Determinants of Glycemic Control among Urban Patients with Type 2 Diabetes: A mediation analysis from real-world evidence

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Abstract

Aims
To explore the determinants of glycemic control (GC) among patients with type 2 diabetes (PwD) to provide insight into the pathways of the effect of diabetes knowledge on GC.

Methods A multicenter cross-sectional study was conducted in PwD from 28 primary outpatient centers located in Mexico City. Using the multivariable-adjusted models, we determined the associations between diabetes knowledge, self-care behaviors, and glycemic control. The mediation analyses used linear regression models, where the significance of indirect effects was calculated with bootstrapping.

Results
The population (N=513) had a mean age of 53.8 years (standard deviation: 11.3 yrs.), and 65.9% were women. Using multivariable-adjusted linear models, we found that diabetes knowledge was associated with glycemic control ($\beta$: -0.102, 95% Confidence Interval [95% CI] -0.189, -0.014). Diabetes knowledge was also independently associated with self-care behavior (for physical activity: $\beta$: 0.181, 95% CI 0.088, 0.273), and self-care behavior was associated with glycemic control (for physical activity: $\beta$: -0.112, 95% CI -0.194, -0.029). The association between diabetes knowledge and glycemic control was lost after adjustment for self-care behaviors, especially physical activity ($\beta$: -0.084, 95% CI -0.182, 0.014, p-value: 0.062). Finally, the mediation models showed that the effect of diabetes knowledge on glycemic control was 17% independently mediated by physical activity (p-value: 0.049).

Conclusions
Self-care activities, particularly physical activity, mediated the effect of diabetes knowledge on glycemic control. Our results indicate that diabetes knowledge should be reinforced in low-income PwD, with an emphasis on the benefits physical activity has on improving GC.

1. Introduction

Diabetes is a major worldwide cause of death and disability. It is estimated that diabetes affects 451 million adults, mainly in low- and middle-income countries (LMICs) [[1, 2]]. Patients with type 2 diabetes (PwD) are at risk of developing a range of complications that can endanger their health, quality of life, and survival. Diabetes also has a considerable financial impact on patients and health care systems [[3, 4]].

The document Healthy People 2020 from the United States government has emphasized the importance of social and environmental factors that affect individuals and their health. The goal is to “reduce the disease and economic burden of diabetes mellitus and improve the quality of life for all persons who have, or are at risk for, diabetes.” [[5]]. Historically, research and the resulting clinical approaches focusing on the individual, including pharmacological treatments, have led to improvements in self-management outcomes and reduction of cardiovascular risk factors. Despite significant advances in treatment, inadequate disease control persists[[6]]. However, researchers have more recently recognized the need to consider factors external to the individual, namely, social determinants of diabetes, to achieve the goal of sustainable improvement in health outcomes [[7]]. Evidence suggests there is a relationship between determinants of health and both risks of diabetes and worse outcomes, especially among individuals with low
socioeconomic status (SES) and education level. It is suggested that urban areas of LMICs, where the burden of disease is particularly high, need further research on this topic [[8, 9]]. For example, diabetes self-care activities are behaviors undertaken by PwD and contribute to successful self-management [[10]]. These self-care behaviors positively correlate with good glycemic control, reduction of complications, and improvement in the quality of life [[11, 12]].

The relationship between diabetes knowledge and health outcomes has been inconsistently reported [[13-17]]. However, few studies have shown the relationship between diabetes knowledge, self-care behaviors, and clinical outcomes in low-income urban populations, where diabetes knowledge could be even more inadequate. Therefore, using mediation analyses, this study aimed to explore the determinants of glycemic control (GC) among PwD and low SES from Mexico City, including SES and clinical factors, and to provide insight into the pathways of the effect of diabetes knowledge on GC.

2. Materials and Methods

2.1 Design and population

A multicenter cross-sectional study was conducted in PwD from 28 primary outpatient centers located in urban areas of Mexico City from January 2017 to May 2018. The patients were beneficiaries of Seguro Popular (public health insurance). PwD who agreed to participate were referred to an outpatient diabetes center located in Iztapalapa, a municipality of Mexico City to complete an assessment.

2.2 Clinical, socio-economic, diabetes knowledge and self-care activities assessments
The data related to demographic characteristics, current treatment, time since diagnosis, comorbidities, and physical medical examination were collected from medical records and confirmed during medical interviews. The biochemical data, including glycosylated hemoglobin (HbA1c) as a measure of glycemic control, were collected from the last blood tests done two weeks before the study To determine the presence of diabetes-related microvascular complications, standardized criteria from international clinical practice guidelines[18] were implemented, such as fundoscopy with mydriatic camera for retinopathy assessment, increased urine albumin/creatinine ratio or decreased estimated glomerular filtration rate for diabetic kidney disease assessment, and abnormal sensitive and vibratory perception for distal diabetic neuropathy assessment [[18, 19]].

SES was determined using the AMAI index (Spanish for Mexican Association of Marketing Research and Public Opinion Agencies [[20]], which integrates updated information of income and expenses of Mexican households from official Mexican government databases. The index provides a numeric value (0 to > 193) and five categories ranging from “A/B”, the highest socioeconomic level, to “E”, the lowest [[21]]. Diabetes knowledge was assessed using the Spoken Knowledge in Low Literacy Patients with Diabetes (SKILLD) Scale [[22]]. The 10-item SKILLD assesses the knowledge of lifestyle interventions, glucose management, recognition and treatment of hypo- and hyperglycemia, and activities to prevent long-term diabetes-related complications. Each item score was summed; it ranged from 0 to 10. The higher the score number, the better the knowledge of diabetes. The SKILLD was originally designed and validated for vulnerable PwD with low literacy, and it has been previously used in Mexican-origin populations [[23–25]].

The 11-item version of the Summary of Diabetes Self-Care Activities (SDSCA) [[26]]
was used to measure participants’ self-care behaviors. It measures the frequency of self-care activities in the last seven days. In the analyses, we included general diet (followed healthy diet), specific diet (fruits/low-fat diet), exercise glucose tests, and foot care.

2.3 Statistical analyses

We examined the role of diabetes knowledge in self-care behavior; we used univariable and multivariable linear models adjusted for age, sex, and time since diagnosis. We also used multiplicative terms to determine the potential interactions between socioeconomic status (SES) in the association between diabetes knowledge and self-care behaviors. We determined the role of education in the association between SES and diabetes knowledge using multivariable logistic regression models. We evaluated the role of self-care behaviors in the association between diabetes knowledge and glycemic control, including diet (specific, global, and total), physical activity, glucometry assessments, foot care, and a self-care global score.

We ran mediation models according to the Baron and Kenny’s steps [[27]]. We assessed whether the effect of diabetes knowledge on glycemic control (HbA1C levels) was mediated by self-care behaviors in a multiple mediator model (Fig. 1). Coefficients were obtained from a linear regression analysis. Indirect effects were calculated based on the product-of-coefficients method (a*b) [[28]]. Standard errors and confidence intervals for mediation analyses were calculated with bootstrapping (5000 samples) [[29]]. Outcome and mediating variables were adjusted for age (as a continuous variable), sex (male vs. female), years of disease (as a continuous variable), and education level (primary vs. higher education). The direct effect (c’ path) did not have to be reduced to zero because an incomplete mediation of the effect was expected. Also, for significant mediating variables, the proportion
mediated was calculated as effect size measure \( ((a*b)/c) \). Finally, we determined the role of diabetes knowledge and self-care behaviors in glycemic control (HbA1c levels, as a continuous variable) and microvascular damage (retinopathy, nephropathy, and neuropathy) using multivariable-adjusted logistic regression models. We performed the analyses using the R software (R Project for Statistical Computing, CRAN, The Comprehensive R Archive Network, Vienna) and we used the command `mediate()` in ‘mediation’ package for bootstrapping. Statistical significance was defined as a value of \( p < 0.05 \).

3. Results

3.1 Characteristics of study participants

A total of 513 PwD were included, of which 66.3% were female. The mean age was 53.7 years (standard deviation [SD] 11.32 years). Most of the population reported primary school or less as their education level (52.4%), and 64% showed low or very low socioeconomic status (D+, D, and E, AMAI categories). Patients had a mean time since diagnosis of 12.2 years (SD: 8.75 years), and 48.4% of them reported coexisting hypertension. The microvascular complications assessment revealed the presence of diabetic retinopathy in 23.9% of the population, diabetic renal disease in 41.3%, and diabetic distal neuropathy in 54.9%. The SKILLD scale, used to measure diabetes knowledge, showed a mean value of 3.06 (SD: 2.37, range 0–10). The best self-care activity performance observed was foot care (mean 3.39 days a week, SD: 3.19 days a week), and glucose blood sugar testing was the least commonly performed (mean 1.7, SD: 2.28 days a week). The mean level of HbA1c was 9.6% (SD: 2.2). Full description of the population included is shown in Table 1.

3.2 Role of socioeconomic factors in diabetes knowledge
We found that SES was linked to education level (p-value < 0.001, Supplementary Fig. 1). Multivariable-adjusted models also showed that SES was associated with diabetes knowledge ($\beta$: 0.009, 95% Confidence Interval [95% CI] 0.003, 0.015, p-value < 0.001, Supplementary Table 1). Finally, univariable and multivariable-adjusted models showed a positive and statistically significant association between education and SES on diabetes knowledge; education had the strongest effect (Supplementary Table 1).

### 3.3 Mediation analysis

Table 2 shows the mediation of self-care behaviors between diabetes knowledge and glycemic control. First, we determined the effect of diabetes knowledge on glycemic control (c path). Multivariable regression models, adjusted for age, sex, years of disease, and education, showed a negative association between diabetes knowledge and glycemic control (HbA1C blood levels, p-value = 0.023). Second, we examined the impact of diabetes knowledge on self-care behaviors using multivariable-adjusted linear models (a path). Diabetes knowledge was significantly associated with all self-care behaviors, including diet (general, specific, and global score), physical activity, blood sugar testing, and foot care, and with the global score for self-care activities. The strongest association was observed for foot care and the weakest for specific diet score. Following the Baron and Kenny’s steps for mediation models [[27]], we determined the role of self-care behaviors in glycemic control (b path). Among self-care behaviors, only physical activity and global diet reached statistical significance. The association between diabetes knowledge and glycemic control was lost after adjustment for self-care behaviors, especially physical activity. Finally, we determined if the mediation effect was statistically significant. We found a partial mediation of physical activity in the association between
diabetes knowledge and glycemic control (Table 2), where physical activity significantly accounted for 17% of the association (p-value: 0.049).

3.4 Role of diabetes knowledge and self-care in microvascular damage

We studied whether diabetes knowledge or self-care behaviors were associated with microvascular damage (retinopathy, nephropathy, and neuropathy). Diabetes knowledge was not associated with any of the surrogates for microvascular damage. However, several self-care behaviors were associated with neuropathy, including diet (general HR: 0.95, 95% CI 0.90, 0.99; global HR: 0.95, 95% CI 0.92, 0.99), physical activity (HR: 0.90, 95% CI 0.83, 0.98), blood sugar testing (HR: 0.86, 95% CI 0.79, 0.93), and self-care global score (HR: 0.97, 95% CI 0.95, 0.99) (Table 5). Global diet score was also associated with retinopathy (HR: 1.04, 95% CI 1.01, 1.09), and physical activity was associated with the presence of any of the surrogates of microvascular damage (HR: 0.83, 95% CI 0.72, 0.96, Supplementary Table 2).

4. Discussion

We showed how diabetes knowledge plays a key role in self-care behavior. Our study found that, among all the self-care behaviors evaluated, physical activity mediated the association between diabetes knowledge and glycemic control in a low-income population of PwD from a large urban area. Both SES and level of education were directly associated with diabetes knowledge, but education showed a stronger impact. To the best of our knowledge, this is the first study that elucidates the pathways between diabetes knowledge and glycemic control in low-income primary care PwD.
The present study is in line with previous studies about the benefit of self-care behaviors, particularly physical activity, and provides additional information on the causal path. This study also shows the relevance of diabetes knowledge and self-care behavior in PwD. The lack of health-related knowledge and poor performance of diabetes self-care habits could partially explain the heavier diabetes burden in populations with social lag indicators. Previously, diabetes was associated with worse prognoses in Mexico than in high-income countries [[30, 31]] which made this research obligatory. For mediation analysis, we used one of the two available approaches: the Sobel test [[32]] and bootstrapping [[33]]. Although the Sobel test has been widely used since 1982, bootstrapping has been strongly recommended in recent years. Hence, we chose bootstrapping for our mediation analysis [[34]].

Health literacy involves the patient’s capacity to obtain, process, and understand basic health information and services needed to make appropriate decisions [[35]]. Health literacy is independently related to disease knowledge, and PwD and limited health literacy have less understanding of their disease and experience more negative outcomes than individuals with higher literacy and more knowledge [[17, 36]]. Then, to perform self-care activities, it is essential for PwD to have basic diabetes knowledge, which is usually associated with self-management behavior [[37]]. Structured therapeutic education in diabetes can determine sustained improvement and maintenance of treatment goals, lower incidence rates of all-cause mortality, and reduce first microvascular and macrovascular outcomes incidence. Therefore, educational strategies are crucial to promote empowerment in diabetes [[38, 39]].

In this study, we described a strong association of diabetes knowledge with all self-care activities evaluated, which highlights the role of diabetes knowledge in the
performance of self-care activities. Eyüboğlu E, Schulz PJ et al [[40]] did not find an interaction between diabetes knowledge and health literacy with the frequency of self-care behaviors. A distinctive feature and strength of our study was that it included a large sample of patients with low socioeconomic and educational level, in whom the burden of having poor diabetes knowledge could be more significant than in other populations. Self-care depends on the knowledge patients have about diabetes, but this knowledge alone cannot guarantee patient’s self-care practicing. An important finding was the elucidation of socioeconomic factors on diabetes knowledge. Both factors evaluated, SES and education level, played a major role in diabetes knowledge, particularly education. This finding suggests there is a causative role of socioeconomic factors in the epidemic of complications of diabetes mellitus in underdeveloped countries. Poverty influences the development of type 2 diabetes and complications [[41, 42]]. Education and socioeconomic levels are associated with the activation of self-care management in chronic diseases [[43]]. These two social determinants could partially influence the poor performance in self-care habits, through the potential contribution and mediating effect of poor diabetes knowledge, which indicates a link between social determinants of health and diabetes self-management. Moreover, socioeconomic status was directly associated with glucose testing, which identifies the restriction PwD and low SES have to execute this behavior. These findings reiterate why health care professionals need to consider their patients’ socioeconomic status when implementing diabetes self-care management and education programs. One strength of this study is that it included a validated tool for diabetes knowledge (SKILLD), which was designed for vulnerable populations [[22, 23]]. We observed that most patients scored low on this scale, even though PwD and long-term
diabetes diagnosis were enrolled, which indicates the need for increasing diabetes education in healthcare programs. The study participants were beneficiaries of Seguro Popular in Mexico City, which attends to the largest number of primary care outpatients in Mexico [[44]]. Therefore, our results were obtained from real-world data among a representative population from a low-income subset of patients from one of the largest urban areas in the world, which is home to more than 20 million people in 1,450 km².

Although our results are novel and potentially useful in the context of diabetes mellitus treatment in low-income countries, our study has several limitations. First, this is a cross-sectional epidemiological study, so we are not able to conclude causality. However, as any other epidemiological study, it is a hypothesis generator, and examines the relevance of education on diabetes knowledge to improve glycemic control. Second, the sample size may seem small in comparison with other diabetes studies. However, our study included a large number of participating health centers in an unprecedented manner. Third, although this study was conducted in Mexico City, a megalopolis, our findings may not be representative of other urban areas across the world. Nevertheless, the study highlights the need to consider social determinants of health and diabetes knowledge across populations that surely share similarities with our sample. Fourth, the SKILLD scale does not have a widespread use among studies that measure diabetes knowledge. Moreover, from our perspective, the traditional tools used for this purpose are difficult to understand for populations with educational lag; hence we decided to administer SKILLD, which has been tested and validated in populations similar to ours. Fifth, despite adjusting for potential confounding factors in our analysis, we did not assess for other factors that may influence glycemic control and self-care behaviors,
such as pharmacological treatments, mental disorders, barriers to self-care, etc.

Adverse diabetes outcomes are complex and multicausal and involve biological, individual, and social factors. In this work, we try to reinforce the relevance of some of them; we recognize the difficulty of including all the factors involved in a study of this nature.

In conclusion, our study revealed that socioeconomic and educational gradients influence diabetes knowledge among primary care patients with type 2 diabetes. We also determined that self-care behaviors, particularly physical activity, mediate the effect of diabetes knowledge on glycemic control. These results may indicate the most relevant pathways to consider in populations with poor access to diabetes care, which could lead to allocating government resources to improve education and diabetes knowledge and to encouraging PwD to increase self-care activities, particularly physical activity. Further research is needed to estimate the size effect of interventions on diabetes knowledge and self-care improvement strategies in socially disadvantaged circumstances, particularly in low-income groups.

Declarations

**Ethics approval and consent to participate**

Approval was obtained from the institutional Bioethics and Research Health Ministry Board (609-010-01-18), and all participants signed an informed consent.

**Consent for publications**

All authors have read and approved the manuscript for submission, accepted responsibility for the manuscript’s contents.

**Availability of data and material**

The datasets generated and/or analyzed during the current study are not publicly
available due that data used are from patients from the Clinic and are under policies for private confidential information, but are available from the corresponding author on reasonable request and using unidentifiable IDs by a third party.

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**Declaration of Interest**

Authors declare no conflicts of interest.

**Authors’ contributions:** R.S.T., T.C.X and V.D.S. designed and developed the research. R.S.T., J.G.G. and D.P, wrote the manuscript. D. P. and R.S.T. made the statistical analysis. E.L.G, J.S.A., AO.T., L.C.M., D.C.L revised the manuscript critically for important intellectual content. R.S.T. is the guarantor of this work and takes the responsibility for the integrity of the data.

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Tables
Table 1. Sociodemographic and clinical characteristics of patients with type 2 diabetes mellitus in Mexico City (n=513).

| Continuous variables | Mean | SD |
|----------------------|------|----|
| Age, yrs.            | 53.75| 11.32 |
| Years of disease     | 12.25| 8.75  |
| Socioeconomic status (score)* | 80.35| 40.51 |
| **Diabetes knowledge (SKILLD score)** | 3.06| 2.37 |

**Self-care behavior**

| Diet               | Specific, days a week | 2.90 | 1.85 |
|--------------------|------------------------|------|------|
|                     | General, days a week   | 2.36 | 2.09 |
|                     | Global, days a week    | 2.63 | 1.68 |
| Physical activity, days a week | 1.85 | 2.31 |
| Blood sugar testing, days a week | 1.70 | 2.28 |
| Foot care, days a week | 3.39 | 3.19 |
| Self-care global score**, days a week | 2.37 | 1.57 |

| HbA1c, %           | 9.6 | 2.2 |

**Categorical variables**

| Sex            | n   | %   |
|----------------|-----|-----|
| Female         | 340 | 66.28% |
| Male           | 173 | 33.72% |

| Education       | n   | %   |
|-----------------|-----|-----|
| Null            | 22  | 4.29% |
| No read, no write | 49  | 9.55% |
| Primary school  | 198 | 38.60% |
| Secondary school | 118 | 23.00% |
| High school     | 79  | 15.40% |
| University      | 33  | 6.43% |
| No information  | 14  | 2.73% |

| Socioeconomic status | n   | %   |
|----------------------|-----|-----|
| A, B (> 193)         | 6   | 1.17% |
| C+ (155 to 192)      | 28  | 5.46% |
| C (128 to 154)       | 45  | 8.77% |
| C- (105 to 127)      | 64  | 12.48% |
| D+ (80 to 104)       | 123 | 23.98% |
| D (33 to 79)         | 189 | 36.84% |
| E (0 to 32)          | 20  | 3.90% |
| No information       | 38  | 7.41% |

| Comorbidities       | n   | %   |
|---------------------|-----|-----|
| Hypertension        | 249 | 48.54% |
| High triglycerides  | 305 | 59.45% |
| High total cholesterol | 248 | 48.34% |

**Microvascular complications**

| Retinopathy        | 123 | 23.98% |
| Nephropathy        | 212 | 41.33% |
| Neuropathy         | 282 | 54.97% |

*AMAI score for socioeconomic status. **Diet, physical activity, glucose, and foot care divided by 4. SD: Standard deviation.

Table 2. Mediation of self-care behaviors between diabetes knowledge and glycemic control in low-income patients with type 2 diabetes mellitus from Mexico City (n=513).

| Diabetes knowledge | X → Y (c path) | X → M (a path) | M → Y (b path) | Indirect effect | Proportion mediated |
|--------------------|----------------|----------------|----------------|----------------|--------------------|
| Crude analysis     | -0.10 (-0.19, -0.01) | -0.10 (-0.19, -0.01) | -0.10 (-0.19, -0.01) | -0.10 (-0.19, -0.01) | -0.10 (-0.19, -0.01) |
|                          | Self-care behavior | Diet | Specfic | 0.13 | (0.06, 0.21) | -0.06 | (0.04, 0.17) | 0.00 | (0.00, 0.03) | -0.06 | (0.04, 0.17) |
|-------------------------|--------------------|------|---------|------|-------------|-------|-------------|------|-------------|-------|-------------|
|                          |                    |      | -0.11  | -0.02 | (0.01, 0.19) | -0.05 | (0.03, 0.13) | 0.07 | (0.05, 0.15) | -0.06 | (0.04, 0.17) |
| Global 09               |                    |      | -0.17  | -0.06 | (0.02, 0.07) | -0.07 | (0.05, 0.15) | 0.01 | (0.01, 0.03) | -0.06 | (0.04, 0.17) |
| Total                   |                    |      | -0.12  | -0.08 | (0.02, 0.10) | -0.08 | (0.05, 0.16) | 0.01 | (0.01, 0.03) | -0.06 | (0.04, 0.17) |
| Physical activity days a week |      |      | -0.08  | -0.18 | (0.00, 0.01) | -0.02 | (0.00, 0.02) | -0.04 | (0.00, 0.02) | -0.06 | (0.04, 0.17) |
| Blood sugar testing days a week |      |      | -0.10  | -0.06 | (0.01, 0.02) | -0.07 | (0.05, 0.16) | 0.01 | (0.01, 0.03) | -0.06 | (0.04, 0.17) |
| Foot care days a week   |                    |      | -0.09  | -0.07 | (0.06, 0.08) | -0.08 | (0.05, 0.16) | 0.01 | (0.01, 0.03) | -0.06 | (0.04, 0.17) |
| Self-care global score days a week |      |      | -0.09  | -0.19 | (0.07, 0.08) | -0.22 | (0.03, 0.04) | 0.05 | (0.02, 0.08) | 0.07 | (0.02, 0.12) |

\[\text{a} \quad \text{c path (total effect): The crude association between diabetes knowledge and glycemic control.}\]

\[\text{b} \quad \text{c' path (direct effect): The association between diabetes knowledge and glycemic control, adjusted for mediator (self-care behavior).}\]

\[\text{c} \quad \text{a path: Association between diabetes knowledge and self-care behavior.}\]

\[\text{d} \quad \text{b path: Association between self-care behavior and glycemic control.}\]

\[\text{e} \quad \text{Indirect effect (}\ a \ b \text{): The indirect effect of the diabetes knowledge on glycemic control through self-care behavior.}\]

\[\text{f} \quad \text{Proportion effect mediated (}\ (a \ b)/c \text{): The proportion of the total effect mediated through self-care behavior.}\]

\[\text{g} \quad \text{Confidence interval for indirect effects were calculated with bootstrapping (5000 samples).}\]
All analyses used linear regression models adjusted for age, sex, years since diagnosis, and SES.

Figures

Figure 1.

Single mediator models for diabetes knowledge effect on glycemic control (y) via

Diabetes knowledge (x) → Self-care behaviors (m) → Glycemic control (y)

Diagram showing pathways:
- a path: Diabetes knowledge to Self-care behaviors
- b path: Self-care behaviors to Glycemic control
- c path: Direct effect of Diabetes knowledge on Glycemic control
- c' path: Indirect effect of Diabetes knowledge on Glycemic control via Self-care behaviors

Figure 1

Single mediator models for diabetes knowledge effect on glycemic control (y) via
Supplementary Files

This is a list of supplementary files associated with the primary manuscript. Click to download.

Supplementary File.docx
Supplementary File.docx