HYPOS IN SUMMER

Seasonal variation in dysglycaemia

HYPERS IN WINTER
A new population-based study from Canada reveals seasonal trends in both episodes of hypoglycaemia and hyperglycaemia requiring hospital attention. Paying attention to this new risk factor may help people with diabetes and healthcare professionals prepare for, or even prevent, such episodes.

It is well established that there are seasonal variations in glycaemia-related laboratory measurements. For instance, fasting plasma glucose and plasma glucagon levels are highest in the winter, while HbA1c values are higher from January to April, compared with values between July to October, suggesting poorer glycaemic control in the winter period.

Factors that might underpin this seasonal variation include changes in diet, bodyweight, physical activity or environmental factors. While it is of interest to discover how these might operate, what is more relevant to the person with diabetes, healthcare providers and policy makers is how this seasonal variation translates into clinically significant outcomes. Previous research on this subject has been limited to single centres in different countries and specific subgroups, such as people with Type 1 diabetes. A new study, led by Kristin Clemens of Western University, London, Ontario, and colleagues, adds to our understanding by looking at the whole population of Ontario, Canada’s biggest province, with respect to seasonal variations in hospital encounters for hypoglycaemia and hyperglycaemia.

Study details
The researchers used linked healthcare databases to perform time series analyses of the rates of hospital encounters with hypoglycaemia and hyperglycaemia in Ontario between 1 January 2003 and 31 December 2012, over one-month time intervals. There are over 13 million residents of Ontario who have universal coverage for hospitalisations, physician visits and diagnostic testing. Information on their utilisation of healthcare is held in the records of several databases held at the Institute for Clinical Evaluative Sciences.

The diabetes status of people was obtained from the Ontario Diabetes Database. The researchers used the Canadian Institute for Health Information’s Discharge Abstract Database and the National Ambulatory Care Reporting System Database to collect diagnostic and procedural information captured during hospital admissions and emergency department visits. Monthly median temperatures were obtained from Environment Canada meteorological data.

The primary outcome of this study was the seasonality in the rates of hospital encounters for hypoglycaemia and hyperglycaemia. Hospital encounter was defined as either an emergency room visit or an inpatient hospital admission. The researchers used the International Classification of Diseases 9th revision, and related classifications, to check the diagnoses.

Various statistical analyses were carried out on the data. The researchers note that the population of Ontario was selected as the denominator, as they were interested in looking at the rate of these diabetes-related outcomes in the general population, and with consideration of the changing prevalence of diabetes.

In additional analyses, seasonality of hypoglycaemia and hyperglycaemia with age were evaluated, along with the seasonal demographic characteristics, concomitant diagnoses and also comorbidities for those who presented with each type of encounter in 2008, the mid-point of the study. Finally, meteorological definitions of the seasons were used. Winter was defined as 1 December to 28/29 February, spring as 1 March to 31 May, summer as 1 June to 31 August and autumn as 1 September to 30 November.

Seasonal trends uncovered
During the study period, 88,685 people had a total of 129,887 encounters with hypoglycaemia (20,916 people had more than one encounter). Over the same time interval, 56,576 people had a total of 79,773 encounters with hyperglycaemia (9,020 had more than one encounter). There were 13,494 people who had an encounter with both hypoglycaemia and hyperglycaemia.

Overall, the rate of hypoglycaemia encounters varied seasonally, with a peak rate between April and June when, on average, there were an additional 49 encounters per month, which represents a five per cent increase. This proved to be statistically significant. The strength of this seasonal relationship was strongest for those aged 17 years and under and those over 65.

For hyperglycaemia, encounters appeared to peak in January when, on average, there were an additional 69 encounters per month, which represents an 11 per cent increase compared with other months. This was also statistically significant. A weaker relationship was observed for those aged 17 and under.

The median age of people at the time of their encounter was similar across the seasons and was 68 years for hypoglycaemia and 53 years for hyperglycaemia. Most of those with encounters had a diagnosis of diabetes and around half were women.

Seasonal influences on blood glucose
This study shows that, in the Ontario region, hospital encounters for hypoglycaemia peak between April and June, while encounters for hyperglycaemia peak in January. The authors believe that these seasonal trends in blood glucose levels result from a complex interplay between social, behavioural, environmental and physiological factors. Social and
**HYPOS AND HYPERS**

Behavioral influences such as calorie consumption, physical activity and weight gain vary throughout the year. In winter, people tend to eat more and exercise less, resulting in weight gain. The winter holiday season has also been linked to poorer glycemic control. Such factors may contribute to the peak in hyperglycemia encounters that is seen in January.

Conversely, in the spring and summer, people may adopt a healthier diet, take more activity and lose weight. This might make them more susceptible to hypoglycemia. There may also be seasonal differences in the likelihood of people seeking medical care, the postponement of medical care during the holiday season and monthly differences in referral patterns.

Then there is the impact of temperature changes upon glucose monitoring devices, insulin absorption and metabolism of anti-hyperglycemic medications in people with diabetes. Extremes of temperature can cause glucose meters and test strips to lose their analytic stability, as well as augmenting the absorption rate of insulin. While it may be possible to adjust kit and medications to account for temperature differences, this may not always happen and diabetes management may be affected. Furthermore, dehydration may occur on hot days, leading to kidney damage and impaired metabolism of medication which, in turn, may cause hypoglycemia.

And there are other physiological processes which can contribute to the seasonal trends observed here. Cortisol, growth hormone and glucagon all play a role in the pathogenesis of diabetic ketoacidosis and levels of all three peak in the winter months, possibly contributing to the excess of hyperglycemia encounters seen at this time. Moreover, there are seasonal trends in hospital encounters for congestive heart failure, myocardial infarction, stroke, infection and sepsis. These too could contribute to associated dysglycemia at those times. Finally, the higher rates of hyperglycemia in January could reflect incident diabetes which has also been observed to peak in the winter.

Some variation in the strength of the seasonal trends with age were noted in this study. Younger and older people were more likely to have seasonal variation in their encounters with hyperglycemia, while the winter trend in hyperglycemia was weaker in younger people. Such age-specific seasonality in healthcare encounters has been described elsewhere. It is not clear whether these findings are due to age-related differences in susceptibility to dysglycemia, the prevalence of different diabetes subtypes within each age category or differences in healthcare-seeking behavior with age.

**Prepare and prevent**

These new findings are similar to those of smaller, single-centre studies which have detected seasonality in hyperglycemia and hyperglycemia in people with Type 1 diabetes. In a single German hospital, a study running from 2007 to 2014 found more severe hypoglycemia encounters in spring and summer than in autumn or winter. There were 1,080 encounters in total, of which 27.7 per cent were in the spring, 28.6 per cent in the summer, 21.5 per cent in the autumn and 22.2 per cent in the winter.

Another study, in a hospital in Tokyo, from 2006 to 2012, showed more people having hypoglycemia in summer than in winter (578 encounters of which 35.2 per cent were in the summer and 18.2 per cent in the winter). In both of these studies, a seasonal trend was not apparent in people with Type 2 diabetes.

Finally, in a Canadian study of people with Type 1 diabetes, from 2004 to 2010, there were 21,568 ketoacidosis encounters and 5,349 hypoglycemia encounters, with the former being highest in winter, and the latter highest in the summer.

However, the new findings do differ from some other reports. In a small study of 67 encounters for severe hypoglycemia in adults aged over 60 presenting to a hospital in Morioka, Japan, from 2004 to 2007, the encounters were less frequent from April to September (3.0 +/- 2.2 encounters) than from October to March (6.7 +/- 2.2). These different findings may have arisen from the study being small and carried out in a different climate.

One major strength of this study lies in its size and scope, covering as it does 129,887 hypoglycemia encounters and 79,773 hyperglycemia encounters over a nine-year period. The whole population of Ontario was used as denominator in order to allow policy makers to monitor cause-specific hospitalisations at population level and inform healthcare planning. However, the authors believe that the same seasonal patterns would have been observed had the study been restricted to people with diabetes.

Weaknesses include the ecological design of the study, which means that results are applicable only at the population level. So it could not be determined whether events were related to the use of specific antihyperglycemic medications, for instance. Furthermore, administrative data was used to look at study covariates and outcomes. These databases have not been specifically linked to hypoglycemia or hyperglycemia in people with diabetes. These databases have not been specifically linked to hypoglycemia or hyperglycemia in people with diabetes.

These seasonal trends in blood glucose levels result from a complex interplay between social, behavioral, environmental and physiological factors.
created to answer the research question posed in this study. The databases did not allow assessment for differences in social or behavioural factors or diabetes subtype. It is also possible that some people with diabetes, including those newly diagnosed after their hyperglycaemia, were not included in the study. The researchers could also only capture those episodes of hypoglycaemia and hyperglycaemia that led to an encounter. There may have been others which were self-treated or treated by emergency medical services out of the hospital. It is likely that the true number of events was underestimated, therefore, because the codings of hypoglycaemia and hyperglycaemia are likely insensitive. Finally, these results relate to Ontario, in the Northern Hemisphere. Trends elsewhere may differ according to climate and season.

The authors say that their findings could help educate people about those times when they are more vulnerable to either hyperglycaemia and hypoglycaemia. Physicians and healthcare providers could also better anticipate and prepare for seasonal fluctuations by, for instance, stockpiling insulin and glucagon. Maybe this is particularly relevant in parts of Canada, where extremes of weather, like heavy snow, could render areas inaccessible. Finally, the underlying mechanism of these seasonal trends in dysglycaemia is, in itself, worthy of further study.