Diabetic ketoacidosis (DKa) is a potentially life-threatening, yet entirely preventable, diabetes complication. A new paper looking at the risk factors for DKA may help identify the most vulnerable and raise awareness of this acute condition among healthcare professionals, as well as preventing cases from occurring.

Risk Factors for Diabetic Ketoacidosis

Diabetic ketoacidosis (DKa) is clinically defined as the biochemical triad of hyperglycaemia, acidosis and ketonuria, has an estimated mortality rate of between 2 and 12 per cent, which makes it the most serious acute metabolic complication faced by people with diabetes and the commonest cause of death in children with diabetes. Although DKA is more common in Type 1 diabetes, it also occurs among those with Type 2 and other forms of diabetes. Developing DKA is also costly in financial terms, accounting for around a quarter of direct medical costs among adults with Type 1 diabetes.

Diabetic ketoacidosis is preventable, and it would clearly be of great value to identify its predictors so that healthcare providers can intervene early to help those patients who are most at risk, thereby potentially preventing significant morbidity and the number of life-threatening episodes. Sonia Butalia of the University of Calgary, and colleagues, carried out a study on patients in a large diabetes clinic in order to identify the clinical and socio-demographic factors associated with hospitalisation for DKA. Though the findings come from Canada, they may well be relevant elsewhere, including in the UK.

The study population

Previous research on DKA risk factors has been in mixed populations (Type 1 and Type 2), among children and adolescents, and in other highly selected groups. Applicability to more general diabetes populations may therefore be limited. These earlier studies show that higher HbA1c and psychiatric...
disorders are linked to DKA. However, it should be borne in mind that there are many differences between children/adolescents in management goals, care models, types and rates of co-morbidities and of chronic complications. Knowledge of the predictors of DKA in adults is limited, hence the value of this new study.

The researchers carried out a data linkage exercise based on adults with Type 1 diabetes resident in Alberta, Canada, who attended the Diabetes, Hypertension and Cholesterol Centre. Those with a duration of diabetes less than six months were excluded. All received diabetes education.

For this study, four sources of data were merged to identify the study population and tease out the DKA predictors. These were:

1. Alberta Inpatient Discharge Abstract Database
   - In Alberta, summary records for discharged or deceased patients are filed with the Canadian Institute for Health Information, where charts, demographics, diagnoses and interventions are recorded.

2. Diabetes, Hypertension and Cholesterol Centre Clinical Database
   - Each patient visit to the Centre mentioned above is recorded alongside data on demographics, diabetes type, diagnosis data, involvement of a diabetes specialist, medical history, blood pressure, BMI, medication and lab results are available.

3. Statistics Canada 2006 Census data
   - This dataset has information on income and education.

4. Alberta Kidney Disease Network Repository of Laboratory Data
   - The Alberta Kidney Disease Network is a computerised repository of select laboratory data for the province, which focuses upon outpatient results.

Clinical, socio-demographic variables in DKA

The clinical variables investigated in this study were: BMI, duration of diabetes, involvement with a diabetes specialist, blood pressure medication and statin use. Co-morbidities and complications noted included: retinopathy, neuropathy, gastroparesis, cardiovascular disease, autoimmune disease, psychiatric disorder.

Lab results for HbA1c and median estimated glomerular filtration rate (eGFR) were noted. Socio-demographic variables included age, sex, household income and education level.

A total of 2,055 patients with Type 1 diabetes were identified in the Diabetes, Hypertension and Cholesterol Centre clinical database. Of these, 261 had already been hospitalised for DKA. Among these, six were excluded because of the duration of their diabetes being less than six months. This left 1,994 patients, of whom 255 had been hospitalised with DKA. The mean age of patients with DKA was 36.2 years and that of those without DKA was 40.5 years. The mean duration of diabetes among those with DKA was 14.1 years and, for those without, 18.4 years. Nearly one-third of those with DKA had been hospitalised two or more times with the condition.

Analysis revealed that hospitalisation for DKA was associated with younger age, lower BMI and shorter duration of diabetes. The use of statins, but not blood pressure medication, was associated with a reduced risk of DKA. A number of co-morbidities and complications were linked to DKA, namely gastroparesis, a psychiatric diagnosis and also increased eGFR. A higher HbA1c was also associated with DKA. Meanwhile, higher income and higher education level decreased the risk of DKA.

The importance of self-management

Having Type 1 diabetes means a lifetime of self-management and this fact alone may account for some of the predictors of DKA observed in this study. For instance, the patient who has had diabetes for a shorter duration is generally less experienced in managing their condition and may have had less time for exposure to diabetes education. The link with higher BMI is perhaps not surprising, as this has also been linked to shorter diabetes duration and greater risk of all-cause hospitalisations. It may be that the underlying reason for this observation is that less successful self-management leads to higher HbA1c.

The finding that gastroparesis is linked to DKA is novel and was the only diabetes-related complication found to be thus associated. Although the findings do not prove causality, there is a plausible biological explanation for the association. Delayed gastric emptying, which is the hallmark of gastroparesis, may lead to nausea, lack of appetite and omission of insulin. Clinicians should therefore be especially attentive to the DKA risk associated with gastroparesis among their patients.

Meanwhile, psychiatric conditions such as depression, anxiety and eating disorders are known to be common among people with Type 1 diabetes. Depression may lead to poorer self-management. Moreover, patients with anxiety may have a fear of hypoglycaemia, needle phobia or worry about glucometer readings, which can lead to chronically elevated blood glucose. Previous studies have shown that psychiatric disorders and depressive symptoms are linked to increased risk of complications, including DKA.

The link between income and education and DKA was not significant, although other studies have shown these socio-demographic factors to be a strong predictor. In this study, it may be because the location of the research, Calgary, is relatively affluent and distribution of income among the study participants was said to be surprisingly narrow. A lack of diversity might therefore explain the lack of impact of these factors.

Another surprise was lack of influence of specialist care on risk of DKA. Other research has been inconsistent. One study showed that not being cared for by an endocrinologist did increase the risk of DKA hospitalisation, while another showed no such association.

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Study implications

The researchers have identified a number of factors linked to increased risk of DKA, so this work has significant implications for those looking after people with diabetes. Some of the risk factors are modifiable or amenable to intervention. For instance, focusing diabetes education on those at higher risk may yield benefit in terms of reduced episodes of DKA. Efforts to reduce HbA1c, treat gastroparesis and address mental health concerns could also pay significant dividends.

The care of adults with diabetes does tend to lay emphasis upon prevention of chronic complications and it may be time to give equal weight to reducing the risk of acute complications like DKA. Future research, looking at DKA risk factors in other populations and social groups, and at the value of specific interventions, would be particularly worthwhile.