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Glycemic control, treatment and complications in patients with type 1 diabetes amongst healthcare settings in Mexico

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Abbreviations: **T1D**, Type 1 diabetes; **RENACED-DT1**, Registro Nacional de pacientes con Diabetes Tipo 1; **CGM**, Continuous glucose monitoring; **BMI**, Body mass index; **SMBG**, Self-monitoring of blood glucose; **FPG**, Fasting plasma glucose; **HbA1c**, Glycated hemoglobin A1c; **MDI**, Multiple daily injections; **DKA**, Diabetic ketoacidosis; **DCKD**, Diabetic chronic kidney disease; **SPB**, Systolic Blood Pressure

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A B S T R A C T

Aims: Type 1 diabetes (T1D) is a growing chronic disease. Evidence of whether the healthcare setting affects management and glycemic control is scarce. We evaluate outcomes in patients with T1D in private and public healthcare settings in Mexico, registered in the National T1D Registry in Mexico (RENACED-DT1).

Methods: Biochemical parameters, diabetes education, and treatment were analyzed considering the data registered in the last visit. Development of chronic complications was determined during follow-up.

Results: We included 1,603 patients; 71.5% (n = 1,146) registered in the public system, and 28.5% (n = 457) in a private institution. Patients in the public setting had higher HbA1c (8.6%, IQR: 7.3%-10.5% vs 7.7%, IQR: 7.0%-8.8%; p < 0.001). Indicators of diabetes education, glucose monitoring, and use of insulin-pumps were lower in the public setting. Patients in the public setting were at higher risk of diabetic chronic kidney disease, retinopathy, and neuropathy. Diabetes knowledge was a mediator between type of healthcare setting and the likelihood of achieving glycemic control.

Conclusions: Patients registered in public healthcare settings have an adverse metabolic profile and higher risk of complications. Social factors need to be addressed in order to implement multidisciplinary measures focused on diabetes education for patients with T1D in Mexico.

1. Introduction

Type 1 Diabetes (T1D) is the most common chronic endocrinological disease diagnosed during childhood [1]. Recent reports have shown that T1D incidence is increasing worldwide, with a growing need for healthcare attention and services to address the disease [2]. Information regarding patients living with T1D in Mexico is limited. Previous reports in Mexico have shown that T1D incidence in patients under 19 years increased from 3.4 to 6.2 per 100,000 persons between 2000 and 2010 [3]. Nevertheless, the real prevalence of T1D in Mexico is unknown and there is scarce information regarding diagnosis, treatment and follow-up. Living with type 1 diabetes requires continuous education, monitoring, and treatment to ensure adequate glycemic control. Ideally, healthcare systems should ensure universal coverage for these patients, however, health disparities have been previously highlighted among racial and ethnic minorities, rural and urban populations, and private and public settings [4,5]. In Mexico, differences in health outcomes amongst the major healthcare settings have also been described [6]. There is an urgent need to understand the socio-demographic context of an increasing chronic disease such as T1D. In order to address the lack of information regarding T1D in Mexico, an online T1D registry (Registro Nacional de pacientes con Diabetes Tipo 1: RENACED-DT1) was developed. RENACED-DT1 is an open online platform endorsed by the Sociedad Mexicana de Nutrición y Endocrinología (SMNE-Mexican Nutrition and Endocrinology Society), that allows recording longitudinal T1D real-life data. Information regarding the sociodemographic characteristics, disparity in access to healthcare and its impact on metabolic control is needed. In this work, we aim to outline the differences in metabolic control, diabetes education, treatment, and associated complications of patients living with T1D in Mexico registered in the RENACED-DT1 receiving care either in public or private healthcare settings. Furthermore, we aim to explore whether diabetes education acts as a mediator in the likelihood of achieving therapeutic goals. Our hypothesis is that deficiencies within the public healthcare setting are associated with a suboptimal glycemic control and a greater risk of T1D complications, and that diabetes knowledge could act as a mediator of glycemic control.

2. Material and Methods

2.1. Study population and data collection

Patients with diagnosis of T1D were captured in the RENACED-DT1 registry by endocrinologists all over the country. The history of RENACED-DT1 conceptualization, the diabetes care centers invited across the country, and their representativeness is presented in the **Supplementary Methods Section**. The first results and methodology of the RENACED-DT1 are reported elsewhere [7,8]. RENACED-DT1 was designed to be an ambispective cohort that could be implemented as an online national registry for data capture based on LAMP (Linux, Apache, MySQL, PHP) technology. It is based on a secure website, following the national laws of privacy and confidentiality (informed consent and notice of privacy). The platform allows for data capture relevant to T1D based on the St. Vincent Declaration [7,8]. We analyzed the data of all patients living with T1D registered in the RENACED-DT1 from 2014 until March of 2020. T1D diagnosis was defined as: 1) diagnosis of T1D by a medical care provider, 2) fulfilling the ADA diagnostic criteria for diabetes, and 3) insulin requirement since diabetes diagnosis. Data capture is performed by the registered attending physician or an assistant, with online access, at each office visit, as an adjunct to the medical record, including follow-up information. Anthropometric and biochemical measurements were also registered. The information can be analyzed at a clinic, state, or national level and according to the healthcare setting (public or private) where the patient's information was captured. The protocol was approved by the medical ethics committee of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. All patients signed informed consent before being registered in the RENACED-DT1 and children provided assent and also an informed consent was signed by the parents or guardians of child participants. This study followed the principles of the declaration of Helsinki.

2.2. Type 1 diabetes-related outcomes

T1D related outcomes were defined using the criteria established by the current ADA guidelines 2020 [9]. Diabetic chronic kidney disease (DCKD) was considered with the presence of albuminuria (albumin-to-creatinine ratio $\geq$ 30 mg/gr) recorded in two or more urine samples, reduced estimated glomerular filtration rate (eGFR < 60 mL/min/1.73 m2), use of dialysis and/or history of a kidney transplant [10]. Diabetic retinopathy was diagnosed by certified ophthalmologists or was considered in those patients with a history of retinal photocoagulation. Peripheral neuropathy was diagnosed when pinprick, vibration perception or 10-g monofilament were recorded as altered in one or both feet. Diabetic foot was reported when the attending physician reported ulceration or deformity attributed to diabetes during physical exploration. Hypoglycemia was defined with a confirmed glucose concentration <70 mg/dL. History of severe hypoglycemia as an event with alteration of mental and/or physical functioning requiring assistance from another person. Furthermore, we registered severe hypoglycemia in the last year if it occurred one year prior to the last recorded clinical visit. Diabetic ketoacidosis (DKA) requiring hospitalization and hospitalizations for any other cause were also registered.

2.2.1. Clinical variables

Age group categories were classified as follows: children included patients aged 0 to 9 years, adolescents aged 10 to 17 years, and adults older than 18 years [11]. We considered exercise when a patient performed at least 150–300 min/week of moderate-intensity, 75–150 min/week of vigorous-intensity, or an equivalent combination of moderate- and vigorous-intensity exercise. [12].

2.3. Statistical analysis

Categorical variables are reported as frequencies and percentages. Continuous data are presented as mean (standard deviation) or median (interquartile range) according to their distribution. To compare differences among those subjects who receive care in a public or private healthcare setting, we performed a χ^2-test for qualitative variables. Differences between quantitative variables were analyzed using Student's *t*-test or Mann-Whitney *U* test, as appropriate.

2.3.1. Associated factors related to an adverse metabolic profile

To identify whether an adverse metabolic profile is associated with the healthcare setting in which patients receive treatment and were registered, we performed a mixed-effects logistic regression model adjusted by age, sex, body mass index (BMI), time since diagnosis, continuous glucose monitoring (CGM) and education level, using the health care setting as a random effect variable.

2.3.2. Risk of complications associated to healthcare setting

In order to investigate the risk for developing T1D associated complications with the healthcare setting, we fitted mixed effects Cox proportional risk regression models. The date of the patient's T1D diagnosis was used for the Cox regression models and the follow-up time was estimated using the date of the acute/chronic complication in those patients who developed the event. In those censored cases, we used the time since T1D diagnosis until the last visit. Finally, we performed Kaplan-Meier analyses to identify the risk associated with the healthcare setting for T1D related outcomes and compared them in private or public healthcare settings using the Breslow-Cox test.

2.3.3. Propensity score matched analyses

To reduce the likelihood of a delayed entry bias in our Cox-regression analyses, we carried out propensity score matching using the *MatchIt* R package (Version 4.1.0). This type of bias could be caused by differences in the time of T1D diagnosis between the public and private settings, which would result in a longer T1D duration and, therefore, a higher time margin in which a patient could develop chronic complications [13].

We used the same population of RENACED-DT1 to obtain a confirmation sub-analysis that would allow us to further isolate the effect of the type of healthcare setting in the propensity matched subsample. We matched a 1:1 ratio independent dataset of our population based on the type of healthcare setting, time since T1D diagnosis, age, sex, and education level. We used a caliper of 0.10 standard deviations with the "nearest neighbor" method as described by D.E. Ho et al [14].

2.3.4. *Mediation analyses*

We hypothesized that the risk of an adverse metabolic profile and associated T1D complications related to the healthcare setting is partially mediated by the disease knowledge of each patient. To test this hypothesis, we conducted casual mediation analyses using the *mediation* R package. We used the cumulative number of clinical educational parameters (carbohydrate counting, glycemic index, treatment for hypoglycemia, and insulin dose adjustment knowledge) known by each patient as a continuous mediator variable to define the diabetes knowledge (**Supplementary** Fig. 1**)**. Confidence intervals were estimated using White's heteroskedasticity-consistent estimator for the covariance matrix, derived from quasi-Bayesian Monte Carlo simulation based on normal approximation. All statistical analyses were performed using R software version 3.6.1. A p-value < 0.05 was considered as statistically significant.

3. Results

3.1. *Sociodemographic and biochemical characteristics*

For this report, we included 1,603 patients living with T1D in Mexico, most of them living in the states of Jalisco (23.8%), Mexico City (21.2%), Mexico State (10.7%), and Hidalgo (7.9%). Details of patients' distribution according to their state of residency is presented in **Supplementary** Table 1 **and** Fig. 1. Our study population has Hispanic ethnicity in its majority; most of our patients were born in Mexico (98.6%). The sociodemographic and biochemical characteristics of included patients are presented in Table 1. We found a female predominance (n = 953; 59.5%) with a median age of 23 years (IQR: 17–33). Most of these patients were diagnosed between six and twelve years of age (n = 605; 42.07%) and median time since diagnosis was 11.3 (IQR: 6.3–18.5) years. Remarkably, 43.4% (n = 638) of the registered patients were diagnosed between 2011 and 2020 (**Supplementary** Fig. 2). Regarding education and socioeconomic level, most of these patients referred to have a high school diploma or higher (n = 888; 55.4%) and reported to have an income lower to 50,000 MXN (2,227 USD) per month (n = 1,512; 94.3%) (Table 1).

3.2. *Metabolic and demographic profile amongst healthcare settings*

Overall, patients receiving care in a public healthcare institution tended to be younger, with higher glycated hemoglobin A1c (HbA1c), fasting plasma glucose (FPG), triglycerides, systolic blood pressure (SPB), diastolic blood pressure (DPB) and creatinine while HDL-c was lower, compared with those patients treated in private healthcare institutions (Table 1 **and Supplementary** Fig. 3). Furthermore, patients who were registered in a public healthcare institution had a lower probability of having HbA1c < 7.0% [53 mmol/mol] (OR 0.58; 95% CI: 0.49–0.69) and SBP < 140 mmHg (OR 0.31 95% CI: 0.20–0.48) compared with those treated in a private setting, after

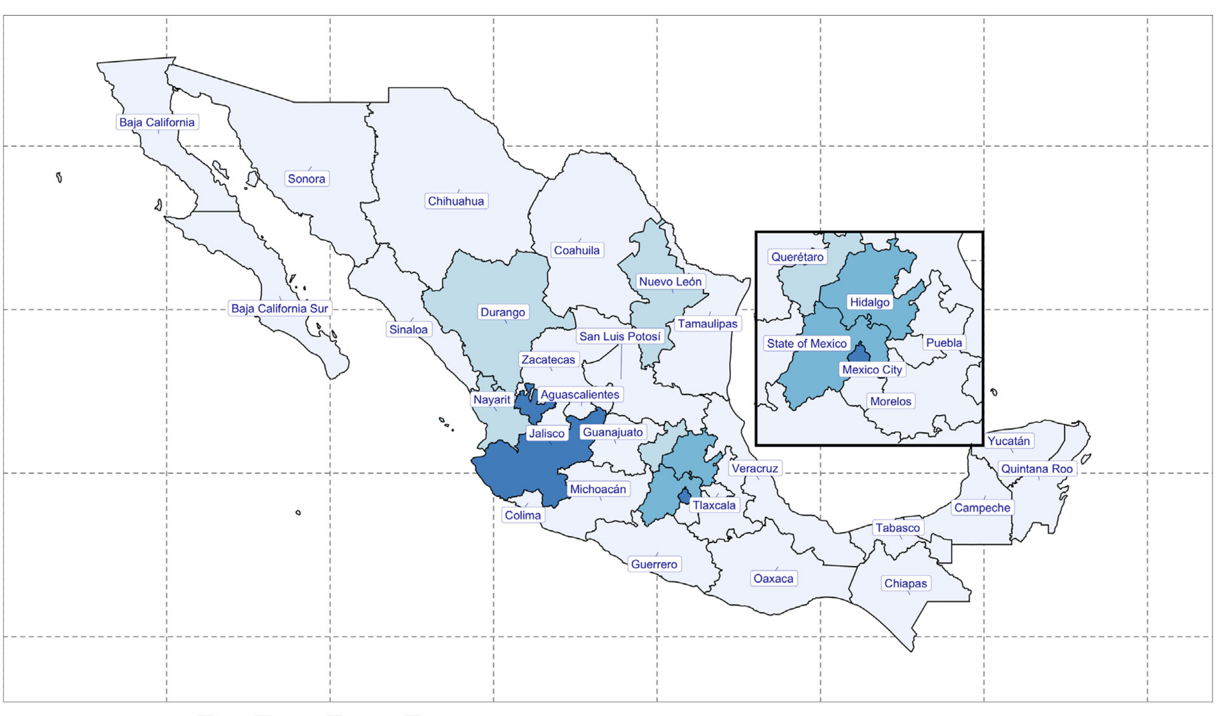

Fig. 1 – Number of patients registered in the RENACED-DT1 in Mexico by state of residency.

Table 1 – Characteristics of subjects living with T1D divided by type of healthcare attention received registered in RENACED-DT1.

Parameters	All-patients n = 1,603	Private HC n = 457	Public HC n = 1,146	P-value
Women (%)	953 (59.5)	247 (54.1)	706 (61.6)	0.006
Age (years)	23 (17–33)	26 (19–39)	21 (16–31)	<0.001
Children (%)	76 (4.7)	58 (5.1)	18 (3.9)	<0.001
Adolescents (%)	381 (23.8)	309 (26.9)	72 (15.8)	
Adults (%)	1146 (71.5)	779 (67.9)	367 (80.3)	
Time since diagnosis (years)	11.3 (6.3–18.5)	14.2 (7.9–20.9)	10.3 (5.9–16.9)	<0.001
Highschool diploma or higher (%)	888 (55.4)	341 (74.6)	547 (47.7)	<0.001
Income lower to 50,000MXN (2,227USD) per month (%)	1512 (94.3)	409 (89.5)	1142 (99.7)	<0.001
Weight (kg)	60.5 (50–70)	63 (54.1–73)	59.4 (48.1–69.3)	<0.001
BMI (kg/m^2)	22.7 (19.9–25.6)	23.0 (20.3–25.5)	22.5 (19.7–25.7)	0.055
$\leq$25 kg/m^2	955 (70.8)	332 (72.6)	878 (76.6)	0.669
25–30 kg/m^2	304 (22.5)	98 (21.4)	206 (18)	
$\geq$30 kg/m^2	89 (6.6)	27 (5.9)	62 (5.4)	
Waist (cm)	79 (71.4–87)	79 (72.8–86)	78.8 (70–88)	0.989
SBP (mmHg)	106 (90–119)	100 (90–119)	107 (95–119)	0.011
DBP (mmHg)	70 (60–76)	60 (60–70)	70 (60–78)	<0.001
FPG (mg/dl)	157 (114–226)	114 (109–213)	157 (108–242)	0.289
HbA1c (%)	8.3 (7.2–10.1)	7.7 (7.0–8.8)	8.6 (7.3–10.5)	<0.001
HbA1c (mmol/mol)	67 (55–87)	61 (53–73)	70 (56–91)	<0.001
HbA1c goal $\leq$ 7% [$\leq$53 mmol/L] (%)	264 (16.5)	93 (20.4)	171 (14.9)	<0.001
Triglycerides (mg/dl)	96.5 (68.3–140)	84 (63.7–123.3)	101 (69.3–142)	<0.001
Total Cholesterol (mg/dl)	172 (148–200)	170 (150–199)	173 (147–200)	0.892
LDL-C (mg/dl)	99 (81–121)	101 (81.5–123)	98.1 (80–120)	0.445
HDL-C (mg/dl)	50.9 (12.3)	54.9 (15.7)	49.6 (14.7)	<0.001
Non-HDL-C (mg/dl)	121 (99–149)	120 (95.3–144)	122 (100–150)	0.206
Creatinine (mg/dl)	0.71 (0.6–0.9)	0.7 (0.6–0.9)	0.8 (0.6–0.9)	0.005
ACR (mg/g)	7.14 (2.88–36.0)	7.34 (3.99–39)	7.14 (1.76–28.8)	0.332
Meal-Plan (%)	850 (53)	259 (56.7)	591 (51.6)	0.237
Exercise (%)	559 (34.8)	211 (46.2)	348 (30.4)	<0.001
Carbohydrate counting (%)	627 (39.1)	293 (64.1)	334 (29.1)	<0.001
SMBG $\geq$ 4 times a day	432 (26.9)	167 (36.5)	265 (14.4)	<0.001
Ketone Measurement (%)	145 (9.0)	86 (18.8)	59 (5.14)	<0.001
Glycemic index knowledge (%)	673 (41.9)	305 (66.7)	368 (32.1)	<0.001
Treatment of hypoglycemia knowledge (%)	1,191 (74.3)	370 (80.9)	821 (71.6)	<0.001
Insulin dose adjustment knowledge (%)	1,002 (62.5)	344 (75.3)	658 (57.4)	<0.001
Hypoglycemia event (%)	219 (13.6)	83 (18.2)	136 (11.0)	<0.001
Severe hypoglycemia (%)	101 (6.3)	61 (13.3)	96 (8.4)	<0.01
Severe hypoglycemia in the last year (%)	34 (2.0)	14 (3.1)	20 (1.74)	0.940
DKA after diagnosis (%)	158 (9.9)	42 (9.2)	116 (10.1)	0.637
Diabetic chronic kidney disease (%)	130 (8.1)	24 (5.3)	106 (9.3)	0.004
Retinopathy (%)	160 (10.0)	38 (8.3)	122 (10.6)	0.189
Neuropathy (%)	107 (6.7)	20 (4.4)	87 (7.6)	0.026

Data expressed as frequencies and (percentage) or median (interquartile range).

Abbreviations: BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, FPG: fasting plasma glucose, HbA1c: glycated hemoglobin, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, ACR: albumin to creatinine ratio, DKA: diabetic ketoacidosis.

adjustment for income, age, sex, time since T1D diagnosis, BMI, use of CGM and education level (Fig. 2).

3.3. *Diabetes education parameters amongst healthcare settings*

Regarding diabetes education and lifestyle, we observed that a lower proportion of patients treated in public healthcare institutions reported practicing any type of exercise, performing carbohydrate counting, glucose monitoring (self-monitoring of blood glucose [SMBG] $\geq$ 4 times/day or CGM use), and ketone measurement. In addition, patients treated in the public healthcare setting had less knowledge of the glycemic index, hypoglycemia treatment, and insulin dose adjustment (Table 1).

3.4. *Insulin regimens and dosage registered*

Regarding insulin treatment administration, patients treated in a public healthcare setting were prescribed with higher insulin doses adjusted per weight in kilograms (**Supplementary** Table 2). Additionally, patients within the public setting had a greater use of MDI (multiple daily injections with insulin analogs), greater use of human insulins and lower use of insulin pumps. The specific insulin regimens and medications utilized in the public and

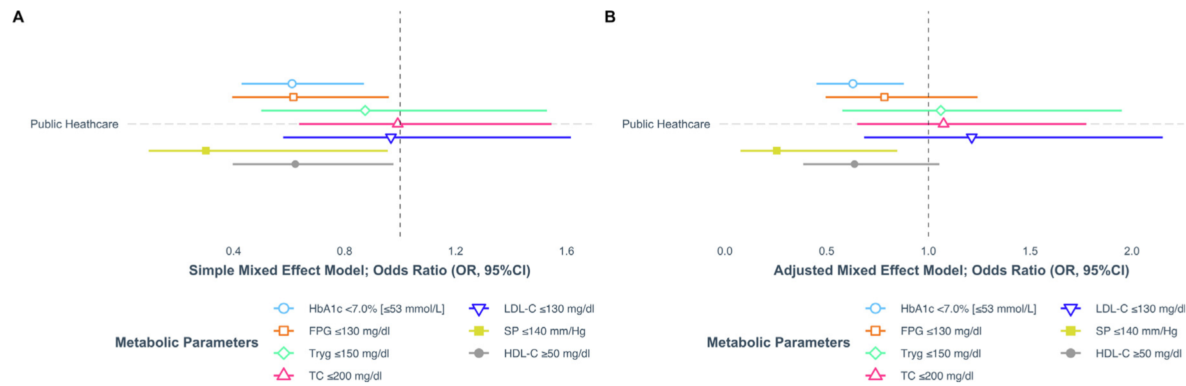

Fig. 2 – Odds-ratio plot representing the likelihood to achieve metabolic goals of patients treated in public healthcare institutions using a single (A) and adjusted (B) mixed effect models. Covariates used for adjustments were high-level of income, time since diagnosis, current age, sex, body mass index, continuous glucose monitoring, and educational level. *Abbreviations*: HbA1c: glycated hemoglobin A1c, FPG: fasting plasma glucose, Tryg: triglycerides; TC: total cholesterol, LDL-C: low-density cholesterol, HDL: high-density cholesterol, SBP: systolic blood pressure.

private healthcare settings are presented in the **Supplementary Tables 2 and 3**.

3.5. *Acute and chronic T1D complications*

In our study population, 13.6% (n = 219) reported any hypoglycemic event, 6.3% (n = 101) reported an event of severe hypoglycemia in their lifetime and 2.0% (n = 34) had a severe hypoglycemia in the last year. Hospitalization for DKA (excluding DKA at diagnosis) was reported in 9.9% (n = 158) of patients. Hospitalization for any cause was reported in 9.3% (n = 149). Regarding diabetes chronic complications we found that 8.1% (n = 130) presented DCKD during follow-up, 10.0% (n = 160) diabetic retinopathy and 6.7% (n = 107) diabetic

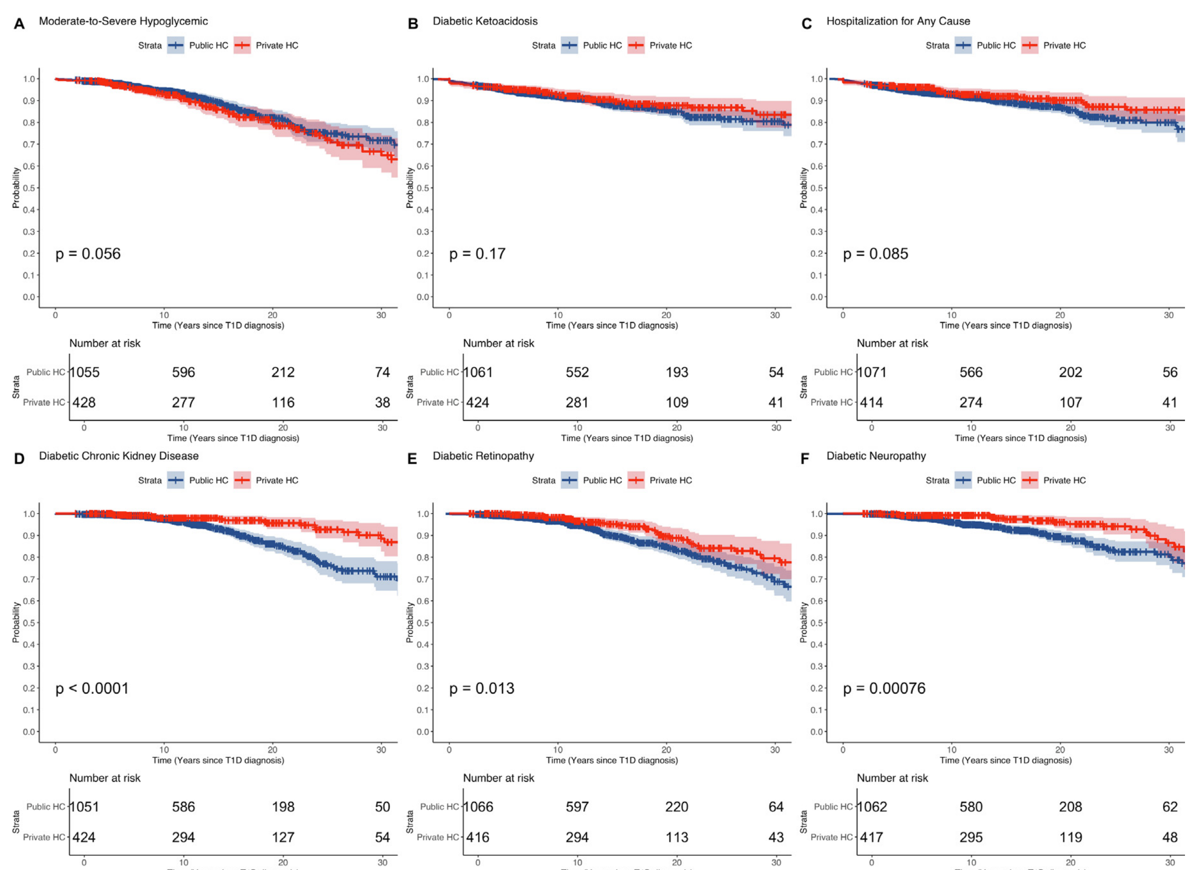

Fig. 3 – Kaplan-Meier Analysis to identify the risk for confirmed moderate-to-severe hypoglycemic events (A), DKA (B), hospitalization for any cause (C), diabetic chronic kidney disease (D), retinopathy (E), and neuropathy (F) divided by healthcare attention using time since T1D diagnosis in patients living with T1D included in the RENACED-DT1. *Abbreviations*: HC: health-care setting. DKA: diabetic ketoacidosis.

Table 2 – Mixed effect Cox proportional regression models and propensity matched score to evaluate the hazard ratio risk for T1D associated complications in patients treated in public healthcare settings.

T1D associated complication	Risk attributable of public healthcare setting			
	Mixed Effects Cox Proportional Hazard Models		Propensity Matched Score	
	Unadjusted Hazard Ratio (95% CI)	Adjusted Hazard Ratio (95% CI)	Unadjusted Hazard Ratio (95% CI)	Adjusted Hazard Ratio (95% CI)
DKA	1.29 (0.90–1.84)	1.13 (0.77–1.65)	1.43 (0.69–3.01)	1.25 (0.57–2.71)
Confirmed hypoglycemic event	0.76 (0.58–1.01)	0.95 (0.69–1.29)	0.54 (0.33–0.89)*	0.61 (0.36–1.04)
Hospitalization for any cause	1.40 (1.01–2.04)*	1.05 (0.70–1.56)	1.24 (0.62–2.45)	1.18 (0.51–2.75)
Diabetic chronic kidney disease	2.51 (1.59–3.96)*	3.00 (1.75–5.17)*	1.98 (1.00–7.12)*	3.22 (1.11–9.36)*
Diabetic retinopathy	1.59 (1.10–2.29)*	2.06 (1.33–3.19)*	1.09 (0.52–2.28)	1.39 (0.61–3.16)
Diabetic neuropathy	2.28 (1.39–3.73)*	3.02 (1.75–5.21)*	6.67 (1.53–29.1)*	9.52 (1.78–50.9)*

Adjusted covariates were socioeconomical income, current age, time since T1D diagnosis, sex, BMI, use of continuous glucose monitoring (CGM) and educational level.
Abbreviations: DKA: diabetic ketoacidosis.
* = p value < 0.01

neuropathy. DCKD individual criteria is presented in **Supplementary Table 4**.

3.6. *Risk of T1D related outcomes amongst healthcare settings*

We observed that those patients registered in the public setting had increased risk for DCKD (HR 3.00, 95% CI 1.75–5.17, $p < 0.001$), retinopathy (HR 2.06 95% CI 1.33–3.19, $p < 0.01$) and neuropathy (HR 3.02, 95% CI 1.75–5.21, $p < 0.001$), after adjusting for covariates (Fig. 3). In the 1:1 ratio propensity score matching, the risk observed in patients living with T1D treated in the public setting was maintained for DCKD (HR 3.22 95% CI 1.11–9.36, $p < 0.05$) and neuropathy (HR 9.52 95% CI 1.78–50.9, $p < 0.01$) after adjusting for covariates (Table 2).

3.7. *Diabetes knowledge acts as mediator of glycemic control and impacts T1D associated complications*

We hypothesize that the differences in educational and nutritional parameters observed between both healthcare settings could have contributed as a mediator of T1D therapeutic goals and associated complications in patients living with T1D. We found that diabetes knowledge mediates an average of 29.2% (95% CI 6.6% to 79%, $p < 0.01$) of the effect of the healthcare setting on glycemic control. Moreover, education impacts on fasting glucose, triglycerides and LDL goals, as well on ketoacidosis incidence and confirmed hypoglycemic events, after adjustment for covariates (**Supplementary Table 5**).

4. Discussion

In this work, we report an overview of patients living with T1D in Mexico focusing on the two major healthcare settings in our country, using data from the RENACED-DT1. To our knowledge, the RENACED-DT1 is the largest database including follow-up information from patients living with T1D in Mexico. We found differences in metabolic control, diabetes education, and treatment between both healthcare settings. Furthermore, we found that patients in the public healthcare setting had a lower probability for achieving treatment goals, coupled with a higher risk for developing T1D associated chronic complications. This risk conferred by the healthcare setting could be partially mediated by the knowledge of the disease, which suggests that diabetes education strategies must be emphasized, regardless of the healthcare setting. Our results highlight the role of inequalities within the two main types of healthcare settings, which overall impacts the quality of care in patients living with T1D in Mexico. Inequalities in healthcare need to be addressed to promote behaviors that improve glycemic control and reduce the risk of long-term complications in patients living with T1D.

As it has been reported, T1D is a chronic disease with increasing worldwide prevalence along with its associated chronic complications [2,15], leading to higher demand for specialized healthcare services [16]. Although the factors associated with the increase in T1D incidence worldwide are not completely understood, it has been proposed that prenatal (e.g. obesity, infections, and increased maternal age) and postnatal (e.g. early introduction of diet, β-cell stress and exposure to pathogens) conditions may play a role in the development of T1D [17-19]. In Mexico, reports have shown an increase in the number of confirmed cases registered with T1D, most of which are diagnosed during childhood [3]. The obtained information from RENACED-DT1 shows an increase in the number of registered cases that were diagnosed in the last two decades. Over 75% of our registered RENACED-DT1 patients living with T1D were adults at the moment of the analysis, allowing to study long term outcomes of patients with T1D in contrast to other cohorts which include patients under 19 years-old [20].

Our results also show differences in patients' biochemical, educational, and treatment parameters among healthcare settings, possibly attributable to social inequalities inherent to both settings. Previous reports have shown differences in metabolic control and adverse outcomes attributable to the type of care provided [4,21-23]. Moreover, an unfavorable socioeconomic status restricts access to technologies for diabetes treatment, which directly impacts on glycemic control [23-25]. The differences found in our results could be explained by several social inequalities such as a longstanding social gap, economic and ethnic differences amongst our country, and long term structural differences within the healthcare system models that have been previously reported [4-6,24]. Moreover, it has been reported that several developing countries in the Middle East and Latin America had a high proportion of patients living with T1D that failed to achieve glycemic control [26-28]. Patients living with T1D in Latin-America have several challenges to address. It has been reported that there is a lack of universal healthcare coverage, a high diabetes underdiagnosis, low health expenditure for T1D, limited access to appropriate insulin regimes, and a strong deficiency of low-cost multidisciplinary interventions for diabetes management within the region [29-32]. Mexico is not the exception, as these challenges and social inequalities persist within healthcare institutions. Overall, these deficiencies increase the gap to access quality healthcare services and promote that patients living with chronic diseases seek attention in private institutions as an alternative [33,34]. Our results highlight that a possible determinant could be diabetes knowledge in each patient, as it acts as a mediator on the likelihood of increasing glycemic control. We observed that 29.2% of the effect of care is mediated by knowledge in diabetes. The time in each clinical visit to deliver educational and nutritional recommendations could be lower in a public healthcare setting, where an increased work overload and excess of daily consults are present [35]. The remaining effect could have a multifactorial component. However, we can hypothesize that this could be explained by structural factors (effect of healthcare policies, technologies and treatments available in each healthcare setting, etc.) and individual factors (adherence to diabetes treatment, healthy lifestyle changes, regular clinical visits, etc.) [36]. Our results should serve as a call to action to implement strategies to strengthen the empowerment of each patient, promote multidisciplinary interventions to improve glycemic control, and to apply measures to capture early cases with T1D in childhood, leading to a significant impact in the quality of life of young patients living with the disease in a single and unified healthcare framework. All these actions could offer timely treatment to improve metabolic control and decrease the risk of adverse outcomes in a context where novel treatment technologies and therapeutics are not available and widely used in Mexico.

5. Strengths and limitations

Our work offers a unique insight of the panorama of patients living with T1D in Mexico. To our knowledge, the RENACED-DT1 represents the first and largest database capturing the characteristics and complications of patients living with T1D in our country. Furthermore, the RENACED-DT1 comprises the effort of 43 certified healthcare providers in private practice and public institutions attending patients living with T1D in Mexico. However, some limitations must be acknowledged. We could not address the real prevalence or incidence of T1D in Mexico. Until now, we have included a small proportion of the whole population living with T1D Mexico and there might be a bias to the registration of patients in cities where endocrinologists and treatment facilities are available. Although there have been previous reports to address the lack of data, no population-based information is available regarding the real prevalence of T1D in adults in Mexico. An average incidence of 1.15/100,000 individuals under 15 years was reported in Veracruz [37]. However, Gomez et. al. reported a higher incidence of 6.2/100,000 individuals under 19 years-old [3]. If we consider the 26,578 cases of T1D in people under 19 years reported by the IDF in 2019 [38] and the 25,695 cases notified in the period between 2010 and 2018 by the Mexican Ministry of Health [39], we are including approximately 6% of the population living with T1D in Mexico. Therefore, we could only evaluate a small proportion of the patients living with the disease. There might be a possible bias when recording hypoglycemic events because technology is available to a small fraction of our population, which could explain the higher prevalence of hypoglycemic events in the private healthcare setting. We captured a higher proportion of women with T1D, which could be a selection bias due to an active involvement of women in this registry. Finally, our mediation analysis should be interpreted as an exploratory analysis that sought to generate a potential answer to the differences observed in metabolic profile within both healthcare institutions. Overall, this reflects the complexity of achieving glycemic control in patients with T1D and represents an area of opportunity for further studies.

In summary, we found differences in metabolic, educational and treatment parameters, alongside an increased risk for diabetic chronic complications between patients treated in public versus private healthcare settings. The disease knowledge could act as a mediator in the likelihood of achieving glycemic control that directly impacts on metabolic treatment goals and associated T1D complications. Our findings unveiled the underlying social inequalities and a lack of a unified healthcare framework in our country, calling to action to consider future public health care policies that focus on implementing cost-benefit strategies to timely educate and empower patients living with T1D. Overall, these strategies should focus on reducing social inequalities and assure a better quality of life for patients living with T1D in our country.

Author contributions

Research idea and study design RNF; data acquisition: MVV, RNF, LIO, JRMS, CZL, AMRM, NEGH, JFBM, GGG, MVC, KLSR, CCG, AEYR, MAPP, JJCM, JCVM, AREO, AFH, ERS, ARZ, SML, MHFA; data analysis/interpretation: RNF, NEAV, AGT, PAV; statistical analysis: NEAV; manuscript drafting: NEAV, AGT, PAV, RNF; supervision or mentorship: PAV, RNF. Each author contributed important intellectual content during manuscript drafting or revision and accepted accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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(https://www.renaced-diabetestipo1.mx/grupo-renaced-diabetes-tipo1/).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2021.109038.

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