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Pererspective in the Identification of the Risk Factors for Develop Type 2 Diabetes Mellitus and Laboratory Tests for Diagnosis

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Abstract

Background: Diabetes is a condition characterized by insulin resistance that triggers hyperglycemia, causing a poor quality of life in the patient and complications with other diseases. Continuous monitoring of blood glucose levels is important for its prevention and control. It is essential. It is important to review, analyze and emphasize information about the main factors of its development, as well as laboratory tests for diagnosis.

Aim: Document the main predisposing factors for developing Type 2 Diabetes Mellitus and the laboratory tests useful for its diagnosis.

Methods: This research is observational and cross-sectional

in nature, written in accordance with the PRISMA 2020 Declaration, using platforms such as Scielo, Elsevier, Governmental, PubMed and ResearchGate, obtaining 23 studies useful in research in the period 2000 – 2023.

Results: 23 references were analyzed in detail, the majority being from the period 2016 to 2020, mainly presenting overweight/obesity, as well as a sedentary lifestyle as the main risk factor.

Conclusion: It is important to keep information up to date. Overweight and obesity, along with a sedentary lifestyle and poor diet, are the main predisposing factors for development.

Keywords: Research, Biochemistry, Literature Review, Diabetes Mellitus, Glucose, Obesity

Introduction

Diabetes mellitus is a condition that belongs to a heterogeneous group of non-communicable metabolic diseases characterized by hyperglycemia that in the long run can cause damage to the heart, eyes, nerves, kidneys and blood vessels. (Pan American Health Organization (PAHO), 2020). In 2019, non-communicable diseases (NCDs) represented 73.6% of deaths worldwide, of which 284,049 were due to type 2 diabetes mellitus. Mortality from this disease has increased by 70% since 2000 and belongs to one of the ten leading causes of death worldwide. In Mexico, Diabetes Mellitus is responsible for 74.6% of total deaths due to both types 1 and 2 (DIABETES Statistics 2022 INEGI), it occupies third place in the epidemiological panorama of non-communicable diseases with a incidence of 186.7 cases per 100,000 inhabitants (Epidemiological Panorama of Non-Communicable Diseases in Mexico 2021 GOB) and in the state of Oaxaca it ranks sixth in mortality with a rate of 13.5 per 100,000 inhabitants. (Statistics a Propocito de la DIABETES 2022 INEGI). Observational and experimental studies have been carried out on factors predisposing to the development of type 2 diabetes mellitus (DM2) in different states of Mexico such as Campeche, Edo. Of Mexico, Sinaloa, particularly, in the state of Oaxaca we do not have extensive and current information on the Internet, which is why it is important to review, analyze and emphasize the information.

T2DM is mainly characterized by insulin resistance (Reyes *et al.*, 2008) ^[27], this peptide produced and secreted in the pancreas (Hubbard, 2013) ^[15] is activated when it binds to an integral membrane glycoprotein (Heesom *et al.*, 1997) ^[13] promoting glucose absorption mainly in muscle and adipose tissue (Gutiérrez-Rodelo *et al.*, 2017) ^[12], this resistance causes pancreatic β cells to enter a process of compensatory hyperinsulinemia, deteriorating the cells, causing a decrease in insulin receptors, increased phosphorylation status in insulin receptor residues, as well as defects in the expression and function of the group 4 glucose transporter, causing glucose integration into muscle and adipose tissue to be reduced, promoting metabolic alterations that give rise to hyperglycemia and DM2 (Reyes *et al.*, 2008) ^[27] previously called non-insulin dependent, in most cases it is not diagnosed early, but until several years later when it already causes complications. Emphasizing the factors that lead to the development of this disease and the main tests for early diagnosis are of great importance to promote the creation of strategies

for the prevention and control of T2DM. The increase in DM2 as a silent epidemic causes a decrease in performance in the population, modifiable and non-modifiable factors contribute, so intervention mainly in modifiable factors causes a positive effect on the development of the disease (Deng *et al.*, 2020) [6]. The risk factors for T2DM are a combination of genetic, metabolic, and environmental factors that are related and contribute to its prevalence (Galicia-Garcia *et al.*, 2020) [11].

For these reason, the objective of this review was to document the main predisposing factors for developing Type 2 Diabetes Mellitus and the laboratory tests useful for its diagnosis in Oaxaca.

Development factors of type 2 diabetes mellitus

Studies have been carried out around the world identifying these factors, there are theories about the causality of DM2, which give an overview of the interaction of the environment with the human genome and other risk factors, the genetic and molecular heterogeneity of DM2 is multifactorial in nature, impacting chronic complications and pharmacological response. The human being presents an epigenetic mark that is inherited and generated. During conception, childhood, adolescence and puberty, epigenetic alterations can occur that cause the development of conditions such as DM2. Unlike non-modifiable factors such as genetic polymorphisms that are permanent, modifiable factors such as stress, little exercise, a poor diet, inflammatory processes, hyperglycemia, obesity and oxidative stress cause overexpression of some of the genes. (Castro-Juárez *et al.*, 2017) [4].

Phenotypes at birth associated with diseases in adulthood have recently been identified. One of the genes that could be involved is the gene that encodes aromatase, CYP19A1, which converts estrogens into androgens in peripheral tissues, such as fatty tissue and the liver. Muscles, thin newborns tend to be resistant to insulin, infants of short stature and high weight are correlated with lower insulin production, causing DM2 in adults, preliminary epidemiological studies in the Mexican population regarding this gene show its association with DM2. (Castro-Juárez *et al.*, 2017) [4].

In the population of western Mexico, the influence of the TNFR1 gene polymorphism, in the -388A/C promoter region, has been found as a risk marker for hepatitis C infection and for the development of DM2. Recently, the importance of melatonin has been regained in the study of DM2; its irregular production is related to IR and DM2, in addition to this, the influence of polymorphisms in the MTNR1B gene (melatonin receptor 1b), with the decrease in response to insulin in its early phase and culminating in the development of DM2. In patients who already have the disease and early onset, the loss of a 1.3 Mb gap in the subtelomeric region of the 4p16.3 locus has also been detected. The Alu insertion in the MUTYH gene has also been associated with T2DM. (Ramirez-Garcia *et al.*, 2013) [16].

In Chile, Ana María Leiva *et al.* (Petermann Rocha *et al.*, 2018) [25] analyzed 4700 people, of which 538 were diabetic, obtaining a lower level of education, low economic income, higher body weight, higher prevalence of general and central obesity, physically inactive, higher consumption of salt, fruits and vegetables, presence of high blood pressure, with greater metabolic complications, being those with a higher

risk of developing DM2 compared to the rest who were non-diabetics, these being modifiable factors, belonging to the group of people with an age > 45 years old and having a family history with DM2 are non-modifiable factors. (Petermann Rocha *et al.*, 2018) [25], on the other hand, in Matanzas Cuba a study of 628 people carried out by Belkis Sánchez *et al.* Demonstrated that inadequate diet and smoking are associated with the highest occurrence of DM2, being statistically significantly modifiable risk factors (Sánchez Martínez *et al.*, 2020) [29], studies have also been carried out on eating habits in the same city, predominating obesity associated with inadequate eating patterns, with a percentage association between poor eating habits and an elevated risk of suffering from DM2 (Vega Jiménez, 2020) [32].

In the community of Joa del Canton, Jipijapa Ecuador, a study was carried out on 58 patients to determine the predisposing factors to the development of DM2 in their population, highlighting mainly overweight and obesity; however, the entire population studied has a history of at least one family member with DM2 and most of them have bad food consumption habits (Bravo Bonoso *et al.*, 2020) [3], in the same country, but in the city of Cuenca, a study was carried out on 379 people, who in their The majority were overweight and obese, had poor eating habits, as well as the presence of high blood pressure and family members who had DM2, which are predisposing factors to the development of DM2 (Uyaguari-Matute *et al.*, 2021) [31]. In Barranquilla Colombia, a study was carried out to know the risk and modifiable factors of developing DM2 by applying the Finnish Diabetes Risk Score test to 362 patients, which showed that the most frequently observed risk factors are sedentary lifestyle, family history of diabetes and overweight/obesity, all of these factors showed a significant association with a higher risk of DM2, a fasting blood glucose test was also performed, finding that 26.67% of the participants had altered blood glucose (Moreno *et al.*, 2020) [20].

In the state of Jalisco Mexico, Luis Flores *et al.* They carried out a study in a low-income population with a sample of 304 mestizos to estimate the association of the repeat (CAG)_n of the ATXN2 gene in a Mexican population with DM2 diabetes mellitus. Obtaining a statistically significant association with a X²=31.8 and p=0.0001 of the (CAG)_n polymorphism of the ATXN2 gene with the development of type 2 DM in this population. (Flores-Alvarado *et al.*, 2016). In the same state Sergio Ramírez *et al.* They carried out a study of the SNP rs1345365 of the ELMO1 gene and its association with DM2, using 148 individuals with DM2, 156 without DM2, but with cardiovascular risk factors and 296 healthy people, using different genetic epidemiology models to establish the association, by purchasing their Distribution of alleles of the SNP rs1345365 found that the G allele occurred more frequently in diabetic patients with 60%, the para-dominant model determined the presence of the G allele, which suggests the association of the SNP rs1345365 with the development of DM2. (Alberto Ramirez-Garcia *et al.*, 2015) [2].

In the state of Sinaloa Mexico, studies have been carried out on the development of DM2, a study with a sample of 256 individuals from a rural community showed that the indicators with the highest risk for the development of DM2 are high blood pressure (HTN) and overweight. And obesity, increasing the risk of DM2 with increasing obesity

and decreasing it with increasing personal education (Heredia & Gallegos Cabriaes, 2022) [14]. Also in the state of Campeche, an observational study was carried out on 213 individuals, between 30 and 60 years of age with a diagnosis of DM2, finding that the risk factors in the population were mainly obesity and cholesterol - triglycerides, as well as hereditary history. Of DM2, these being predominant in women, increasing the risk in proportion to age (Sarabia Alcocer *et al.*, 2016) [30]. In the state of Oaxaca, only 1 study was found on factors for the development of DM2, Fernando Luna *et al.* Studied 130 women from the Isthmus of Tehuantepec, more than 90% were overweight and obese, reporting having low schooling, being factors in the development of DM2 taking into account the population studied [9].

Diagnostic tests of diabetes mellitus

It is well known that tests for T2DM include fasting plasma glucose (FPG), oral glucose tolerance test (OGTT) and glycated hemoglobin HbA1c test. (Meijnikman *et al.*, 2017) [19] Venous plasma glucose is the conventional method to measure and report diabetes mellitus, it should be analyzed immediately after obtaining the sample, if this is not the case, it should be collected in a tube with glucose inhibitors.

glycolysis, centrifuge immediately to obtain the plasma and freeze until the time of analysis, however, in low-resource settings, patients who monitor their blood glucose levels with personal glucometers (Pan American Health Organization (PAHO), 2020) are recommended. Perform a periodic checkup with laboratory tests to verify the values obtained by your glucometer with acceptable limits of ±15% [18].

The new diagnostic criteria are based on lower glucose values in order to detect in time the stage in which the patient is, facilitating management strategies and starting effective treatment. Normal fasting glucose values less than 100 mg/dL and 140 mg/dL two hours after an OGTT present normoglycemia; abnormalities in glucose metabolism prior to the development of DM2 are altered fasting glucose with values of between 100 mg/dl and 125 mg/dl and intolerance to the glucose test when the values at 2 hours range between 140 mg/dl and 199 mg/dl, after ingesting 75 g of glucose, this known stage as hyperglycemia and values that exceed the upper normal limits in a causal glycemia of 200 mg/dl is a glycemia causal of diabetes mellitus. [28] (ALAD, 2019) [1]. The Pan American Health Organization in its 2020 cut presents the diagnostic criteria for diabetes mellitus represented in Table 1.

Table 1: Diagnostic criteria for diabetes mellitus (Pan American Health Organization (PAHO), 2020) Pan American Health Organization PAHO

Measurement	Diagnostic limit value	Observation
Fasting venous or capillary plasma glucose	≥ 7.0 mmol/L 126 mg/dL	The least expensive measurement, but it is difficult to ensure fasting status
Venous plasma glucose 2 hours after oral glucose loading	≥ 11.1 mmol/L 200 mg/dL	Difficult to carry out and expensive, it is difficult to ensure the fasting state
Capillary plasma glucose 2 hours after oral glucose loading	≥ 12.2 mmol/L 220 mg/dL	Difficult to carry out and expensive, it is difficult to ensure the fasting state
Random plasma glucose	≥ 11.1 mmol/L 200 mg/dL	Use only in the presence of symptoms
HbA1c	≥ 6.5 % ≥ 48 mmol/mol	Indirect method Lower viability in the same person than in basal glycemia Fasting is not needed It is more expensive than basal blood glucose It may be inaccurate in the case of certain conditions (hemoglobinopathies, renal failure, some anemias, disorders with rapid erythrocyte turnover)

However, it is well known that HbA1c can be performed non-fasting, being preferred by doctors and leaving aside the OGTT. Abraham S. Meijnikman *et al.* Conducted a study demonstrating that not performing an OGTT is of great relevance in the diagnosis of DM2 in patients with risk factors such as overweight and obesity (Meijnikman *et al.*, 2017) [19]. Patients who carry these factors in their daily lives without realizing that they are getting closer to suffering from diabetes, studies have been carried out that demonstrate poor glycemic control in patients already diagnosed. In Villavicencio Colombia, a study of 453 patients showed that individuals with hyperglycemia with HbA1c values > 7% have a greater risk of having inadequate glycemic control (Piñeros-Garzón & Rodríguez-Hernández, 2018) [26].

In the State of Mexico, a study was carried out consisting of 239 people previously diagnosed with DM2, which demonstrated that low quality of life and low education are factors that lead to poor self-care of the disease, increasing the risk in women who They have less social support, cultural history, their beliefs, less satisfaction in quality of

life that contributes to a lack of self-care and the development of complications. (Cruz-Bello *et al.*, 2014) [5]. Each population in the world has different physical, geographical, biological, cultural and ethnic characteristics. In Mexico, diabetes mellitus is governed under the control of the Official Mexican Standard 015 for the prevention, treatment and diagnosis of diabetes mellitus NOM-015-SSA1 -2010, which is developed specifically in the Mexican population, the detection of prediabetes and the diagnosis of DM2 must be carried out in the population from the age of 20, even if at puberty the patient presents alarm due to obesity and factors risk assessment every three years must be carried out beforehand. Early detection occurs when capillary blood glucose is <100 mg/dl and there are no risk factors.

At least the same test will be performed over a period of 3 years, if capillary blood glucose detection is <100. mg/dl and the patient has obesity, a sedentary lifestyle, smoking, he or she must be attended to and trained to have a correct diet, a physical activity plan and stop smoking, and repeat the detection in a year, however, if the blood glucose is

>100 mg/dl fasting or casually >140 mg/dl, the diagnosis is confirmed with the measurement of fasting plasma glucose for at least 8 hours. NOM 015 SSA1 2010 establishes a diagnosis of prediabetes when the patient has a fasting glucose ≥ 100 mg/dl and when the oral glucose load 2 hours after loading 75 g of anhydrous glucose is ≥ 140 mg/dl and ≤ 199 mg/dl. Likewise, the diagnosis of diabetes mellitus is established if any of the following characteristics are met: Presence of classic symptoms and a casual plasma glucose > 200 mg/dl, fasting plasma glucose > 126 mg/dl or a glucose > 200 mg /dl two hours after an oral load of 75 g of anhydrous glucose dissolved in water, without ruling out that in the fasting glucose test or in the OGTT or even in the absence of symptoms of hyperglycemia, these criteria must be confirmed by repeating the test on a different day^[19].

Methods

This research is cross-sectional observational in nature, written in accordance with the PRISMA 2020 Statement: An updated guide for reporting systematic reviews. A randomized search of articles was carried out on the population, it consists of articles from the network belonging to scientific dissemination platforms, for the selection of the articles a series of inclusion criteria were included such as articles from the year 2000 to 2023, articles on factors of DM2, articles with 1 or more descriptions of predisposing factors, experimental and observational articles on the development of DM2, articles on patients with DM2

already diagnosed, excluding those articles that referred to the development of DM1, articles on metabolic diseases in children, articles on signs and symptoms of T2DM and eliminating articles that do not contain references, fragments of incomplete articles, and outdated information from years before 2000. There were no rejections of articles based on criteria of sex, language, and population size.

On September 5, 2022, the search for literature on the Internet regarding the development factors of DM2 internationally, nationally and stately, as well as laboratory tests for its diagnosis, belonging to scientific dissemination platforms such as, PubMed, ResearchGate, Elsevier, Scielo and official government pages, international organizations, using keywords to construct specific and comprehensive searches on the topic, eligible information was identified in the first instance by titles and summaries of the text, subsequently an analysis of the text was carried out complete in conjunction with the inclusion, exclusion and elimination criteria, to end with an analysis of the full text of the articles that were selected by inclusion, analyzing the factors to the development of DM2 in each article, thus compiling the data from each publication to be attached to the database on the Excel platform and to the Mendeley platform for the management of bibliographic references and research documents. Table 2 shows the platform of origin of the information, the name of the publication and the date of review.

Table 2: Presentation of information by scientific platform and search date

Platform	Qualification	Review date
Governmental	ALAD 2019	22 of january 2023
	Prevalence and factors associated with DM2 in the indigenous population of Mexico: Systematic review	22 of january 2023
	Manual of technical and administrative standards of the diabetes mellitus program	24 of may 2023
	Official Mexican Standard NOM-015-SSA2-2010, For the prevention, treatment and control of diabetes mellitus	25 of may 2023
Scielo	Factors Associated with the Development of Type 2 Diabetes Mellitus in Chile	5 of october 2022
	Risk of DM2 and its determinants	5 de october 2022
	Case-control study on risk factors for DM2 in older adults	5 of october 2022
	Risk factors associated with glycemic control and metabolic syndrome in patients with DM2	24 of october 2022
	Definition, classification and diagnosis of Diabetes mellitus.	1 of june 2023
	Association between type 2 diabetes and physical activity in individuals with family history of diabetes	23 of august 2023
	Modifiable factors and risk of type 2 diabetes mellitus in young adults: A cross-sectional study	28 of august 2023
	Eating habits and risk of DM2 in individuals with a diagnosis of obesity	30 of august 2023
PubMed	Risk factors for developing diabetes mellitus II	1 of september 2023
	Gender and self-care of DM2 in the State of Mexico	1 of september 2023
	Diet, lifestyle, and the risk of type 2 diabetes mellitus in women.	19 of september 2023
Elsevier	Not performing an OGTT results in significant underdiagnosis of (pre)diabetes in a high-risk adult Caucasian population	23 of june 2023
	Hematic biochemistry	1 of june 2023
ResearchGate	Epidemiology and social determinants associated with obesity and DM2 in Mexico	1 of september 2023
	Epidemiology, risk factors across the spectrum of age-related metabolic diseases. Journal of Trace Elements in Medicine and Biology	5 of september 2022
ResearchGate	Characterization of risk factors for DM2 using the Findrisk test in a population aged 30 to 50 years from Medellín, Colombia	5 of october 2022
	Lifestyle and risk of suffering from diabetes mellitus in the Joa community.	24 of october 2022

For all scientific dissemination platforms, phrases such as “risk factors for the development of type 2 diabetes mellitus” “development of type 2 diabetes” “diagnostic tests for diabetes mellitus” “history of type 2 diabetes mellitus” were used, using the filter year of publication and based on

the inclusion criteria, until September 1, 2023, identifying the terms searched in the Titles and summaries of the article. For the review of each selected article, the title was read followed by the abstract by 2 reviewers independently, before the complete analysis of the text. If the article met the

selection and inclusion criteria, the full text was read. To precisely identify the predisposing factors for the development of DM2 and the laboratory tests for its diagnosis mentioned by the corresponding author, once the full text was analyzed, the information was taken and reported in the database, to continue with the addition of the full text to the Mendeley platform, the articles in English were translated by the “Site translator” software. For the study, independent variables were used such as the “information providing platform” “the year of publication” “type of information found, article, book or report” “origin of international, national and state information” and “background mentioned about DM2”. Because the research refers to a systematic review, the factors described are only informative; it is not intended to identify them in the population through experimental research. The analysis of the results was carried out with the database obtained from the collected articles, grouping the factors to develop DM2 in the population.

Results

120 eligible references in the network on DM2 were analyzed, of which 77 were discarded due to the exclusion and elimination criteria, the remaining 43 studies were included in the study, of which, 23 for the identification of the factors to develop DM2. And diagnostic tests, as shown in Fig 1.

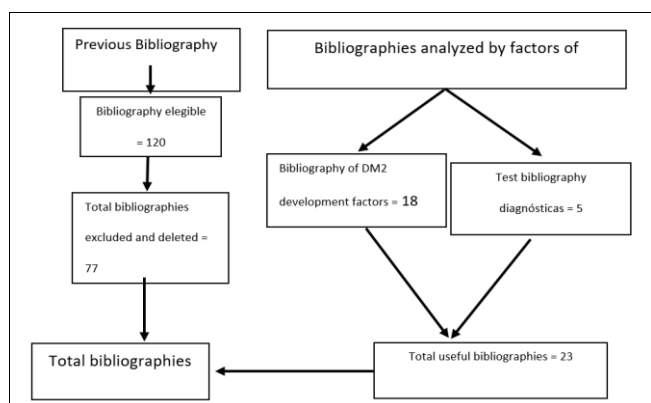


Fig 1: Bibliography analyzed in the study

Of the bibliography selected according to inclusion criteria, 53.48% correspond to those analyzed for the identification of predisposing factors to the development of DM2 and laboratory tests for its diagnosis. Of the 23 references analyzed, 56.52% correspond to Scielo, 13.04% to the Elsevier platform, 13.04% to government, 8.69% to PubMed and 8.69% to the ResearchGate platform. According to the year of publication of each bibliography with the established periods 2000 – 2023, 5-year groups were established, from 2000 to 2005 8.69% corresponds to this group; from 2006 to 2010 4.34%; 2011 to 2015 21.73% of the bibliography; from 2015 to 2020 52.17% and from 2021 to 2023 13.04% of the references analyzed. At the international level, 69.56% corresponds to Latin America, 26.08% at the national level and 4.34% at the state level. The risk factors for the development of DM2 were associated by convenience in groups, 60.86% of the articles mention overweight/obesity, higher BMI and poor diet as risk factors; 52.17% mention a sedentary lifestyle and low quality of life as risk factors; 17.39% document that low/no education, poverty and

belonging to a certain indigenous population serve as risk factors; Likewise, 17.39% mention that having a family history with diabetes mellitus increases the risk of developing the disease and 8.69% detail that alcoholism and smoking without factors promote the development of T2DM, as shown in Fig 2.

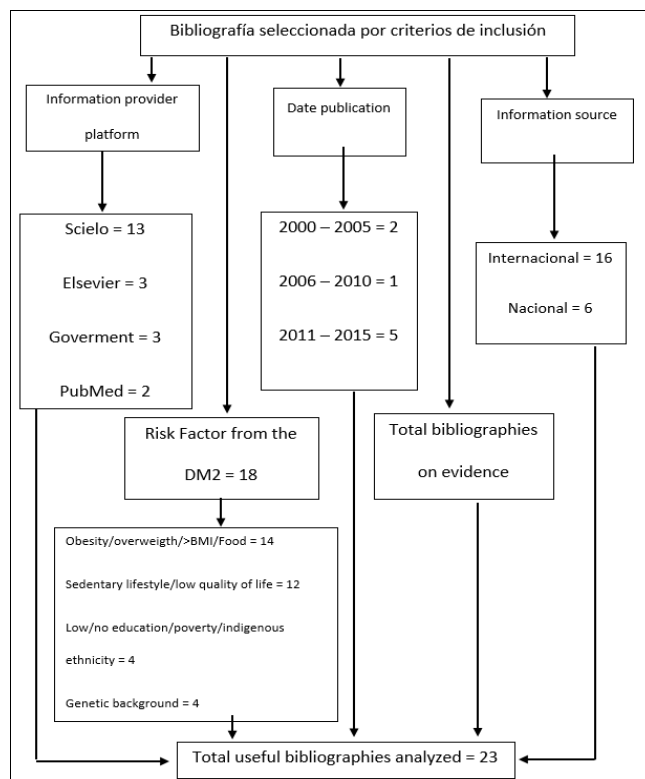


Fig 2: Bibliography analyzed in the study

Discussion

This review highlights the importance of the factors that lead to the development of DM2 that go unnoticed by the general population every day, increasing the morbidity caused by the untimely detection of the disease and the tests that must be performed to achieve a good outcome. Glycemic control and reduce or avoid the risk of suffering from type 2 diabetes mellitus, the majority of international literature mentions overweight/obesity and a higher body mass index (BMI) as a decisive factor in contracting the disease, experimental research with different sample numbers that show similar results, the majority of the population has this condition, however these studies show that obesity and overweight are related to other factors.

In Chile, the study of 4700 people by Ana María *et al.* Which shows that they also have high blood pressure, live in poverty and are of adult age; in Cuba by Vega Jiménez *et al.* The study carried out on 628 patients where they also had a poor diet; in Ecuador by Bravo Bonoso *et al* with a sample of 379 people with risk factors such as high blood pressure and poor diet, in Colombia by Moreno CEB *et al* where a population of 362 patients at risk due to a sedentary lifestyle and a family history of diabetes mellitus was studied. Finding the same results at the national level, in the state of Sonora by Heredia *et al* with a sample of 256 patients presenting mainly overweight/obesity and high blood pressure; as well as in Campeche by Sarabia Alcocer *et al* where it was documented that belonging to the female gender, having high cholesterol and triglycerides, being of

legal age and having a family history add to the risk factors with a population of 213 patients; and finally the state of Oaxaca by Fernando Luna *et al.*, obtaining results from 130 women that low schooling and family history are also at risk for promoting the development of T2 DM.

The combination of several factors further favors the development of the disease, which develops chronically until it generates moderate, severe and serious complications, which is why performing a fasting glucose test is of utmost importance to know and maintain good control with values ≤ 100 mg/dl indicated by NOM 015 SSA1 2010. The best strategy to identify risk factors and maintain good control in their laboratories with the person who has DM2, is the direct observation of their behaviors in daily life and actions that the individual assumes in the face of his illness. (Cruz-Bello *et al.*, 2014) [5] The state of Oaxaca presents the last update in 2016 on the state strategy for the prevention and control of overweight, obesity and diabetes in this state, being important to update said information to the current knowledge of researchers about this disease and generate the necessary research for prevention and control strategies.

Conclusion

It is important to keep the information updated to know and reaffirm the monitoring and changes that the diseases have over the years, DM2 condemns patients to a low quality of life, considering their risk factors associated with its development is essential to generate strategies for prevention and control. Overweight and obesity, combined with a sedentary lifestyle and poor diet, are the main predisposing factors for the development of DM2; however, having a family history with diabetes mellitus increases the risk and its complications mentioned in the literature. The measures to be taken in the population such as the change in their daily activities, encouraging the population to undergo control studies, such as fasting glucose, oral glucose tolerance and glycosylated hemoglobin, can prevent or know the phase of the disease., thus improving the patient's quality of life, this research is useful for the generation of public health strategies to reduce the increase in new cases of DM2.

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