**ABSTRACT**

**Objective:** The objective of the study was to identify the frequencies of chronic complications (micro- and macrovascular) in adult T2D patients of the Instituto Mexicano del Seguro Social (IMSS) treated from 2011 to 2017 and to determine risk factors, including the presence of overweight and obesity.

**Methods:** The data used in this retrospective cohort study were obtained from the Non-Communicable Diseases Analysis System (SANENT)® of the IMSS.

**Results:** This study included 3,807,621 T2D patients with an average age of 61.1 years and a female predominance of 58.8%. A total of 46.5% of the patients presented obesity, 30% were overweight, 16.8% had arterial hypertension (HT), and 1.05% had dyslipidemia. A total of 32.6% had uncontrolled or poor glycemic control, and 29.44% had some type of comorbidity. Age and the largest number of comorbidities were consistent risk factors for the presence of complications micro- and macrovascular. Regarding hospital mortality, uncontrolled or poor glycemic control, HT, age and comorbidities were risk factors. It should be noted that the factor with the greatest impact was the presence of comorbidities.

**Conclusion:** The risk factors that had the greatest impact on chronic complications were the number of comorbidities, age and HT. Likewise, for hospital mortality.

**Keywords:** Type 2 diabetes; Chronic diabetic complications; Macrovascular; Microvascular

**Abbreviations:** BMI: Body Mass Index; BP: Blood Pressure; A1c: Glycated Hemoglobin; IMSS: Instituto Mexicano del Seguro Social; IR: Interquartile Range; ICD-10: International Classification of Diseases; SANENT®: Non-Communicable Diseases Analysis System; T2D: Type 2 Diabetes; UMF: Family Medicine Unit; WHO: World Health Organization.
prevalence in the adult population between 20 and 69 years of age [4,5]; and between 2000 and 2012, there was an almost 60% increase in subjects with T2D [6]. The data from ENSANUT 2018 (the Mexican National Survey on Health and Nutrition) showed a T2D prevalence of 10.3% was reported.

In addition, T2D is one of the three chronic diseases responsible for the most hospitalizations and costs to health institutions [7]. However, these figures do not account for patients with arterial hypertension (HT); or chronic kidney disease (CKD), which is the most frequent chronic complication of T2D and are among the ten chronic diseases that most strongly affect hospitalizations at the same institutions [8,9]. These complications lead to increased medical visits and hospitalizations, negatively affecting quality of life and increasing the cost of health [10-12]. Macrovascular complications include Peripheral arterial disease, myocardial infarction (MI), congestive heart failure, stroke, and peripheral artery disease. Patients with T2D have a two to four times higher risk of MI and stroke compared to people without diabetes. Specifically, MI and stroke are more likely in patients with uncontrolled T2D and high glycated hemoglobin (A1c) [12].

Obesity influences the vascular system, with endothelial damage promoting cellular changes and causing atheromatous plaques [13,14] and low-grade chronic inflammation. These changes ultimately lead to endothelial dysfunction in individuals with mild untreated dyslipidemia, promoting metabolic alterations that increase the development of atherosclerosis and, finally, cardiovascular complications, as stroke and MI [15]. Few studies have examined the clinical burden of T2D in adult patients with IMSS with a long follow-up period, a large cohort, and patient-level data.

The objective of the study was to identify the frequencies of chronic complications (micro- and macrovascular) in adult T2D patients of the Mexican Social Security Institute (Instituto Mexicano del Seguro Social-IMSS) treated from 2011 to 2017 and to determine the chronic and acute complications (micro- and macrovascular) in adult T2D patients with T2D and acute and chronic complications treated from 2011 to 2017 at the IMSS. The patients were clinically diagnosed by IMSS physicians.

Data Sources
The sources of data for this study were records compiled through the Comprehensive Healthcare Information System, the hospital records of the Medical Statistics System (DataMart) and SANENT® of the IMSS, and the Family Medical Units (FMU) database. The IMSS database contains records for each patient, including those who attended medical check-ups at the first-, second- and third-level care clinics. Diseases are reported using International Classification of Diseases (ICD10) codes.

Baseline Variables and Follow-up
This study included patients aged 18 years or older who were treated from January 2011 to December 2017 and whose records included the following ICD10 codes: E10 (Insulin-dependent diabetes mellitus), E11 (Type 2 diabetes mellitus), E12 (Malnutrition-related diabetes mellitus), E13 (Other specified diabetes mellitus), and E14 (Unspecified diabetes mellitus).

Chronic complications of T2D were defined when, in addition to having the diabetes-related codes [E11-E14], patients presented one of the following diagnoses: coronary heart disease [I20-I25]; ischemic stroke [I63-I69]; chronic kidney disease with kidney complications [E11.2]; terminal kidney failure [N18.0]; hypertensive kidney disease with kidney disease [I12.0]; other chronic kidney disease [N18.8]; unspecified chronic kidney disease [N18.9]; chronic kidney disease [N18X]; nonspecific kidney disease [N19X]; glomerular disorders in diabetes mellitus [N08.3]; diabetic retinopathy [H33-H36]; E11.3, E12.3, E13.3, E14.3; with peripheral circulatory complications [E105, E115, E125, E135, E145], peripheral angiopathy, gangrene and diabetic ulcer [E14.5]; or major lower limb amputation [ICD-9: 8415-8419], excluding traumatic causes of amputations [ICD-10: S77, S78, S87, S88, S98, T053, T055 and T136].

Acute complications of T2D were defined when, in addition to having the codes E11-E14, patients presented the diagnoses of hypoglycemia (E15-E16) and hyperosmolar state (E11.0). Subsequently, to define the study population and results and to describe the epidemiological profile of this group of patients, the codes were searched in the database of patients who received outpatient care at a first-, second- or third-level facility. Age, sex, BMI, HT and mortality, and the chronic and acute complications of these patients were described. Glycemic control, the presence of overweight/obesity and HT were recorded.

Glycemic control was evaluated according to the hemoglobin A1c records in the patient database and was considered uncontrolled when hemoglobin A1c was greater than 7%. All patients had at least one recorded A1c determination, which was analyzed. If more than one measurement was reported, the annual average hemoglobin A1c value was obtained [17].

HT was defined according to ICD10 codes [I10-I15] or when the blood pressure values recorded in the database were ≥ 140/90 mmHg [18]. The presence of dyslipidemia was defined according to ICD10 codes (E.78). The BMI was calculated for the somatometric blood pressure values recorded in the database were ≥ 140/90 mmHg [18]. The presence of dyslipidemia was defined according to ICD10 codes (E.78). The BMI was calculated for the somatometric values of the patients (weight and height) and classified as follows: low weight when the BMI was <18.4 kg/m², normal weight when the BMI was between 18.5 and 25.9 kg/m², overweight when the BMI was between 25.1 to 30 kg/m², class I obesity with a BMI of 30 to 34.9 kg/m², class II obesity with a BMI of 35 to 39.9 kg/m², and class III obesity with a BMI ≥ 40.0 kg/m² [19]. Comorbidities were defined as the presence of HT, dyslipidemia.

Statistical analysis
For quantitative variables, the Kolmogorov-Smirnov normality test was performed, and a parametric distribution was demonstrated. Quantitative variables were described as means and standard deviations. Proportions and frequencies were calculated for qualitative variables. The patients were divided into 3 groups according to nutritional status measured by BMI (normal weight, overweight, and obesity). To compare quantitative variables between the groups, ANOVA with Bonferroni’s test was used; chi-square was used for the qualitative variables.

To identify the factors related to cardiovascular complications and mortality, a multiple logistic regression model was performed. A value of p<0.05 was considered statistically significant, and STATA v.14.0 was used for the statistical analyses.

According to the requirements of the Helsinki Declaration, the
RESULTS

From 2011 to 2017, a total of 3,807,621 patients with T2D were identified; they had an average age of 61.1 years, a 58.8% predominance of females, and an average of 59.6 months of T2D evolution. A proportion of 46.5% of the patients had obesity, 30% were overweight, 16.8% had HT, and 1.05% had dyslipidemia. The average A1c reported was 6.5%, and 32.6% of the patients had uncontrolled or poor glycemic control. It is noteworthy that only 7.6% of patients had more than one determination of A1c during the 6-year evaluation period; the rest of the patients had only one A1c analysis. Figure 1 shows the association of hemoglobin A1c with the patients' complications. When the patients' general characteristics were compared according to nutritional status, it was identified that the subjects with obesity had a lower age and shorter time of evolution compared to patients with normal and overweight; however, the HT, uncontrolled or poor glycemic control and comorbidity frequencies were higher in patients with obesity compared to the other groups (Table 1).

Acute complications (hypoglycemia and hyperosmolar state) occurred in 2.09% of patients, with hyperosmolar state being the more frequent. In terms of nutritional status, patients with normal BMI had a higher frequency of this acute complication.

Of the chronic macrovascular complications identified in patients with T2D, the most common was peripheral arterial disease in 7.3%, while of the microvascular complications, the most common were chronic kidney disease in 4.8% and diabetic retinopathy in 2.4%. When comparing chronic complications according to nutritional status, it was observed that patients with a BMI<25 kg/m² had a higher proportion of these complications, and the difference was statistically significant (Table 2).

Of the total number of patients identified, 29.44% of patients had some type of comorbidity. Specifically, 25.25% (n=961,242) had one comorbidity, 3.86% (n=146,813) had two comorbidities, 0.31% (n=11,850) had three comorbidities, and 0.02% (n=970) had four or more comorbidities. The most frequently occurring comorbidity was HT. When the number of comorbidities was compared according to nutritional status, patients with obesity had a significantly higher proportion and number of comorbidities (Figure 2).

Regarding mortality, during the study period (6 years), a total of 152,811 deaths (4.01%) were identified, of which 13.47% (n=20,585) were in-hospital deaths. When the crude and adjusted annual mortality rates were analyzed, a statistically significant gradual decline over the years was identified (Figure 3).

Multivariate analysis was performed to identify the factors that had an impact on chronic complications. Age and number of comorbidities were constant risk factors for the presence of these alterations, followed by the presence of HT, which was a risk factor for cardiovascular disease, and follow by chronic kidney disease.
Although the bivariate analysis showed that patients with a BMI<25 kg/m² had a higher proportion of chronic complications, the multivariate analysis indicated that overweight and obesity were significant risk factors for coronary heart disease and peripheral arterial disease (Table 3).

Uncontrolled or poor glycemic control was identified as a risk factor for the presence of diabetic retinopathy (OR=1.03), with a very low impact, and for the presence of limb amputation (OR=1.36).

Regarding in-hospital death, uncontrolled or poor glycemic control, HT, age and number of comorbidities were risk factors. It is worth noting that the factor with the greatest impact was the number of comorbidities (Table 3).

DISCUSSION

The present study aimed to investigate the epidemiological data on the presence of micro- and macrovascular complications in IMSS subjects with T2D in Mexico, taking into account the presence of overweight and obesity. According to ENSANUT 2018, the combined prevalence of overweight and obesity was 75.2% (39.1% overweight and 36.1% obesity), which is lower than that observed in our population (42.73% were obese). However, it is expected that

Although the bivariate analysis showed that patients with a BMI<25 kg/m² had a higher proportion of chronic complications, the multivariate analysis indicated that overweight and obesity were significant risk factors for coronary heart disease and peripheral arterial disease (Table 3).

Uncontrolled or poor glycemic control was identified as a risk factor for the presence of diabetic retinopathy (OR=1.03), with a very low impact, and for the presence of limb amputation (OR=1.36).

Regarding in-hospital death, uncontrolled or poor glycemic control, HT, age and number of comorbidities were risk factors. It is worth noting that the factor with the greatest impact was the number of comorbidities (Table 3).

Table 1: Description of patients with T2D and stratification according to the nutritional status classified by the BMI.

<table>
<thead>
<tr>
<th>Nutritional Status</th>
<th>All</th>
<th>Normal</th>
<th>Overweight</th>
<th>Obesity</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.1 ± 13.2</td>
<td>64.8 ± 13.7</td>
<td>61.8 ± 12.6</td>
<td>58.8 ± 12.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>1,567,839 (41.2)</td>
<td>416,320 (46.4)</td>
<td>524,398 (48.0)</td>
<td>627,121 (35.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Evolution time of the T2D</td>
<td>59.6 ± 54.2</td>
<td>69.1 ± 57.6</td>
<td>62.1 ± 54.8</td>
<td>52.8 ± 51</td>
<td>0.001</td>
</tr>
<tr>
<td>Systemic arterial hypertension</td>
<td>640,499 (16.8)</td>
<td>92,024 (10.2)</td>
<td>134,755 (11.8)</td>
<td>413,720 (23.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>39,985 (1.05)</td>
<td>8,615 (0.96)</td>
<td>14,114 (1.24)</td>
<td>17,256 (0.98)</td>
<td>0.001</td>
</tr>
<tr>
<td>Poor glycemic control (A1c&gt;7%)</td>
<td>1,244,152 (32.6)</td>
<td>270,851 (30.1)</td>
<td>338,780 (29.7)</td>
<td>634,522 (35.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>1,120,875 (29.4)</td>
<td>242,379 (27)</td>
<td>288,897 (25.3)</td>
<td>589,599 (33.3)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

The patients were divided into 3 groups according to nutritional status measured by BMI (normal weight, overweight, and obesity). To compare quantitative variables between the groups, ANOVA with Bonferroni’s test was used.

Table 2: Frequency of chronic and acute complications of patients with T2D and stratification according to the nutritional status classified by the BMI.

<table>
<thead>
<tr>
<th>Nutritional status</th>
<th>All</th>
<th>Normal</th>
<th>Overweight</th>
<th>Obesity</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral arterial disease</td>
<td>278,880 (7.3)</td>
<td>73,339 (8.1)</td>
<td>81,159 (7.1)</td>
<td>124,382 (7.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>35,811 (0.94)</td>
<td>9,319 (1.04)</td>
<td>11,278 (0.99)</td>
<td>15,214 (0.86)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>18,917 (0.5)</td>
<td>6,312 (0.70)</td>
<td>5,069 (0.44)</td>
<td>7,536 (0.43)</td>
<td>0.001</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>183,199 (4.8)</td>
<td>62,101 (6.9)</td>
<td>51,706 (4.5)</td>
<td>69,392 (3.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>91,268 (2.4)</td>
<td>28,929 (3.2)</td>
<td>29,776 (2.6)</td>
<td>32,563 (1.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Amputation</td>
<td>5,815 (0.15)</td>
<td>2,416 (0.27)</td>
<td>1,249 (0.11)</td>
<td>2,150 (0.12)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hyperosmolar state</td>
<td>71,207 (1.87)</td>
<td>19,534 (2.18)</td>
<td>22,360 (1.96)</td>
<td>29,313 (1.66)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>8,333 (0.22)</td>
<td>3,337 (0.37)</td>
<td>2,163 (0.19)</td>
<td>2,833 (0.16)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>20,585 (0.54)</td>
<td>6,537 (0.73)</td>
<td>4,115 (0.36)</td>
<td>9,933 (0.56)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Macrovascular complications identified in patients with T2D, the most common was peripheral arterial disease, while of the microvascular complications, the most common were chronic kidney disease and diabetic retinopathy.
According to the literature, overweight and obesity worsen the evolution of patients with T2D because they worsen glycemic control and increase the risk of developing macrovascular and microvascular comorbidities. Subjects with T2D may also present with acute complications such as hypoglycemia or hyperosmolar state, the former being the more common. This is due to variations in diet and the use of antihyperglycemic treatments, for which hypoglycemia is the main side effect. However, while an acute condition does not require hospitalization except in cases of severe hypoglycemia, all patients presenting with a hyperosmolar state should be hospitalized because this complication cannot be resolved on an outpatient basis. This explains why our results show a higher proportion of patients with a hyperosmolar state than patients with hypoglycemic events. Regarding macrovascular complications, the results of the present study are comparable since subjects with obesity had a higher frequency of Peripheral arterial disease and a greater number of comorbidities. Although this study identified that 29.44% of patients had some type of comorbidity, this did not include overweight and obesity, which occurred in 76.41% of the subjects analyzed [20-22]. It is known that the presence of comorbidities is a risk factor for secondary chronic complications and death; our results show that the presence of comorbidities was the only factor that increased the risk of chronic complications and death in a person with T2D (OR>5).

Currently, the frequency of dyslipidemia in patients with T2D is approximately 28% - 41% [20,21]. In this study, a low frequency of dyslipidemia (1.05%) was identified regardless of nutritional status. Although the diagnosis of dyslipidemia includes an increase in total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C) and a decrease in high-density lipoprotein cholesterol (HDL-C), this study defined this condition through ICD10 classifications and not by lipid profile, which suggests a sub diagnosis of dyslipidemia [20,22]. However, despite the low frequency of identified dyslipidemia, the multivariate analysis indicated that dyslipidemia was a risk factor for the presence of coronary heart disease. This finding shows the important impact of this medical condition and the importance of considering dyslipidemia in patients with T2D and, above all, providing early and intensive management of this condition.

Macrovascular complications encompassing retinopathy, nephropathy and diabetic neuropathy are usually asymptomatic until they reach advanced stages, when they manifest as blindness, chronic kidney failure and the need for limb amputations [23]. In this context, chronic kidney disease had more severe manifestations that require patients to seek medical care, which explains why it was the most frequently, identified macrovascular complication. It is also important to mention that, according to reports, microvascular alterations are present in a high percentage of subjects with T2D (30% to 50%), given that the disease is detected in early stages [24].

### Table 3: Multivariate logistic regression analysis to identify the factors that impact on the presence of macrovascular, microvascular and mortality alterations in patients with T2D.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Ischemic heart disease</th>
<th>Cerebrovascular disease</th>
<th>Peripheral arterial disease</th>
<th>Chronic kidney disease</th>
<th>Diabetic retinopathy</th>
<th>Amputation</th>
<th>Hospital death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overweight/obesity</td>
<td>1.15</td>
<td>0.87</td>
<td>1.21</td>
<td>0.87</td>
<td>0.87</td>
<td>0.87</td>
<td>(0.89, 1.01)</td>
</tr>
<tr>
<td>(1.13, 1.17)**</td>
<td>(0.89, 1.01)</td>
<td>(1.20, 1.22)**</td>
<td>(0.89, 1.01)</td>
<td>(0.89, 1.01)</td>
<td>(0.89, 1.01)</td>
<td>(0.89, 1.01)</td>
<td></td>
</tr>
<tr>
<td>A1c ≥ 7</td>
<td>0.93</td>
<td>0.91</td>
<td>1.12</td>
<td>0.91</td>
<td>1.03</td>
<td>1.36</td>
<td>1.13</td>
</tr>
<tr>
<td>(0.99, 1.02)</td>
<td>(0.99, 1.02)</td>
<td>(1.11, 1.13)**</td>
<td>(0.99, 1.02)</td>
<td>(1.02, 1.05)**</td>
<td>(1.28, 1.45)**</td>
<td>(1.09, 1.17)**</td>
<td></td>
</tr>
<tr>
<td>T2D (months)</td>
<td>0.99</td>
<td>0.99</td>
<td>0.99</td>
<td>1.01</td>
<td>0.99</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td>(0.99, 1.01)</td>
<td>(0.99, 1.01)</td>
<td>(0.99, 1.01)</td>
<td>(1.01, 1.01)**</td>
<td>(0.99, 1.01)</td>
<td>(0.99, 1.01)</td>
<td>(0.99, 1.01)</td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1.16</td>
<td>1.11</td>
<td>1.15</td>
<td>0.91</td>
<td>1.38</td>
<td>1.01</td>
<td>1.01</td>
</tr>
<tr>
<td>(1.05, 1.29)*</td>
<td>(0.95, 1.30)</td>
<td>(1.11, 1.20)**</td>
<td>(0.95, 1.30)</td>
<td>(1.30, 1.46)**</td>
<td>(0.95, 1.01)</td>
<td>(0.99, 1.01)</td>
<td></td>
</tr>
<tr>
<td>Hypertension arterial</td>
<td>0.87</td>
<td>1.21</td>
<td>0.99</td>
<td>1.6</td>
<td>1.13</td>
<td>1.34</td>
<td>1.39</td>
</tr>
<tr>
<td>(0.84, 1.01)</td>
<td>(1.16, 1.26)**</td>
<td>(0.99, 1.01)</td>
<td>(1.58, 1.62)**</td>
<td>(1.11, 1.15)**</td>
<td>(1.23, 1.45)**</td>
<td>(1.32, 1.45)**</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.01</td>
<td>1.02</td>
<td>1.02</td>
<td>1.02</td>
<td>1.01</td>
<td>1.02</td>
<td>1.02</td>
</tr>
<tr>
<td>(1.01, 1.01)**</td>
<td>(1.02, 1.02)*</td>
<td>(1.01, 1.02)**</td>
<td>(1.02, 1.02)**</td>
<td>(1.01, 1.02)**</td>
<td>(1.01, 1.02)**</td>
<td>(1.01, 1.02)**</td>
<td></td>
</tr>
<tr>
<td>Number of comorbidities</td>
<td>13.7</td>
<td>11.7</td>
<td>21.5</td>
<td>70.4</td>
<td>22.1</td>
<td>25.1</td>
<td>5.25</td>
</tr>
<tr>
<td>(13.4, 13.9)**</td>
<td>(11.5, 12.9)**</td>
<td>(21.8, 22.8)**</td>
<td>(69.2, 71.6)**</td>
<td>(21.8, 22.8)**</td>
<td>(24.8, 26.4)**</td>
<td>(5.14, 5.36)**</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.001.
However, we identified only the patients with the most severe manifestations of microvascular disease, including chronic kidney disease and limb amputations, which is why our frequency was lower than that reported in other studies.

Our results show a lower mortality range than that reported in the literature; however, our data are comparable with those reported in the literature, since our results show that A1c, HT and the presence of comorbidities are a risk factor for hospital mortality. Glycemic control it is the most important factor in the follow up of patients with T2D since it is key to the progression of the disease and development of complications. However, in Mexico, only 5.3% of subjects with T2D have adequate glycemic control [25]. In this study the analysis of glycemic control should be mentioned as a limitation since we classified glycemic control using hemoglobin A1c, and more than 90% of patients had only one A1c measurement; this percentage was higher than that reported by ENSANUT 2016, in which only 15.2% of the sample had a single A1c determination [26]. However, A1c provides information about glycemic control over approximately 3 months, which is not enough time to evaluate the control and identify whether it determines the presence of chronic complications, which would explain why its impact was only demonstrated in some chronic complications.

CONCLUSION

We suggest that the acute and chronic complications in T2D patients were a short-term due to the characteristics of the population, with diagnosis time of 60 months. Thus, we can conclude that in this population the risk factors are established by the greatest impact in the number of comorbidities and age. Besides, the importance of controlling risk factors and the implication that overweight and obesity have in control patients must be considered.

AUTHORS’ CONTRIBUTIONS

JEFG, LMA and NCG to the conceptualization originally and designed of the study. RACG, MLBA and MLAF contributed to data collection, validation and interpretation; JNZC and MLBA performed the formal analyses. JEFG, LMA, and NCG critically reviewed the manuscript for Writing - Original Draft content and wrote the manuscript and all co-authors critically edited the manuscript. NCG is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethics approval was provided by the National Research and Health Ethics Committee of IMSS, with the registry number R-2014-785024.

Conflict of interest

The authors declare that they have no competing interests.

Acknowledgements

Not applicable.

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