Prevalence of obesity in people with and without type 1 diabetes across Belgium, Kuwait, and Mexico: an IMI2 SOPHIA study

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Summary

Background Individuals with type 1 diabetes (T1D) are traditionally perceived as lean, but recent evidence suggests an increasing trend of obesity. To provide global estimates, this study explored the prevalence of obesity among adults with and without T1D across three distinct global regions.

Methods An observational, cross-sectional study was performed utilizing data from T1D registries and national health surveys to assess the prevalence of obesity (BMI $\geq$ 30 kg/m^2) and the prevalence of overweight and obesity (BMI $\geq$ 25 kg/m^2) across Belgium, Kuwait, and Mexico. Demographic and clinical characteristics of adults with and without T1D were assessed. Prevalence estimates were calculated through a binomial generalized linear mixed-effects model adjusting for age, sex, HbA1c, and survey year. As a sensitivity analysis, propensity score matching was performed for confounder adjustment of age and sex.

Findings The study encompassed 3594 individuals with T1D (from 2003 to 2022) and 9898 without T1D (from 2014 to 2021). After model adjustment for confounders (age, sex, HbA1c% and data-collection year), individual obesity prevalence was lower in individuals with T1D in Kuwait and Mexico than among those without type 1 diabetes (Kuwait: 22% (CI: 18–26%) vs. 44% (CI: 41–48%); Mexico: 5% (CI: 3–7%) vs. 40% (CI: 38–42%)). In contrast, individuals with T1D in Belgium showed a more comparable proportions to those without T1D (12% (CI: 9–16%) vs. 16% (CI:11–22%)).

Interpretation Our data reveal that obesity is prevalent among people with T1D. These findings underscore the need for targeted strategies in T1D care that address the growing concern of obesity.

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Keywords: Obesity; Type 1 diabetes

Research in context

Evidence before this study

Contrary to the historical belief, a substantial proportion of individuals with type 1 diabetes is living with obesity. This study provides global estimates by examining the prevalence of obesity in adults with type 1 diabetes across Belgium, Kuwait, and Mexico, and by comparing these estimates with the corresponding populations without diabetes.

Added value of this study

The study highlights notable geographic variations in individual and combined prevalence across countries and populations. In Kuwait and Mexico, out data indicate a significantly lower obesity prevalence in the population with type 1 diabetes compared to their counterparts without diabetes. In contrast, Belgium exhibits a non-significant but marginally higher obesity prevalence in people with type 1 diabetes than those without diabetes.

Implications of all the available evidence

These findings challenge existing notions and emphasize the need for tailored type 1 diabetes care that addresses the disease of obesity, highlighting its growing significance.

Introduction

In recent decades, the global rise in the prevalence of the disease of obesity has become a significant health concern. While people with type 1 diabetes have been stereotypically viewed as lean, there has been a noticeable increase in obesity prevalence among those with type 1 diabetes.[1,2] Recent studies have even indicated that the prevalence of obesity in people with type 1 diabetes has surpassed that of the general population.[3] Despite these findings, comprehensive data on the incidence and prevalence of type 1 diabetes remains limited, particularly among adults, and vary considerably across different demographics and geographic regions.[4]

In the past several decades, the advent of intensive insulin therapy and technological advances in devices and insulin therapeutics have substantially enhanced the management of type 1 diabetes, offering people with type 1 diabetes better tools to achieve optimal glycaemic control. This progress has reduced the risk of developing diabetes-related complications.[5] Notably, continuous glucose monitors and automated insulin delivery systems have enabled users to attain better glycaemic management with reduced risk of hypoglycaemia, as well as enhanced quality of life.[6,7] The evolution of insulin development from crude animal extracts to highly refined and precisely dosed formulations has revolutionized its use, ensuring greater consistency, predictability, and efficacy in treatment.[8]

However, the improved ability to prevent the catabolic state that historically characterized people with type 1 diabetes has introduced new challenges, notably the increasing presence of obesity among this population. Different factors may predispose individuals with type 1 diabetes to gain weight including high levels of exogenous (injected) insulin, genetic susceptibility to obesity, and frequent low blood sugar (hypoglycaemia) episodes requiring extra snacking.[9,10] This trend mirrors the global obesity epidemic, implicating individuals with type 1 diabetes in the dual burden of managing both diabetes-related and obesity-related health complications.[11] These include but are not limited to an increased risk of cardiovascular disease, stroke, and various cancers.[12] Therefore, understanding the global impact of obesity on people with type 1 diabetes requires thorough investigation.[13] Estimating the magnitude of obesity among individuals with type 1 diabetes has significant challenges, especially due to scarcity of data. Moreover, the dual treatment of obesity and type 1 diabetes is complex, and there is a lack of evidence-based guidelines for lifestyle modification for this population.[14] This report focuses on analysing the individual prevalence of obesity and the combined prevalence of overweight and obesity among individuals with and without type 1 diabetes across three diverse geographic regions: Europe, the Middle-East, and Latin America.

Methods

Study design and study population

This observational study was performed to analyse the individual prevalence of obesity and the combined prevalence of overweight and obesity among adults with and without type 1 diabetes across Belgium, Kuwait, and Mexico. This observational study was performed to analyse the individual prevalence of obesity and the combined prevalence of overweight and obesity among adults with and without type 1 diabetes across Belgium,

Kuwait, and Mexico. This study is part of the SOPHIA—Stratification of Obesity Phenotypes to Optimize Future Therapy project which is a public-private partnership that has brought together healthcare professionals, academia, industry leaders, and patient organizations to change the future of obesity care. SOPHIA aims to better predict the risks of obesity and responses to treatment—making care more personalized and patient centric. In attempt to obtain a global view on the prevalence of obesity in people living with type 1 diabetes and based on ongoing collaborations within the SOPHIA project, we have chosen one country per continent available within this collaboration. Belgium, Mexico and Kuwait have more granular datasets with relevant variables for this analysis."

Data for the population with type 1 diabetes was available from patient registries. In Belgium, patient data were sourced from the University Hospital Leuven type 1 diabetes registry. This is a tertiary hospital located in the northern region of Belgium (Flemish Brabant). All patients with type 1 diabetes attending this hospital were eligible to be included in the registry. Clinical diagnosis of type 1 diabetes by a medical care provider was needed. The most recent endocrinologist visit available within the 2010 to 2021 timeframe from electronical medical records was used. For Kuwait, data were obtained from the Dose Adjustment for Normal Eating (DAFNE) clinic registry at the Dasman Diabetes Institute. The latest available clinical visit between 2003 and 2022 was used. For Mexico, data were available from the National Type 1 Diabetes Registry (RENACED-DT1).[15,16] This is an online registry with information from both public and private centres all over Mexico, with longitudinal follow-up supported and endorsed by Mexican Nutrition and Endocrinology Society. All patients with type 1 diabetes are eligible to be included in the registry. Clinical diagnosis of type 1 diabetes by a medical care provider, fulfillment of the ADA diagnostic criteria for diabetes with insulin requirement at diagnosis and thereafter was considered to establish type 1 diabetes diagnosis. Data from their latest available visit with the endocrinologist between 2008 and 2022 was used in the analysis.

Data for people without type 1 diabetes was available from three national household-based health surveys. For Belgium, the Health Interview Survey 2018 served as the source for data on individuals without type 1 diabetes.[17] For Kuwait, data were derived from the 2014 STEPS survey. For Mexico, data were collated from the ENSANUT national health surveys conducted in 2016, 2018, and 2021.[18–20] Ethical approval was acquired from local ethics committees for the ethical conducts of human research (Ethics Committee Research UZ/KU Leuven, DDI Research Ethical Committee, Comité de Ética del Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán). All personal identifiers were anonymized to ensure the participants' privacy. Written consent was obtained.

A cross-sectional analysis was performed with data that was gathered from the six previously mentioned sources. For both groups (people with and without type 1 diabetes), the study population consisted of adult, non-pregnant individuals aged 18 years and above. People with a reported diagnosis of diabetes or taking medication for diabetes were excluded. In addition, to prevent undiagnosed or uncontrolled diabetes from polluting the sample, individuals with glycated haemoglobin (HbA1c) levels above 6.5% were excluded in the group of people without type 1 diabetes.

Statistical analysis

Demographic and clinical characteristics are reported as mean ± standard deviation for continuous variables, and frequencies with percentages for categorical variables. The Kruskal–Wallis rank sum test and Pearson's Chi-squared test were applied to test for differences in demographic or clinical variables between countries per population. The prevalence of obesity (defined as a body mass index $\geq$ 30 kg/m^2) and the prevalence of overweight and obesity (defined as a body mass index $\geq$ 25 kg/m^2) was calculated in both populations as adjusted rates employing suitable techniques and weighting procedures to accommodate for the intricate data structure. Marginal prevalence ratios were estimated from binomial generalized linear mixed-effects model (logit function) per country adjusted for the type of population (with or without diabetes), age, sex, HbA1c and data collection year as random effect since it differed within type of population.). The prevalence ratio estimates were obtained by marginal conditional methods as described by Wilcosky & Chambless (marginal prevalence ratio)[21] in each stratum (male/female) and for each age, HbA1c and year value included in the dataset. The marginal prevalence ratio is the ratio between the average of the prevalences in each stratum. Confounding is a major concern in nonexperimental, observational studies. Therefore, as a sensitivity analysis for confounding adjustment, propensity score matching (PSM) was performed. PSM is a quasi-experimental technique that can effectively control for baseline confounding by balancing measured baseline confounders and risk factors and creating comparable populations. Propensity scores were calculated via generalized linear model with logit function, and age and sex as covariates. The propensity score difference was used as a distance measure for matching. The method used for the matching was a distance-based method referred to as optimal pair matching. Optimal pair matching attempts to pair each treated unit with one or more control units, here it was 1:1, it chooses matches that collectively optimize an overall criterion, which in this case is the sum of the absolute pair distances in the matched sample.[22,23] To further reduce the distance between pairs, exact matching was chosen for sex. Unpaired units were dropped from the sample. Age and sex were

assessed in the matched sample with standardized differences. Prevalence ratios were calculated on the matched data. All prevalence estimates are reported in combination with the 95% confidence intervals. To assess the association between HbA1c and BMI, Spearman correlations were calculated. Complete case analysis was used. All tests were performed as two-sided ones with significance level below 0.05. All analyses were conducted using R version 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

Role of the funding source

The funding body of the study had no role in study design, data analysis, data interpretation, or writing of the report.

Results

Characteristics of people with and without type 1 diabetes

The study encompasses a group of 3593 individuals with type 1 diabetes and 8256 individuals without type 1 diabetes prior to the matching process. With this sample size, we can expect a precision between 2% and 4% for the prevalence of obesity. Demographic and clinical characteristics of both populations in each country are provided in Table 1. The proportion of the population that is female was higher in Mexico and Kuwait compared to Belgium in both the group with type 1 diabetes (Belgium: 49.9%; Kuwait: 55.3%; Mexico: 61.7%; $P < 0.0001$) and in the group without diabetes (Belgium: 51.9%; Kuwait: 60.1%; Mexico: 60.1%; $P < 0.0001$). In both groups, the age distribution varied across countries. In the group with type 1 diabetes, individuals from Kuwait and Mexico were on average younger than those from Belgium (Belgium: 47.0 ± 17.9; Kuwait: 28.8 ± 9.9; Mexico: 32.1 ± 11.6; $P < 0.0001$). However, individuals without diabetes were older in Mexico and Belgium compared to those from Kuwait (Belgium: 48.6 ± 15.8; Kuwait: 35.4 ± 11.1; Mexico: 53.7 ± 18.7; $P < 0.0001$). Glycaemic control, as measured by HbA1c levels, varied between countries in both individuals with type 1 diabetes and individuals without type 1 diabetes. A significant difference was observed for HbA1c levels between individuals without diabetes across countries, although all were below the clinical threshold of 6.5%. Individuals with type 1 diabetes in Belgium exhibited a more favourable glycaemic control compared to those in Kuwait and Mexico (Belgium: 7.80% ± 1.22; Kuwait: 8.51% ± 1.72; Mexico: 8.55% ± 1.90; $P < 0.0001$). Additionally, the use of insulin pump delivery systems was higher in Belgium compared to Kuwait and Mexico (Table 2). The year of availability of the cross-sectional information presented is for population-based surveys from 2018 (Belgium), from 2014 (Kuwait) and from 2016 (46%), 2018 (28%) and 2020 (26%). In terms of the registries for people with type 1 diabetes, for Belgium 72% is from 2020 to 2021, for Kuwait 63% is between 2018 and 2022, and for Mexico 81% is between 2018 and 2022.

Individual prevalence proportion of obesity in people with and without type 1 diabetes

The model-based prevalence estimates of obesity in each population per country are presented in Table 3. When examining the groups with type 1 diabetes, Mexico demonstrated the lowest prevalence of obesity among individuals with type 1 diabetes with 5% (CI: 3–7%) according to the adjusted model, and 10% (CI: 8–11%) after matching (Supplemental Table S1). These numbers are markedly lower than those observed in Belgium and Kuwait, where the model reported a prevalence of 12% (CI: 9–16%) and 22% (CI: 18–26%), respectively, and after matching adjustments indicating a prevalence of 16% (CI: 14–18%) for Belgium and 22% (CI: 20–24%) for Kuwait (Supplemental Table S1). Conversely, a higher prevalence of obesity was observed within the population without type 1 diabetes with notable differences across the countries. Kuwait and Mexico exhibit a higher prevalence of obesity compared to Belgium (Kuwait: 44% (CI: 41–48%); Mexico: 40% (CI: 38–42%), Belgium: 16% (CI: 11–22%)). Similar proportions were obtained after propensity score matching with slightly lower rates for all countries

Variable	People with type 1 diabetes			P-value	People without type 1 diabetes			P-value
	Belgium	Kuwait	Mexico		Belgium	Kuwait	Mexico	
Sample size	1502	1272	819		994	1955	5307	
Age (years)	47.0 ± 17.9	28.8 ± 9.9	32.1 ± 11.6	<0.0001	48.6 ± 15.8	35.4 ± 11.1	53.7 ± 18.8	<0.0001
Sex (n (%))								
Male	753 (50.1)	569 (44.7)	314 (38.3)	<0.0001	478 (48.1)	731 (37.4)	2119 (39.9)	<0.0001
Female	749 (49.9)	704 (55.3)	505 (61.7)		516 (51.9)	1224 (62.6)	3188 (60.1)	
HbA1c (%)	7.80 ± 1.22	8.51 ± 1.72	8.55 ± 1.90	<0.0001	5.38 ± 0.33	5.35 ± 0.39	5.34 ± 0.39	0.0002
BMI (kg/m^2)	25.7 ± 4.34	26.4 ± 4.78	24.6 ± 4.0	<0.0001	25.3 ± 4.35	29.1 ± 5.57	28.1 ± 5.35	<0.0001

Data presented as mean ± standard deviation or number (frequencies). P-values by Kruskal–Wallis rank sum test or Pearson's Chi-squared test. BMI: body mass index.

Table 1: **Baseline characteristics of people with and without type 1 diabetes.**

Variable	People with type 1 diabetes			P-value
	Belgium	Kuwait	Mexico	
Multiple daily injections	1058 (70.4)	1100 (86.6)	695 (84.9)	<0.0001
Insulin pump	444 (29.6)	171 (13.4)	124 (15.1)	

Data presented as number (percentage). P-value by Pearson's Chi-squared test.

Table 2: **Use of multiple daily injections and pump per country among people with type 1 diabetes.**

(Supplemental Table S1). When comparing the obesity prevalence between both populations, a higher prevalence of obesity was observed in people without type 1 diabetes for both Kuwait and Mexico ($P < 0.0001$). In contrast, no significant difference was observed between people with or without type 1 diabetes for obesity prevalence in Belgium ($P = 0.08$).

Combined prevalence rate of overweight and obesity in people with and without type 1 diabetes

The adjusted and matched combined prevalence estimates of overweight and obesity in each population per country are presented in Table 4. The combined prevalence of overweight and obesity was highest in Kuwait, followed by Belgium, and Mexico when examining the groups with type 1 diabetes both before and after matching (Supplemental Table S2). Conversely, a higher combined prevalence of overweight and obesity was observed within the population without type 1 diabetes with the highest prevalence observed in Kuwait, followed by Mexico, and then Belgium. When comparing the combined prevalence between both populations per country, a higher combined prevalence of overweight and obesity was observed in people without type 1 diabetes for both Kuwait and Mexico. In contrast, a higher combined prevalence of overweight and obesity was observed in people with type 1 diabetes in Belgium.

Across all three countries, a weak correlation was present between HbA1c levels and BMI in people with and without type 1 diabetes (Fig. 1).

Country	Population	Model-based prevalence of obesity (%)
Belgium	Type 1 Diabetes	12 (9–16)
	No diabetes	16 (11–22)
Kuwait	Type 1 Diabetes	22 (18–26)
	No Diabetes	44 (41–48)
Mexico	Type 1 Diabetes	5 (3–7)
	No Diabetes	40 (38–42)

Data are presented as percentage -%- with 95% confidence intervals between brackets (). Leveraging a cross-sectional analysis, a generalized linear mixed-effects model was first performed adjusting for the type of population, age, sex, HbA1c, and data collection year (as a random effect). BMI: body mass index.

Table 3: **Individual prevalence estimates of obesity among people with and without type 1 diabetes.**

Country	Population	Model-based prevalence of overweight and obesity (%)
Belgium	Type 1 Diabetes	49 (43–55)
	No diabetes	55 (46–63)
Kuwait	Type 1 Diabetes	61 (57–66)
	No Diabetes	80 (77–82)
Mexico	Type 1 Diabetes	33 (27–39)
	No Diabetes	76 (74–77)

Data are presented as percentage -%- with 95% confidence intervals between brackets (). Leveraging a cross-sectional analysis, a generalized linear mixed-effects model was first performed adjusting for the type of population, age, sex, HbA1c, and data collection year (as a random effect). BMI: body mass index.

Table 4: **Combined prevalence estimates of overweight and obesity among people with and without type 1 diabetes.**

Discussion

In this study, we investigated the prevalence of obesity in adults with type 1 diabetes across three geographically diverse regions: Belgium, Kuwait, and Mexico. By conducting a comparative analysis with the adult population without diabetes in each of these countries, our research applied a systematic and comprehensive approach to quantify the extent of the rise in obesity prevalence in people living with type 1 diabetes.

Our results demonstrate that the global increase in obesity is mirrored within the adult population with type 1 diabetes. In Kuwait, and particularly in Mexico, the prevalence of obesity is significantly higher in the population without diabetes compared to the population with type 1 diabetes, corroborating previous data from these countries.[15,24] Conversely, individuals with type 1 diabetes exhibit a non-significant but marginally higher propensity towards obesity in Belgium compared to their counterparts without diabetes. This trend is consistent with observations from other Western European countries and North America, though data remain scarce.[25,26]

While it is tempting to conclude that the glycaemic control in Belgian adults with type 1 diabetes, which resembles that of the population without type 1 diabetes, explains their tendency to be living with obesity, this conclusion seems overly simplistic and warrants a nuanced interpretation.[27] Although a positive association between BMI and HbA1c exists within the Belgian adults with type 1 diabetes, it remains extremely weak and well below the association between BMI and HbA1c in those without diabetes. This outcome suggests that effective glycaemic control is not necessarily a predicament to excessive weight gain. In Mexico, the weak negative correlation between BMI and HbA1c potentially highlights the catabolic state induced by poor glycaemic control,[28] that might lead to weight loss. Conversely, there was no statistically significant

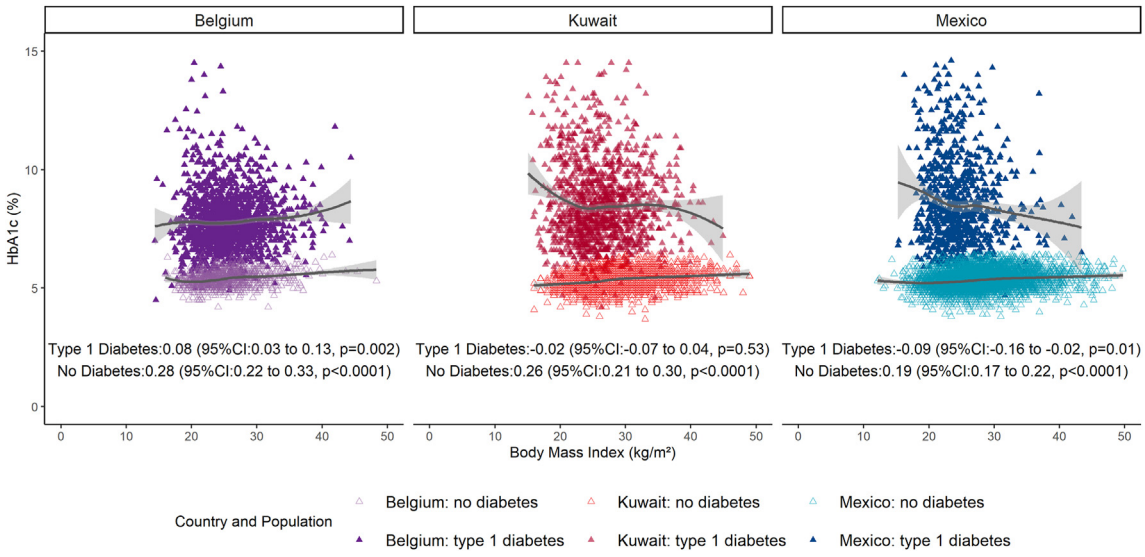

Fig. 1: Correlation between BMI and HbA1c levels across countries in individuals with and without type 1 diabetes fitted with a smoothed conditional means with shaded 95% confidence intervals.

correlation between BMI and HbA1c in Kuwait. This emphasizes that although weight management and glycaemic control are linked, the relationship is more complex than sometimes assumed. The catabolic state of badly controlled type 1 diabetes may help patients to avoid unwanted weight gain, but people with type 1 diabetes and obesity may find it more difficult to attain good glycaemic control due to insulin resistance, which is clearly associated with excess adiposity.[29]

Our investigations included large, well-characterized cohorts from distinct global regions. The sample survey data used provides representative data about the general population that allows generalizability while the registry data is from large, nationally representative registries that had no stringent inclusion criteria meaning that all patients with type 1 diabetes were eligible for inclusion raising the likelihood that the results obtained adequately reflect the prevalence in the respective countries and regions. Nevertheless, to what extent these three countries' reality (access to healthcare, socioeconomic status, age distribution, family/societal support, among others) accurately reflects the diversity and key attributes of the population in other countries of the respective geographical regions could be considered as a shortcoming. Moreover, the cross-sectional design limits our ability to draw longitudinal causal inference on the relationship between obesity and type 1 diabetes and poses the risk of underestimation due to accounting for only existing cases (prevalence) and not for new cases (incidence) and unmeasured confounders. Nevertheless, we have taken into account bias of known confounders such as age and sex. Age and sex are both well-known factors to impact human biology. Previous research has already shown the importance of including these factors in models on obesity and related health problems.[30] There are several reasons why we deem it important to include them in our study as well. Firstly, obesity is more commonly found in women compared to men, with additional differences in the way they deal with this condition.[31,32] Moreover, a study in young adults reported that especially women with type 1 diabetes are more often living with abdominal obesity in comparison to women without type 1 diabetes.[33] Aging is associated with an increase in abdominal obesity and contributes to the development of obesity comorbidities as well.[34] Although more factors such as ethnicity and the level of education are also associated with obesity,[35] we do not have data on these factors. Considering the limited factors that we could include based on the data available, as well as the importance of age and sex in the context of our research, these are the factors we chose to include. The cohorts in Belgium were similar in age, while in Kuwait and Mexico the group without type 1 diabetes were older. Obesity incidence increases with age and hence our interpretation that the patients with type 1 diabetes in Kuwait and Mexico had less obesity compared to those without type 1 diabetes might possibly be a conservative interpretation. There has also been a time-change in the prevalence of obesity worldwide which could potentially affect our estimates which is why we have included the year of study to our adjusted model for estimating prevalence. Furthermore, the lack of granularity in the data precludes detailed comparisons in terms of diabetes, cardiovascular and/or

other complications. Overall, our study reinforces the growing concern of obesity becoming a relevant problem in people with type 1 diabetes.

Given the substantial global prevalence of obesity among individuals with type 1 diabetes, there is a compelling need for further research. A study from Sweden by Edqvist et al. demonstrated that the risk of major cardiovascular disease, heart failure, cardiovascular death, and mortality escalates with increasing BMI in adults with type 1 diabetes with more pronounced associations in men compared to women.[36] This underscores the necessity for more comprehensive, prospective studies to univocally ascertain the interplay between obesity and type 1 diabetes. Moreover, further understanding of not only biological but also behavioural, psychological, and social characteristics -socioeconomic status, access to healthcare-contributing to obesity and their potential differences across countries is needed. Furthermore, there is an unmet need in evidence based management guidelines that are specific to type 1 diabetes including what lifestyle approaches will be most efficacious for prevention and control of weight gain, if medication can be used as adjunctive therapy to counteract the effects of intensive insulin therapy and improve glycaemic control.

In conclusion, our findings highlight that worldwide a substantial proportion of adults with type 1 diabetes are living with obesity. In Belgium, individuals with type 1 diabetes exhibit obesity prevalence rates similar to those without diabetes. However, in Kuwait and Mexico, the prevalence rate of obesity is lower in people with type 1 diabetes. The variations in obesity prevalence between countries may offer insights into the drivers of obesity among those living with type 1 diabetes. This calls for additional attention on weight management strategies for individuals with type 1 diabetes to mitigate the onset of obesity and the resulting comorbidities.

Contributors

EO, NS, SP, and NEAV: accessed and verified the data as well as contributed to literature search, study design, data collection, data analysis, data interpretation, writing, review and editing.

BV, and CR: literature search, study design, data collection, data interpretation, writing, review and editing.

ATA, JAK, PAV, CD, RNF, AGT, MI, JCL, JR, CHdP, TS, AL, and CM: study design, data collection, data interpretation, writing, review and editing.

Data sharing statement

The data that support the findings of this study are available on request from the corresponding author. The data for the ENSANUT national health surveys are openly available at https://ensanut.insp.mx/.

Declaration of interests

EO, NS, SP, ATA, JAK, NEAV, RNF, AGT, MI, JCL, CHdP, AL, and BV: declare no competing interests.

CR declared grants, consulting fees, payment of honoraria for lectures, presentations, support for attending meetings, and stocks. CD declared being employed by Novo Nordisk. JR declared a leadership position at Breakthrough T1D. PAV declared payment of honoraria, support attending meetings and participation on a data safety monitoring or advisory board. TS declared to hold shares in Novo Nordisk. CM declared to receive payment of honoraria for lectures, presentations and participation on a data safety monitoring or advisory board.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102869.

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