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*Scientific articles*

## **Factores de riesgo de la enfermedad renal oculta en pacientes diabéticos**

***Risk factors that trigger the disease of hidden renal failure in diabetic patients***

***Fatores de risco para doença renal oculta em pacientes diabéticos***

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## Resumen

**Introducción:** La insuficiencia renal (IR) ha emergido como un significativo problema de salud pública en México. El Instituto Nacional de Estadística y Geografía (INEGI) la ha clasificado como la décima causa de mortalidad en el país en la población femenina. Por ende, la detección temprana se ha vuelto esencial, especialmente en el caso de la enfermedad renal oculta (ERO), que afecta de manera notable a la población diabética. **Objetivo:** Identificar los factores de riesgo que inciden en la presencia de ERO en pacientes con diabetes tipo II (DM2). **Metodología:** Se llevó a cabo un estudio transversal, analítico y descriptivo en un muestreo de 352 pacientes, de los cuales 149 procedían de la ciudad de Chilpancingo de los Bravo, Guerrero, y 206 del municipio de Olinalá, en la Región Montaña del Estado de Guerrero. Los pacientes que aceptaron participar lo ratificaron a través de la firma de la carta de consentimiento informado.

En este estudio, se realizaron mediciones antropométricas, se midió la presión arterial y se recopilaron parámetros bioquímicos. Los resultados se registraron en una hoja de cálculo de Excel 2021 y para el análisis estadístico se utilizó el *software* STATA, versión 16.

**Resultados:** De la población estudiada, el 3.5 % (12 pacientes) presentó ERO, de los cuales el 50 % eran diabéticos. Entre los factores de riesgo identificados en la población con diabetes se incluyeron la edad mayor de 60 años (11.29 %), niveles elevados de albumina (16 %), urea (42.8 %) y ácido úrico (30.76 %). **Conclusión:** La enfermedad renal oculta afecta tanto a comunidades rurales como urbanas. Encontrándose un total de 12 pacientes con presencia de ERO, de los cuales el 25 % proceden de la ciudad de Chilpancingo, y 75 % del poblado de Olinalá (rural), lo que subraya la importancia de su detección temprana y un monitoreo oportuno. Esto es particularmente relevante en la población rural con diabetes mellitus.

**Palabras clave:** diabetes mellitus, insuficiencia renal crónica, enfermedad renal oculta.



## Abstract

**Introduction:** Renal failure (RF) has emerged as a significant public health issue in Mexico, ranking as the tenth leading cause of mortality among women, according to the National Institute of Statistics and Geography (INEGI). Early detection has become imperative, particularly in cases of Occult Renal Disease (ORD), which notably affects individuals with DM2. **Objective:** To identify the risk factors that contribute to the presence of ORD in patients with type II diabetes (DM2). **Methodology:** A cross-sectional, analytical and descriptive study was carried out in a sample of 352 patients, of whom 149 came from the city of Chilpancingo de los Bravo, Guerrero, and 206 from the municipality of Olinalá, in the Montaña region of the State of Guerrero. The patients who agreed to participate ratified their participation by signing the letter of informed consent.

In this study, anthropometric measurements were taken, blood pressure was measured and biochemical parameters were collected. The results were recorded in an Excel 2021 spreadsheet and STATA software, version 16, was used for statistical analysis.

**Results:** Of the population studied, 3.5% (12 patients) presented ORD, of which 50% having diabetes. Risk factors identified in the population with diabetic included age over 60 years (11.29%), elevated albumin levels (16%), urea (42.8%), and uric acid (30.76%). **Conclusion:** ORD affects both rural and urban communities. Out of 12 patients with ORD, 25% were from Chilpancingo, and 75% were from the rural area of Olinalá, which highlights the importance of early detection and timely follow-up. This is particularly relevant in the rural population with diabetes mellitus.

**Keywords:** Diabetes mellitus, Chronic Renal Failure, Occult Renal Disease.

## Resumo

Introdução: A insuficiência renal (IR) emergiu como um problema significativo de saúde pública no México. O Instituto Nacional de Estatística e Geografia (INEGI) classificou-a como a décima causa de mortalidade na população feminina do país. Portanto, a detecção precoce tornou-se essencial, especialmente no caso da doença renal oculta (ERO), que afeta notavelmente a população diabética. Objetivo: Identificar os fatores de risco que influenciam a presença de ERO em pacientes com diabetes tipo II (DM2). Metodologia: Foi realizado um estudo transversal, analítico e descritivo com uma amostra de 352 pacientes, dos quais 149 eram provenientes da cidade de Chilpancingo de los Bravo, Guerrero, e 206 do município de



Olinalá, na Região Serrana do Estado de Guerreiro. Os pacientes que concordaram em participar ratificaram-no assinando a carta de consentimento informado.

Neste estudo foram realizadas medidas antropométricas, aferida a pressão arterial e coletados parâmetros bioquímicos. Os resultados foram registados em planilha Excel 2021 e foi utilizado o software STATA, versão 16, para análise estatística.

Resultados: Da população estudada, 3,5% (12 pacientes) apresentavam ERO, dos quais 50% eram diabéticos. Os fatores de risco identificados na população com diabetes incluíram idade superior a 60 anos (11,29%), níveis elevados de albumina (16%), ureia (42,8%) e ácido úrico (30,76%). Conclusão: A doença renal oculta afeta comunidades rurais e urbanas. Foram encontrados 12 pacientes com presença de ERO, dos quais 25% eram provenientes da cidade de Chilpancingo e 75% da cidade de Olinalá (rural), o que ressalta a importância da detecção precoce e do monitoramento oportuno. Isto é particularmente relevante na população rural com diabetes mellitus.

**Palavras-chave:** diabetes mellitus, insuficiência renal crônica, doença renal oculta.

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## Introduction

Renal Failure (RD) has been declared a public health problem, defined as a decrease in renal function, with a glomerular filtration rate (GFR) less than 60 ml/min/1.73 m<sup>2</sup>, coupled with persistent kidney damage lasting three months, as detected by serum creatinine and creatinine clearance (Fácil et al., 2009). Additionally, Reduced Glomerular Filtration Rate (RGFR) includes patients with normal creatinine levels but a GFR less than 60-ml/min/1.73 m<sup>2</sup> (Labrador et al., 2007a).

Current classifications of CKD stages often do not account for the expected physiological decline in glomerular filtration rate associated with the nephroaging process. The concept of kidney health and nephroaging are not mutually exclusive; rather, they are complementary, encompassing biological, sociological, economic, and even political components. Therefore, defining CKD without adjusting for the expected decrease based on age, estimated through current clinical formulas, complicates the accurate determination of its real incidence (Álvarez, 2020).

Formulas have been developed to estimate the Glomerular Filtration Rate (GFR) and assess the extent of Reduced Glomerular Filtration Rate (RGFR) involvement, including well-known ones such as *Cockcroft-Gault* and *MDRD-4* (Galiano et al., 2019). Additionally,



studies have indicated that patients with CKD face an increased likelihood of mortality, emphasizing the importance of assessing risk factors in cases of Reduced Glomerular Filtration Rate (ROS) (Sánchez et al., 2020). Furthermore, certain factors can expedite kidney deterioration independently of the CKD progression rate, many of which are reversible. Recognizing and correcting these factors becomes crucial for effective management (García et al., 2014).

Research conducted on patients with chronic diseases identifies systemic arterial hypertension (SAH), body mass index, age, and sex as risk factors for ORD. Notably, DM2 is a chronic disease that is closely linked to ROS (Balderas et al., 2019; López et al., 2020). In Mexico, DM2 holds the position of the third leading cause of mortality in 2020, trailing behind cardiovascular diseases, as reported by the National Institute of Statistics and Geography (INEGI, 2023). Concerningly, both before and during the pandemic, a significant majority of diabetes patients exhibited poor glycemic control. Notably, studies conducted during the pandemic revealed the worst glycemic control among these patients (Mares et al., 2023).

In the epidemiological study of renal failure in Spain in 2010 (EPIRCE), by random sampling, a prevalence of 3.3% of CKD was reported in patients between 40-64 years of age and 21.42% in patients over 64 years of age (Otero *et al.* , 2010 ) . In 2018, the Spanish Nutrition and Cardiovascular Risk Study (ENRICA) reported that 15.1% of patients have CKD (Gorostidi *et al.* 2018) . In the United States, CKD prevails at 15% in adults, which has increased over time (Centers for Disease Control and Prevention, 2 021) . In Cuba, CKD increases with age and affects older adults in 21.4% (Lastre *et al.* , 2019) .

In Mexico, according to INEGI's technical note on registered death statistics, renal failure appeared among the top ten causes of death in women in 2020; in this year, 15 455 deaths due to renal failure were registered. This disease was the cause of death of 6618 (42.8%) women and 8835 (57.2%) men. Of this total of deaths due to Renal Failure, those from CKD represent 72.4% with 11,188 events (INEGI, 2021a) . In this context, primary care (PC) is primordial in the detection and stratification of RF in different populations, as well as for correct management of the situation presented (Labrador *et al.* , 2018b).

The recognition of abnormal glomerular filtration rates in individuals with normal serum creatinine levels prompts us to consider the necessity for regular evaluations of this parameter at the primary care level. This practice is crucial for the timely diagnosis and treatment of diabetic nephropathy, ensuring patients a better quality of life (Leyva et al., 2013).



The INEGI pointed out that, according to the 2018 National Health and Nutrition Survey (ENSANUT), in Mexico, there is a mortality rate due to DM2 of 11.95 people per 10,000 inhabitants, which is equivalent to 1,086,743 deaths per year ( INEGI , 2021b) . One of the complications of DM2 is the development of diabetic nephropathy. Indeed, it is estimated that between 25% and 40% of the diabetic population have some degree of nephropathy (Enríquez & Hernández , 2021) .

In the State of Guerrero, a notable 13.2% of individuals were recorded to have ROS within the family medicine unit of the Mexican Social Security Institute (UMF-IMSS). The early identification of ROS in patients with chronic diseases at the primary health care level serves as a crucial preventive measure to mitigate the risk of progression to end-stage renal failure (Balderas et al., 2019)

Adequately determining renal function is of great importance in clinical practice, both for the early diagnosis of nephropathy and for monitoring the progression and predicting the initiation of renal replacement treatment (Castaño *et al.* , 2009).

Therefore, the current investigation aims to identify the risk factors influencing the presence of Occult Renal Disease (ORD), particularly among patients diagnosed with type 2 diabetes (DM2). The primary goal is to provide information that facilitates early identification of kidney disease in its initial stages by first-contact doctors, while also elucidating the relationships with associated factors.

## Materials and methods

A cross-sectional, analytical, and descriptive study was conducted to investigate the risk factors associated with ORD in diabetic patients. The study included individuals from the Guillermo Soberón Acevedo Health Center in Chilpancingo de los Bravo, Guerrero, as well as patients from the municipality of Olinalá in the Mountain Region of the State of Guerrero, Mexico. The inclusion criteria encompassed individuals of both sexes clinically diagnosed with type 2 diabetes, without a pre-existing diagnosis of kidney disease.

To conduct the sampling, permission was sought from the authorities responsible for the sample centers. Following approval, patients were extended invitations to participate, and those who agreed affirmed their willingness by signing an informed consent letter.

Blood pressure measurement was performed using a previously calibrated and verified baumanometer . The samples obtained were processed *in Roche's Cobas Integra 400* equipment, previously calibrated and verified through quality control, to determine the



following variables: glucose, creatinine, urea, uric acid, cholesterol, and triglycerides. To measure the anthropometric variables—such as body mass index (BMI), age, and height—a scale with a previously calibrated and verified stadiometer was used. The Chronic formula was used to determine the GFR. Kidney disease Epidemiology Collaboration (CKD-EPI).

The present investigation implies a minimal risk for the patient in accordance with the General Health Law; However, health safety measures were considered during sampling, in accordance with chapter 1 of the second title Ethical Aspects of Research on Human Beings of the regulations of the general health law on health research. (General health law on research, 2014)

The results were concentrated in an Excel spreadsheet and the statistical analysis was carried out with STATA software, version 16, determining the maximum, minimum, mean and standard deviation values of each group of the study population (diabetics, non-diabetics and prediabetics). Likewise, through an ANOVA statistical test, the differences in the means were considered statistically significant when the value of  $p = \leq 0.05$ .

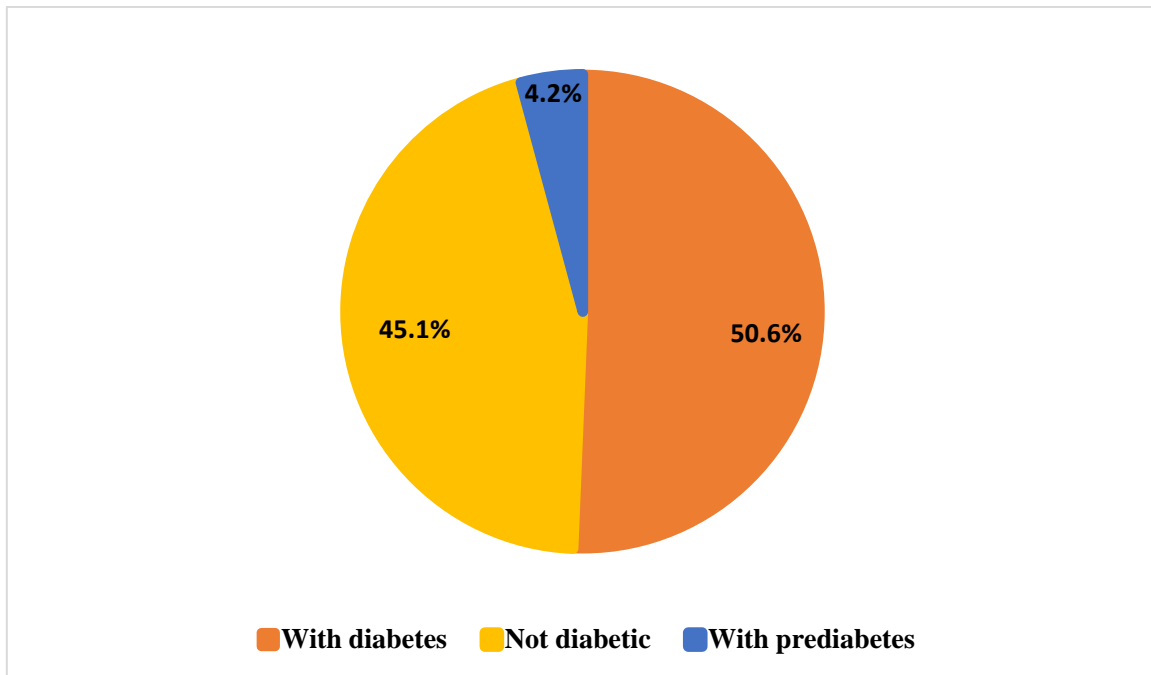
To measure the association between the variables included as risk factors and ORD, a bivariate analysis was performed using the Odds Ratio test, with a 95% confidence interval (95% CI).

## Results

The total population included 352 patients: 204 from the town of Olinalá and 148 from the city of Chilpancingo. 65% belonged to the female sex and 35% to the male. Patients aged 12 to 88 years were included.

Based on the determination of blood glucose levels, the patients exhibited the following distribution: 50.6% (178) were diagnosed with diabetes, 45.1% (159) did not have diabetes, and 4.2% (15) had prediabetes. It is noteworthy that all patients with prediabetes belonged to the population of Olinalá, and none of them had prior knowledge of this condition. (Figure 1)

**Figure 1.** Distribution of study patients according to their diagnosis on the presence of diabetes.



Source: self-made.

In the city of Chilpancingo de los Bravo, out of a total of 148 participants, 3 (2.02%) presented ORD. Conversely, in the rural area of Olinalá, 9 (4.41%) exhibited ORD. Furthermore, 12 patients with ROS were identified, with 25% belonging to Chilpancingo and 75% to Olinalá (refer to Table 1).



**Table 1.** Results of patients with kidney disorders in the study population

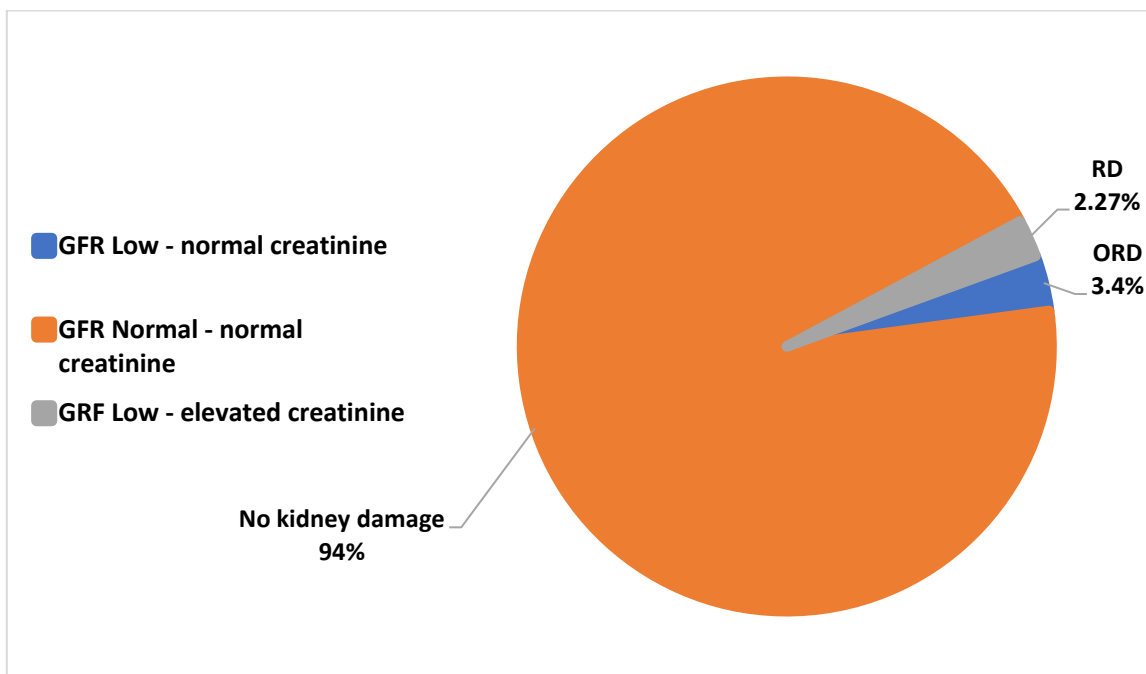
| P.R. | MUN | SEX | STAT | AGE | F.G. | C.R.S. | ALB | BMI   | SBP | DBP | GLU | U    | AU    | CHOL | TRIG | HDLc | LDLc  | AI   |
|------|-----|-----|------|-----|------|--------|-----|-------|-----|-----|-----|------|-------|------|------|------|-------|------|
| ORD  | OLI | F   | CD   | 57  | 52   | 1.156  | 150 | 24.64 | 110 | 60  | 249 | 52.8 | 4.74  | 202  | 112  | 71   | 90.6  | 2.8  |
| ORD  | OLI | M   | CD   | 56  | 50   | 1.152  | 150 | 34.07 | 130 | 80  | 192 | 37.6 | 10.41 | 148  | 249  | 28   | 90.4  | 5.3  |
| ORD  | OLI | M   | CD   | 75  | 52   | 1.318  | 80  | 28.85 | 120 | 70  | 85  | 63.2 | 11    | 111  | 96   | 28   | 60.8  | 3.9  |
| ORD  | OLI | M   | CD   | 85  | 51   | 1.276  | 10  | 59.03 | 124 | 77  | 143 | 28.3 | 8.41  | 193  | 301  | 36   | 118.4 | 5.4  |
| ORD  | OLI | F   | S/D  | 74  | 55   | 1.008  | 10  | 37.47 | 134 | 62  | 88  | 46.3 | 5.81  | 203  | 154  | 55   | 107.4 | 3.7  |
| ORD  | OLI | F   | S/D  | 72  | 55   | 1.023  | 10  | 24.87 | 117 | 67  | 78  | 43.8 | 4.96  | 157  | 256  | 37   | 88.6  | 4.2  |
| ORD  | OLI | F   | C/P  | 57  | 52   | 1.169  | 10  | 32.02 | 116 | 72  | 109 | 41.6 | 4.93  | 220  | 222  | 55   | 121   | 4    |
| ORD  | OLI | F   | S/D  | 76  | 53   | 1.020  | 10  | 29.75 | 125 | 70  | 89  | 31.3 | 7.4   | 241  | 260  | 38   | 154.8 | 6.3  |
| ERO  | OLI | M   | N.D. | 84  | 59   | 1.138  | 10  | 24.69 | 133 | 68  | 94  | 25.4 | 6.55  | 158  | 103  | 46   | 80.4  | 3.4  |
| ORD  | CH  | F   | CD   | 53  | 59   | 1.07   | 8   | 26.5  | 113 | 72  | 136 | 51   | 7.5   | 211  | 162  | 45   | 123   | 4.69 |
| ORD  | CH  | F   | CD   | 85  | 54   | 0.96   | 20  | 32    | 125 | 78  | 98  | 65   | 6.8   | 222  | 126  | 64   | 113.6 | 3.5  |
| ORD  | CH  | F   | S/D  | 72  | 56   | 1      | 10  | 28.7  | 122 | 82  | 77  | 36   | 3.9   | 184  | 127  | 69   | 89.6  | 2.67 |
| RD   | OLI | F   | CD   | 78  | 39   | 1.317  | 10  | 21.1  | 120 | 75  | 473 | 72.4 | 6.74  | 157  | 116  | 51   | 74.6  | 3.1  |
| RD   | OLI | F   | CD   | 85  | 8    | 4.72   | 10  | 30.40 | 120 | 60  | 76  | 201  | 12.1  | 176  | 101  | 48   | 92.8  | 3.6  |
| RD   | OLI | M   | S/D  | 87  | 28   | 2.060  | 10  | 22.93 | 110 | 71  | 82  | 59   | 6.52  | 139  | 108  | 38   | 73.2  | 3.7  |
| RD   | CH  | M   | CD   | 70  | 46   | 1.5    | 150 | 30.8  | 196 | 110 | 183 | 42   | 6.9   | 158  | 185  | 28   | 98.4  | 5.64 |
| RD   | CH  | F   | CD   | 59  | 44   | 1.32   | 80  | 30.7  | 120 | 75  | 141 | 73   | 3.6   | 298  | 241  | 49   | 189.4 | 6.08 |
| RD   | CH  | F   | CD   | 60  | 45   | 1.28   | 150 | 28.4  | 123 | 57  | 157 | 130  | 8.7   | 251  | 201  | 50   | 150.8 | 5.02 |
| RD   | CH  | M   | CD   | 49  | 15   | 4.4    | 150 | 32.71 | 132 | 85  | 142 | 132  | 6.2   | 226  | 298  | 65   | 115.8 | 3.5  |
| RD   | CH  | M   | CD   | 64  | 34   | 2.02   | 150 | 21.7  | 186 | 86  | 157 | 61   | 6.1   | 236  | 188  | 50   | 50    | 4.72 |

Source: self made. Processed in Excel.

Abbreviations: Renal pathology (PR), Occult renal disease (ORD), Renal disease (RD), Municipality (MUN), Olinalá (OLI), Chilpancingo (CH), Female (F), Male (M), Status (ESTAT), With Diabetes (C/D), Without diabetes (ND), With Prediabetes (C/P), Glomerular filtration rate (GFR), Serum creatinine (CRS), Albuminuria (ALB), Body mass index (BMI), Blood pressure systolic (SBP), Diastolic blood pressure (DBP), Glucose (GLU), Urea (U), Uric acid (UA), Cholesterol (CHOL), Triglycerides (TRIG), High-density cholesterol (HDLc), Low-density cholesterol (LDLc), Atherogenic index (AI).

After determining the GFR and serum creatinine levels, a group of 8 patients was found with a decrease in GFR  $< 60$  ml/min/1.73 m<sup>2</sup> and high creatinine levels, which indicates the presence of kidney disease, representing 2.27% of the study population. In addition, patients with a GFR  $< 60$  ml/min/1.73 m<sup>2</sup> and normal creatinine were identified, with ROS data representing a percentage of 3.40% (12 patients) (figure 2).

**Figure 2.** Distribution of study patients according to GFR rate and serum creatinine values.



Source: self made.

Table 2 shows the comparison of age, BMI, and systolic and diastolic blood pressure of patients with diabetes, prediabetes and non-diabetics, where only significant values are observed in age. Unlike Table 3, where an analysis of the biochemical parameters of the study population was carried out, albuminuria, urea and cholesterol were found to have significant values ( $p = < 0.05$ ).

**Table 2.** Analysis of variables between patients with diabetes, prediabetes and non-diabetics.

| Variable | Sex | Status           | Half   | D.S.  | Min.  | Max.  | p* value |
|----------|-----|------------------|--------|-------|-------|-------|----------|
| AGE      | F   | With diabetes    | 58.45  | 11.55 | 22    | 85    | 0.0001   |
|          |     | With prediabetes | 55.5   | 10.76 | 40    | 78    |          |
|          |     | Not diabetic     | 44.77  | 16.93 | 12    | 84    |          |
|          | M   | With diabetes    | 58.42  | 13.42 | 12    | 85    | 0.2712   |
|          |     | With prediabetes | 59     | -     | 59    | 59    |          |
|          |     | Not diabetic     | 53.11  | 17.85 | 22    | 88    |          |
| BMI      | F   | With diabetes    | 29.05  | 5.10  | 15.49 | 47.78 | 0.0532   |
|          |     | With prediabetes | 31.15  | 8.53  | 20.02 | 51.75 |          |
|          |     | Not diabetic     | 27.85  | 5.47  | 16.5  | 52.59 |          |
|          | M   | With diabetes    | 28.51  | 5.84  | 18.97 | 59.03 | 0.2636   |
|          |     | With prediabetes | 31.86  | -     | 31.81 | 31.81 |          |
|          |     | Not diabetic     | 26.91  | 4.36  | 19.72 | 42.3  |          |
| SBP      | F   | With diabetes    | 123.21 | 18.60 | 80    | 180   | 0.1671   |
|          |     | With prediabetes | 125.42 | 23.91 | 98    | 173   |          |
|          |     | Not diabetic     | 118.72 | 21.23 | 82    | 200   |          |
|          | M   | With diabetes    | 130    | 31.11 | 90    | 288   | 0.8066   |
|          |     | With prediabetes | 128    | -     | 128   | 128   |          |
|          |     | Not diabetic     | 127.11 | 17.14 | 89    | 167   |          |
| DBP      | F   | With diabetes    | 73.41  | 11.15 | 48    | 100   | 0.2648   |
|          |     | With prediabetes | 78.28  | 7.80  | 66    | 97    |          |
|          |     | Not diabetic     | 73.68  | 10.30 | 52    | 101   |          |
|          | M   | With diabetes    | 78.26  | 15.73 | fifty | 148   | 0.9568   |
|          |     | With prediabetes | 82     | -     | 82    | 82    |          |
|          |     | Not diabetic     | 78.76  | 12.06 | 61    | 113   |          |

Source: self made.

\*ANOVA analysis for one factor, with Fisher probability.

Abbreviations: Body mass index (BMI), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Female (F), Male (M), Standard deviation (SD), Non-assessable data, n = 1 (-) .

**Table 3.** Biochemical variables among patients with diabetes, prediabetes and non-diabetics.

| Variable | Sex | Status           | Half   | D.S.   | Min.  | Max.  | <i>p</i> value * |
|----------|-----|------------------|--------|--------|-------|-------|------------------|
| SC       | F   | With diabetes    | 0.64   | 0.38   | 0.27  | 4.72  | 0.4432           |
|          |     | With prediabetes | 0.73   | 0.16   | 0.54  | 1.16  |                  |
|          |     | Without diabetes | 0.68   | 0.11   | 0.43  | 1.02  |                  |
|          | M   | With diabetes    | 0.92   | 0.57   | 0.39  | 4.4   | 0.8061           |
|          |     | With prediabetes | 1,033  | -      | 1.03  | 1.03  |                  |
|          |     | Without diabetes | 0.87   | 0.23   | 0.58  | 2.06  |                  |
| ALB      | F   | With diabetes    | 31.89  | 38.55  | 5     | 150   | 0.0001           |
|          |     | With prediabetes | 10     | 0      | 10    | 10    |                  |
|          |     | Without diabetes | 16.75  | 16.37  | 6     | 100   |                  |
|          | M   | With diabetes    | 47.87  | 48.54  | 8     | 150   | 0.0003           |
|          |     | With prediabetes | 10     | -      | 10    | 10    |                  |
|          |     | Without diabetes | 14.95  | 15.92  | 8     | 80    |                  |
| Urea     | F   | With diabetes    | 30.84  | 20.24  | 12.28 | 201.4 | 0.0432           |
|          |     | With prediabetes | 29.29  | 8.45   | 12.8  | 41.62 |                  |
|          |     | Without diabetes | 25.63  | 9.07   | 7.79  | 57    |                  |
|          | M   | With diabetes    | 34.08  | 17.94  | 12.74 | 132   | 0.1622           |
|          |     | With prediabetes | 36.77  | -      | 36.77 | 36.77 |                  |
|          |     | Without diabetes | 28.15  | 10.28  | 12.27 | 61    |                  |
| A.U.     | F   | With diabetes    | 5.14   | 1.86   | 1.8   | 12.1  | 0.1404           |
|          |     | With prediabetes | 4.95   | 0.98   | 3.69  | 7.17  |                  |
|          |     | Without diabetes | 4.72   | 1.29   | 2.0   | 9.09  |                  |
|          | M   | With diabetes    | 34.08  | 17.94  | 12.74 | 132   | 0.9417           |
|          |     | With prediabetes | 6.56   | -      | 6.56  | 6.56  |                  |
|          |     | Without diabetes | 6.0    | 1.39   | 2.6   | 8.7   |                  |
| CHOL     | F   | With diabetes    | 194.85 | 41.91  | 94    | 338   | 0.0111           |
|          |     | With prediabetes | 196.71 | 53.40  | 116   | 309   |                  |
|          |     | Without diabetes | 178.69 | 42.50  | 85    | 320   |                  |
|          | M   | With diabetes    | 184.40 | 50.41  | 109   | 404   | 0.3000           |
|          |     | With prediabetes | 132    | -      | 132   | 132   |                  |
|          |     | Without diabetes | 173.73 | 35.99  | 120   | 259   |                  |
| TRIG     | F   | With diabetes    | 223.11 | 225.35 | 51    | 1957  | 0.1382           |
|          |     | With prediabetes | 200.5  | 117.38 | 43    | 468   |                  |
|          |     | Without diabetes | 176.76 | 101.63 | 48    | 690   |                  |
|          | M   | With diabetes    | 213.73 | 261.93 | 40    | 950   | 0.8743           |
|          |     | With prediabetes | 281    | -      | 281   | 281   |                  |
|          |     | Not diabetic     | 196.59 | 135.56 | 60    | 660   |                  |
| AI       | F   | With diabetes    | 4.42   | 1.36   | 1.8   | 11.2  | 0.3723           |
|          |     | With prediabetes | 4.48   | 1.40   | 2.1   | 7.4   |                  |
|          |     | Without diabetes | 4.20   | 1.23   | 1.8   | 7.6   |                  |
|          | M   | With diabetes    | 4.54   | 1.04   | 2.5   | 8.6   | 0.8959           |
|          |     | With prediabetes | 5.1    | -      | 5.1   | 5.1   |                  |
|          |     | Without diabetes | 4.53   | 1.34   | 23    | 8.3   |                  |

Source: self-made



\*ANOVA analysis for one factor, with Fisher probability.

Abbreviations: Serum creatinine (SC), Albuminuria (ALB), Urea (U), Uric acid (AU), Cholesterol (CHOL), Triglycerides (TRIG), Atherogenic index (AI), Female (F), Male (M), Non-assessable data, n=1 (-).

Table 4 shows the relationship of the variables associated with a 95% confidence index. To estimate the risk factor, the Odds ratio analysis was used, which made it possible to establish indices that allow the differences in significance between the risk variables to be observed. Four factors were found to be significantly associated with ORD, including age equal to or greater than 60 years, presence of albuminuria, elevated urea and uric acid.

**Table 4.** Bivariate analysis of factors associated with occult renal failure

| FACTOR |         | ODDS RATIO | 95% CI     | <i>Q</i> |
|--------|---------|------------|------------|----------|
| Sex    | Female  | 1.96       | 0.67-5.43  | 0.1462   |
|        | Male    |            |            |          |
| Age    | ≥ 60    | 4.70       | 1.63-15.29 | 0.0008   |
|        | < 60    |            |            |          |
| BMI    | ≥ 25    | 0.80       | 0.27-2.63  | 0.6627   |
|        | < 25    |            |            |          |
| SBP    | 121-300 | 1.34       | 0.49-3.77  | 0.5195   |
|        | 80-120  |            |            |          |
| DBP    | 81-150  | 0.60       | 0.14-1.94  | 0.3762   |
|        | 40-80   |            |            |          |
| Alb    | ≥ 30    | 4.63       | 1.52-13.01 | 0.0007   |
|        | < 30    |            |            |          |
| Urea   | ≥ 44    | 29.62      | 9.38-94.31 | 0.0001   |
|        | < 44    |            |            |          |
| AU     | ≥ 8.5   | 8.97       | 1.79-36.23 | 0.0001   |
|        | < 8.5   |            |            |          |
| CHOL   | ≥ 240   | 1.77       | 0.31-6.66  | 0.3742   |
|        | < 240   |            |            |          |
| TRIG   | ≥ 200   | 1.18       | 0.40-3.26  | 0.7145   |
|        | < 200   |            |            |          |
| AI     | ≥ 5     | 0.86       | 0.23-2.63  | 0.7865   |
|        | < 5     |            |            |          |
| HDLc   | ≥ 50    | 2.01       | 0.71-5.52  | 0.1268   |
|        | < 50    |            |            |          |
| LDLc   | ≥ 160   | 0.91       | 0.02-6.47  | 0.9354   |
|        | < 160   |            |            |          |
| Glu    | ≥ 126   | 1.78       | 0.64-4.93  | 0.2019   |
|        | < 126   |            |            |          |

Source: self made



Abbreviations: Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Albuminuria (ALB), Uric acid (UA), Cholesterol (CHOL), Triglycerides (TRIG), Atherogenic index (AI), High-density cholesterol (HDLc) , Low-density cholesterol (LDLc) , Glucose (Glu) .

## Discussion

Abnormally high plasma glucose concentrations (hyperglycemia) are a common consequence of poor diabetes control. This condition can lead to various long-term complications, including kidney disease (García *et al.* , 2014) . In the present study, 53.6% of the patients were diabetic, of which the average glucose is 181.3 mg/dl. This reflects poor glycemic control, which generates a greater impact on the economic and health systems.

In this sense, these high glucose levels may be influenced by the effects of the disappearance of the Prospera and Seguro Popular programs, which were a health monitoring and prevention tool for the population, as well as the presence of the pandemic, which together formed a difficult environment for medical care throughout the country.

For example, Seas *et al.*, (2023) conducted a comparative study of glycemic control in a pre-pandemic and pandemic group. The results show that in the pre-pandemic, patients under 50 years of age had an HbA1 level of  $8.1 \pm 2.4$  compared to the pandemic, where the level was  $8.4 \pm 2.4$ . Furthermore, as age increases, a decrease in the HbA1 level is observed, since those over 70 years of age in the pre-pandemic had an HbA1 level of 7.1, in contrast to the pandemic group, which was  $7.3 \pm 1.8$ . These data reveal deficiencies in prevention, especially during the Covid-19 pandemic, where glycemic uncontrol was significantly greater compared to pre-pandemic levels. In other words, the deficiency in primary care, together with isolation, favored a sedentary lifestyle, smoking, alcoholism and comorbidities, which increased the probability of poor glycemic control in the Mexican population (Mares *et al.*, 2023).

In our study, diabetic patients exhibited a comparable prevalence of Reduced Glomerular Filtration Rate (ROS) to a study conducted in Guanajuato, Mexico, where the prevalence was 7.4%. The Guanajuato study revealed that diabetics with a Glomerular Filtration Rate (GFR)  $<60 \text{ ml/min/1.73m}^2$  had elevated levels of cholesterol, triglycerides, and blood pressure (Leyva *et al.*, 2013). In contrast to the present study, diabetic patients with ROS exhibited normal creatinine and blood pressure levels, while 50% had elevated triglyceride levels, and 33% had elevated cholesterol values. This suggests that patients in our study are likely being identified in the early stages of ROS. Therefore, emphasizing the



importance of seeking GFR with normal serum creatinine in the patient's evaluation during diagnosis.

Likewise, in the present investigation, a higher percentage of ROS was observed in female patients with 66.6%, while in male patients it was 33.30%. In studies carried out in Cuba by López *et al.* (2020) show that there was also a higher percentage in the female sex, with 54.9% in their study population. From a population point of view, it is believed that this is associated with the fact that demographically there are more women than men, since, in Mexico, according to data from the 2020 census carried out by the INEGI, of the total population, 48.8% are men and 51.2% are women (INEGI, 2021c). Furthermore, it is worth highlighting the fact that more women than men go to health centers, which can generate under-reporting of the male sex.

On the other hand, it is worth highlighting, in the case of this research, that most of the participants come from the town of Olinalá, where the male population usually works in the field, which did not make it easier for them to attend sampling. This was a factor that affected the monitoring of health status in the male population. In addition to this, it should be mentioned that, in terms of the health sector, there are currently more campaigns for prevention and health for female population.

Even so, the bivariate analysis allowed us to find four factors associated with the presence of ROS in our study population. Aging was found as an associated factor (OR:4.70, 95% CI; 1.63-15.29), since age equal to or greater than 60 presented significance with a *p value* = 0.008. This result coincides with what was pointed out by Balderas *et al.* (2019), who during 2021 conducted a study where they found age  $\geq 60$  years to be one of the main factors associated with ROS.

Furthermore, it is important to note the expected physiological decrease in the GFR rate associated with the nephroaging process (kidney aging), in which biological aspects are considered due to this relationship. Therefore, greater importance should be given to monitoring kidney age, the speed of progression of physiological deterioration at this level, as well as the aspects specific to each sex and age group (Álvarez, 2020).

Other factors associated with ROS were levels of albuminuria  $>20$  mg/ dL, since as diabetic nephropathy progresses, albumin losses become more evident, which contributes to the progressive loss of GFR ( Vergara *et al.* , 2020) . In this study, 16% of the population has high levels of albuminuria and are diabetic. The presence of albuminuria may be one of the first manifestations of kidney damage due to the decrease in the GFR rate (Labrador *et al.* , 2018b).



Uric acid (UA) has a great impact on health, since it is a precursor in the development of several pathologies when it occurs at high levels. UA at levels  $> 7$  mg/dl has been determined as hyperuricemia (Ríos *et al.* , 2020) and some studies have indicated that high levels of UA have a strong link with the development of kidney disease (UA is eliminated in two thirds by the kidney and increases with the deterioration of GFR). Hyperuricemia produces several lesions at the kidney level, which impair renal autoregulation responses and cause glomerular hypertension (Goicoechea *et al.* , 2021) .

Two studies conducted in Japan—one by Tomita *et al.* (2000) to examine the relationship between UA and ER—determined that having UA  $>8.5$  mg/dl increased the risk of developing CKD by 8 times compared to levels of moderate hyperuricemia 5-6.4 mg/dl. The second study, conducted by Kunitoshi *et al.*, 2004, evaluated the incidence of CKD, where the levels in men with UA turn out to be  $>7$  mg/dl and in women  $> 6$  mg/dl.

Building upon the earlier discussion, hyperuricemia emerges as a noteworthy factor, with a notable representation of 30.76% in patients with renal pathology and diabetes when utilizing  $> 8.5$  mg/dl as a reference. This implies that individuals with sustained high levels of uric acid may face an increased likelihood of developing ROS in the long term. This, if not addressed through appropriate treatment, could lead to the progression of CKD.

Finally, the estimation of GFR, in addition to the use of equations, can be determined from the average clearance of urea and creatinine. Urea is completely eliminated by the kidney through filtration, so its concentration increases when tubular flow is lower (Castaño *et al.* , 2009) . In the present study, urea is shown as a risk indicator, since it reached high levels in 42.85% of diabetic patients with ROS.

## Conclusion

ROS exhibits a heightened prevalence among diabetic patients, especially those hailing from rural communities. Notably, 75% of our ROS prevalence is attributed to the town of Olinalá, with associated factors identified, including age over 60 years, albuminuria, and elevated levels of urea and uric acid.

This underscores the imperative of implementing timely detection measures for ROS, extending beyond the diabetic population to include non-diabetic individuals. Such an approach is crucial to prevent the progression to CKD. Additionally, special attention should





be given to prediabetic patients, who currently lack programs aimed at preventing and delaying the onset of diabetes and its complications.

### Future lines of research

It would be beneficial to investigate the impact of treatment effectiveness and adherence, as well as the influence of lifestyle factors, on the development of ORD in diabetic patients. Understanding how these variables contribute to the occurrence of ORD can provide valuable insights for improving patient outcomes.

Furthermore, conducting research to identify factors contributing to the higher prevalence of ROS and diabetes in female patients compared to male patients would be valuable. This investigation could shed light on gender-specific risk factors and aid in developing targeted interventions for both prevention and management.

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