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Factors Associated with Insulin Nonadherence in Type 1 Diabetes Mellitus Patients in Mexico

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Keywords
Diabetes mellitus · Type 1 diabetes · Insulin · Depression · Disordered eating behavior

Abstract
Background: Lack of adherence to insulin therapy is common among patients with type 1 diabetes. Factors associated with insulin omission in adult persons with type 1 diabetes in Latin America have not been studied in detail. ***Objectives:*** To investigate factors associated with insulin nonadherence including the presence of psychological disorders (disordered eating behaviors and depression) in adult patients with type 1 diabetes. ***Methods:*** Cross-sectional study including 104 consecutive adults (≥18 years old) attending a tertiary care center in Mexico City. Adherence to insulin therapy was measured with a specific item in a questionnaire. Sociodemographic data and factors related to insulin omission, including validated questionnaires to evaluate disordered eating behavior and depression, were collected and compared between the nonadherent and adherent groups with parametric or nonparametric statistical tests, as appropriate. ***Results:*** We classified 51 (49.1%) patients as nonadherent and 53 (50.9%) as adherent. Adherent subjects reported that they planned their activities around insulin application more often than the nonadherent subjects did (43.4 vs. 23.5%, $p = 0.032$). In a logistic regression model, fear of hypoglycemia (OR = 11.39) and economic reasons (OR = 6.02) were independently associated with insulin adherence. Presence of disordered eating behavior was identified in 14.4% of subjects, the majority belonging to the nonadherent group. ***Conclusions:*** Only 50% of the patients with type 1 diabetes were adherent. The principal factors associated with nonadherence were economic reasons and fear of hypoglycemia.

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Introduction

The World Health Organization defines adherence as "the extent to which a patient's behavior – taking medication, following a prescribed diet, and/or executing lifestyle changes – corresponds with agreed recommendations from the health care provider" [1].

Lack of adherence is common among patients with type 1 diabetes (T1D) ranging from 23 to 77%, with a higher frequency in developing countries [2, 3]. Factors associated with poor adherence in diabetes patients include age, gender, duration of disease, social and family factors, physician-related attitudes, regimen complexity, socioeconomic status, psychiatric disorders and medication side effects [4].

With respect to insulin adherence, Peyrot et al. [5] found that 31% of patients with T1D (including 19% Hispanics) reported insulin omission. Patients felt that injecting insulin was intrusive in their lives. The main factors related to omission were the number of daily insulin injections, lack of adherence to a healthy diet and interference with activities of daily living [5].

We currently have limited information regarding insulin adherence in adults with T1D in developing countries such as Mexico. One study in Pakistan reported that common factors associated with poor insulin adherence in children with T1D were fear of hypoglycemia, misunderstanding of medical treatment and low parental education level [2].

Regarding data in adults (aged 30 ± 11.90 years) with T1D, a Brazilian study reported moderate (42.2%) and minimal (48%) adherence to insulin treatment, evaluated using an adapted 4-item Morisky medication scale questionnaire. Patients in the highest adherence group had lower mean glycated hemoglobin (HbA_{1c}) in comparison to patients in the moderate and minimal adherence groups. The significant independent variables related to greater insulin adherence were older age, higher adherence to diet, lower rate of self-reported hypoglycemia in the last month, low economic status and living in the southeast region of the country [6].

People with T1D are at risk for depression, anxiety disorder, eating disorder, distress and anxiety. These psychosocial aspects are often associated with nonadherence to treatment and poor glycemic control [7]. A recent meta-analysis of 19 studies in juvenile populations reported a moderate association between depression and treatment adherence [8].

With regard to eating disorders, the prevalence of clinical and subclinical disease (anorexia nervosa, bulimia nervosa and other unspecified eating disorders) is more frequent (about 21–37%) in patients with T1D, predominantly in young women, and in overweight or obese patients. Some of these patients omit insulin doses in order to avoid weight gain, resulting in worsening glycemic control [9, 10].

Disordered eating behaviors (DEB) are abnormal eating conducts that are not practiced at a high enough frequency or severity to merit the formal diagnosis of an eating disorder, yet they confer an increased risk for developing one in the future. The prevalence of DEB in adolescents with T1D increases with age and weight, showing a predominance in girls [9].

Eisenberg et al. [11] confirmed in youth with T1D that the presence of DEB was associated with higher HbA_{1c}, mean glucose and percentage of glucose >180 mg/dL on the continuous glucose monitoring trace, and with worse diabetes adherence.

Finally, another barrier for insulin adherence is economic difficulties, which is particularly relevant in out-of-pocket markets, where patients have to pay for their insulin [12, 13].

In Mexico, to our knowledge no study has been conducted to explore insulin adherence among adult patients with T1D. Moreover, there are no data regarding the presence of eating disorders in this population. The aim of this study is to evaluate insulin adherence in adult patients with T1D treated at a tertiary care center and to identify the factors associated with insulin omission, including the presence of psychological disorders (DEB and depression).

Materials and Methods

We performed a cross-sectional study in patients with T1D (defined as the presence of anti-GAD (glutamic acid decarboxylase) and/or C peptide levels <0.2 nmol/L), attending the Type 1 Diabetes Clinic of a tertiary care center in Mexico City. Between March and December 2016, patients were recruited consecutively by convenience sampling. Our study sample represents 80% of the clinic population. Inclusion criteria were patients with T1D, aged ≥16 years, under treatment with an insulin regimen (basal-bolus regimen or subcutaneous continuous insulin infusion [$n = 7$]). Exclusion criteria were other types of diabetes (e.g. type 2, MODY or secondary to pancreatitis), pregnancy and analphabetism. Patients were recruited the day of their appointment and underwent a personal interview.

The study was approved by the Comité de Ética en Investigación del Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (study reference 1967), and informed consent was obtained from all participants. Patients were excluded if they had type 2 diabetes mellitus, a secondary cause of diabetes or dementia.

We obtained a medical history and current laboratory results. The main outcome was adherence to insulin therapy. This was evaluated in a self-administered questionnaire using a Likert scale (never, rarely, few times and often). Patients who referred to never omitting insulin were the adherent group, the rest of the population was considered nonadherent. This group included patients who reported omitting insulin rarely, occasionally (few times) or often in the last month. The questionnaire also evaluated factors associated with omission [14, 15]. This included 23 questions regarding the impact of insulin application, experience with insulin injections, feelings regarding insulin application, fear of hypoglycemia and economic factors. The questions were structured with answers on a 5-point Likert scale [16]. The results were compared between the adherent and nonadherent groups. In addition, the ability to perform carbohydrate counting was evaluated with a question in which participants were asked to write the total grams of carbohydrates in four types of food. In addition, we asked the patients' physician (not involved in this project) if he/she considered that the patient knew how to count carbohydrates.

For the assessment of microvascular complications (retinopathy, nephropathy and neuropathy), an ophthalmologist performed a funduscopic evaluation. For nephropathy, we measured the albumin-creatinine ratio and calculated creatinine clearance using the Chronic Kidney Disease Epidemiology Collaboration equation. Finally, for neuropathy screening, we applied the Michigan neuropathy-screening instrument. This consists of a self-administered questionnaire and a clinical examination; a score ≥7 on the questionnaire and/or ≥2 in the clinical examination indicates the presence of neuropathy.

For the assessment of DEB, we conducted the Diabetes Eating Problem Survey (DEPS). This is a 16-item diabetes-specific self-reported questionnaire to test for diabetes-specific eating disorders. Answers are scored on a 6-point Likert scale, with higher scores (range 0–80) indicating DEB and a total score of ≥20 indicating a high risk for eating disorders. For the screening of depression, we performed the Patient Health Questionnaire (PHQ). A result ≥10 is indicative of possible depressive disorder.

The questionnaires for evaluating adherence and related factors were self-administered with supervision from one of the study investigators.

Statistics

The distribution of continuous variables was assessed by the Kolmogorov-Smirnov test. In the statistical analysis, adherent versus nonadherent patients were compared. Continuous variables were compared between adherence groups using the Student *t* test (parametric) or the Mann-Whitney U test (nonparametric). The χ^2 test or Fisher's exact test were used to compare categorical variables, as appropriate. We performed a logistic regression analysis with adherence as the dependent variable and including as independent variables the identified factors related to omission: economic reasons, fear of hypoglycemia, planning activities around insulin injections and the presence of DEB. A p value <0.05 was considered as statistically significant. Analyses were performed using SPSS version 21.

Results

One hundred four subjects fulfilled the selection criteria and were included in this study. The majority were women (60.6%), with a mean age of 32 years (25–45.7) and a mean duration of diabetes of 15.9 ±11.0 years. The mean HbA_{1c} was 8.8 ± 1.6%. Almost all of the patients lived in an urban area (only 4 were reported living in a rural setting). With respect to employment status, 57 (54.8%) were employed, 23 (22.1%) were students, 21 (20.2%) were unemployed and 3 (2.9%) were pensioners. Concerning educational level, 58.7% (n = 61) of the participants had completed college or postgraduate training. Of the remaining patients, 26.9% (n = 28) had completed high school and 14.4% (n = 15) only had middle or elementary school education.

The number of adherent subjects (those who answered that they never omitted insulin doses) was 53 (50.9%), the remaining 51 (49.1%) patients where considered nonadherent. Table 1 shows the characteristics of the population according to the adherent and nonadherent categories. There were no differences between groups with respect to gender (p = 0.720), age (p = 0.296) and duration of diabetes (p = 0.904). When we compared the educational status between groups, a significantly greater proportion of nonadherent patients had completed high school, college or postgraduate training (98 vs. 81.1%, respectively, p = 0.005). There was no difference between groups concerning basal or prandial insulin analogue use (p = 0.408 and p = 0.735, respectively). In addition, a similar proportion of adherent and nonadherent patients reported carbohydrate counting (p = 0.561). However, when the physician in charge was asked which patients he or she considered carried out carbohydrate counting, they preferentially indicated adherent subjects (p = 0.026). In the carbohydrate counting test there was no difference between groups, only 16 (48.5%) in the adherent group and 17 (51.5%) in the nonadherent group answered all the questions correctly (p = 0.177).

There was no difference between adherence groups regarding biochemical variables (Table 2). Concerning microvascular complications, comparing adherent versus nonadherent groups, retinopathy was identified in 24 (48%) versus 23 subjects (54.8%), respectively (p = 0.518), and albuminuria in 27 (54%) versus 25 subjects (52.1%), respectively (p = 0.849). A significant greater proportion of nonadherent subjects had neuropathy as evaluated with the Michigan score: 10 (19.2%) in the adherent group versus 18 (35.3%) in the nonadherent group (p = 0.049). A logistic regression model was created to explore

Table 1. Characteristics of study participants, classified by adherence category

Variable	Adherent (n = 53)	Nonadherent (n = 51)	p value
Gender			0.720
Men	20 (37.7)	21 (41.2)	
Women	33 (62.3)	30 (58.8)	
Age, years	36.9±13.9	34.2±12.1	0.296
Weight, kg	63.5±12.0	65.0±10.8	0.511
BMI	23.9±3.6	23.8±3.2	0.948
Duration of diabetes, years	15.7±11.2	16.0±11.1	0.904
Education level			*0.005*
None/elementary school	10 (18.9)	1 (2)	
High school/college/postgraduate	43 (81.1)	50 (98)	
Basal insulin			0.408
NPH	5 (10.4)	3 (5.9)	
Basal insulin analogue (glargine and degludec)	43 (89.6)	48 (94.1)	
Preprandial insulin			0.735
Regular	3 (5.9)	4 (7.5)	
Rapid insulin analogue (lispro, aspart or glulisine)	48 (94.1)	49 (92.5)	
Carbohydrate counting	39 (76.5)	43 (81.1)	0.561
Physician considers that patient performs carbohydrate counting	46 (86.8)	35 (68.6)	*0.026*
Capillary glucose measurement per week			0.127
≤2	15 (29.4)	7 (13.2)	
>2	35 (68.6)	45 (84.9)	
Hypoglycemia (<70) in the previous week	35 (66.0)	34 (66.7)	0.946
Severe hypoglycemia in the previous 6 months	16 (31.4)	14 (26.4)	0.577

BMI, body mass index (weight/height^2); NPH, neutral protamine Hagedorn. Data expressed as means ± standard deviation or number (percentage) as appropriate. Italicized p values indicate statistically significant differences.

Table 2. Participants' biochemical parameters and microvascular complications according to adherence category

Variable	Adherent (n = 53)	Nonadherent (n = 51)	p value
HbA_{1c}, %	8.8 [7.9–9.3]	8.6 [7.5–9.9]	0.802
mmol/mol	73 [63–78]	70 [58–85]	
Triglycerides, mg/dL	76.0 [61.0–119.0]	93.5 [71.2–122.5]	0.210
Total cholesterol, mg/dL	176.6±35.9	179.0±42.5	0.748
HDL cholesterol, mg/dL	59.6±17.5	54.2±10.6	0.061
LDL cholesterol, mg/dL	102.2±28.0	111.8±38.6	0.153
Albuminuria, mg/dL	10.0 [4.9–31.6]	8.2 [5.0–30.0]	0.922
Albuminuria >30 mg/dL	25 (52.1)	27 (54)	0.849
Neuropathy (Michigan score)	10 (19.2)	18 (35.3)	0.049
Retinopathy	24 (48)	23 (54.8)	0.518

HbA_{1c}, hemoglobin A_{1c}; HDL, high-density lipoprotein; LDL, low-density lipoprotein. Data expressed as median [interquartile range], means ± standard deviation or number (percentage) as appropriate.

Table 3. Interference of insulin application with daily activities according to adherence category

	Adherent (n = 53)	Nonadherent (n = 51)	p value
How much do insulin injections interfere with your eating?			0.162
Not at all	33 (62.3)	28 (54.9)	
A little	9 (17)	11 (21.6)	
A moderate amount	1 (1.9)	6 (11.8)	
A great deal	10 (18.9)	6 (11.8)	
How much do insulin injections interfere with your exercise?			0.468
Not at all	33 (62.3)	33 (64.7)	
A little	7 (13.2)	7 (13.2)	
A moderate amount	7 (13.2)	3 (5.9)	
A great deal	6 (11.3)	6 (11.8)	
Do you plan your activities around insulin injections?			*0.032*
No	30 (56.6)	39 (76.5)	
Yes	23 (43.4)	12 (23.5)	
Do insulin injections have a negative effect on your social activities?[1]	43 (81.1)	33 (64.7)	0.125
Do insulin injections have a negative effect on your recreational activities?[1]	41 (77.4)	36 (70.6)	0.200
Do insulin injections have a negative effect on your sexual activity?[1]	50 (94.3)	43 (84.3)	0.241
Do insulin injections have a negative effect on your work/career?[1]	41 (77.4)	32 (62.7)	0.176
Do insulin injections have a negative effect on your family care giving?[1]	48 (90.6)	44 (86.3)	0.517

[1] Number and percentage of patients answering 0 (no negative effect of insulin injections). The italicized p value indicates statistically significant differences.

the association between adherence and neuropathy adjusted for HbA_{1c} and time since diagnosis. When this model was generated, it showed that only HbA_{1c} (OR = 1.36, 95% CI = 1.01–1.82, p = 0.038) and time since diagnosis (OR = 1.06, 95% CI = 1.02–1.11, p = 0.004) remained significantly associated with neuropathy (R^2 = 0.211), the association with adherence was lost.

Regarding factors associated with insulin adherence, we evaluated the influence of insulin application on activities of daily living. Adherent subjects reported that they planned their activities around insulin application more often than the nonadherent subjects did (43.4 vs. 23.5%, p = 0.032). In general, insulin application was not a significant concern in either group (Table 3).

Next, the experience and attitudes regarding insulin application were evaluated. There were no differences between the adherence groups concerning insulin application. However, the nonadherent group had a significantly greater fear of hypoglycemia compared to the adherent group, with a median score of 2 [1.5–2.5] in the adherent group versus 2.5 [2–3] in the nonadherent group, p < 0.001 (Table 4).

Finally, 17 (16.3%) subjects reported omitting insulin due to economic reasons, 3 (5.7%) in the adherent group versus 14 (27.5%) in the nonadherent group (p = 0.017). Accordingly, the majority of subjects for whom insulin was an out-of-pocket expense (n = 82) were in the nonadherent group, 46 (90.2%) versus 36 (67.9%), p = 0.005.

Subsequently, the association between psychological disorders (DEB and depression) and insulin adherence was evaluated. DEB was identified in 15 (14.4% subjects (indicated by a DEPS score >20); a significant proportion of these belonged to the nonadherent group, 12 (23.5%) versus 3 (5.7%), respectively, p = 0.010.

There was a higher prevalence of DEB in women (86.7% vs. 13.3%, p = 0.027). In addition, patients with DEB had higher HbA_{1c} and fasting triglycerides concentrations compared to patients without DEB 10.2% [8.4–11.6] versus 8.6% [7.7–9.4], p = 0.008, and 86 mg/dL [62–119] versus 111.5 mg/dL [77.7–165.7], p = 0.034, respectively. Concerning diabetes self-care activities, subjects with DEB performed less glucose monitoring than subjects without DEB, (less than 2 self-monitorings of glucose per day, 46.7 vs. 16.9%, p = 0.030, respectively). Con-

Table 4. Experience and attitudes associated with insulin application according to adherence category

	Adherent (n = 53)	Nonadherent (n = 51)	p value
How do you describe your experience regarding the time needed for insulin application?			0.793
Very satisfied	22 (42.3)	21 (48.8)	
Satisfied	24 (46.2)	25 (49)	
Somehow satisfied	5 (9.6)	5 (9.8)	
Unsatisfied	1 (1.9)	0	
How do you describe your experience regarding the difficulty for insulin application?			0.341
Very satisfied	33 (63.5)	25 (50)	
Satisfied	17 (32.7)	21 (42)	
Somehow satisfied	2 (3.8)	4 (8)	
Unsatisfied	0	0	
How do you describe your experience regarding pain due to insulin application?			0.345
Very satisfied	15 (28.3)	19 (37.3)	
Satisfied	24 (45.3)	15 (29.4)	
Somehow satisfied	10 (18.9)	14 (27.5)	
Unsatisfied	4 (7.5)	3 (5.9)	
How do you describe your experience regarding bruising due to insulin application?			0.786
Very satisfied	16 (30.2)	11 (21.6)	
Satisfied	13 (24.5)	15 (29.4)	
Somehow satisfied	15 (28.3)	16 (31.4)	
Unsatisfied	9 (17)	9 (17.6)	
How do you describe your experience regarding embarrassment due to insulin application?			0.562
Very satisfied	27 (50.9)	27 (52.9)	
Satisfied	14 (26.4)	9 (17.6)	
Somehow satisfied	9 (17)	9 (17.6)	
Unsatisfied	3 (5.7)	6 (11.8)	
Total score	1.8 [1.4–2.2]	2.0 [1.4–2.4]	0.807
I dread insulin injections			0.410
Disagree	40 (75.5)	43 (84.3)	
Somehow disagree	4 (7.5)	4 (7.8)	
Somehow agree	4 (7.5)	3 (5.9)	
Agree	5 (9.4)	1 (2.0)	
Injecting insulin is the most difficult part of my diabetes treatment			0.847
Disagree	35 (66.0)	36 (70.0)	
Somehow disagree	5 (9.4)	6 (11.8)	
Somehow agree	9 (17.0)	6 (11.8)	
Agree	4 (7.5)	3 (5.9)	
I have to mentally prepare before injecting insulin			0.450
Disagree	45 (84.9)	43 (84.3)	
Somehow disagree	1 (1.9)	4 (7.8)	
Somehow agree	2 (3.8)	1 (2.0)	
Agree	5 (9.4)	3 (5.9)	
Fear of hypoglycemia[1]	2 [1.5–2.5]	2.5 [2–3]	<0.001

[1] Score from 0 (not at all) to 5 (a great deal).

cerning factors associated with insulin omission, patients with probable DEB reported that insulin significantly interfered with eating compared to subjects without DEB (20 vs. 14.6%, $p = 0.004$, respectively). Similarly, patients with DEB scored negatively regarding experience with insulin application (2.4 [1.9–2.6] vs. 1.8 [1.4–2.2], $p = 0.019$, respectively). Furthermore, fear of hypoglycemia was also greater in subjects with possible DEB (2.5 [2.5–3] vs. 2 [2–2.5], $p = 0.002$, respectively). The frequency of omission due to economic factors was not different whether disordered eating was present or absent.

Finally, we did not find differences between adherence groups with respect to the PHQ score (adherent group 3 [1–9] vs. nonadherent group 3 [0.5–8], $p = 0.872$). However, the group of subjects with a probable DEB had a greater chance of showing features of depression (PHQ score >10) than patients without DEB (7 (46.7% vs. 12 [13.3%], $p = 0.002$).

A logistic regression model was generated with adherence as the dependent variable (adherence yes or no). The independent variables were selected from the bivariate analysis. Educational level, economic factors, fear of hypoglycemia, presence of DEB and planning of activities around insulin application were included as the independent variables. The results of this model indicated that only economic factors (OR = 6.02, 95% CI = 1.3–27.3, $p = 0.020$) and fear of hypoglycemia (OR = 11.39, 95% CI = 3.7–34.8, $p < 0.001$) were independently associated with insulin nonadherence ($R^2 = 0.39$, $p < 0.001$).

Discussion

In this study, we evaluated the factors related to insulin nonadherence in adults with T1D treated in a tertiary care center in Mexico City. About half (49%) of the subjects reported current insulin nonadherence. In addition, 14.4% of the population showed features of DEB, the majority of which were in the nonadherent group. The main factors associated with insulin nonadherence were fear of hypoglycemia and economic factors.

To our knowledge there is no information exploring factors associated with insulin omission in adult persons with T1D in Latin America. The Global Attitudes of Patients and Physicians (GAPP) study similarly explored factors associated with insulin injection omission. The authors confirmed an association between frequency of hypoglycemia and insulin omission/nonadherence ($p = 0.06$) [17]. In our study, fear of hypoglycemia was associated with nonadherence; nonetheless, there were no differences in the adherence groups about the frequency of any or severe reported hypoglycemia episodes.

A higher educational level was observed in the nonadherent group, but in this study we could not explore the reasons for this finding. Few studies have explored insulin adherence in adults with T1D; as a result, there is little information regarding this association.

In this study, patients who omitted insulin injections did not plan their activities around insulin injections and did not consider that insulin interfered with their daily activities. When asked for the main reason for omitting insulin, almost 20% of subjects mentioned forgetting their insulin injection. In contrast, in the GAPP study subjects who omitted insulin reported interference with daily activities (43.3%) [17].

Economic reasons were another factor associated with insulin omission; individuals who obtained their insulin free of cost were less likely to skip injections. This may be common in countries where insulin is an out-of-pocket expense [2].

Regarding psychological disorders, the prevalence of probable depression in this population with T1D was higher in women (28.1% women vs. 2.4% men, $p = 0.001$); this is in accordance with previous reports [18]. However, we did not find a difference in the PHQ score between adherence groups. This result differs from the findings of the study of Gonzalez et al. [7], where the authors reported a significant association between the presence of depression and insulin omission; this difference may be due to instruments used to evaluate the presence of depression.

Concerning DEB, there was a significantly higher prevalence of probable DEB in the nonadherent group. Of the patients with DEB, 86.7% were women and the presence of DEB was associated with uncontrolled metabolic parameters. Markowitz et al. [19], when validating the DEPS tool, also described an association between insulin omission and a higher score (presence of DEB). Wisting et al. [9] investigated the prevalence of DEB and insulin omission among 770 children and adolescents with T1D. They reported that 27.7% of the girls and 8.6% of the boys scored above the DEPS threshold. In line with our results, they also found a significantly higher HbA_{1c} in the DEB group (10.2% [88 mmol/mol] vs. 8.6% [70 mmol/mol], $p < 0.001$). The prevalence of depressive symptoms was also greater in the group with a score ≥20 (indicating DEB). This is in accordance with previous reports highlighting the association between depression and DEB, particularly in women [20].

To our knowledge, this is the first study in a Mexican population that has explored factors related to insulin nonadherence in adult patients with T1D. The results of this study indicate that insulin nonadherence is common even in patients treated in specialized clinics. The findings of this study should be used to develop strategies to address this problem in patients with T1D. Screening algorithms tailored to detect the factors associated with insulin omission may be generated. Education programs, patient empowerment and specific interventions targeting newly diagnosed individuals may be implemented to address insulin omission.

Some limitations of this study must be acknowledged. Insulin omission was evaluated through questionnaires and not directly. Patient self-reporting may either underestimate or overestimate adherence [21]. In addition, despite the fact that not all the patients attending the clinic were included, we believe that the results are representative and relevant for this population. The effect of participating in a study may have influenced the way participants responded.

In this study, about half of the subjects reported omitting insulin doses. The principal factors associated with insulin nonadherence were economic reasons and fear of hypoglycemia. It is essential that health care providers are aware that insulin omission is common in patients with T1D. A multidisciplinary team must evaluate patients, and risk factors associated with insulin omission should be promptly addressed.

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Statement of Ethics

Subjects have given their written informed consent. The research institute's committee on human research has approved the study protocol.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

P.A.-V. designed, wrote and reviewed the manuscript, J.P.R. conducted the research, K.W.Z.C. wrote the manuscript, D.R.P. conducted the research, J.B.C. conducted the research, F.J.G.-P. reviewed the manuscript, C.A.A.-S. reviewed the manuscript, and R.M. designed, wrote and reviewed the manuscript.

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