Clinical Characterization and Frequencies of Acute and Chronic Complications in Diabetes

José Esteban Fernández-Gárate[1], Nelly Cisneros Gonzalez[1], Leticia Manuel-Apolinar[2*], María de Lourdes Basurto Acevedo[2], María Luisa Arellano Flores[2], Roberto Alejandro Correa González[2] and Jessie Nallely Zurita-Cruz[3,4]

[1]Epidemiological Surveillance Coordination, Instituto Mexicano del Seguro Social, Mexico City, México

[2]Endocrine Research Unit, Instituto Mexicano Seguro Social, Mexico City, México

[3]Facultad de Medicina Universidad Nacional Autónoma de México, Hospital Infantil de México Federico Gómez, Mexico City, México.

[4]Unit of Research in Medical Nutrition, Pediatric Hospital "Centro Médico Nacional Siglo XXI", Instituto Mexicano del Seguro Social, Mexico City, México.

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.

INTRODUCTION

Mexico is experiencing the socioeconomic impact of the "epidemiological transition", with the prevalence of chronic non-communicable diseases experiencing exponential growth [1-3]. One consequence is that dietary patterns emphasizing foods with high energy density, overweight and obesity, high cholesterol and arterial hypertension (HT), which are the factors responsible for the global burden of the disease, have been modified [3].

Type 2 diabetes (T2D) is a chronic degenerative disease, and its involvement in morbidity and mortality in Mexico has been progressive. Its incidence appears to be increasing, which may be due to both an increase in life expectancy and greater exposure to known risk factors related to the Western lifestyle. At the same time, longer survival of patient with T2D has led to a secondary increased in the prevalence of the disease [4]. According to the Organization for Economic Cooperation and Development (OECD), among its member countries, Mexico ranks first in T2D

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 risk factors, including the presence of overweight and obesity [16].

MATERIALS AND METHODS

Study Population

A retrospective, comparative study was conducted in adult 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 variables of the patients (weight and height) and classified as follows: low weight when the BMI was <18.4 kg/m^2, normal weight when the BMI was between 18.5 and 25.9 kg/m^2, overweight when the BMI was between 25.1to 29.9 kg/m^2,class I obesity with a BMI of 30 to 34.9 kg/m^2, class II obesity with a BMI of 35 to 39.9 kg/m^2, and class III obesity with a BMI ≥ 40.0 kg/m^2 [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

protocol was evaluated and approved by the National Research and Health Ethics Committee of IMSS with registry number R-2014-785-024.

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/m^2 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,
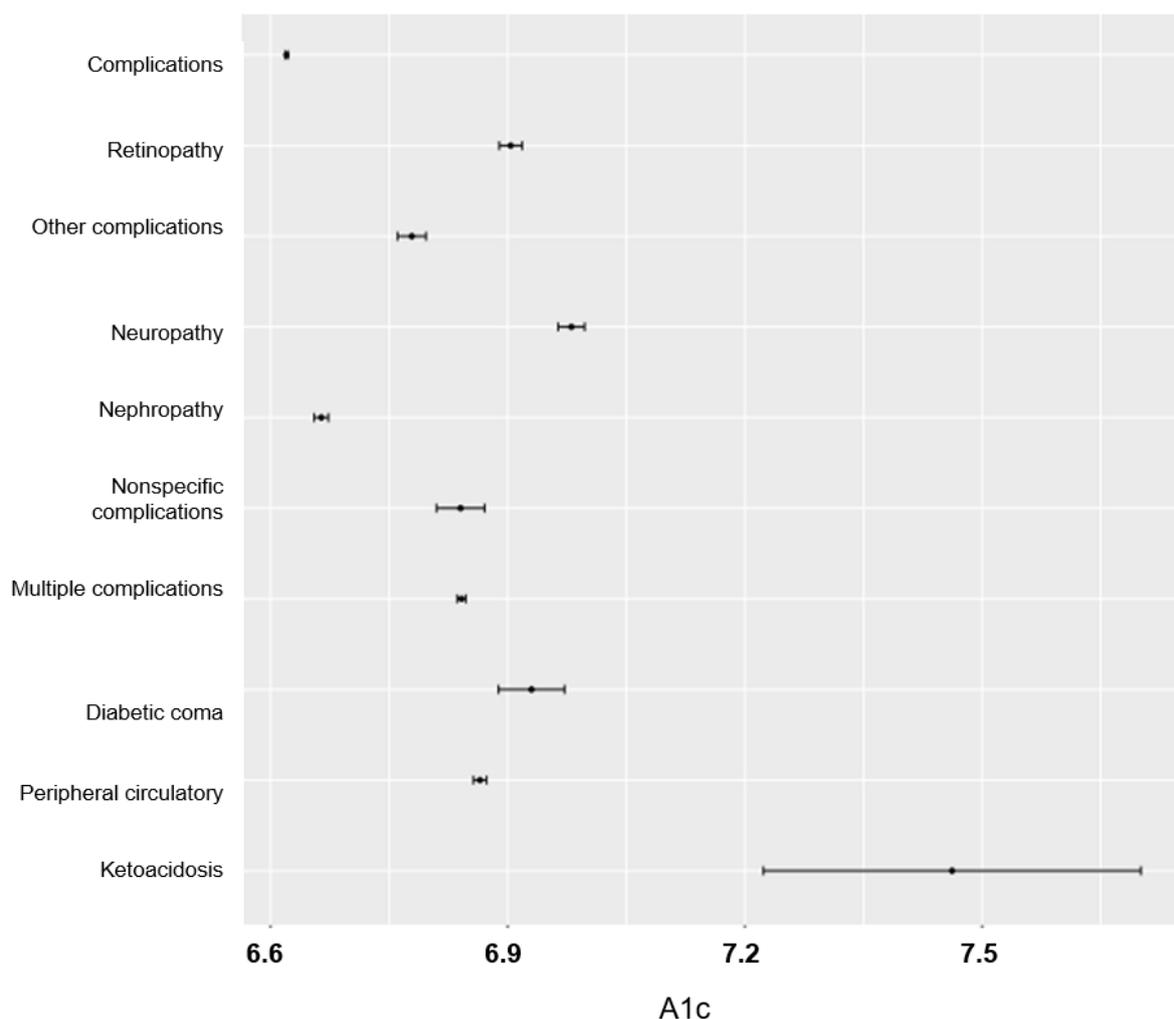

Figure 1: Hemoglobin A1c levels with complications in T2D.

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

	Nutritional Status				
	All	Normal	Overweight	Obesity	
	n=3,807,621	n=898,052	n=1,140,495	n=1,769,074	p
	Frequencies (%)				
Age (years)*	61.1 ± 13.2	64.8 ± 13.7	61.8 ± 12.6	58.8 ± 12.9	0.001
Male sex	1,567,839 (41.2)	416,320 (46.4)	524,398 (46.0)	627,121 (35.5)	0.001
Evolution time of the T2D (months)*	59.6 ± 54.2	69.1 ± 57.6	62.1 ± 54.8	52.8 ± 51	0.001
Systemic arterial hypertension	640,499 (16.8)	92,024 (10.2)	134,755 (11.8)	413,720 (23.4)	0.001
Dyslipidemia	39,985 (1.05)	8,615 (0.96)	14,114 (1.24)	17,256 (0.98)	0.001
Poor glycemic control (A1c>7%)	1,244,152 (32.6)	270,851 (30.1)	338,780 (29.7)	634,522 (35.9)	0.001
Comorbidities	1,120,875 (29.4)	242,379 (27)	288,897 (25.3)	589,599 (33.3)	0.001

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.

	Nutritional status				
	All	Normal	Overweight	Obesity	p
	n=3,807,621	n=898,052	n=1,140,495	n=1,769,074	
	Frequencies n (%)				
Peripheral arterial disease	278,880 (7.3)	73,339 (8.1)	81,159 (7.1)	124,382 (7.0)	0.001
Ischemic heart disease	35,811 (0.94)	9,319 (1.04)	11,278 (0.99)	15,214 (0.86)	0.001
Cerebrovascular disease	18,917 (0.5)	6,312 (0.70)	5,069 (0.44)	7,536 (0.43)	0.001
Chronic kidney disease	183,199 (4.8)	62,101 (6.9)	51,706 (4.5)	69,392 (3.9)	0.001
Diabetic retinopathy	91,268 (2.4)	28,929 (3.2)	29,776 (2.6)	32,563 (1.8)	0.001
Amputation	5,815 (0.15)	2,416 (0.27)	1,249 (0.11)	2,150 (0.12)	0.001
Hyperosmolar state	71,207 (1.87)	19,534 (2.18)	22,360 (1.96)	29,313 (1.66)	0.001
Hypoglycemia	8,333 (0.22)	3,337 (0.37)	2,163 (0.19)	2,833 (0.16)	0.001
Hospital mortality	20,585 (0.54)	6,537 (0.73)	4,115 (0.36)	9,933 (0.56)	0.001

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.
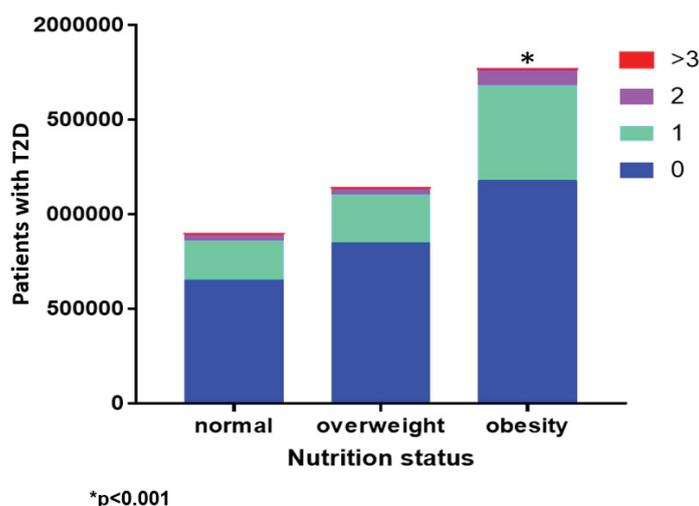

*p<0.001

Figure 2: Comparison of the number of complications in patients with T2D according to their nutritional status.

retinopathy and amputation (Table 3). The time of evolution only proved to be a risk factor for the presence of chronic kidney disease, and its impact was very low (OR=1.01).

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).

Regardingin-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

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.

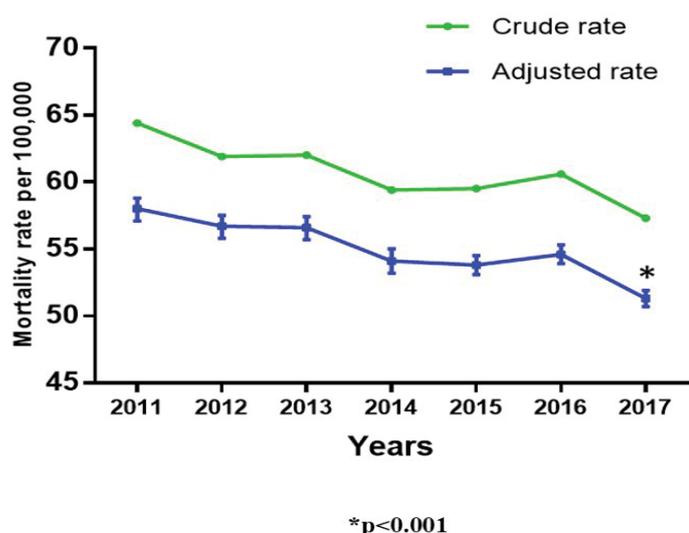| Factors	Ischemic heart disease	Cerebrovascular disease	Peripheral arterial disease	Chronic kidney disease	Diabetic retinopathy	Amputation	Hospital death
	Odds Ratio (Confidence interval 95%)						
Overweight /obesity	1.15	0.87	1.21	0.87	0.87	0.87 (0.89, 1.01)	0.87
	(1.13, 1.17)**	(0.89, 1.01)	(1.20, 1.22)**	(0.89, 1.01)	(0.89, 1.01)		(0.89, 1.01)
A1c ≥ 7	0.93	0.91	1.12	0.91	1.03	1.36	1.13
	(0.99, 1.02)	(0.99, 1.02)	(1.11, 1.13)**	(0.99, 1.02)	(1.02, 1.05)**	(1.28, 1.45)**	(1.09, 1.17)**
T2D (months)	0.99	0.99	0.99	1.01	0.99	1.01	0.99
	(0.99, 1.01)	(0.99, 1.01)	(0.99, 1.01)	(1.01, 1.01)**	(0.99, 1.01)	(0.99, 1.01)	(0.99, 1.01)
Dyslipidemia	1.16	1.11	1.15	0.91	1.38	1.01	1.01
	(1.05, 1.29)*	(0.95, 1.30)	(1.11, 1.20)**	(0.95, 1.30)	(1.30, 1.46)**	(0.95, 1.01)	(0.99, 1.01)
Hypertension arterial	0.87	1.21	0.99	1.6	1.13	1.34	1.39
	(0.84, 1.01)	(1.16, 1.26)**	(0.99, 1.01)	(1.58, 1.62)**	(1.11, 1.15)**	(1.23, 1.45)**	(1.32, 1.45)**
Age (years)	1.01	1.02	1.02	1.02	1.02	1.01	1.02
	(1.01, 1.01)**	(1.02, 1.02)*	(1.01, 1.02)**	(1.02, 1.02)**	(1.01, 1.02)**	(1.01, 1.02)**	(1.01, 1.02)**
Number of comorbidities	13.7	11.7	21.5	70.4	22.1	25.1	5.25
	(13.4, 13.9)**	(11.5, 12.9)**	(21.8, 22.8)**	(69.2, 71.6)**	(21.8, 22.8)**	(24.8, 26.4)**	(5.14, 5.36)**

* p<0.05; ** p<0.001.

*p<0.001

Figure 3: Mortality rate T2D of 2011 to 2017.

this prevalence is higher in individuals with T2D. 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.

Microvascular 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 microvascular 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].

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 3months, 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.

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-2014-785-024.

Conflict of interest

The authors declare that they have no competing interests.

REFERENCES

1. Kuri-Morales PA. La transición en salud y su impacto en la demanda de service os. Gac Med Mex. 2011;147:451–454.

2. Stevens G, Dias RH, Thomas KJA, Rivera JA, Carvalho N. (2008) Characterizing the epidemiological transition in Mexico: National and subnational burden of diseases, injuries, and risk factors. PLoS Med. 5: e125.

3. Zhang M, Hu T, Zhang S ZL. Associations of Different Adipose Tissue Depots with Insulin Resistance: A Systematic Review and Meta-analysis of Observational Studies. Sci Rep. 2015;5:18495.

4. American Diabetes Association. 2. Classification and diagnosis of diabetes. Diabetes Care. 2015; 38:S8–S16.

5. Rtveladze K, Marsh T, Barquera S, Sanchez-Romero LM, Levy D, Melendez G, et al. Obesity prevalence in Mexico: impact on health and economic burden. Public Health Nutr. 2014; 17:233–239.

6. Córdova-Villalobos JA, Barriguete-Meléndez JA, Lara-Esqueda A, Barquera S, Rosas-Peralta M, Hernández-Avila M, et al. Chronic non-communicable diseases in Mexico: epidemiologic synopsis and integral prevention. Salud Publica Mex. 2008;50:419–427.

7. Juan-López M RPL. CONSEJO DE SALUBRIDAD GENERAL [Internet]. Estándares para certificar hospitales. 2015;341.

8. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 2013;36:1033–1046.

9. Bannier K, Lichtenauer M, Franz M, Fritzenwanger M, Kabisch B, Figulla HR, et al. Impact of diabetes mellitus and its complications: Survival and quality-of-life in critically ill patients. J Diabetes Complications. 2015.

10. Steinberger J. Obesity, Insulin Resistance, Diabetes, and Cardiovascular Risk in Children: An American Heart Association Scientific Statement From the Atherosclerosis, Hypertension, and Obesity in the Young Committee (Council on Cardiovascular Disease in the Young) and Circulation. 2003;107:1448–1453.

11. Velasco-Contreras ME. Evolution of the type 2 diabetes mellitus epidemia in insured population at the IMSS. Rev Med Inst Mex Seguro Soc. 2016;54:490–503.

12. American Diabetes Association. Standards of medical care in diabetes-2016. Diabetes Care. 2016;39:S1–S2.

13. Väätäinen S, Cederberg H, Roine R, Keinänen-Kiukaanniemi S, Saramies J, Uusitalo H, et al. Does future diabetes risk impair current quality of life? A cross-sectional study of health-related quality of life in relation to the Finnish diabetes risk score (FINDRISC). PLoS One. 2016;11:1–15.

14. Zurita-Cruz JN, Manuel-Apolinar L, Arellano-Flores ML, Gutierrez-Gonzalez A, Najera-Ahumada AG, Cisneros-González N. Health and quality of life outcomes impairment of quality of life in type 2 diabetes mellitus: A cross-sectional study. Health Qual Life Outcomes. 2018;16.

15. Gayda M, Juneau M, Tardif JC, Harel F, Levesque SNA. Cardiometabolic and traditional cardiovascular risk factors and their potential impact on macrovascular and microvascular function: preliminary data. Clin Hemorheol Microcirc. 2015;59:53–65.

16. Stroker R KJ. New insights on oxidative stress in the in the artery Wall. J ThrombHaemost. 2005;3:1825–1834.

17. Verma S, Hussain ME. Obesity and diabetes: An update. Diabetes MetabSyndr Clin Res Rev. 2017;11:73–79.

18. Carey RM WP 2017 AHGWC. Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Synopsis of the 2017 American College of Cardiology/American Heart Association Hypertension Guideline. Ann Intern Med. 2018;168:351–358.

19. Engin A. The Definition and Prevalence of Obesity and Metabolic Syndrome. Adv Exp Med Biol. 2017;960:1–17.

20. Mata-Cases M, Franch-Nadal J, Real J, Cedenilla MD. Prevalence and coprevalence of chronic comorbid conditions in patients with type 2 diabetes in Catalonia: a population-based cross-sectional study. BMJ Open. 2019;9:e031281.

21. Hermans MP DN. Prevalence and co-prevalence of comorbidities in Belgian patients with type 2 diabetes mellitus: a transversal, descriptive study. Acta Clin Belg. 2018;73:68–74.

22. Iglay K, Hannachi H, Joseph Howie P, Xu J, Li X, Engel SS, et al. Prevalence and co-prevalence of comorbidities among patients with type 2 diabetes mellitus. Curr Med Res Opin. 2016;32:1243–1252.

23. Stehouwer CDA. Microvascular Dysfunction and Hyperglycemia: A Vicious Cycle With Widespread Consequences. Diabetes. 2018;67:1729–1741.

24. Pérez-Pevida B, Llavero M, Gargallo J EJ. Complicaciones microvasculares de la diabetes. Medicine (Baltimore). 2016;12:958–970.

25. Meza R, Barrientos-Gutierrez T, Rojas-Martinez R, Reynoso-Noverón N, Palacio-Mejia LS, Lazcano-Ponce H-ÁM. Burden of Type 2 Diabetes in Mexico: Past, Current and Future Prevalence and Incidence Rates. Prev Med. 2015;81:445–550.

26. Rojas-Martínez R, Basto-Abreu A, Aguilar-Salinas CA, Zárate-Rojas E, Villalpando S B-GT. Prevalencia de diabetes por diagnóstico médico previo en México. Salud Publica Mex. 2018;60.