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COMMENTARY

Type 1 diabetes, obesity and PCOS: Is type 1 stepping into the shoes of type 2 diabetes?

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In recent decades, improvements in type 1 diabetes (T1D) therapy have led to an increasingly positive outlook for persons living with this condition. Prolonged life expectancy, an extended time without microvascular complications and improved fertility are some factors that have experienced significant improvement. However, young women and adolescents living with T1D experience abnormal weight gain, menstrual irregularity and polycystic ovarian syndrome (PCOS), but the relationship among these abnormalities has not been clarified in women with T1D.

The prevalence of weight problems in persons living with T1D is higher than the prevalence observed in the general population.[1-3] Intensive insulin therapy and efforts to achieve near-normal glucose levels are associated with weight gain.[1] During childhood, obesity in patients with T1D is not especially prevalent, but from peri-puberty onward, progressive weight gain often occurs, especially in females.[4,5] Obesity in T1D is linked to increased mortality, an increased risk of macrovascular disease, the development of subclinical cardiovascular disease and insulin resistance.[1,6] Obese females with T1D experience abnormally high C-reactive protein levels, a marker of subclinical inflammation, especially during the luteal phase of the menstrual cycle[7]; this has been postulated to be one of the mechanisms explaining subclinical cardiovascular disease in obese women with T1D.

In this issue of *Clinical Endocrinology*, Thong et al reported the prevalence of weight gain, PCOS and menstrual irregularity in young adult women with and without T1D who participated in *the Australian Longitudinal Study in Women´s Health*, a longitudinal community-based cohort study.[8] In this study, women aged 18-23 years answered a questionnaire (T1D n = 115, controls n = 15 811); a proportion of them were followed for two years (T1D n = 61; controls n = 8332). At baseline, more than half of the women with T1D were overweight/obese, which was significantly higher than 32%, as observed in the control group. The level of physical activity was similar in both groups; therefore, it could not explain the excess weight observed in women with T1D. During the observation period, women with T1D gained 4 kg, which was higher than 2 kg, as observed in the control group. The most striking finding of the study was that for the first time, a longitudinal study showed that excessive weight gain in T1D women confers a risk of developing PCOS and menstrual irregularity. Obesity was associated with a fourfold increased risk of developing PCOS and a 37 percent increased risk of menstrual irregularity in the two-year observation period.

In the 2000s, two independent groups described the association of T1D and PCOS.[9,10] Subsequently, several groups replicated their findings, and recently, a meta-analysis concluded that 24% of women with T1D have PCOS, a prevalence that is far beyond the prevalence observed in the general population.[11] Until now, this association had been explained by the exposure of the ovary and other glands to hyperinsulinaemia due to nonphysiological, exogenous insulin administration, leading to hyperandrogenemia and polycystic ovarian morphology.[12] The study published in this issue suggests that excessive weight gain is another mechanism involved in the pathophysiology of PCOS in T1D women. Only one previous study has shown an association of elevated serum androgen levels with elevated body mass index (BMI) in young women with T1D.[13]

While the paper published in this issue of *Clinical Endocrinology* has limitations, it also adds information regarding diabetes care in young women with T1D. The fact that the *Australian Longitudinal Study in Women´s Health* used a self-reported outcome of weight, height and menstrual irregularity represents a weakness of the study. The questionnaires asked if the subjects had received a diagnosis of T1D or PCOS, and there is no certainty about which criteria

were used in making these diagnoses. However, this is the first study to perform a longitudinal assessment of a community-based cohort and determine the relationship between obesity development and PCOS in women with T1D.

The association of obesity and PCOS in women with T1D suggests that these patients may exhibit some pathophysiologic mechanisms of PCOS similar to those in nondiabetic obese women.[14] Hyperinsulinaemia and insulin resistance are known factors involved in the pathophysiology of PCOS in nondiabetic women.[14] Patients with T1D, even if they are of normal weight, exhibit a certain degree of insulin resistance that has been explained by hyperglycaemia.[15] Obesity exacerbates metabolic dysregulation in patients with T1D,[1] and frequently, a very high daily insulin dose is required to treat obese patients with T1D. Hyperinsulinaemia, a second mechanism involved in the pathophysiology of PCOS, is also present in women with T1D. By definition, T1D is due to deficient insulin secretion by β cells; paradoxically, patients with this condition exhibit hyperinsulinaemia due to exogenous insulin therapy. Insulin is administered via subcutaneous tissue and does not undergo hepatic first-pass clearance, leading to hyperinsulinaemia. Therefore, in that setting, obese patients with T1D are insulin resistant yet exhibit hyperinsulinaemia. All these elements may explain the association between T1D, obesity and PCOS.

In conclusion, a longitudinal community-based study has shown that excessive weight gain is associated with PCOS in women with T1D. These data suggest that, unfortunately, T1D follows the steps of T2D; both entities may be merging, and the clear clinical signs that once were characteristic of each type of diabetes may no longer be straightforward. Hopefully, in the future, we will have new therapeutic options for T1D that will allow the achievement of optimal metabolic control without excessive weight gain.

CONFLICT OF INTEREST

The author does not report any significant conflicts of interest.

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