 3.7% of those admitted had utilized the Grady Diabetes Center in the past year while 43% utilized the emergency department and 38% were hospitalized in the following year. Individuals with T1D had significantly more hospitalizations in the following year compared with T2D (42.5% vs 24.7%, $p<0.05$).

Diabetes and hyperglycemic emergency characteristics are presented in Table 4. The majority of young adults admitted were diagnosed with T1D (73.3%). Compared to patients with T2D, patients with T1D had a significantly younger age at diagnosis (14.9 ± 6.5 years vs 25.6 ± 6.1 years, $p<0.001$) and had a significantly longer duration of disease (10.3 ± 6.9 years vs 2.7 ±4.5 years, $p<0.001$). HbA1c increased significantly with shorter duration of disease ($p<0.05$). The precipitating factor for 60% of young adult's primary admissions was classified as medication non-adherence. Admissions in T1D patients for non-adherence and infections were higher than in T2D (non-adherence: T1D-61.5% vs T2D-47.9%, $p<0.05$; infection: T1D-21.5% vs T2D-9.6%, $p<0.05$); however 36% of primary admissions in T2D patients were attributed to an untreated new diabetes diagnosis (vs 3.5% in T1D $p<0.001$).

Table 4: Admitted Young Adult Diabetes and Hyperglycemic Emergency Characteristics

Characteristic	All admissions (n=273) Mean (SD) or %	T1D (n=200) Mean (SD) or %	T2D (n=73) Mean (SD) or %	HbA1c<9.0% (n=20) Mean (SD) or %	9.0%≤HbA1c<12.0% (n =75) Mean (SD) or %	HbA1c≥12.0% (n=116) Mean (SD) or %
Diabetes Type (n=273)						
Type 1	73.3	73.3	0.0	90.0	74.7	67.2
Type 2	26.7	N/A	26.7	10.0	25.3	32.8
Age at Diagnosis, years (n=192)	18.40 (8.15)	14.86 (6.53)	25.63 (6.1)**	14.42 (5.33)	18.78 (8.76)	19.39 (8.25)
Duration of Disease, years (n=192)	7.80 (7.19)	10.30 (6.92)	2.68 (4.54)**	13.56 (5.32)	8.06 (7.69)	6.32 (6.25)*[ab]
Precipitating Factors (n=240)						
Non-adherence	57.9	61.5	47.9*	55.0	57.3	62.1
Infection	18.3	21.5	9.6*	30.0	18.7	16.4
New Onset	12.1	3.5	35.6*	0.0	16.0	14.7
Other	11.2	13.5	6.8	15.0	8.0	6.9
Length of Stay, days (n=271)	3.75 (3.6)	3.60 (3.28)	4.15 (4.32)	4.75 (4.83)	4.00 (3.81)	3.8 (3.74)
Admission to ICU (n=272)						
ICU Admission	13.2	15.0	5.5	25.0	18.7	7.8
ICU Length of Stay, days	0.39 (1.37)	0.46 (1.49)	0.21 (0.94)	1.70 (3.76)	0.51 (1.21)	0.14 (0.56)*[ab]
Glycemic Control (n=211)						
Admission HbA1c, %	12.38 (2.61)	12.11 (2.69)	13.07 (2.29)*	7.78 (0.78)	10.51 (0.86)	14.37 (1.39)**
Prior HbA1c, %	11.00 (2.71)	10.94 (2.70)	11.38 (2.83)	9.30 (2.41)	10.12 (2.60)	12.29 (2.57)**

*significant at alpha $p<0.05$
**significant at alpha $p<0.001$
[a] significant difference between HbA1c <9.0% and HbA1c >=12.0% at alpha $p<0.05$
[b] significant difference between HbA1c <9.0% and 9.0%<=HbA1c<12.0% at alpha $p<0.05$

Patients' time in the ICU decreased as HbA1c increased (*p*<0.05). Uncontrolled diabetes with a HbA1c greater than 9% was present in 90.5% of the study sample. The average HbA1c of admitted young adults was 12.4±2.61%. T2D patients had a significantly higher HbA1c compared to T1D patients (13.1% vs 12.1%, *p*=0.02).

Chronic Complications and Co-morbidities are presented in Table 5. Chronic complications related to diabetes (microvascular, macrovascular, or other complications) were present in 45% of the young adults admitted. Significantly more patients with T1D had complications than T2D patients (46.0% vs 41.1%, *p*=0.04). T2D diabetes patients had a significantly higher BMI than T1D patients (35.8 8kg/m^2 vs 24.8 8kg/m^2 , *p*<0.001). A history of psychiatric conditions (depression, substance abuse, or other psychiatric condition) was present in 36%, with significantly more patients with T1D having a history of substance use (16.5% vs 11.0%, *p*=0.02).

Table 5: Admitted Young Adult Chronic Complications and Co-morbidities

Characteristic	All admissions (n=273) Mean (SD) or %	T1D (n=200) Mean (SD) or %	T2D (n=73) Mean (SD) or %	HbA1c<9.0% (n=20) Mean (SD) or %	9.0%≤HbA1c<12.0% (n =75) Mean (SD) or %	HbA1c≥12.0% (n=116) Mean (SD) or %
Chronic Diabetes Complications (n=219)						
Any Diabetes complication	44.7	46.0	41.1*	60.0	44.0	43.1
Macrovascular complications	0.7	0.5	1.4	0.0	0.0	0.9
Microvascular complications	18.7	19.0	17.8	25.0	16.0	14.7
Other Diabetes Complications	35.2	37.0	35.2	55.0	37.3	31.9
Obesity (n=240)						
BMI (std.ev)	27.76 (8.85)	24.83 (5.76)	35.83 (10.72)**	25.64 (5.99)	29.81 (11.27)	27.33 (8.04)
Underweight	3.7	4.5	1.4	0.0	5.3	4.3
Normal weight	37.0	46.5	11.0*	50.0	33.3	36.2
Overweight	20.9	22.5	16.5	25.0	20.0	23.3
Obese	26.4	14.5	58.90*	20.0	30.7	26.7
Mental Health (n=196)						
Any psychiatric co-morbidity	35.5	35.5	35.6	30.0	34.7	36.1
Substance use	21.2	16.5	11.0*	25.0	17.3	12.1
Depression	15.0	20.0	24.7	5.0	17.3	21.6

*significant at alpha p<0.05
**significant at alpha *p*<0.001

Discussion

The major findings of this study were a descriptive analysis of the young adult patient admitted to an inner city hospital for DKA/HHS and the lack of primary diabetes care in the young adult population. DKA/HHS young adult patients were characterized as individuals in their mid-twenties, Black and non-Hispanic. These patients had limited access to care as demonstrated by low insurance rates and minimal usage of diabetes care clinics.

The majority had a type T1D diagnosis and over 90% had poor glycemic control. Additionally, there was a substantial prevalence of chronic diabetes complications and psychiatric co-morbidities. These are risk factors that healthcare providers can use to identify young adults at risk of hyperglycemic emergencies.

The high rate of uncontrolled diabetes in this young adult population emphasizes the importance of primary diabetes care for young adults moving from pediatric to adult healthcare systems. 34% of young adults report a gap between pediatric and adult diabetes care (Findley et al., 2015; Garvey et al., 2012). In this sample only 4% utilized diabetes care services the year before their primary DKA/HHS admission, suggesting that there are challenges to accessing and utilizing routine primary diabetes care, which is critical to preventing emergency hospitalizations.

The high rate of uncontrolled diabetes in this population correlates with the high rate of chronic diabetes complications observed. These complications will greatly affect morbidity and mortality in this young adult population, as well as substantially increase health care costs. Optimal glycemic control during young adulthood reduces the likelihood of serious long-term microvascular and macrovascular complications and can reduce the economic burden of diabetes (Blonde, 2012; Silverstein et al., 2005). There is a lack of attention to young adult diabetes transitional care and diabetes primary care research in vulnerable subgroups that have barriers to optimal diabetes treatment (Findley et al., 2015). Research, development, and implementation of transitional care programs and diabetes care specific to young adults in vulnerable populations such as this study sample are essential to effectively maintain glycemic control and prevent chronic diabetes complications during young adulthood.

Other findings in this study were the comparison of patients with T1D versus T2D presenting in DKA. These differences aligned with prior research differentiating characteristics of T1D and T2D. The risk of developing T2D increases with age and obesity (American Diabetes Association, 2017b). In this study sample, T2D patients were older, had a later age of diagnosis, shorter duration of disease, and their BMI was significantly greater. Previous studies exploring DKA in adult populations found that there was a significant difference between patients with T1D and T2D in regards to age of admission, duration of disease, the precipitating factor for DKA being new onset diabetes, and BMI (Balasubramanyam, Zern, Hyman, & Pavlik, 1999; Barski et al., 2013; Newton & Raskin, 2004; E. Nyenwe et al., 2007). These differences between hyperglycemic emergencies in T1D and T2D were the same in the current young adult study; however, HbA1c was also found to be significantly higher in individuals with T2D. The current study also found that T2D patients had fewer chronic diabetes complications, which corresponds to the overall shorter duration of disease compared to those with T1D. Patients with T2D also had a lower rate of substance use. Glycemic control, chronic diabetes complications, and psychiatric co-morbidities associated with DKA in young adults need to be further explored to determine if these differences between individuals with T1D and T2D hold true in similar populations.

The data collected in this study was limited to information within the Grady Health System EHR and did not capture information from the patient's utilization of other hospital systems. Additionally, if a patient's diagnosis was originally miscoded they were missing from the sample. Much of the data extracted from the EHR was found in provider notes which are a subjective source of information and can lead misinterpretation. Some study variables were not always recorded for every patient. There was bias in the data towards patients who have high utilization rates of the Grady Health System as there were more encounters in the chart from which to pull data. There may have been additional bias towards T1D classification in this sample because diabetes type was primarily extracted from emergency department notes due to limited utilization of the diabetes clinic. In the emergency department patients with T1D were often not diagnosed with autoantibody screening which is the ADA standard of diagnosis (American Diabetes Association, 2017b).

Finally, patients did not have consistent follow-up time. The study spanned five years of EHR data, but patients who were admitted at the beginning of the study period have five years of follow-up readmission while patients who were admitted later in the study period have a shorter follow-up. The average length of follow-up was 3.24 years (SD=1.30). Since not all patients were followed for five years, the readmission rates in this population may be even higher than the study results suggest. Despite the limitations in this study, the descriptive results characterize young adults at risk of hyperglycemic emergencies and highlight gaps in care and research that need to be further addressed and explored.

The characteristics of the young adult at risk for hyperglycemic emergencies are especially relevant in continuing current diabetes research. It is essential to identify young adults that are at the highest risk for readmission. The four categories of risk factors used in this study to characterize the young adult patient admitted to an inner city hospital for DKA/HHS can serve as the basis for building a model that could indicate young adults at risk for DKA/HHS hospital admissions and readmissions. Once this at risk population can be identified, interventions can be developed to target these young adults and decrease morbidity, mortality, and hospital utilization.

Paper 2: Risk Factors Associated with Recurrent Hospital Admissions for Hyperglycemic Emergencies in an Inner City Young Adult Population

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Abstract

Background: Young adults (18-35 years) with diabetes have disproportionally high rates of recurrent hyperglycemic emergencies that are associated with increased short-term mortality and high healthcare costs. The purpose of this study was to characterize and identify young adults at risk for recurrent hyperglycemic emergencies.

Methods: A retrospective chart review of 273 young adults admitted to an inner city hospital over a 5 year period determined risk factors associated with recurrent hyperglycemic emergencies. These risk factors served as the basis for a parsimonious multiple logistic regression model.

Results: During the study period, 43.6% of the young adult sample had more than one hyperglycemic emergency admission. Risk factors significantly associated with recurrent hyperglycemic emergencies included non-Hispanic ethnicity (8.4% vs 0.8%, $p=0.05$), race (90.8% vs 77.9%, $p=0.017$), lower household income (\$39,048±14,421 vs \$44,107±15,633, $p=0.007$), type 1 diabetes (82.4% vs -66.2%, $p=0.003$), younger age at diagnosis (16.95±7.40 vs 19.41±8.51, $p=0.039$), presence of chronic diabetes complications (53.8% vs 37.7%, $p=0.01$), lower BMI (25.96±8.07 vs 29.17±9.20, $p=0.005$), and psychiatric co-morbidities (58.0% vs 25.0%, $p<0.001$; depression: 26.9% vs 5.8%, $p<0.001$; substance use 26.9% vs 16.9%, $p=0.02$).

Conclusion: This study highlights unique risk factors for recurrent hyperglycemic emergencies in young adults that differ from risk factors associated with hyperglycemic emergencies in adult or pediatric studies. This suggests that conventional interventions may not be optimal in young populations. Modifiable risk factors specific to young adults can be targeted in future interventions to decrease hyperglycemic emergency hospital admissions, morbidity, mortality, and diabetes economic burden. (Word Count: 244)

Paper 2: Risk Factors Associated with Recurrent Hospital Admissions for Hyperglycemic Emergencies in an Inner City Young Adult Population

Introduction

There is an abundance of diabetes research focusing on pediatric patients under the age of 18 and all adult patients over the age of 18; however, young adults ages 18 to 35 are a distinctive group that are often overlooked. Due to a growing prevalence of diabetes in youth, the population of young adults with diabetes is expected to considerably increase over the next several years (Hamman et al., 2014; Patterson et al., 2012; Vehik & Dabelea, 2011). Young adults are a vulnerable population due to changes in diabetes care and self-management as a result of the need to transition from pediatric to adult health care providers coupled with significant normative life changes. During this transitional period, young adults often have large gaps in care and substantial alterations in risk taking behaviors, financial and social autonomy that leads to changes self-management (Findley et al., 2015) and poor glycemic control (Ali et al., 2013; Bryden et al., 2001; Insabella et al., 2007) and disproportionally high rates of hyperglycemic emergencies (Bradford et al., 2017; Randall et al., 2011).

Optimal diabetes control is notably more difficult to achieve within the young adult population (Bryden et al., 2001; Insabella et al., 2007). The American Diabetes Association (ADA) recommends glycemic control corresponding to a hemoglobin A1c (HbA1c) of less than 7% for adults over the age of 18 (American Diabetes Association, 2017d). Due to young adults moving from pediatric to adult health care providers and subsequently having changes in resources, different support systems, and alterations to their standard self-management and self-care, the ADA recommends a less stringent HbA1c target (<8%) for some young adults (American Diabetes Association, 2017d). Diabetes control is essential during young adulthood to prevent the development and progression of diabetes complications. Better glycemic control in young adulthood is associated with significantly decreased rates of microvascular complications (American Diabetes Association, 2017d; Holman, Paul, Bethel, Matthews, & Neil, 2008; Ohkubo et al., 1995; UK Prospective Diabetes Study (UKPDS) Group, 1998) and macrovascular complications (American Diabetes Association, 2017d; Holman et al., 2008; Nathan et al., 2005; Nathan et al., 2009) in those with type 1 diabetes (T1D) and type 2 diabetes (T2D). Despite the more flexible HbA1c recommendations, many young adults still fail to meet glycemic control standards. If optimal glycemic control is not achieved during young adulthood, diabetes complications will increase as these young adults age.

The young adult population also has disproportionally high rates of hyperglycemic emergencies such as diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar syndrome (HHS) (Bradford et al., 2017; Randall et al., 2011). Hospital admissions due to hyperglycemic emergencies have increased by 226% in the last three decades (Centers for Disease Control and Prevention, 2017) and have an estimated annual cost of $2.4 billion in the United States (Kitabchi et al., 2009). As the population of young adults with diabetes grows, DKA/HHS hospitalizations will continue to escalate. The increased hospital utilization from diabetes complications and hyperglycemic emergencies will have a significant economic impact.

Mortality of adult hyperglycemic emergencies has reduced to less than 1% in the United States (Kitabchi et al., 2009); however, hyperglycemic emergencies are associated with an increased short term risk of death within the five years after hospital admission (Gibb et al., 2016). Mortality rates are significantly associated with increased DKA/HHS hospital admissions (Gibb et al., 2016; Mays et al., 2016). A single hyperglycemic emergency is associated with a 10.6% short-term mortality rate. The mortality rate in those with more than four DKA/HHS admissions within five years is approximately 30% (Gibb et al., 2016). This increased short-term risk of death, is especially pertinent in young adult populations because young adults are at the highest risk for recurrent hyperglycemic emergencies (Bradford et al., 2017; Randall et al., 2011).

The population for this study was young adults admitted to an inner-city hospital serving a primarily uninsured population for a hyperglycemic emergency. This study population has added vulnerability due to the socioeconomic, ethnic and racial inequalities that exist in access to healthcare and affect diabetes outcomes (American Diabetes Association, 2017i; Campbell et al., 2012; H. Y. Lee et al., 2015; Ricci-Cabello et al., 2010). This study adapts the World Health Organization framework of non-communicable diseases (Noncommunicable Diseases and Mental Health World Health Organization, 2003) and distributes risk factors into a four category theoretical model that includes demographic factors, access to care, diabetes and hyperglycemic emergency characteristics, and chronic complications and co-morbidities. This theoretical model is explained in detail in Paper 1: Hospital Admissions for Hyperglycemic Emergencies in Young Adults at an Inner-City Hospital (Paper 1 Figure 1: Four Category Theoretical Model for Characterization and Identification of Young Adults at Risk for Hyperglycemic Emergencies—p.33). The purpose of the current study was to characterize and identify young adults at risk for multiple DKA/HHS hospital admissions in order to develop future intervention that can be used to target this vulnerable population.

Methods

Population and data sources

Electronic health records (EHR) (Epic Systems Corporation, Veronia, WI) from the Grady Health System in Atlanta, Georgia were used as the data source for this study. International Classification of Diseases (ICD)-9 codes indicating DKA or HHS were used to identify cases from patients admitted to Grady between January 2010 and November 2015. During the five year study period, Grady admitted 2,427 cases with an ICD-9 classification indicating DKA or HHS. There were a total of 703 young adult admissions during this period with 326 unique MRN's. Cases were excluded if there was no DKA/HHS admission during the study period at which the patient was 18 to 35 years old, if the patient was only seen in the emergency department or clinic and not admitted to GMH, if there was no evidence in the EHR of a hyperglycemic emergency, or if the patient did not have a diagnosis of T1D or T2D (gestational diabetes and other diabetes types were excluded). These exclusions resulted in a final sample of 273 unique patient records.

IRB approval was obtained from Emory University and authorized by the Grady Hospital Research Oversight Committee. All analyses and study procedures complied with HIPAA regulations.

Data collection

The list of all DKA/HHS admission during the study was used to determine the readmission rates of the young adults and adults over the age of 35. Data were collected from the EHR using retrospective chart reviews completed between December 2015 and December 2016. The first hyperglycemic emergency that occurred between 2010 and 2015 in which the patient was 18 to 35 years old was identified as the primary DKA/HHS admission. Data was extracted relating to the primary admission; however, all EHR documentation was examined in order to gather patient history and information about previous and subsequent encounters and hospital admissions. All demographic variables, diabetes characteristics, co-morbidities, and access to care data were extracted from the EHR. EHR sections that were analyzed included the history and physical (H&P), laboratory results, encounter log, and health care provider notes from physicians, nurses, social workers, dietitians, and diabetes educators (Paper 1 Table 1: Variables within the Four Category Model of Risk Factors Associated with Hyperglycemic Emergencies—p.38)). All data was compiled and de-identified. A further details of the methods can be found in Paper 1: Hospital Admissions for Hyperglycemic Emergencies in Young Adults at an Inner-City Hospital

Data Analysis

All data was reviewed for implausible values. Missing data was assumed to be at random and complete case analysis was used for all analyses. Single admissions were compared to multiple admissions for each study variable within the four categories of risk factors. Independent t-tests were used for continuous measures, and Chi-square tests of independence were used to determine association between categorical variables with z-tests to compare stratified groups and *p*-values adjusted by Bonferroni correction.

Univariate logistic regression was used to calculate unadjusted odds ratios for risk factors that had a significant difference between one DKA/HHS admission and multiple admissions. For this analysis, more than one DKA/HHS admission compared to one DKA/HHS admission was treated as the primary outcome of interest while the demographic, diabetes characteristics, co-morbidities, and access to care variables were the exposures. Multiple binomial logistic regression was used to model all variables associated with multiple DKA/HHS readmissions. A parsimonious model was created using forward conditional stepwise selection. The significance level for entry into the model was set at 0.05. The Nagelkerke R^2 value was used to estimate variation in DKA/HHS recurrence explained by the model. The Hosmer and Lemeshow Goodness of Fit Test was used to evaluate the model's fit. The significance level was set at 0.05 and all analyses were performed in SPSS (SPSS Version 22, Armonk, NY)

Results

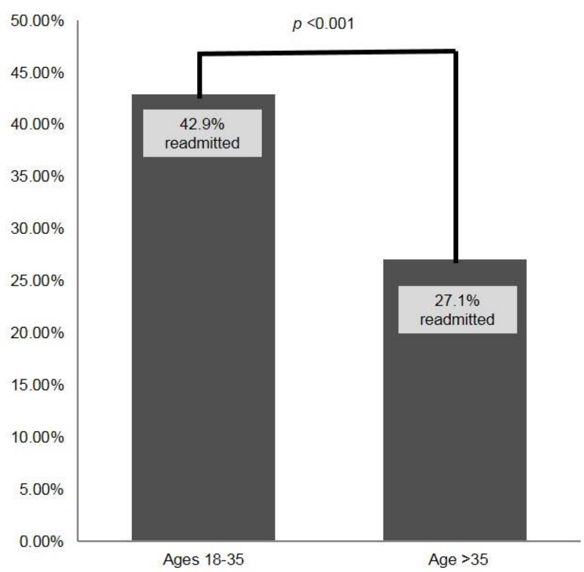

Figure 1: **Percent of DKA/HHS Patients Readmitted Over a 5 Year Period Stratified by Age.** Young adults ages 18-35 had a significantly higher percent of readmission for DKA/HHS in a five year period compared to adults over the age of 36 (42.9% vs 27.1%, *p* <0.001)

Between January 2010 and November 2015, 2427 admissions for DKA/HHS were identified at Grady. In these cases, there were 703 (29%) young adult admission of which accounting for 326 unique patients. Overall, 30.7% of all patients admitted to GMH for DKA/HHS were readmitted at least once during the 5 year period; 42.9% of young adults were readmitted for DKA/HHS compared to 27.1% of adults over the age of 35 ($p<0.001$) (Figure 2). Young adult DKA/HHS readmissions ranged from 2 to 22 times during the five year study period.

Data were extracted from the EHR of the 273 unique patients who fit the inclusion/exclusion criteria for this study. Significant differences between risk factors predicting one DKA/HHS admission versus multiple DKA/HHS admissions were analyzed. In the 273 patient study sample, 43.6% of individuals had multiple admissions. The number of admissions ranged from 1 to 22 times in the five year study period, and readmissions accounted for 75.8% of all admissions.

Demographic risk factors indicated that there was a significant difference associated with readmissions in race and ethnicity. Significantly more Black patients had recurrent DKA/HHS admissions versus a single admission (90.8% vs 77.9%, $p<0.05$) and significantly fewer Hispanic patients had recurrent DKA/HHS versus a single admission (0.8% vs 8.4%, $p<0.05$). Socioeconomic status, as indicated by median household income associated with the patient's zip code (2011-2015 American Community Survey 5-Year Estimates, 2017), showed that lower incomes were associated with multiple admissions ($p<0.05$). There were no differences in sex or age at admission (Table 1- Demographic Factors).

Utilization of acute care hospital services was found to be significantly associated with multiple DKA/HHS admissions. Emergency visits and hospitalizations were significantly higher in individuals with multiple DKA/HHS admissions compared to single admissions (Emergency visits: 70.6% vs 22.1%, $p<0.001$; Hospitalizations: 68.9% vs 13.6%, $p<0.001$) ;however diabetes clinic attendance was not significantly different. (Table 1- Access to Care).

Diabetes characteristics indicated that the percent of patients with T1D who had recurrent admissions was significantly higher than those who had a single admission (82.4% vs 66.2%, $p<0.05$), and younger age at diagnosis was also associated with multiple DKA/HHS admissions (16.95 $\pm$7.40 years vs 19.41$\pm$8.51 years, $p<0.05$). There were no characteristics related to the hyperglycemic emergency hospitalization (precipitating factors, length of stay, ICU) that were indicative of multiple DKA/HHS admissions compared to a single admission (Table 1- Diabetes and Hyperglycemic Emergency Characteristics).

There were significant associations with recurrent DKA/HHS admissions compared to single admissions with higher prevalence of chronic diabetes complications, mental health, and obesity. Patients with chronic diabetes complications and psychiatric co-morbidites had

Table 1: Admitted Young Adult Characteristics Stratified by Single vs Multiple DKA/HHS Admissions

Characteristic	All admissions (n=273) Mean (SD) or %	Single Admission (n=154) Mean (SD) or %	Multiple Admissions (n=119) Mean (SD) or %
Demographic Factors			
Age at primary admission, years (n=273)	26.01 (4.52)	26.47 (4.54)	25.42 (4.34)
Sex (n=273)			
Male	52.7	51.3	54.6
Female	47.3	48.7	45.4
Ethnicity (n=273)			
Hispanic	5.1	8.4	0.8*
Non-Hispanic	94.9	91.6	99.2
Race (n=271)			
Black	83.5	77.9	90.8*
Not Black	15.4	20.8	8.4
Median Household Income, $10k (n=271)	41.89 (15.30)	44.11 (15.63)	39.05 (14.42)*
Access to Care			
Insurance (n=166)			
Any Insurance	30.8	29.2	32.8
Private Insurance	11.4	13.0	9.2
Public Insurance	19.4	16.2	23.5
No Insurance	49.4	70.8	67.2
Healthcare Utilization (n=271)			
Emergency Visits	43.2	22.1	70.6**
Hospitalization	37.7	13.6	68.9**
Diabetes Clinic Attendance	3.7	3.2	4.2
Diabetes and Hyperglycemic Emergency Characteristics			
Diabetes Type (n=273)			
Type 1	73.3	66.2	82.4*
Type 2	26.7	33.8	17.6
Age at Diagnosis, years (n=192)	18.40 (8.15)	19.41 (8.51)	16.95 (7.40)*
Duration of Disease, years (n=192)	7.80 (7.19)	7.18 (6.99)	8.67 (7.42)
Precipitating Factors (n=240)			
Non-adherence	57.9	55.8	60.5
Infection	18.3	19.5	16.8
New-Onset	12.1	14.9	8.4
Other	11.2	9.7	14.3
Length of Stay, days mean (n=271)	3.75 (3.60)	3.93 (3.66)	3.50 (3.50)
Admission to ICU (n=272)	13.2	14.9	10.9
Glycemic Control (n=211)			
HbA1c previously recorded, %	11.00 (2.71)	10.87 (2.77)	11.10 (2.68)
HbA1c at Admission, %	12.38 (2.61)	12.41 (2.57)	12.33 (2.67)
Chronic Complications and Co-Morbidities			
Chronic Diabetes Complications (n=219)			
Any chronic complication	44.7	37.7	53.8*
Macrovascular	0.7	0.6	0.8
Microvascular	18.7	14.3	24.4
Other Complications	35.2	31.8	39.5
Obesity (n=240)			
BMI kg/m^2	27.76 (8.85)	29.17 (9.20)	25.96 (8.07)*
Mental Health (n=196)			
Any psychiatric co-morbidity	35.5	25.3	48.7**
Substance use	21.2	16.9	26.9*
Depression	15.0	5.8	26.9**

*significant at alpha p<0.05
**significant at alpha *p*<0.001

significant associations with recurrent admissions (complications: 53.8% vs 37.7%, $p<0.05$) (psychiatric: 48.7% vs 25.3%, $p<0.001$). BMI was significantly lower for those with multiple versus single admissions(25.96±8.07 vs 29.17±9.20, $p=0.005$) (Table 1-Chronic Complications and Co-morbidities).

Table 2: Odds Ratios for Risk Factors Significantly Associated with Multiple DKA/HHS Admissions

Risk Factor	Beta (SE)	Odds Ratio (95% CI)
Demographic		
Ethnicity		
Hispanic	-2.387 (1.045)	0.092 (0.012-0.713)
Non-Hispanic	Reference	1
Race		
Black	1.058 (0.386)	2.880 (1.252-6.125)
Non-Black	Reference	1
Median Household Income (OR_{10k})	-0.233 (0.10)	0.792 (0.671-0.942)
Diabetes Characteristics		
Diabetes Type		
Type 1 Diabetes	0.867 (0.295)	2.379 (1.335-4.239)
Type 2 Diabetes	Reference	1
Age at Diagnosis (OR_{year})	-0.38 (0.19)	0.963 (0.928-0.998)
Chronic Complications and Co-Morbidities		
Diabetes Complications		
Yes	0.854 (0.283)	2.349 (1.248-4.094)
No	Reference	1
BMI		
>25, Overweight or Obese	-0.646 (0.63)	0.524 (0.312-0.878)
<25, Underweight or Normal	Reference	1
Mental Health		
Any psychiatric co-morbidity		
Yes	1.352 (0.368)	3.867 (1.881-7.949)
No	Reference	1
Substance Abuse		
Yes	0.804 (0.318)	2.235 (1.198-4.172)
No	Reference	1
Depression		
Yes	1.946 (0.435)	7.000 (2.982-16.429)
No	Reference	1

Odds ratios indicated that the odds of readmission significantly decreased with Hispanic ethnicity (OR 0.092, 95% CI: 0.012-0.713, $p=0.022$) and increase of median income (OR_{10k} 0.792, 95% CI: 0.671-0.942, $p=0.039$). T1D patients had a 2.4 increased odds of readmission vs patients with T2D (95% CI: 1.335-4.239, $p=0.003$). Chronic diabetes complications also increased odds of readmissions (OR 2.349, 95% CI: 1.248-4.094, $p=0.003$) as did any psychiatric co-morbidities (OR 3.867, 95% CI: 1.881-7.949, $p<0.001$). Obese and overweight patients had a 0.5 decreased odds of readmission (95% CI: 0.312-0.878, $p=0.014$) (Table 2).

Multiple binomial logistic regression using risk factors listed in Table 2 were used to build a parsimonious model by forward conditional stepwise selection that indicated the strongest predictors of recurrent DKA/HHS. This model explained 38% of variance in recurrent admissions (Nagelkerke R^2) and correctly classified 68% of recurrent admissions (cut off 0.5). The Hosmer and Lemeshow test indicated the model was a good fit (p=0.098). The variables included in the parsimonious model were income, age at diagnosis and substance use. For every $10,000 in household income, the odds of recurrent DKA/HHS admissions were reduced by 46%. With each additional year in age at diagnosis, the odds of recurrent DKA/HHS admissions were reduced by 11%. Substance use had an 8.246 increase in odds of readmission (Table 3).

Table 3: Parsimonious Multiple Binomial Logistic Regression Model of Variables Associated with Multiple DKA/HHS Admissions

Risk Factor	Beta	Standard Error	Odds Ratio	Confidence Interval
Household Median Income (OR_{10k})	-0.62	0.024	0.538	0.337-0.868*
Age at Diagnosis (OR_{year})	-0.122	0.043	0.885	0.814-0.963*
Substance Abuse	2.11	0.815	8.246	1.670-40.712*

*significant at alpha $p<0.05$

Discussion

Factors significantly associated with recurrent DKA/HHS admissions in this young adult study population include non-Hispanic Black race, low SES, T1D versus T2D, younger age at diagnosis, the presence of diabetes complications, normal or underweight BMI, and a history of mental illness or substance use. Many of the factors identified align with the results of previous pediatric and adult studies looking at recurrent DKA/HHS. Multiple hyperglycemic emergency admissions have been consistently associated with ethnic and racial minorities (Bradford et al., 2017; Estrada, Danielson, Drum, & Lipton, 2009; Malik et al., 2016; Mays et al., 2016; Weinstock et al., 2013), low SES populations (Estrada et al., 2009; Weinstock et al., 2013), T1D (Estrada et al., 2009), and a history of a range of mental health conditions including substance use (Bradford et al., 2017; Gibb et al., 2016; Isidro & Jorge, 2013; Malik et al., 2016; Randall et al., 2011).

Chronic microvascular and macrovascular complications have been associated with recurrent DKA/HHS in adult studies that generally have an older sample population (mean age 62 years) (Mays et al., 2016); however a study with a younger population (mean age 31 years) did not find an association with any chronic diabetes complications (Cooper et al., 2016). The presence of chronic diabetes complications increased the odds of recurrent DKA/HHS admissions by 2.3 times in the current study's young adult population with a mean age of 26 years. Although the Cooper et al. study had a similar mean age and participants had a similar durations of diabetes (Cooper et al.- 8.8 years versus current study- 7.8 years), the current study population had a higher HbA1c at admissions (Cooper et al. --10.6% versus current study--12.4%). Although age and duration of diabetes were similar and you would expect similar rates of chronic complications, the higher rate of complications differences seen in the presence of complications could be related to the rate of uncontrolled diabetes. which could be related to the differences seen in association between chronic diabetes complications and multiple DKA/HHS admissions.

Sex, insurance status, and glycemic control are commonly seen as risk factors in DKA/HHS studies. In pediatric studies females are associated with higher rates of multiple hospital admissions (Estrada et al., 2009; Malik et al., 2016) and in adult studies males are associated with recurrent DKA/HHS (Mays et al., 2016); however, in this young adult population sex was not a significant risk factor. In the current study insurance status was not found to be significantly associated with recurrent DKA/HHS; however multiple other studies have indicated that insurance is a predictor of multiple admissions (Bradford et al., 2017; Estrada et al., 2009; Malik et al., 2016; Randall et al., 2011; Weinstock et al., 2013).

This difference could be due to the low insurance rate of entire sample with only 11% having private insurance and 19% having public insurance. Higher HbA1c is often associated with recurrent DKA/HHS (Bradford et al., 2017; Gibb et al., 2016; Weinstock et al., 2013); however over 90% of the current study sample had uncontrolled diabetes with HbA1c above 9% which skewed the data and made it difficult to associate DKA/HHS with glycemic control.

This study suggests that this sample of young adults do have different risk factors for recurrent DKA/HHS compared to adult and pediatric populations. Race/ethnicity, SES, diabetes type and mental health continue to be risk factors; however insurance status, sex, and glycemic control are not as significant. Important factors that may put individuals at risk for recurrent DKA/HHS in this population are a young age of diagnosis and the presence of microvascular or macrovascular complications.

The final parsimonious model of recurrent DKA/HHS presented in this study included SES, age at diagnosis, and substance use. Substance use is the only modifiable risk factor that could be addressed through primary, secondary, or tertiary prevention. Substance use is not a new risk factor in DKA/HHS research, specifically in the adolescent and young adult populations. There is a pathophysiological relationship between drug use and DKA in the alteration of metabolic control (P. Lee, Greenfield, & Campbell, 2009). Additionally, drug use can increase the incidence of chronic complications and co-morbidities through poor compliance to treatment plans (E. A. Nyenwe et al., 2007; Umpierrez et al., 1997; Warner, Greene, Buchsbaum, Cooper, & Robinson, 1998). DKA that is associated with drug use leads to longer ICU and hospital stays, higher mortality rates, and higher treatment costs (E. A. Nyenwe et al., 2007). Due to the detrimental effects of substance use, it is an important issue to address in pediatric, young adult, and adult diabetes populations.

Unfortunately, even in interventional studies that address mental health in diabetes care, it has been difficult to engage or maintain patients with a history of substance use (Maldonado, D'Amico, Rodriguez, Iyer, & Balasubramanyam, 2003; Simmons et al., 2015). The first step in addressing substance use is education for healthcare providers acknowledging substance use as a risk factor for recurrent DKA/HHS and how to educate patients around this topic (P. Lee, Greenfield, & Campbell, 2008; Ng, Darko, & Hillson, 2004; E. A. Nyenwe et al., 2007). All DKA/HHS patients should be asked about drug use in an open and non-judgmental way because non-reporting and under reporting are common (P. Lee et al., 2008; Ng et al., 2004; E. A. Nyenwe et al., 2007). Education should focus on harm minimization rather than advocating for abstinence (P. Lee et al., 2009). In addition to these first steps in reporting drug use and education surrounding drug use, more research is still needed on how to capture this population and what interventions work in addressing substance use.

This study had a number of strengths. It is one of the first studies to focus on young adults with diabetes in an urban, inner-city hospital where the patient population is predominantly black. This population is particularly vulnerable to recurrence and the associated risks of morbidity and mortality. This work is the foundation to create innovative multi-disciplinary interventions for young adults with diabetes that will decrease hyperglycemic emergencies and lead to lower healthcare costs and decreased morbidity and mortality. However, the data collected in this study were limited to information in the EHR. Much of the data extracted were found in provider notes which are a subjective source of information and could lead to misinterpretation. Some study variables were not always recorded for every patient. There is bias in the data towards patients who have high utilization rates of the Grady Health System as there are more encounters in the chart from which to pull data. There may be an additional bias towards T1D classification in this sample because diabetes type was primarily extracted from emergency department notes due to limited utilization of the diabetes clinic. In the emergency department patients are often not classified by autoantibody screening which is the ADA standard of diagnosis (American Diabetes Association, 2017b).

The Grady Health System EHR does not capture information from the patient's utilization of other hospital systems. Additionally, patients did not have a consistent five year follow-up time in this study due to primary admissions spanning the entire study period (Average follow-up time 3.2 ±1.3 years). The readmission rates in this population may be even higher than the study results suggest since not all hospital utilization was captured and not all patients were followed for a full five years.

Differing risk factors between young adult and adult populations highlight that young adults are a unique population in which conventional methods to identify at risk patients and standard interventions to decrease DKA/HHS may not be optimal. The characterization of this at risk population will help to develop intervention that focus on modifiable risk factors such as the development of chronic complications and mental health care that is focused on the young adult. Although interventions may have a significant upfront cost, hopefully these costs would offset the economic burden of diabetes by decreasing recurrent hospital admissions and long term morbidity.

Paper 3: Factors Associated with High Rates of Hospital Readmission and Frequent Hyperglycemic Emergencies in an Inner City Young Adult Population

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Abstract

Background: High rates of diabetic ketoacidosis and hyperglycemic hyperosmolar syndrome (DKA/HHS) hospitalizations are associated with increased morbidity, mortality, and healthcare costs. Young adults are at increased risk of recurrent hyperglycemic emergencies. Patients with high rates of DKA/HHS have a significantly increased risk of short term mortality and those with frequent DKA/HHS are a key population to target first with interventions so that recurrent DKA/HHS can be prevented quickly.

Methods: A retrospective chart review of 273 young adults admitted to an inner city hospital over a five year period analyzed risk factors to determine associations with high rates and frequent DKA/HHS.

Results: Factors associated with greater than four admissions when compared to 2-4 admissions were related to high utilization of health care services (diabetes clinic use in the past year 13.9% vs 0.0%, $p<0.05$; emergency department (ED) use in following year 88.9% vs 62.7%, $p<0.05$; and hospitalization in the following year 88.9% vs 60.2%, $p<0.05$). Precipitating factors of DKA/HHS hospitalization were associated with readmission within one year, with a new diagnosis of diabetes being less likely to be readmitted within one year (4.2% vs 14.9%, $p<0.05$).

Conclusions: Any patient who is seen in the ED or hospitalized for any reason within one year of DKA/HHS admission should be considered at risk of high rates of recurrent hyperglycemic emergencies. Interventions are needed to increase access to comprehensive primary care that addresses risk factors associated with recurrent DKA/HHS including the development of chronic complications, mental health care, and substance use.

Word Count: 247

Paper 3: Factors Associated with High Rates of Hospital Readmission and Frequent Hyperglycemic Emergencies in an Inner City Young Adult Population

Introduction

Recurrent hyperglycemic emergencies, such as diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar syndrome (HHS) are acute complications among individuals with diabetes. In the United Sates there are approximately 145,000 cases of DKA each year , and in the last three decades there has been a 226% increase in DKA/HHS hospitalizations (Centers for Disease Control and Prevention, 2017) . These hyperglycemic emergencies have a critical impact on the morbidity and mortality of diabetes patients and have significant economic consequences.

Although the mortality of adult hyperglycemic emergencies has reduced to less than 1% in the United States (Kitabchi et al., 2009), DKA/HHS still has a significant associated short-term mortality rate. A recent retrospective analysis of over 600 episodes of DKA in 300 patients over 5 years recorded no inpatient mortality; however, DKA/HHS was associated with an increased short term risk of death (Gibb et al., 2016). A single hyperglycemic emergency was associated with a 10.6% short-term mortality rate (Gibb et al., 2016) , and mortality rates were significantly associated with the number of DKA/HHS hospital admissions (Gibb et al., 2016). The mortality rate of those who had more than four DKA/HHS admissions within five years was approximately 30% (Gibb et al., 2016). Uncontrolled diabetes increases the risk of chronic microvascular (American Diabetes Association, 2017d; Holman et al., 2008; Lachin et al., 2015; Nathan et al., 1993; Ohkubo et al., 1995; UK Prospective Diabetes Study (UKPDS) Group, 1998) and macrovascular complications (American Diabetes Association, 2017d; Holman et al., 2008; Nathan et al., 2005; Nathan et al., 2009), as well as risk for hyperglycemic emergencies.

In the United States, the average length of stay for a DKA/HHS admission is 3.4 days (Nyenwe & Kitabchi, 2016). The cost of managing each hospitalization is approximately $17,500 (Kitabchi et al., 2009). DKA hospital admissions are responsible for a half a million hospital days per year (Nyenwe & Kitabchi, 2016), with a total annual cost of $2.4 billion (Kitabchi et al., 2009). Hyperglycemic emergencies represent more than $1 of every $4 spent on direct medical care for adult patients with diabetes, and $1 for every $2 in those patients that have recurrent hyperglycemic emergencies (Javor et al., 1997). There is a current emphasis on decreasing healthcare spending while also increasing the quality of care. Hospital readmissions, such as those seen in recurrent hyperglycemic emergencies, are a major source of health care costs in the United States with all hospital readmissions costing approximately $41 billion (Hines, Barrett, Jiang, & Steiner, 2006). In order to decrease the morbidity, mortality, and economic burden of diabetes, it is essential to decrease DKA/HHS hospital readmissions and target interventions toward those patients who have the highest risk of recurrent hyperglycemic emergencies.

Young adults with diabetes are a vulnerable population with demonstrated poor glycemic control (Bryden et al., 2001; Insabella et al., 2007) and an increased risk of diabetes complications (American Diabetes Association, 2017d; Holman et al., 2008; Lachin et al., 2015; Nathan et al., 1993; Ohkubo et al., 1995; UK Prospective Diabetes Study (UKPDS) Group, 1998). Adults under the age of 35 have disproportionally high rates of recurrent hyperglycemic emergencies (Bradford et al., 2017; Randall et al., 2011). Stemming from an increased prevalence of diabetes in youth, the population of young adults with diabetes is expected to considerably increase over the next several years (Hamman et al., 2014; Patterson et al., 2012; Vehik & Dabelea, 2011); however, the population is often overlooked in diabetes studies.

The population for this study was young adults admitted to an inner-city hospital for a hyperglycemic emergency. This study population has added vulnerability due to the socioeconomic, ethnic and racial inequalities that exist in access to healthcare and affect diabetes outcomes (American Diabetes Association, 2017i; Campbell et al., 2012; H. Y. Lee et al., 2015; Ricci-Cabello et al., 2010). This study adapts the World Health Organization framework of non-communicable diseases (Noncommunicable Diseases and Mental Health World Health Organization, 2003) and distributes risk factors into a four category theoretical model that includes demographic factors, access to care, diabetes and hyperglycemic emergency characteristics, and chronic complications and co-morbidities. This theoretical model is explained in detail in Paper 1: Hospital Admissions for Hyperglycemic Emergencies in Young Adults at an Inner-City Hospital (Paper 1 Figure 1: Four Category Theoretical Model for Characterization and Identification of Young Adults at Risk for Hyperglycemic Emergencies—p.33). The purpose of the current study was to characterize young adults who have high rates of DKA/HHS hospital admissions (more than four admissions in five years) and frequent DKA/HHS admissions (more than one admission within one year). Patients with high rates of DKA/HHS have a significantly increased risk of short term mortality and those with frequent DKA/HHS are a key population to target first with interventions so that high rates of recurrent DKA/HHS can be prevented.

Methods

Population and data sources

Electronic health records (EHR) (Epic Systems Corporation, Veronia, WI) from the Grady Health System in Atlanta, Georgia were used as the data source for this study. International Classification of Diseases (ICD)-9 codes indicating DKA or HHS were used to identify cases from patients admitted to Grady between January 2010 and November 2015.

During the five year study period, Grady admitted 2,427 cases with an ICD-9 classification indicating DKA or HHS. There were a total of 703 young adult admissions during this period with 326 unique MRN's. Cases were excluded if there was no DKA/HHS admission during the study period at which the patient was 18 to 35 years old, if the patient was only seen in the emergency department or clinic and not admitted to GMH, if there was no evidence in the EHR of a hyperglycemic emergency, or if the patient did not have a diagnosis of T1D or T2D (gestational diabetes and other diabetes types were excluded). These exclusions resulted in a final sample of 273 unique patient records.

IRB approval was obtained from Emory University and authorized by the Grady Hospital Research Oversight Committee. All analyses and study procedures complied with HIPAA regulations.

Data collection

The list of all DKA/HHS admission dates during the study was used to determine which individuals between the ages of 18 to 35 had been admitted more than one time within a year of their firs DKA/HHS admission and which individuals had been admitted more than four times during the study period. Data were collected from the EHR using retrospective chart reviews completed between December 2015 and December 2016. The first hyperglycemic emergency that occurred between 2010 and 2015 in which the patient was 18 to 35 years old was identified as the primary DKA/HHS admission. Data was extracted relating to the primary admission; however, all EHR documentation was examined in order to gather patient history and information about previous and subsequent encounters and hospital admissions. All demographic variables, diabetes characteristics, co-morbidities, and access to care data were extracted from the EHR. EHR sections that were analyzed included the history and physical (H&P), laboratory results, encounter log, and health care provider notes from physicians, nurses, social workers, dietitians, and diabetes educators (Paper 1 Table 1: Variables within the Four Category Model of Risk Factors Associated with Hyperglycemic Emergencies—p.33). All data was compiled and de-identified. A further details of the methods can be found in Paper 1: Hospital Admissions for Hyperglycemic Emergencies in Young Adults at an Inner-City Hospital

Data Analysis

Compiled information from the extractors was uploaded to SPSS software for all analyses (SPSS Version 22, Armonk, NY). All data were reviewed for implausible values. Missing data was assumed to be at random and complete case analysis was used for all analyses. Single admissions were compared to 2-4 admissions and greater than four admissions for each study variable. Analysis of variance (ANOVA) was used for continuous measures, and Chi-square tests of independence were used to determine association between categorical variables. In order to compare the stratified groups, z-tests with *p*-values adjusted by Bonferroni correction were utilized. Patients who were readmitted within one year of their primary admission were compared to patients who were readmitted 1-5 years after the primary admission. Independent t-tests were used for continuous measures, and Chi-square tests of independence were again used to determine association between categorical variables. Alpha was set at 0.05 for all analyses.

Univariate logistic regression was used to calculate unadjusted odds ratios for risk factors that had a significant difference among the comparison groups. For this analysis, the risk factors were treated at exposures and more than 4 admissions and admissions within one year were considered the primary outcomes of interest. Multivariate logistic regression was used to model all variables associated with the primary outcomes. The Nagelkerke R^2 value was used to estimate how much variation in the outcome could be explained by the model. Based on the study model, each of the categories of risk factors was added in a stepwise manner to determine the added variance for each category and the overall variance explained by the model.

Results

Of the 2427 admissions during the study period, 703 (29.0%) of these admissions were young adults ages 18 to 35 of which 326 had a unique MRN. Young adults had a higher readmission rate than adults over the age of 35 (42.9% vs 27.1%, $p<0.001$). Additionally, young adults had a higher percentage of cases that were readmitted five or more times (percent of total cases 10.7% vs 3.3%, $p<0.001$; percent of readmitted cases 25.0% vs 12.6%, $p<0.005$) (Figure 1).

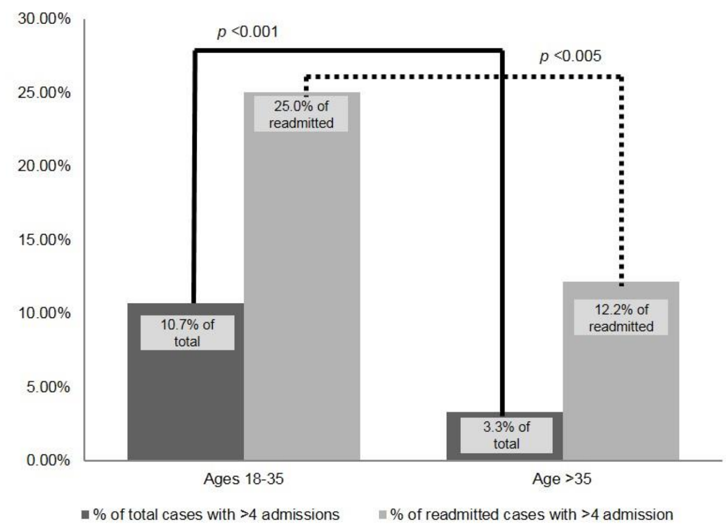

Figure 1: Percent of Total and Readmitted DKA/HHS Cases with >4 Admissions Over a 5 Year Period Stratified by Age. 10.7% of all young adult cases were admitted more than 4 times in a five year period which is significantly greater than adults over 36 (10.7% vs 3.3%, $p<0.001$). 25% of young adults who were readmitted during the five year period, were admitted more than 4 times which is significantly greater than adults over 36 (25% vs 12.2%, $p<0.005$).

Of the 326 unique patients identified, 273 individuals fit the inclusion/exclusion criteria for this study. The 273 included individuals had a total of 636 DKA/HHS admissions during the five year study period. In the study sample, 43.6% were readmitted with the range of admissions between 2 and 22 times during the study period (mean 4.05 ±2.88). Individuals who were admitted more than four times during the study period were 13.2% of the sample and accounted for 41% of the total admissions during the study period. Of patients readmitted, 22.7% were had at least one DKA/HHS readmissions within one year of the

Table 1: Admitted Young Adult Characteristics Stratified by Number of DKA/HHS Admissions

Characteristic	All admissions (n=273) Mean (SD) or %	Single Admission (n=154) Mean (SD) or %	2-4 admissions (n=83) Mean (SD) or %	>4 admissions (n=36) Mean (SD) or %
Demographic				
Age at primary admission, years (n=273)	26.01 (4.52)	26.47 (4.54)	25.82 (4.53)	24.54 (4.13)
Sex (n=273)				
Male	52.7	51.3	55.4	52.8
Female	47.3	48.7	44.6	47.2
Ethnicity (n=273)[a]				
Hispanic	5.1	7.8	1.2	0
Non-Hispanic	94.9	92.2	98.8	100
Race (n=271) [a, c]				
Black	83.5	77.9	88.0	97.2
Non-Black	15.4	22.1	12.0	2.8
Median Household Income, $10k (n=271) [a, c]	41.89 (15.30)	44.11 (15.63)	40.14 (15.50)	36.52 (11.34)
Access to Care				
Insurance (n=166)				
Any Insurance	30.8	29.2	36.1	25.0
Private Insurance	11.4	13	10.8	5.6
Public Insurance	19.4	16.2	25.3	19.4
No Insurance	49.4	74.8	63.9	75.0
Healthcare Utilization (n=271)				
Emergency Department [a, c, d]	43.2	22.1	62.7	88.9
Hospitalization [a, c, d]	55.7	13.6	60.2	88.9
Diabetes Clinic Attendance [a, c, d]	3.7	3.2	0	13.9
Diabetes and Hyperglycemic Emergency Characteristics				
Diabetes Type (n=273) [a, b]				
Type 1	73.3	66.2	79.5	88.9
Type 2	26.7	33.8	20.5	11.1
Age at Diagnosis, years (n=192)	18.40 (8.15)	19.41 (8.52)	16.79 (8.00)	17.35 (5.81)
Duration of Disease, years (n=192)	7.80 (7.19)	7.18 (6.99)	9.13 (7.51)	7.57 (7.23)
Precipitating Factors (n=240)				
Non-Adherence	57.9	55.8	57.8	66.7
Infection	18.3	19.5	15.7	19.4
New-Onset	12.1	14.9	9.6	5.6
Other	11.7	9.7	16.9	8.3
Length of Stay, days mean (n=271)	3.75 (3.59)	3.93 (3.66)	3.33 (2.31)	3.92 (5.34)
Admission to ICU (n=272)	13.2	14.9	7.2	19.4
Glycemic Control (n=211)				
HbA1c previous recorded, %	11.00 (2.71)	10.87 (2.77)	10.90 (2.55)	11.42 (2.92)
HbA1c at Admission, %	12.38 (2.61)	12.41 (2.57)	12.34 (2.54)	12.30 (3.06)
Chronic Complications and Co-Morbidities				
Diabetes Complications (n=219)				
Any Diabetes complication	44.7	37.7	54.2	52.8
Macrovascular	0.7	0.6	1.2	0
Microvascular	18.7	14.3	22.9	27.8
Other Complications	35.2	31.8	39.8	38.9
Obesity (n=240)				
BMI kg/m^2 [a]	27.76 (8.85)	29.17 (9.20)	26.15 (7.81)	25.50 (8.79)
Overweight or Obese [a, c]	40.7	53.2	44.6	27.8
Mental Health (n=196)				
Any psychiatric co-morbidity [a, b, c]	35.5	25.3	45.8	55.5
Substance Abuse [a]	21.2	16.9	26.5	30.6
Depression [a, b, c]	15	5.8	25.3	27.8

[a] significant at alpha $p<0.05$
[b] pairwise comparison between single admission and 2-4 admissions significant at alpha $p<0.0.5$
[c] pairwise comparison between single admission and >4 admissions significant at alpha $p<0.05$
[d] pairwise comparison between 2-4 admissions and >4 admissions significant at alpha $p<0.05$

primary admission and 37.5% of these patients went on to be readmitted more than 4 times during the 5 year study period.

More than four DKA/HHS admissions were different from single admissions in race, SES, diabetes type, BMI, psychiatric co-morbidities, and healthcare utilization (Table 2).

The only risk factor that differentiated over four admissions and 2-4 admissions was health care utilization. High rates of DKA/HHS admissions were related to more utilization of the diabetes clinic in the past year (13.9% vs 0.0%, $p<0.05$), more emergency department use the year after the primary DKA/HHS hospitalization (88.9% vs 62.7%, $p<0.05$) , and higher rates of hospitalization the year after the DKA/HHS hospitalization (88.9% vs 60.2%, $p<0.05$). (Table 1).

Table 2: Odds Ratios for Risk Factors Significantly Associated with Greater than Four DKA/HHS Admissions

Risk Factor	Beta (SE)	Odds Ratio (95% CI)
Demographic		
Race		
Black	2.006 (1.029)	7.435 (0.99-55.833)*
Non-Black	Reference	1
Median Household Income (OR_{10k})	-0.33 (0.14)	0.719 (0.544-0.961)*
Access to Care		
Hospital Utilization		
Clinic Attendance		
Yes	2.004 (0.661)	7.419 (2.032-27.090)*
No	Reference	1
Emergency Department		
Yes	2.622 (0.547)	4.324 (1.282-14.582)*
No	Reference	1
Hospital Admission		
Yes	2.923 (0.549)	8.382 (2.519-27.89)*
No	Reference	1
Diabetes Characteristics		
Diabetes Type		
Type 1 Diabetes	1.19 (0.549)	3.286 (1.120-9.642)*
Type 2 Diabetes	Reference	1
Co-Morbidities		
BMI		
<25, Underweight or Normal	1.021 (0.409)	2.777 (1.246-6.187)*
>25, Overweight or Obese	Reference	1
Mental Health		
Any psychiatric co-morbidity		
Yes	1.485 (0.645)	4.416 (1.247-15.630)*
No	Reference	1
Depression		
Yes	1.887 (0.579)	6.600 (2.121-20.534)*
No	Reference	1.000

*significant at alpha $p<0.05$

Odds Ratios for risk factors significantly associated with greater than four DKA/HHS admissions include a lower median household income (OR 0.719, 95% CI: 0.544-0.961, $p<0.05$), healthcare utilization (clinic attendance OR 7.419, 95% CI: 2.032-27.90 $p<0.05$), $p<0.05$); ED OR 4.324, 95% CI: 1.282-14.582 $p<0.05$; Admission OR 8.382, 95% CI: 2.519-27.89 $p<0.05$), BMI under 25kg/m^2 (OR 2.777 , 95% CI: 1.246-6.187 $p<0.05$) and history of a mental health condition or depression (Any psych. co-morbidity OR 4.416, 95% CI: 1.247-15.630 *p*<0.05; Depression OR 6.600, 95% CI: 2.121-20.534, *p*<0.05). (Table 2). Demographic factors contributed to 6.6% of the explained variance of high rates of recurrent DKA/HHS, diabetes characteristics contributed an additional 3.8% and co-morbidities an additional 7.5%. In sum, the demographic, diabetes characteristics, co-morbidities, and access to care risk factors explained 28.4% of the variance of high DKA/HHS readmission rates (Table 3).

Table 3: Explained Variance by Categories of Risk Factors Associated with Greater than four DKA/HHS Admissions

Adjusted multivariate model				
Risk Factor	Nagelkerke R^2	Added Variance	Hosmer-Lemeshow	C-Statistic
Demographic	0.066	---	0.215	0.657
Demographic, Co-morbidities	0.179	0.113	0.709	0.758
Demographic, Co-morbidities, Access to Care,	0.276	0.097	0.968	0.816
Demographic, Access to Care, Co-morbidities, Diabetes Characteristics	0.284	0.008	0.860	0.827

Characteristics of readmitted patients that had less than one year between their primary admission and readmission were compared to those that had greater than one year between admissions. If the primary admission was due to new onset diabetes there was a decreased chance of being readmitted within one year (4.2% vs 14.9%, *p* <0.05).

Discussion

Results of this study indicate that there are similar risk factors for all DKA/HHS readmissions. The only risk factors that differentiated between 2-4 admissions and greater than four admissions were related to healthcare utilization. Patients with other chronic diseases who have a high health care utilization rates have poorer health outcomes and higher mortality rates (J. Bell, Turbow, George, & Ali, 2017; Hansagi, Olsson, Sjoberg, Tomson, & Goransson, 2001). This aligns with the finding that diabetes patients who are at highest risk of short term mortality (greater than four DKA/HHS hospitalizations in five years) have higher utilization of health care services including the Grady Diabetes Center in the year prior to DKA/HHS hospitalization and the Emergency Department or hospitalization for any reason the year following the DKA/HHS admission.

These results suggest that if a patient returns to Grady for any reason within one year of a hyperglycemic emergency they should be recognized as a risk of high rates of recurrent DKA/HHS hospital admissions and are also at increased risk of mortality. Several factors that are associated with recurrent DKA/HHS overlap with factors that are associated with increased risk of short-term mortality, specifically psychological issues, microvascular complications and substance use (Gibb et al., 2016). These risk impact on short-term and long-term morbidity and mortality and are thus key risk factors to assess clinically and address in future interventions.

The young adults in this population are not utilizing primary diabetes healthcare services. Only 4% of the sample had been to an appointment at the Grady diabetes clinic within the year prior to their hospitalization; however 43% utilize emergency services the year after hospitalization. Those at risk of high rates of recurrent DKA/HHS do use the diabetes clinic more frequently; however, these patients are most likely to have more chronic complications that would need more frequent follow-up care and treatment. In order to prevent acute and chronic complications from developing it is imperative that young adults with diabetes use primary preventative care. This young adult population often has a gap in healthcare as they age out of the pediatric healthcare systems and move to adult clinics and providers (Findley et al., 2015); however the low resources and barriers to healthcare that exist in this population compound the difficulties associated with transitional care and could contribute to the extremely low levels of primary diabetes care seen in this population.

In order to address the most significant modifiable risk factors of recurrent DKA/HHS, comprehensive holistic care is needed. Mental health and substance use are factors consistently associated with DKA/HHS in adolescents, young adults, and adult populations (Bradford et al., 2017; Gibb et al., 2016; Isidro & Jorge, 2013; Malik et al., 2016; Randall et al., 2011). Mental health and substance use are especially important in young adult populations as they are at risk for the on-set of many mental health conditions and substance use become more prominent. Poor mental health has a significant impact on self-management leading to poor glycemic control (American Diabetes Association, 2017e). Uncontrolled diabetes can also alter neurological signaling and function leading to psychiatric co-morbidities (Champaneri et al., 2010; Dantzer et al., 2008; Duman & Monteggia, 2006; Haroon et al., 2012; Ising et al., 2007; Korczak et al., 2011; Musselman et al., 2003; Osborn & Olefsky, 2012; Stuart & Baune, 2012). Substance use alters metabolic control and is associated with DKA/HHS (P. Lee et al., 2009). Psychosocial interventions can improve HbA1c and mental health outcomes (American Diabetes Association, 2017e; Anderson et al., 2001; Anderson et al., 2002; Delahanty et al., 2007). Incorporating the mental health provider into the diabetes treatment team and integrating mental and physical healthcare can improve outcomes (American Diabetes Association, 2017c; Katon et al., 2010).

A pediatric residential treatment intervention that combined diabetes care and education with intensive psychological treatment showed a significant decline in diabetes related hospitalizations during the intervention and after the intervention (Geffken et al., 1997); however, residential treatment is not a feasible option for most young adults. A study in an adult population designed as a multidisciplinary approach to the prevention of recurrent DKA/HHS found that participants were difficult to engage and maintain in psychological treatment. Participants often refused mental health assessments and did not attend therapy sessions; however in this study the mental health care was separated from physical care in that they were look at as separate entities and not integrated and also physically separated in different locations (Simmons et al., 2015). An intensive home-based psychotherapy intervention for adolescents with poorly controlled diabetes did significantly reduce DKA hospital admissions (Ellis et al., 2008). There are substantial costs associated with home-based programs; however in this study the costs were offset from the reduction in DKA admission (Ellis et al., 2008). In low-resource young adult populations home-based interventions may reduce barriers to care but may also require a change in location of services if patients are homeless or in transient housing situations.

In primary diabetes care settings young adults are interested in topics that effect their current everyday lives. It is difficult for them to related to chronic complications that they may not yet be experiencing (Findley et al., 2015). It may be necessary to teach providers how to interact with young adult patients and implement education including mental health and substance use that have an effect on their current wellbeing. Creating a holistic healthcare environment that integrates mental and physical health care can benefit all diabetes patients. In young adults, if this integrated care could help achieve better glycemic control and mental health it could potentially save in DKA/HHS hospitalization costs and the economic burden of long term chronic complications.

The data collected in this study were limited to information in the EHR. Much of the data extracted were found in provider notes which are a subjective source of information and can lead to misinterpretation. Some study variables were not always recorded for every patient. There is bias in the data towards patients who have high utilization rates of the Grady Health System as there are more encounters in the chart from which to pull data. There may be an additional bias towards T1D classification in this sample because diabetes type was primarily extracted from emergency department notes due to limited utilization of the diabetes clinic. In the emergency department patients are often not classified by autoantibody screening which is the ADA standard of diagnosis (American Diabetes Association, 2017b).

The Grady Health System EHR does not capture information from the patient's utilization of other hospital systems. Additionally, patients did not have a consistent five year follow-up time in this study due to primary admissions spanning the entire study period. The readmission rates in this population may be even higher than the study results suggest since not all hospital utilization was captured and not all patients were followed for a full five years.

Work needs to be done in order to improve accessibility to primary diabetes care for young adults and develop interventions that could improve glycemic control and prevent hyperglycemic emergencies. One critical step is to incorporate mental health care into young adult diabetes care. Developing programs that would integrate mental and physical health for young adult diabetes patients could have a high upfront cost, but if the intervention prevented hyperglycemic emergencies and promoted the appropriate use of healthcare services these programs could lead to decreased morbidity, mortality, and diabetes associated healthcare costs.

Integrative Summary

This research proposed a theoretical model of risk factors for recurrent hyperglycemic emergencies in young adults admitted to an inner-city hospital. These risk factors were divided into four categories based on the WHO STEPS framework of non-communicable diseases (Noncommunicable Diseases and Mental Health World Health Organization, 2003). The factors in each category were analyzed to determine their association with hyperglycemic emergencies in order to characterize the young adult population admitted to an inner city hospital for treatment of a hyperglycemic emergency and identify factors associated with recurrent hospitalizations.

Studies have identified that young adults less than 35 years old have disproportionally high rates of diabetic emergencies (Bradford et al., 2017; Randall et al., 2011; Rewers et al., 2002). Hyperglycemic emergencies are associated with an increased risk of short-term mortality. The mortality rate in those with more than four DKA/HHS admissions within five years is approximately 30% (Gibb et al., 2016). In addition to the increased morbidity and mortality, hyperglycemic emergencies have a significant economic impact with an estimated annual cost of $2.4 billion in the United States (Kitabchi et al., 2009). Hyperglycemic emergencies represent more than $1 of every $4 spent on direct medical care for adult patients with diabetes, and $1 for every $2 in those patients that have recurrent hyperglycemic emergencies (Javor et al., 1997). As the population of young adults with diabetes grows, DKA/HHS hospitalizations will continue to escalate. In order to decrease the morbidity, mortality, and economic burden of diabetes, it is essential to decrease DKA/HHS hospital readmissions and target interventions toward those patients who have the highest risk of recurrent hyperglycemic emergencies.

The proposed theoretical model included four categories of risk factors: demographic factors, access to care, diabetes and hyperglycemic emergency characteristics, and chronic complications and co-morbidities. Based on these four categories Figure 1 delineates the characteristics of a young adult admitted to an inner city hospital for the treatment of a hyperglycemic emergency.

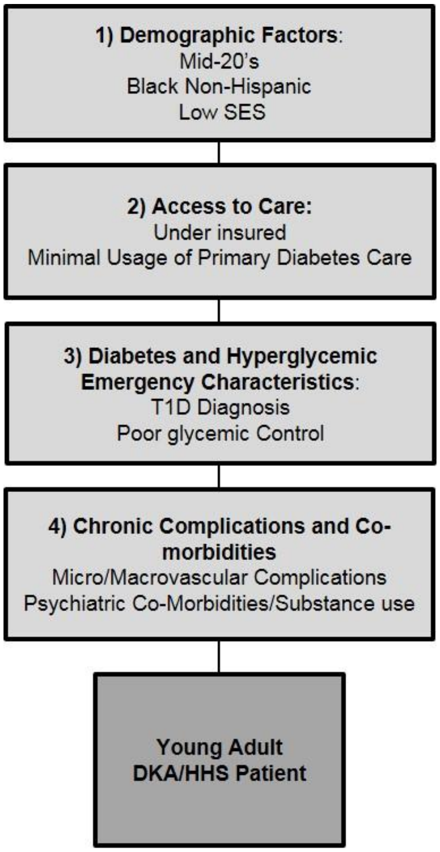

Figure 1: **Profile of the Young Adult DKA/HHS Patient.** The proposed four category theoretical model was used to characterize the young adult DKA/HHS patient admitted to an inner city hospital.

Figure 2 highlights the factors associated with recurrent hyperglycemic emergencies in the young adult population and also lists the level of intervention needed in order to address each category. Many of the factors identified align with the results of previous pediatric and adult studies looking at recurrent DKA/HHS. Multiple hyperglycemic emergency admissions have been consistently associated with ethnic and racial minorities (Bradford et al., 2017; Estrada et al., 2009; Malik et al., 2016; Mays et al., 2016; Weinstock et al., 2013), low SES populations (Estrada et al., 2009; Weinstock et al., 2013), T1D (Estrada et al., 2009), and a history of a range of mental health conditions including substance use (Bradford et al., 2017; Gibb et al., 2016; Isidro & Jorge, 2013; Malik et al., 2016; Randall et al., 2011). A younger age of diagnosis, (Estrada et al., 2009; Gibb et al., 2016; Randall et al., 2011) and chronic microvascular and macrovascular complications(Cooper et al., 2016; Mays et al., 2016) differ in their association with DKA/HHS depending on the study population. Sex (Estrada et al., 2009; Malik et al., 2016), insurance status (Bradford et al., 2017; Estrada et al., 2009; Malik et

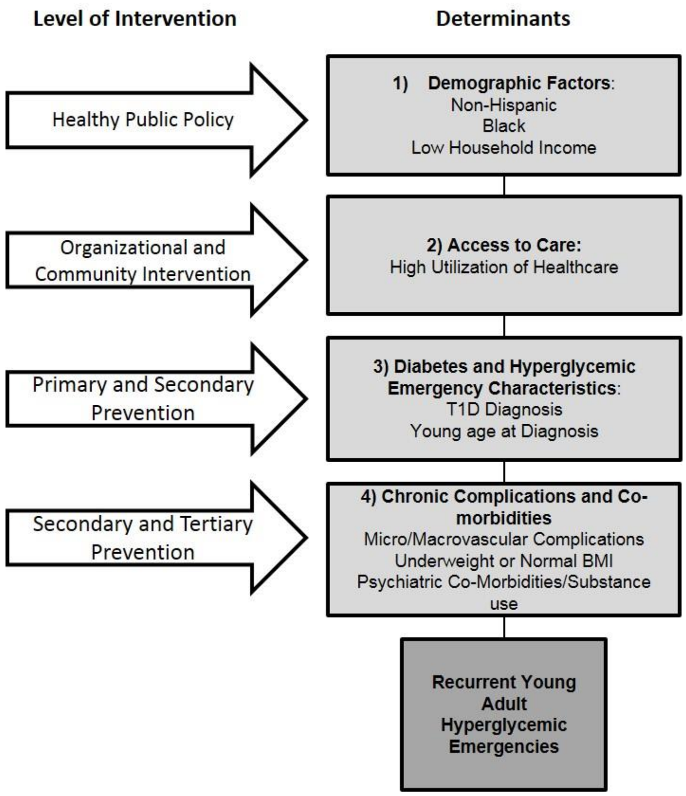

Figure 2: **Risk Factors Associated with Young Adult Recurrent Hyperglycemic Emergencies and Levels of Intervention**. The proposed four category theoretical model was used to outline risk factors significantly associated with young adults admitted to an inner city hospital with recurrent hyperglycemic emergencies. Levels of intervention need to address significant risk factors are matched with each category.

al., 2016; Randall et al., 2011; Weinstock et al., 2013), and glycemic control (Bradford et al., 2017; Gibb et al., 2016; Weinstock et al., 2013) are commonly seen as risk factors in DKA/HHS studies but were not found to be significant in the current study. This study suggests there are differing risk factors for recurrent hyperglycemic emergencies in young adults and that conventional interventions may not be optimal in this population. In order to address all risk factors interventions would need to include public health policies, community interventions, and primary and secondary care.

The major finding from this research is that there are two significant gaps in young adult diabetes care: transitional and young adult primary diabetes care and the integration of mental healthcare into primary diabetes care. In order to address these gaps interventions would be needed at both the community and primary care level. The high rate of uncontrolled diabetes in this young adult population emphasizes the importance of transitional care for young adults moving from pediatric to adult healthcare systems. The young adults in this population are not utilizing primary diabetes healthcare services. Only 4% of the sample had been to an appointment at the Grady diabetes clinic within the year prior to their hospitalization; however, 43% utilize emergency services the year after hospitalization. In order to prevent acute and chronic complications from developing it is imperative that young adults with diabetes use primary preventative care. The young adult population often has a gap in healthcare as they age out of the pediatric healthcare systems and move to adult clinics and providers (Findley et al., 2015). The low resources and barriers to healthcare that exist in this population compound the difficulties associated with transitional care leading to the extremely low levels of primary diabetes care seen in this study. Work needs to be done in order to improve accessibility to primary diabetes care for young adults and develop interventions that could improve glycemic control and prevent hyperglycemic emergencies.

One critical step in improving access to care and preventing hyperglycemic emergencies is to build a comprehensive holistic care model that integrates mental health care into young adult primary diabetes care. Mental health and substance use are factors consistently associated with DKA/HHS in adolescents, young adults, and adult populations (Bradford et al., 2017; Gibb et al., 2016; Isidro & Jorge, 2013; Malik et al., 2016; Randall et al., 2011). Mental health and substance use are especially important in young adult populations as they are at risk for the on-set of many mental health conditions and substance use become more prominent. Poor mental health has a significant impact on self-management leading to poor glycemic control (American Diabetes Association, 2017e). Uncontrolled diabetes can also alter neurological signaling and function leading to psychiatric co-morbidities (Champaneri et al., 2010; Dantzer et al., 2008; Duman & Monteggia, 2006; Haroon et al., 2012; Ising et al., 2007; Korczak et al., 2011; Musselman et al., 2003; Osborn & Olefsky, 2012; Stuart & Baune, 2012). There is pathophysiological relationship between drug use and DKA in the alteration of metabolic control (P. Lee et al., 2009). Additionally, substance use can increase the incidence of chronic complications and co-morbidities through poor compliance to treatment plans (E. A. Nyenwe et al., 2007; Umpierrez et al., 1997; Warner et al., 1998). DKA that is associated with drug use leads to longer ICU and hospital stays, higher mortality rates, and higher treatment costs (E. A. Nyenwe et al., 2007).

Incorporating the mental health provider into the diabetes treatment team to create a holistic care team can improve outcomes (American Diabetes Association, 2017c; Katon et al., 2010). In primary diabetes care settings, young adults are interested in topics that effect their current everyday lives. It is difficult for them to relate to chronic complications that they may not yet be experiencing (Findley et al., 2015). It may be necessary to teach providers how to interact with young adult patients and implement education including mental health and substance use that have an effect on their current wellbeing. Unfortunately, even in interventional studies that address mental health in diabetes care, it has been difficult to engage or maintain patients with a history of substance use (Maldonado, D'Amico, et al., 2003; Simmons et al., 2015). More research is needed on how to capture this population and what interventions work in addressing substance use. Developing programs that would integrate mental and diabetes for young adult diabetes patients could have a high upfront cost, but if the intervention prevented hyperglycemic emergencies and promoted the appropriate use of healthcare services these programs could lead to decreased morbidity, mortality, and diabetes associated healthcare costs.

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