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# Comprehensive approach to type 2 diabetes mellitus: Crucial links to obesity, kidney and cardiovascular disease

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**ABSTRACT**
Type 2 Diabetes Mellitus (DM2) is a systematic inflammatory disease with high prevalence and incidence worldwide. The objective of this article is to make an updated review of the disease, its new definitions, the cardiovascular and renal risk and other pathologies that it entails, as well as its incidence in overweight and obese patients. This document focuses on addressing the most relevant pathophysiological and clinical aspects of the disease.

**Keywords:** Type 2 diabetes, Obesity, Kidney disease, Treatment.

## 1 INTRODUCTION

Type 2 diabetes is a chronic disease that affects how the body uses sugar, or glucose, as an energy source. This condition is characterized by two main problems: insulin resistance and insufficient insulin production by the pancreas (1).

Insulin is a hormone produced by the pancreas that plays a key role in controlling blood sugar levels. This allows the body's cells to absorb glucose from the blood and use it as an energy source. However, in type 2 diabetes, the cells become insulin resistant, meaning they can't respond properly to the hormone. As a result, blood sugar can't enter the cells efficiently, leading to a spike in blood sugar called hyperglycemia. In addition to insulin resistance, in type 2 diabetes, the pancreas does not produce enough insulin to compensate for cellular resistance. This further exacerbates the problem and leads to high blood sugar levels. Type 2 diabetes is a chronic disease that may require lifelong treatment and risk factors include genetics, obesity, physical inactivity, and diet. Treatment usually involves lifestyle changes, such as diet.

In addition to these specific complications, type 2 diabetes increases the risk of other serious diseases, such as certain types of cancer, liver disease, sleep disorders, and mental health problems. Importantly, proper blood sugar control through medication, diet, and exercise can help reduce the risk of these complications and improve the quality of life for people with type 2 diabetes (2).

Therefore, people with this condition should work closely with their healthcare professionals to maintain optimal blood sugar levels and minimize the associated risks. Based on the above, it was decided to review the following formulation of the problem: What are the relationships between type 2 diabetes, obesity, and the combined treatment of kidney and cardiovascular diseases, and what are the most effective strategies to prevent and treat these conditions together? Analyze the key links between integrated treatment approaches for type 2 diabetes, obesity, kidney disease, and cardiovascular disease to identify and develop effective preventive and combination treatment strategies that meet their respective overall goals. these conditions.

About 62 million people in the United States (422 million worldwide) are living with type 2 diabetes, mostly in low- and middle-income countries, and 244,084 deaths per year (1.5 million worldwide) are directly linked to diabetes. The incidence and prevalence of diabetes have steadily increased in recent decades. The number has tripled in the region since 1980 and is expected to reach 109 million by 2040, according to the ninth edition of the Diabetes Atlas (3).

A comprehensive response to type 2 diabetes from a global public health perspective is essential. It includes not only early diagnosis of the disease and appropriate treatment, but also focuses on prevention. Promoting a healthy lifestyle, including a balanced diet and regular physical activity, is essential to preventing type 2 diabetes and its complications. In addition, there is a need to improve access to health care and medicines and treatments for people with diabetes in low- and middle-income countries, where the burden of the disease is particularly high (4).

According to data from Paraguay's National Diabetes Program, from January to October 2020, 10% of the Paraguayan population suffers from diabetes, approximately 700,000 people live with this pathology, of which only 50% are aware of their disease (5). 90% of people with this disease have type 2 diabetes mellitus, while 10% have type 1. In the latter group, most of those affected are minors. The Ministry of Public Health is responsible for 100,000 persons, of whom 66 per cent are women and 34 per cent are men. As for pregnant women, the number of participants reached 3,500 and the number of children and adolescents with type 1 diabetes reached 1,800. Investments in injecting insulin to patients amounted to Gs. 36,767,044.00, medicines and supplements to a total of Gs. 54,667,336,000 (6)

Based on this previous knowledge, the need for research arises due to its high prevalence since this disease affects millions of people worldwide and its incidence continues to increase due to factors such as population aging, urbanization and changes in lifestyle, complexity and diversity.

## 2 MATERIALS AND METHODS

In this research, the methodology used was the literature review, which involved a systematic approach to identify, compile, evaluate and analyze the existing literature on the particular topic. Initially, the research topic was defined, the problem statement and the objective of the literature

review. Subsequently, the sources of information that were used were determined, such as academic databases, digital libraries, scientific journals and relevant books such as Scopus, Medline, Cicco, SciELO and PubMed. Inclusion and exclusion criteria were defined to determine the various articles that meet the research requirements, taking into account the year of publication, language, and type of study. The selected articles were organized in a logical and structured manner, of which 11 were selected based on criteria and relevance to the objectives. Using charts, graphs, and concept maps to aid in the process. A literature review was written, including an introduction, a literature review, and an analysis and discussion of the findings and conclusions. Finally, a list of bibliographic references was prepared that includes all the documents and studies cited in its review.

## 3 DIABESITY

Obesity is a chronic relapsing disease with a complex etiology developed from interactions of genetic, social, behavioral, psychological, metabolic, cellular, and molecular factors (Figure 1). It is defined as an abnormal or excessive accumulation of adipose tissue associated with body weight, which can be harmful to health. It is a risk factor for chronic diseases such as type 2 diabetes, affecting both sexes and all socioeconomic and age groups, although in different ways. Treatment should be multidisciplinary, based on lifestyle changes (diet and physical activity) (7).

Figure 1. Relationship of the development of obesity.



Source: Prepared by author Kaufer-Horwitz M, Pérez Hernández JF, 2022.

There are different diseases that are associated with a higher incidence in obese patients, such as systemic arterial hypertension, cerebral vascular event, acute myocardial infarction, dyslipidemia, diabetes mellitus 2, depression, obstructive sleep apnea syndrome, osteoarthritis, among others. Excess weight is associated with insulin resistance, impaired glucose homeostasis, and other cardiovascular risk factors seen in patients with diabetes mellitus 2, including hypertension and dyslipidemia. The localization of fat in the body has a significant effect on health; Especially in the visceral area, liver, muscle, and pancreatic beta cells may worsen glucose tolerance in patients with diabetes mellitus 2 (8).

Obesity is one of the most important risk factors for type 2 diabetes mellitus and it is estimated that between 60 and 90% of patients are overweight or obese before diagnosis. Being overweight increases the risk of coronary heart disease in healthy individuals and this association may be even more important in people with diabetes, it is responsible for more than 75% of deaths. A recent cross-sectional study of 44,000 patients with diabetes mellitus2 reported that 80% were overweight, of whom 37% were obese (8).

The link between obesity and diabetes has long been known, and obesity has been shown to be a strong predictor of type 2 diabetes. The risk of developing diabetes is proportional to the degree of obesity and even increases with weight gain; This is particularly evident in childhood and in populations that are genetically predisposed to the disease and predominantly obese (7).

This relationship has led to the creation of the term "diabesity", which is considered the new disease of the 21st century. Insulin resistance is a key factor in the progression to type 2 diabetes and is the response of adipose tissue to elevated levels of free fatty acids (lipotoxicity), a consequence of obesity, which causes the pancreas to secrete large amounts of insulin, leading to insulin production. resistance over time. resistance. This hurts its performance. Currently, there are several herbal, pharmaceutical and surgical alternatives for the treatment of diabetes, in which prevention is a crucial aspect (7).

Diabetes prevention should be considered an important part of public health policy around the world. A healthy diet and adherence to the patient's lifestyle are essential in the treatment of diabetes. Diabetics are advised to eat moderate amounts of slow-absorbing carbohydrates found in certain legumes and grains, fish and poultry proteins, and to cut back on red meat and dairy products. As for fats, trans or processed fats should be avoided because they raise LDL cholesterol levels, and unsaturated fats should be preferred over saturated fats (9).

## 4 DIABETIC KIDNEY DISEASE

One of the most frequent chronic complications presented by diabetic patients is diabetic kidney disease (DKD), a pathology whose incidence has doubled in the last decade mainly due to the concomitant increase in patients with diabetes mellitus. It is estimated that approximately 30% to 50% of adults with T2DM have renal involvement from the time of diagnosis, which is a marker of prognosis and quality of life. Recent data suggest that 843 million people worldwide have CKD with an increase in mortality, being more prevalent in patients with DM (diabetes mellitus), hypertension (hypertension), the elderly, and women (10).

International guidelines for the management of diabetes mellitus recommend screening for DRD in all people with type 2 DM by measuring renal function and albuminuria at the time of diagnosis and annually thereafter. The diagnosis of DRD is clinical and is based on three basic aspects: decreased

renal function, reduced GFR and the presence of albuminuria. Knowledge of the pathophysiology and natural history of DRD has allowed us to restructure its treatment along specific axes, which include: metabolic control, reducing or slowing the progression of kidney disease, and reducing cardiovascular outcomes (10).

One of the pillars in the treatment of DKD is blood pressure control. Blood pressure (BP) in the glomerular capillary is an impact factor in the incidence and progression of RDD, strict control of BP levels decreases the degree of albuminuria, slows the progression of CKD and decreases the incidence of cardiovascular events. For the use of finerenone, it is recommended for use with GFR greater than 25 cc/min and with serum potassium levels less than 5 meq/l. Regarding antidiabetic drugs, in 2008, the Food and Drug Administration (FDA) of the United States gave guidelines to the pharmaceutical industry on the need to evaluate the cardiovascular risk of new antidiabetic drugs in their research studies, this led to studies with dipeptyl peptidase inhibitors (DPP-4i), new insulins, sodium glucose-type 2 cotransporter (iSGLT-2) inhibitors and glucagon-like peptide receptor type 1 (aGLP-1) agonists from a cardiovascular safety perspective. Despite all the advances in antidiabetic treatment, metformin remains a first-line drug (10).

## 5 PREVALENCE OF DIABETES

A study was also conducted at the Hospital Italiano de Buenos Aires (HIBA) in the Autonomous City of Buenos Aires, Argentina; In order to estimate the prevalence of DM, where patients with a diagnosis as a history were identified, defined by means of a multiple capture strategy and compliance with one of the following criteria: active diabetes problem (or corresponding terminological subset) loaded in the EHR, and/or a glycated hemoglobin (HbA1c) record greater than or equal to 7%, and/or two records of HbA1c greater than or equal to 6.5% (at the discretion of the investigator), and/or record of effective purchase (pharmacy withdrawal) of any hypoglycemic drug for exclusive use in diabetes or insulin in the last year. Variables related to demographics, comorbidities, metabolic control, and diabetes-related complications were requested. Macrovascular complications were defined as acute myocardial infarction (AMI), stroke, and peripheral vascular disease (PVD); and microvascular complications, retinopathy and neuropathy. Other complications included diabetic foot and amputations (11)

A total of 12,832 patients diagnosed with DM were detected out of a total of 150,725 active adult affiliated members. The overall prevalence of DM in adult patients aged 18 years as of March 2019 was 8.5% (95% CI: 8.3-8.6) (11).

Table 1 shows the overall prevalence stratified by sex and the overall prevalence stratified by age group. Figure 2 shows the stratified prevalences by sex and age group. As can be seen, the prevalence increases according to age group and seems to be consistently higher in males (11).

Table 1. Stratified prevalences.

| Variables | Prevalence | 95% confidence interval |
|---|---|---|
| Stratified by sex | | |
| Female | 7.4% (6,756/90,434) | 7.3-7.6% |
| Male | 10.1% (6,076/60,291) | 9.8-10.3% |
| Stratified by Age Group | | |
| 18-64 years | 3.9% (3,652/91,669) | 3.8-4.1% |
| 65-80 years | 15.7% (5,885/37,379) | 15.3-16.1% |
| Age 81 or older | 15.2% (3,295/21,677) | 14.7-15.6% |

Fuente: Russo, M. P., Grande-Ratti, M. F., Burgos, M. A., Molaro, A. A., & Bonella, M. B. (2023).

Figure 2. Diagram of the flow of inclusion of patients in the study.
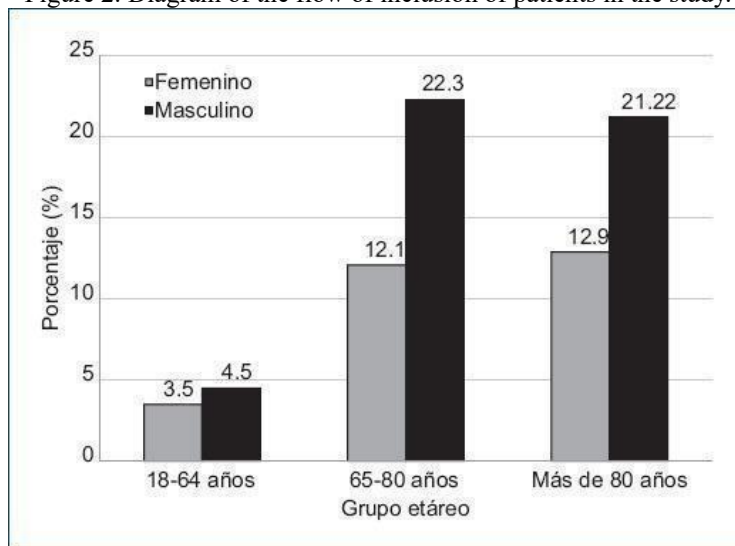


Fuente: Russo, M. P., Grande-Ratti, M. F., Burgos, M. A., Molaro, A. A., & Bonella, M. B. (2023).

Table 2 presents baseline, sociodemographic and comorbidities of patients diagnosed with diabetes. The majority of patients were female (52.6%), with an average age of 70 years, and the chronic non-communicable cardiovascular diseases that were the most frequent comorbidities were: 88% dyslipidemia, 75% hypertension, 55% obesity, 35% smoking and 7% sedentary lifestyle. Complications related to the disease are presented in Table 3, with the most frequent antecedents being AMI (11%) and stroke (8%) (11).

Table 2. Baseline characteristics of the population.

| Variables | DM (n: 12,832) |
|---|---|
| Age, in years* | 70.4% (14.4) |
| Male | 47.3% (6,076) |
| BMI, numerical value* | 29.8% (5.6) |
| Dyslipidemia (problem y/o c-LDL>100) | 88.8% (11,395) |
| High blood pressure | 74.8% (9,601) |
| Obesidad (IMC > 30) | 55.2% (7,086) |
| Overweight (BMI 25-29) | 35.6% (4,572) |
| Smoking | 34.5% (4,437) |
| Sedentary lifestyle | 6.5% (838) |
| Congestive heart failure | 8.5% (1,096) |
| Osteoporosis/osteoporotic fracture | 11.3% (1,457) |
| Depression | 17.6% (2,268) |
| Solid tumors | 15.1% (1,949) |
| Oncohaematological disease | 1.6% (206) |

Fuente: Russo, M. P., Grande-Ratti, M. F., Burgos, M. A., Molaro, A. A., & Bonella, M. B. (2023).
*Mean (standard deviation).
DM, diabetes mellitus; BMI, body mass index; LDL-C: low-density lipoprotein-linked cholesterol.

Table 3. Chronic complications associated with diabetes mellitus (DM).

| Variables | DM (n: 12,832), % (n) |
|---|---|
| Macrovascular | |
| Acute myocardial infarction | 11.5% (1,477) |
| Stroke | 8.3% (1,073) |
| Peripheral vascular disease | 3.9% (507) |
| Microvascular | |
| Retinopathy | 1.7% (222) |

| | |
|---|---|
| Neuropathy | 3.8% (496) |
| Other | |
| Diabetic foot | 7.5% (964) |
| Amputations | 0.3% (45) |

Fuente: Russo, M. P., Grande-Ratti, M. F., Burgos, M. A., Molaro, A. A., & Bonella, M. B. (2023).

Data on metabolic control are presented in Table 4. Most had at least one lipid profile measurement in the last two years (90% total cholesterol, 81% high-density lipoprotein-linked cholesterol, 80% triglyceridemia, and 78% low-density lipoprotein-linked cholesterol), and 60% had at least one HbA1c measured in the last year, with 70% of these being less than 7% (11).

Table 4. Metabolic control.

| Variables | DM (n = 12,832) |
|---|---|
| Glycemic profile in the last year | 59.8% (7,682/12,832) |
| HbA1c measured in the past year | 6.7 (1.25) |
| HbA1c, expressed in %* | 68.4% (5,257/7,682) |
| HbA1c menor has 7% | 40.95% (5,257/12,832) |
| Lipid profile in the last 2 years | |
| LDL-C measured in the last 2 years | 78.5% (10,075/12,832) |
| c-LDL, and mg/dl* | 97.9 (35.2) |
| c-LDL equal to less than 100 mg/dl | 55.76% (5,618/10,075) |
| HDL-C measured in the last 2 years | 81.4% (10,457/12,832) |
| c-HDL, and mg/dl* | 48.2 (12.9) |
| HDL-C greater than 40 mg/dL (male) | 55.9% (2,840/5,074) |
| HDL-C greater than 50 mg/dL (female) | 52.9% (2,847/5,376) |
| Triglyceridemia measured in the last 2 years | 80.8% (10,376/12,832) |
| Triglycerides, mg/dL* | 146.0 (93.7) |
| Triglycerides less than 150 mg/dl | 65.2% (6,767/10,376) |
| Total cholesterol measured in the last 2 years | 90.6% (11,629/12,832) |
| Total cholesterol, mg/dL* | 171.7 (42.8) |

| Vascular damage | |
|---|---|
| Consultation with ophthalmology in the last year** | 56.2% (7,211/12,832) |
| Creatininemia measured in the last 2 years | 91.3% (11,718/12,832) |
| Creatinine one mg/dl* | 0.9 (0.5) |

Fuente:  Russo, M. P., Grande-Ratti, M. F., Burgos, M. A., Molaro, A. A., & Bonella, M. B. (2023).
*Stocking (standard deviation).
**Fundus proxy variable.
DM, diabetes mellitus; HDL-C: high-density lipoprotein-linked cholesterol; LDL-C: cholesterol linked to low-density lipoproteins; HbA1c: glycated hemoglobin.

In the article "Prevalence of diabetes, epidemiological characteristics and vascular complications", the prevalence of diabetes increases with age, where the prevalence in older adults was 15.7%, being somewhat lower than that reported by IDF in Latin America (22.7%; CI95%: 18.3-29.3), although similar to the European rate (20.1%; 95%CI: 15.3-25.8), according to a CDC report that estimated a prevalence of 21.4% (95%CI: 18.7-24.2) in adults over 65 years of age. Diabetes may intensify many of the geriatric syndromes because it causes cognitive dysfunction, depression, malnutrition, incontinence, fractures and falls, chronic pain, and loss of sense; In turn, geriatric syndromes can lead to greater complications in diabetes (11).

## 6 CONCLUSIONS

This research shows that type 2 diabetes mellitus represents an extremely serious problem at a global level, which leads to other health complications such as obesity, cardiovascular diseases and diabetic kidney disease, which is one of the most important complications with defined repercussions on quality of life and the overall prognosis of the disease.

By way of conclusion, after analyzing the main relationships between type 2 diabetes, obesity, kidney and cardiovascular diseases, and the objective of identifying and developing effective strategies for the prevention and combined treatment of these diseases. Several key observations can be made:

1. There are complex relationships between risk factors for type 2 diabetes, obesity, and cardiovascular and kidney disease, including insulin resistance, chronic inflammation, and metabolic dysfunction. These factors increase the risk of several health conditions.

2. A comprehensive approach to the management of type 2 diabetes is essential to effectively treat the cardiovascular and kidney diseases that are often associated with the disease. This includes not only controlling blood sugar, but also managing other cardiovascular risk factors such as blood pressure, cholesterol, and preventing metabolic syndrome.

3. Obesity is a major risk factor for type 2 diabetes and cardiovascular and kidney disease. Prevention and treatment of obesity are critical to reducing the burden of these diseases and promoting health.

4. Educating and empowering people with type 2 diabetes is critical to self-care and effective disease management. This includes promoting a healthy diet, increasing physical activity, and following medical treatment.

5. Prevention and treatment strategies should be tailored to the patient's individual needs, taking into account factors such as genetics, age, and comorbidities.

Analyzing the relationship between type 2 diabetes, obesity, and cardiovascular and kidney disease is essential to developing effective prevention and treatment strategies, and a comprehensive approach to addressing these issues is necessary to improve the quality of life of people with type 2 diabetes and reduce the burden of related diseases in the general population.

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