Review Article

Hospitalization for Acute Diabetic Complications: Are We Aware?

Joann C. Harper

Associate Professor, National University, California.

ABSTRACT

The aim of this paper was to explore the reason for the findings reported by the Healthcare Cost and Utilization Project (H-CUP). It cited a 23 percent increase in hospitalization rates for short term diabetes complications between 2005 and 2010.

The literature was reviewed to address this intriguing statistic for which an understanding may launch a different approach to discharge protocols and outpatient management. While the number of potentially preventable admissions for adults and children decreased between 2005 and 2010, for the same time period, rates of potentially preventable hospital admissions among adults increased for short-term diabetes complications, i.e. diabetic ketoacidosis, hyperosmolarity, and coma (23 percent), and hypertension (33 percent).There were no statistically significant changes in rates for long term diabetes complications (i.e. renal, visual, neurological, and circulatory disorders).

The inquiry was unable to link current evidence in a way that adequately explains the results reported. There was not an exhaustive literature search which might have revealed different information. Despite the lack of an identifiable cause for the hospitalization rate observed, a different approach to monitoring patients with diabetes in the outpatient setting may reduce acute episodes.

Key Words: Diabetes, Hospitalization, Readmission, Complications, Healthcare Cost and Utilization Project (H-CUP)

INTRODUCTION

Diabetes and its complications account for an important and potential source of preventable hospital admissions, a lead topic for practice reform. Yet, healthcare and medical communities may be unaware of the substantial increase in the types of complications which require individuals to be hospitalized. The Healthcare Cost and Utilization Project (H-CUP) published[1]: Between 2005 and 2010, the total number of potentially preventable admissions for adults and children decreased 6.2 percent and nearly 40 percent respectively. But, the rates among adults significantly increased for short-term diabetes complications (23 percent) and hypertension (33 percent).Short term complications included diabetic ketoacidosis, hyperosmolarity, and coma. There were no statistically significant changes in rates for long term diabetes complications (i.e. renal, visual, neurological, and circulatory disorders), for diabetes-related lower extremity complications, or for uncontrolled diabetes without complications. [1] This paper explores the literature for possible

explanations to the diabetes short-term complication admission increase reported. Then, discusses what value a better understanding of this increase might shape care.

Since the report did not distinguish between index admissions and readmissions by a time interval, the assumption was made that the rate reported represented all preventable admissions. Rates for selected conditions were developed using the Agency for Healthcare Research and Quality (AHRQ) Prevention Quality Indicators (PQI's): bacterial pneumonia, chronic obstructive pulmonary disease, dehydration, congestive heart failure, hypertension, short term diabetic complications, uncontrolled diabetes, and urinary tract infection. [1]

Incidence and prevalence of diabetes

In 2001, Boyle et al. published a projection of diabetes burden through 2050, and, unlike other studies, included changes in the demographic characteristics, including race composition and increasing trends in age-, sex- and race-specific prevalence rate of diabetes. [2] Both the U. S. Census Bureau projections and the U. S. representative National Health Interview Survey (NHIS) were used. Their projections reflected a steady increase in the overall prevalence of diabetes from 3.99% in 2000 to 7.21 % in 2050. Predictions based on these assumptions indicate that the total number of people with diabetes would rise from approximately 11 million in 2000 to almost 20 million by 2025, and by 2050, surpass 29 million people. Projections used three different scenarios, the "most likely scenario", projected that by 2010, 14.1 million or an additional 3.1 million people would have diabetes, with demographic changes accounting for the largest share of the increases (38.7%), followed by increases in prevalence rates (35.5%) and population growth (25.8%). Consistent with the CDC data, [3] the largest increases projected were among those aged ≥75years. [2]

Between 2004 and 2007, the number of Americans diagnosed with diabetes increased from 14.7 million in 2004 to 17.9 million in 2007, affecting 7.8 % of the population. [4] According to the CDC, Diabetes for 2010 affected 25.8 million people or 8.3% of the U.S. population. [3] Sources have attributed the increase to changes in the population. For instance, Andrews et al. [5] reported the prevalence of diabetes had increased 41% over the nineties reaching 6.5% in 1999 and "is projected to continue to increase due to an aging population, changing racial/ethnic composition, and rising disease incidence". [5] (p1) According to Inzucchi et al. both the prevalence and incidence of type 2 diabetes are increasing worldwide, particularly in developing countries, in conjunction with increased obesity rates, and westernization of lifestyle. [6]

Despite the preceding information, what remains puzzling is the reported incidence for diabetes. According to the CDC, from 1980 to 2011, the incidence of diagnosed diabetes varied by age group. [7] Among adults aged 18–44 years, incidence increased from 1980 to 2003. However, among adults aged 45–64 years, incidence of diagnosed diabetes changed little during the 1980s with increases beginning in the 1990s through 2002. For these two age groups, incidence showed no significant change from the early 2000's to 2011. [7] The adult age group which demonstrated significant increases was among those aged 65–79, for which the incidence of diagnosed diabetes has increased from 6.9 per 1000 in 1980 to 15.4 per 1000 in 2011. [7] Importantly, while the number of new cases of diabetes has increased since the early 1990s to 2006, from 2006 to 2011, the number of new cases of diagnosed diabeteshad no significant change. [8]

At H-CUP's baseline year 2005, age adjusted percentages of diabetes were 7.4 percent, and 8.8 percent for year 2010, the end point, representing a 1.4 percent change. The 65-74 age group comprised 19.1 percent and 22.0 percent of that number for 2005 and 2010 respectively. For persons age 75 years and older, there was an increase from 15.6 percent in 2005 to 21.7 percent in 2010. The combined age group of 65 to 75 years and older represented a change from 34.7 percent in 2005 to 43.7 percent in 2010. [9,10] Therefore, during the period between the years of 2005 and 2010 when hospitalizations increased for acute complications, the remarkable incidence increase was amongst a specific age group, ages 65-79 according to the CDC (7), and ages 65 to >75 years according to data reported by the NIHS. [9,10]

Other factors as contributions

In one meta-analysis, the literature was reviewed to determine what factors are associated with preventable readmissions. [11] The authors identified thirty seven studies, but found there were clear gaps preventing workable guidance to healthcare organizations related to a variety of timeframes, conditions, and readmit conditions, which represented 15 different combinations.

In another study, Ronksley et al., identified patients with incident diabetes in Alberta, Canada, in an attempt to identify which patients were at the highest risk of subsequent hospitalization. [12] While patients did not reside in the US, the study merited review. They identified adults (≥18 years) who had at least one hospitalization following their diabetes diagnosis between Jan 1, 2004 and March 31, 2011. The investigators used Cox regression to estimate the association between factors related to health care engagement (prior emergency department use, primary care visits and discharge dispositions (i.e.

whether the patient left against medical advice) and the risk of subsequent all-cause hospitalization within one year. Of the 33,811 adults with diabetes and at least one hospitalization, 11,095 (32.8%) experienced a subsequent all-cause hospitalization within a mean follow-up time of .68 (.03) years. Limited and increased use of primary care was both associated with increased risk of a subsequent hospitalization. [12] Charlson comorbidities described participant characteristics, but these did not include the acute diabetic illnesses cited in the H-CUP report. [1]

Kimet et. al. reported rates of unscheduled and "scheduled" (scheduled at least 24 hours in advance)readmits using the 2006 California State Inpatient Dataset (124, 967 patients 50 years and older, mostly aged 65-79 years, female, white, and Medicare beneficiaries, with diabetes discharged from acute care hospitals between April and September 2006). [13] They looked at a three month period following patients' index hospitalizations. They chose a three month versus a 30-day period to better assess patient readmit risk from the "perspective of patients", for whom both an early and/or later readmission is important."About" 26.3% of patients were readmitted -87.2% of which were unscheduled readmissions, almost one fifth of unscheduled readmissions. Readmissions were potentially preventable based on definitions of the eight PQI's identified by AHRQ. [13]

While the study's aim was to examine factors associated with scheduled readmissions vs. unscheduled admissions, other findings were equally important. The most common reason for the index hospitalization was congestive heart failure (7.9%), followed by Diabetes Mellitus (DM) with complications (7.5%).Notably, for unscheduled and scheduled readmissions, DM with complications was the second and third most common diagnosis respectively.

[13] An unscheduled readmit was more likely to occur among patients who had one or more hospitalizations in the 3 months preceding the index hospitalization. The risk for an unscheduled readmission increased when the index hospitalization was an unscheduled admission or when it ended with a transfer to another post-acute or long term institution. As length of stay rose, the likelihood of an unscheduled readmission increased. In addition, 12.8% of readmissions were scheduled at least 24 hours in advance, suggesting scheduled vs. unscheduled should be differentiated in studies. [13] However, there were no distinctions made between acute, short term complications versus long-term complications.

Other studies were examined. Several investigators have concluded poor glycemic control is either the most significant predictor for hospitalization among people with diabetes or one of the most controllable for ambulatory management. [14,15] Ackerson, et al. created a model to validate a prediction rule for identifying diabetic members who were at high short-term risk of complications. [16] They grouped complications into macro- (e.g. myocardial infarction, congestive heart failure, etc.), and microvascular complications (e.g. chronic renal failure, diabetic eye disease, etc.), infectious complications (e.g. pneumonia, septicemia, etc.) and metabolic complications (e.g. diabetic ketoacidosis, hyperosmolar coma, etc.).

Prior hospitalizations for similar events were the strongest predictors for both metabolic and infectious events, and the second strongest predictor for macro and microvascular events (16). These findings are consistent with Kim et al. [13] Use of insulin alone was associated with all three complication sets. Hyperglycemia with an average level greater than 10.0%

(HgA.sub.1c), no measure during the baseline period, and elevation of total or LDL cholesterol were each associated with both macro- and microvascular and metabolic complications. Other findings pertinent to macro- and microvascular or infectious complications were elevated serum creatinine levels, two or more different anti-hypertensive medications, and the presence of albuminuria or microalbuminuria. [16] Age was inversely related to metabolic complications.

Admission, readmission and outpatient continuity

Publications were explored for a relationship between admission or readmission and outpatient care. In a study by Warner and Ziboh patients with an Ambulatory Care Sensitive Condition (ACSC) related to DM were evaluated for which characteristics of ambulatory patients with diabetes were associated with an ACSC hospitalization. [17] Diagnoses included both longer term complications (e.g. renal, eye, neurological and circulatory) and short term complications (e.g. ketoacidosis, hyperosmolarity, and coma). Patients identified had poor glucose control [mean A_1c 9.24 (77mmol/mol) vs. 7.68 (60 mmol/mol); $P<0.001$], but there was no difference in blood pressure or lipid control. The authors concluded prevention of diabetes-related hospitalization related more closely to glycemic control, rather than other important aspects of comprehensive care. Similar findings of poor glucose levels were cited by others. [14-16] Comparatively, lipid control was also a factor in the Ackerson study, [16] and in other studies; blood pressure has been a factor. [5,15]

In contrast to the dangers of persistently high HbA1c levels, the seminal findings of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study group, revealed the hazards of aggressive lowering of HbA1c

[<6%(<42mmol/mol)]. Their findings resulted in a discontinuation of intensive therapy as a result of increased mortality. [18] A reduction in cardiovascular events after long term intensive glucose lowering remains a question, particularly for individuals who do not have additional cardiovascular risk factors. Of particular consequence, was the rate of study participants (N= 5128, intensive therapy; N= 5123, standard therapy) who required assistance for hypoglycemic episodes: 538(10.5%) for those individuals requiring medical assistance, and 830 (16.2%)for those requiring "any assistance" (not defined), as compared to the standard therapy group: 179 (3.5%) and 261 (5.1%), respectively. Each group had significant hypoglycemic adverse events (p<0.001). Whether the hypoglycemic conditions or other acute episodesrequired hospitalization were not reported. [18]

In addition to glycemic control amongst others as factors for readmission risk, [14-17] documentation irregularities have been reported, which could discernibly affect outpatient treatment. Robbins and Webb found that patients with diabetes frequently did not have the proper diabetic coding evident in their discharge summaries. [19] The absence of a diabetes diagnosis (when there should have been) was a highly significant predictor of re-hospitalization after adjustment for age, year, gender, race/ethnicity, insurance status, admission type, severity code, length of stay, discharge status and number of previous hospitalizations. [19]

Inconsistent provider assignment to patients with visits over multiple outpatient episodes, may also affect hospitalization. Using the Community Tracking Study Household Survey (2000-2001), Hunt et al. reviewed emergency department visits and the characteristics of frequent users (≥ 4 visits). [20] While the study was not exclusive to patients with DM, they found individuals who were treated by the same physician at every visit were less likely than those who were treated by different physicians to report frequent emergency department use. Emergency department presentation is associated with hospitalization. However, the proportion of emergency department visits which resulted in hospitalization from the period of 1997 through 2007 remained remarkably stable from 13.5% in 1997 to 14.2 % in 2007. [21] Additionally, there was no significant change in visit rates amongst persons 65 years and older, [21] for which the incidence of diagnosed diabetes had increased. [7]

Clinical inertia during hospitalization also has been labeled as a culprit of poor diabetic management, having implications for continuity of care, outpatient management and hospitalization. Clinical inertia is defined as failure to initiate or intensify therapy when it is clinically indicated. [22] It has been documented in outpatient settings within the Veteran Affairs (VA) health system. [22] Investigators reported male patients admitted from July 1, 2002 to August 31, 2009 were receiving therapy for HgbA1c >8 (>64 mmol/mol). Of 2025 admissions for 1359 patients, 454 had some change in diabetes medication at discharge (22.4%). In an adjusted analysis a total of 656 admissions (32%) demonstrated aggregate clinical inertia with no change in therapy, no documentation of HgbA1c within 60 days of discharge and no follow-up appointment within 30days of discharge. The investigators posited admissions to the hospital represent an important opportunity to improve glycemic control among poorly controlled patients by adjusting outpatient medications at discharge and providing appropriate outpatient clinical follow-up. In this study, no changes in the diabetic regimen at discharge were observed even when it was clear due to the HgbA1c data

that the preexisting outpatient regimen was ineffective. The study also found that patients admitted for acute endocrine problems, nutritional deficits, or metabolic disorders were less likely to have changes in diabetic therapy upon discharge. The investigators also cited the inattention to diabetes during inpatient admission when it is not the primary focus or reason for admission. [22]

Cagliero et al, found that while disruptions in outpatient regimens, intercurrent illness and medication changes may cause hyper- and hypoglycemia during hospitalization, the availability of frequent monitoring, skilled nursing care, and glucose lowering medications should limit both in the hospital setting. [23] However, their study amongst 999 patients across 44 academic and community hospitals revealed persistent hyperglycemia was very common and often treated by sliding scales alone. Sliding scales were prescribed as the sole treatment on an inpatient basis in 41% of the UHC (University Health System Consortium) cohort and 45% of the "VHA Inc" cohort. [23]

Quality and readmissions

The literature suggests that readmissions observed within a longer follow-up period are mostly related to the progression of chronic disease, and are thus a gauge of the quality of outpatient care. [24] Jiang et al. alluded that readmissions occurring soon after a hospital stay are related to quality of care problems during the initial admission. [14] Yet McKay et al found even in a 30 day readmit study, disease chronicity prevailed as the principal reason for readmission, not quality of care. [24] Conditions included by Jiang et al were broadly defined to cardiovascular and renal diseases, and not focused to the acute complications of diabetes.[14]Benbassat and Taragin's literature review found mixed results in their evaluation of readmissions as

a measure of quality of care. [25] They described multiple and stratified risk indicators for readmission related to advancing age, geographic variability (i.e. hospital bed availability), disposition post discharge (e.g. personal home vs nursing home), and a variety of demographic factors. While some studies revealed care-related causes in patients with diseases, such as diabetes, [25,26] avoidable readmissions reported varied between 9% and 50%, with a number of attributing factors, such as, hospital, clinician and patient factors, along with interrater inconsistency for the detection of preventable determinations. [25]

DISCUSSION

Despite rising prevalence and incidence rates, these increases alone are unlikely to account for the acute hospitalization rates reflected in H-CUP's data. Data maps to the older age group as one target for an explanation. Precise clinical guidelines for glycemic control during patient hospitalization remain under discussion. [27,28] Many studies predate important changes in therapy when newer pharmaceutical agents available have altered the drug treatment landscape. For example, in 2012, an update by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) was published, given the new uncertainties resulting from a widening array of pharmacological agents available, with more deliberation on the benefits of intensive glycemic control. [6,29] One of the key points expressed by the joint effort is that *glycaemic* targets must be individualized. Reported by Inzucchi, et al: "Our guidelines are less prescriptive than and not as algorithmic as prior guidelines". [29] (p 1578) While this was a statement attributed to the lack of comparative-effectiveness research, it follows that in the absence of clear treatment guidance,

attention to individual variation may be essential.

In 2003, sentinel recommendations for the reclassification of DM changed the cut point values of fasting plasma glucose (FPG) from ≥ 140 mg/dL (7.77mmol/L) to ≥ 126 mg/dL(6.99 mmol/L) as a criterion for a diabetic diagnosis. [30] Other conditions within which the diagnosis should be considered includes a second, confirmatory value on a subsequent day. The recommendations also included that the estimates for prevalence and incidence should also be changed to FPG ≥ 126mg/dL(6.99 mmol/L) for epidemiological studies. How widely or immediately these changes were adopted to change when a diagnosis was made could be a factor in the increase reported. But, new cut-offs may not have resulted in a change in acute hospitalizations. Since the value is lowered, an earlier diagnosis would encourage treatment management, rather than a late diagnosis. While the lowered cut point was adopted prior to 2005, the new value is unlikely to have substantially and negatively affected the treatment of individuals, if diagnosis was presumably made sooner, not later, reducing the need for acute intervention. In anticipation of adopting the new definition, the implications for disease prevalence was forecasted and reported to be 1.7 million new cases, representing a 14% increase. [31] Lowering the threshold exposes more to treatment, and the potential for harm. [31,32] But, lowered thresholds are not as likely to precipitate hyperglycemic acute illnesses and acute hospitalization increases.

Evidence suggests that acute episodes might be thwarted by closer monitoring of not just HbA1c, but patients who are receiving insulin alone, elevation of total cholesterol or LDL, the presence of albuminuria or microalbuminuria, [16] and who have had prior hospitalizations for similar events. [13] Findings indicated an unscheduled readmit was more likely to occur among patients who had one or more hospitalization in the 3 months preceding the index hospitalization, or when the index hospitalization was an unscheduled admission, or when it ended with a transfer to another post-acute or long term institution. [13] For unscheduled and scheduled readmissions DM with complications was the second and third most common diagnoses respectively. [13] In part, this finding supports the H-CUP data reported without revealing an underlying cause.

As suggested by the research, attention to outpatient management and its effects on clinical stability and hospital admission are considerations. The position statement of ADA and the EASD reflect the increasing complexity of diabetic management. [6,29] It calls for an approach to control by applying multiple factors, each of which is patient-centric, based on disease duration, established vascular complications, life expectancy, associated risks of hypoglycemia, and patient attitude, adherence, and resources, amongst others. [6,29] A plea for individualized therapy may be simply made by the consensus that "type 2 diabetes is a disease that is heterogeneous in both pathogenesis and clinical manifestation". [6,29] (p 1366) There are inherent challenges to balance physiology with lifestyle to attain optimal glycemic levels while supporting patients in their choices. Yet, avoid emergent glycemic episodes.

Perhaps, we haven't honed in enough on the factors that make a critical difference. What makes a patient more adherent, for instance? Adherence and compliance have been challenged on the basis that alternative terms or constructs such as self-management, "autonomy motivation" or "autonomy support" are more useful to address the psychological process that drives patient behavior change. [33] Disease and

case management may affect outcomes, and other mediators such as self-efficacy may in turn predict self-care. [34-36] While studies [36,37] demonstrate a lower adherence rate to diet vs. a medication regimen, on the assumption that adaptation to medication regimes requires less life style adjustment, there is also evidence to suggest patient participation in care and continued follow-up make a difference. For instance, early post discharge follow up by telephone with a diabetes nurse specialist has been shown to improve HbA1c. [37] Inpatient diabetes education has also been associated with a reduction in hospital readmissions. [38] These studies are worthy of renewed attention to inform a patient discharge protocol or a community-directed support program.

The practice of post discharge protocols have extended into the community for some time. With the Affordable Care Act, care through community agencies is being revisited to achieve patient–centered outcomes. Diabetes is a disease for which treatment usually requires self-monitoring in some measure. A patient-centered, collaborative approach between providers and patients which encourages self-determination through informed choices and control, acknowledges as Glasgow and Anderson so aptly stated: "We cannot share in the risk of developing retinopathy, neuropathy, or cardiovascular disease nor can we share the cost to the patient's quality of life for making a commitment to rigorous blood glucose control". [33] (p 2091)

Using the findings presented, post discharge protocols could be tested to evaluate which ones make a difference. Establishing an 'at risk' screen with an outpatient protocol should match the monitoring intensity required of patients. Specific protocols might address a variety of factors, including patients' psychosocial aptitude. Each protocol, guided by a number of patient characteristics, may be adjusted to patients' status, from the extremely fragile to the highly stable. Protocols such as these might mitigate or redirect acute episodes.

Strengths and Weaknesses

There was not an exhaustive literature search which might have revealed different information. A comparison of other diseases and their acute hospitalization rates during the same time period might uncover trends due to extraneous or common factors, which contribute to the overall increase in acute hospitalization rates. An investigation of the changes in, and or use of, a variety of pharmaceutical agents was not made, an exploration of which, may shed more light. Yet, a variety of factors were posited, each one having a potential value to the rate increase observed. Further research about any one of these topics may uncover an explanation.

CONCLUSION

In the literature reviewed, no studies were found that had a specific focus aimed at finding contributions for the acute diabetic admissions increase reported, but hint at possible causes. While increases in the prevalence of disease during the reported period may predictably cause a consequential increase in the acute conditions attributed to hospitalizations, the literature reviewed did not substantially verify a relationship. The dynamics and variation of diagnoses, reporting, and timing across geographic regions with multiple populations may preclude a reasonably applied statistical test. The inquiry was unable to link current evidence in a way that adequately explains the results reported by the H-CUP data.

While links to the increase in the hospitalization rates for acute diabetic diagnoses remain elusive, research to date should inform patient preparation for discharge, post-discharge protocols, and

focus points, which direct specific attention to short term diabetic complications. Hospitalization may be mitigated by better management of patients in the community setting to avoid *clinical inertia* in both the inpatient and outpatient settings. Future research may guide us on the clinical instructions for post discharge follow-up protocols, which are packaged in a way to create program elements that can adequately individualize care and monitoring.

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