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# Evaluation and comparison of diabetic and non-diabetic patients infected by COVID-19 and phenotypes of severity: an analytical and cross-sectional study in a reference hospital of the Federal District, Brazil

**Avaliação e comparação de pacientes diabéticos e não diabéticos infectados pelo COVID-19 e fenótipos de gravidade: um estudo analítico e transversal em hospital de referência do Distrito Federal, Brasil**

**Evaluación y comparación de pacientes diabéticos y no diabéticos infectados por COVID-19 y fenotipos de severidad: un estudio analítico y transversal en un hospital de referencia del Distrito Federal, Brasil**

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**Marina Grazziotin Pasolini**
ORCID: https://orcid.org/0000-0003-0480-2222
Hospital Regional de Taguatinga, Brazil
e-mail: marinagpasolini@yahoo.com.br
**Fernanda Silveira Tavares**
ORCID: https://orcid.org/0000-0002-9743-7916
Hospital Regional de Taguatinga, Brazil
e-mail: fernanda.endocrino@gmail.com
**Mariani Carla Prudente Batista**
ORCID: https://orcid.org/0000-0002-0979-4754
Hospital Regional de Taguatinga, Brazil
e-mail: mariani.carla@terra.com.br
**Amanda Sena Nunes Canabrava**
ORCID: https://orcid.org/0000-0002-6068-6521
Escola Superior de Ciências da Saúde, Brazil
e-mail: amandasena.nc@gmail.com
**Lisandra Vieira da Cruz Souza**
ORCID: https://orcid.org/0000-0002-9284-6681
Escola Superior de Ciências da Saúde, Brazil
e-mail: lisandravcsouza@gmail.com
**Isabela Yumi Saito Delage**
ORCID: https://orcid.org/0000-0002-9731-6751
Escola Superior de Ciências da Saúde, Brazil
e-mail: iydelage99@gmail.com
**Fábio Siqueira**
ORCID: https://orcid.org/0000-0001-5849-3037
Hospital Regional de Taguatinga, Brazil
e-mail: fabiosqr@gmail.com
**Hugo de Luca Correa**
ORCID: https://orcid.org/0000-0002-3080-9391
Universidade Católica de Brasília, Brazil
e-mail: hugo.efucb@gmail.com
**Thiago dos Santos Rosa**
ORCID: https://orcid.org/0000-0003-0418-0945
Universidade Católica de Brasília, Brazil
e-mail: thiagoacsdkp@yahoo.com.br

**Abstract**

Introduction: In March 2020 the World Health Organization (WHO) declared a pandemic for the disease called COVID 19, caused by a new acute severe coronavirus respiratory syndrome 2 (SARS-CoV-2), being a public health emergency of international interest. Since the beginning of the pandemic, diabetes mellitus has emerged as a complicating factor, with unfavorable outcomes compared to the non-diabetic population. Thus, our study aimed to evaluate and compare, through an analytical, cross-sectional and descriptive study, the phenotypes of severity among people with diabetic and non-diabetic COVID-19 in a reference hospital in the Federal District, Brazil. Material and methods: Through an active

search of data in the medical records of hospitalized patients diagnosed with COVID-19 by the"Real Time Polymerase Chain Reaction" (RT-PCR) method, 2041 individuals who, after exclusion criteria, selected a total of 762 for the proposed study were selected, comparing clinical and laboratory data between the group with diabetes and without diabetes. Descriptive statistics were performed with mean and standard deviation values, absolute frequency and relative percentage. The normality and homogeneity of the data were calculated with the Shapiro-Wilk and Levene test, respectively. The student's t-test for independent samples was used to compare the continuous variables and the chi-square test was used to compare categorical variables between diabetic and non-diabetic patients. Findings: Individuals with diabetes presented a more severe clinical picture when compared to those without the disease. Evidencing an independent risk factor for a worse prognosis. Discussion: our findings are in line with other studies already conducted, showing that the chronic inflammatory component of the disease seems to be the main trigger for unfavorable outcomes. Conclusion: Considering the epidemiological importance of diabetes, urgent research is made that elucidate the above-mentioned doubts, aiming at more appropriate therapeutic interventions and, therefore, improving outcomes in this population. In the case of a new and still little known disease, with several questions, probably many of the answers will only come over time, through more robust, prospective and randomized studies, with larger and more diverse populations.
**Keywords:** COVID-19; Diabetes mellitus; Risk factors; Indicators of morbidity and mortality; Systemic inflammatory response syndrome.

**Resumo**

Introdução: Em março de 2020 a Organização Mundial da Saúde (OMS) declarou uma pandemia pela doença denominada COVID 19, causado por uma nova síndrome respiratória aguda grave coronavírus 2 (SARS-CoV-2), sendo uma emergência de saúde pública de interesse internacional. Desde o início da pandemia, o diabetes mellitus emergiu como um fator complicador, com desfechos desfavoráveis em comparação à população não diabética. Dessa forma, nosso estudo objetivou avaliar e comparar, através de um estudo analítico, transversal e descritivo, os fenótipos de gravidade entre pessoas com COVID-19 diabéticas e não diabéticas em um hospital de referência no Distrito Federal, Brasil. Material e métodos: Através de busca ativa de dados em prontuários de pacientes internados com diagnóstico com COVID-19 pelo método “Real Time Reação de Cadeia de Polimerase” (RT-PCR), foram recrutados 2041 indivíduos que, após critérios de exclusão, selecionados um total de 762 para o estudo proposto, comparando dados clínicos e laboratoriais entre o grupo com diabetes e sem diabetes. A estatística descritiva foi realizada com valores média e desvio-padrão, frequência absoluta e percentual relativo. A normalidade e homogeneidade dos dados foram calculadas com o teste de Shapiro-Wilk e Levene, respectivamente. O teste t de student para amostras independentes foi usado para comparar as variáveis contínuas e o teste qui-quadrado foi utilizado para comparar as variáveis categóricas entre os pacientes diabéticos e não diabéticos. Resultados: Indivíduos com diabetes apresentaram um quadro clínico mais severo quando comparados àqueles sem a doença. Evidenciando um fator de risco independente para um pior prognóstico. Discussão: nossos achados vão de encontro a outras pesquisas já realizadas, mostrando que o componente inflamatório crônico da doença parece ser o principal gatilho para desfechos desfavoráveis. Conclusão: Considerando a importância epidemiológica do diabetes, fazem-se urgentes pesquisas que elucidem as dúvidas acima expostas, visando intervenções terapêuticas mais apropriadas e, portanto, melhorando os desfechos nesta população. Em se tratando de uma doença nova e ainda pouco conhecida, com várias interrogações, provavelmente muitas das respostas só virão com o tempo, através de estudos mais robustos, prospectivos e randomizados, com populações maiores e mais diversificadas.
**Palavras-chave:** COVID-19; Diabetes mellitus; Fatores de risco; Indicadores de morbimortalidade; Síndrome de resposta inflamatória sistêmica.

**Resumen**

Introducción: En marzo de 2020 la Organización Mundial de la Salud (OMS) declaró una pandemia por la enfermedad denominada COVID 19, provocada por un nuevo síndrome respiratorio agudo severo por coronavirus 2 (SARS-CoV-2), siendo una emergencia de salud pública de interés internacional. Desde el comienzo de la pandemia, la diabetes mellitus ha surgido como un factor de complicación, con resultados desfavorables en comparación con la población no diabética. Así, nuestro estudio tuvo como objetivo evaluar y comparar, a través de un estudio analítico, transversal y descriptivo, los fenotipos de gravedad en personas con COVID-19 diabéticos y no diabéticos en un hospital de referencia del Distrito Federal, Brasil. Material y métodos: Mediante una búsqueda activa de datos en las historias clínicas de pacientes hospitalizados diagnosticados de COVID-19 por el método "Reacción en cadena de la polimerasa en tiempo real" (RT-PCR), 2041 individuos que, tras criterios de exclusión, seleccionaron un total de Se seleccionaron 762 para el estudio propuesto, comparando datos clínicos y de laboratorio entre el grupo con diabetes y sin diabetes. Se realizó estadística descriptiva con valores de media y desviación estándar, frecuencia absoluta y porcentaje relativo. La normalidad y homogeneidad de los datos se calcularon con la prueba de Shapiro-Wilk y Levene, respectivamente. Se utilizó la prueba t de Student para muestras independientes para comparar las variables continuas y la prueba de chi-cuadrado para comparar variables categóricas entre pacientes diabéticos y no diabéticos. Hallazgos: las personas con diabetes presentaban un cuadro clínico más grave en comparación con las que no tenían la enfermedad. Evidenciando un factor de riesgo independiente de peor pronóstico. Discusión: nuestros hallazgos están en línea con otros estudios ya

realizados, que muestran que el componente inflamatorio crónico de la enfermedad parece ser el principal desencadenante de resultados desfavorables. Conclusión: Considerando la importancia epidemiológica de la diabetes, se realizan investigaciones urgentes que dilucidan las dudas mencionadas, con el objetivo de realizar intervenciones terapéuticas más adecuadas y, por tanto, mejorar los resultados en esta población. En el caso de una enfermedad nueva y aún poco conocida, con varias preguntas, probablemente muchas de las respuestas solo lleguen con el tiempo, a través de estudios más robustos, prospectivos y aleatorizados, con poblaciones más grandes y diversas.
**Palabras clave:** COVID-19; Diabetes mellitus; Factores de riesgo; Indicadores de morbimortalidad; Síndrome de respuesta inflamatoria sistémica.

## 1. Introduction

In March 2020, the World Health Organization (WHO) declared a pandemic for the disease called COVID 19, caused by a new acute acute coronavirus 2 (SARS-CoV-2) syndrome, and is a public health emergency of international interest. The first case took place in China in early December 2019(Ramanathan et al., 2020). In Brazil,on February 3, 2020, the Ministry of Health declared a Public Health Emergency of National Importance (ESPIN)(Brasil, 2020). The new coronavirus disease 2019 (COVID-19) is highly contagious and the clinical features are varied, ranging from asymptomatic state to acute respiratory distress syndrome and multiple organ dysfunction (Fadini et al., 2020).

Pre-existing conditions, such as diabetes, hypertension, cardiovascular diseases and obesity, are pointed out by epidemiological studies common markers of higher mortality and morbidity in COVID-19(Zhou, 2020; Williamson et al., 2020). Diabetes mellitus (DM) is undoubtedly one of the most important causes contributing to an unfavorable outcome in hospitalization rates, severe complications and mortality (Corona et al., 2021).

The evidence is well established that people with diabetes are more susceptible to infections in general and have a worse prognosis compared to the non-diabetic population (Xu et al., 2019). In addition, this susceptibility has been previously reported for other epidemics by SARS (Yang et al., 2006). In this context, when comparing the clinical characteristics between COVID-19 patients with and without diabetes, they found that people with diabetes are not more likely to contract COVID 19 than the general population, but it is a high-risk group for complications, admission to the intensive care unit or invasive ventilation or death in COVID-19(Blanke, 2020; Klein, 2020).

The population with diabetes is highly heterogeneous, there is epidemiological evidence that reinforces the role of diabetes to a more critical prognosis in viral conditions, with emphasis mainly on COVID-19. In this study, we identified the clinical characteristics and evaluated the association of disease severity and mortality of people with diabetes hospitalized because of COVID-19 in a reference hospital for diabetes in the Federal District.

## 2. Materials and Methods

### Type of study

This is an analytical, descriptive and cross-sectional study, with the objective of analyzing and comparing the epidemiological characteristics and phenotypes of people with and without diabetes mellitus infected by Covid-19 from March 2020 to December 2020 at the Regional Hospital of Taguatinga - Federal District (HRT-DF).

### Sample

Through an active search of data in the medical records of hospitalized patients diagnosed with COVID-19 by the"Real Time Polymerase Chain Reaction" (RT-PCR) method, 2041 individuals who, after exclusion criteria, selected a total of 762 for the proposed study were recruited.

Inclusion criteria were: over 18 years, both sexes, laboratory confirmation of Sars-COV-2 infection by RT-PCR method, symptomatic or not, treated at home or in hospital. Exclusion criteria were: pregnant women or those with incomplete data in

the medical records and who, therefore, did not meet the purposes of the research.

This study was submitted and approved by the Ethics and Research Committee (CEP) under the certificate of approval of ethical appreciation (CAAE) 37271120.8.0000.5553, and it was waived from the Informed Consent Form (TCLE).

**Data collection**

Data collection was performed via electronic medical records by the study hospital's management system, such records provide the history of each patient, as well as the laboratory tests that are collected in the same unit, the evolution and clinical outcomes of each individual. The data collected included clinical data such as gender, race, age, body mass index (BMI), existence or not of diabetes and, if so, its classification in type 1 or 2. For those with DM, regardless of type, the following were evaluated: use of oral antidiabetics, insulin, glycemic control in the last six months, using glycated hemoglobin (A1c) as the main parameter and the presence of chronic complications. The presence of previous existing diseases such as obesity, systemic arterial hypertension (SAH), chronic kidney disease (CKD) and pulmonary disease (asthma, chronic obstructive pulmonary disease (COPD) and others) were collected in both groups, as well as habits and lifestyle such as smoking, alcohol consumption and sedentary lifestyle. In addition to clinical data, laboratory values of creatinine, ferritin, C-reactive protein (CRP), oxalace transaminase (TGO) and pyruvic transaminase (PGT) were evaluated. clinical outcomes (hospitalization, clinical status, use of mechanical ventilation and death) completed the evaluation of the groups.

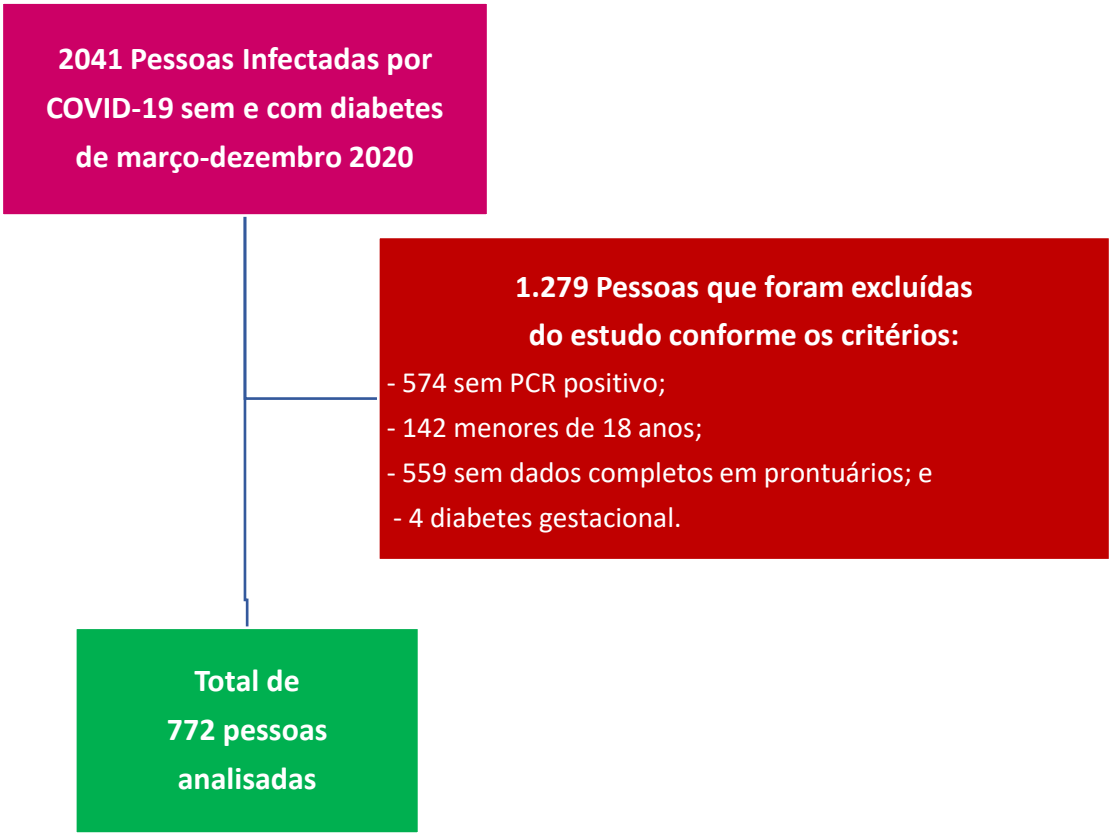
**Data analysis**

Descriptive statistics were performed with mean and standard deviation values, absolute frequency and relative percentage. The normality and homogeneity of the data were calculated with the Shapiro-Wilk and Levene test, respectively. The student's t-test for independent samples was used to compare the continuous variables and the chi-square test was used to compare categorical variables between diabetic and non-diabetic patients. The results were considered significant for $p < 0.05$. All statistical analyses were performed using IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. And GraphPad Prism version 8.0.0 for Windows, GraphPad Software, San Diego,California, USA, www.graphpad.com.

## 3. Results

A total of 2041 individuals were identified. Of the 2,041 participants, 1,279 were excluded from the study, including 574 without RT-PCR performed or not catalogued, 142 individuals under 18 years of age, 559 without complete medical records and 4 diagnosed with gestational diabetes (Figure 1).

**Figure 1** - Summary flowchart of study.




Source: Authors (2021).

Of the 762 infected with COVID-19, approximately 70% of them were diagnosed with DM (2.6% with type 1 diabetes and 97.4% with type 2 diabetes) with an average of 12.05±8, 97 years with the disease, however, data regarding dm time were obtained only 12.38% of patients. In addition, 13.4% of patients were also diagnosed with chronic kidney disease (mean creatinine of 1.32±1,17). The results regarding age, weight and BMI are described in Table 1. In this sense, it is observed that diabetic patients have a higher mean age (66.27±0.81 vs. 51.44±0.78), $p < 0.0001$) and have a higher BMI (30.29±0.92 vs. 27±1.06, $P = 0.021$) when compared to those without diabetes.

**Table 1 -** Difference of continuous variables between diabetics and non-diabetics. Values expressed in mean and standard deviation.

| Variables | Total (n=762) | No diabetes (n=229) | With diabetes (n=533) | Average Difference | 95%IC | P-value |
|---|---|---|---|---|---|---|
| **Age (years)** | 55.9±17.76 | 51.44±0.78 | 66.27±0.81 | 14,828 | 12,629 - 17,029 | <0,0001 |
| **Weight (kg)** | 74.4±22.98 | 72.15±2.62 | 76.83±2.07 | 4,674 | -1,979 - 11,327 | 0,141 |
| **BMI (kg/m2)** | 28.58±8.52 | 27±1.06 | 30.29±0.92 | 3,288 | 0,502 - 6,074 | 0,021 |

BMI: body mass index. Source: Authors.

Table 2 illustrates the demographic characteristics of covid-19-infected patients stratified among people with and without diabetes. Apparently, there are no differences between men, women and race($p > 0.05$). However, individuals with diabetes had a higher prevalence of obesity and smoking (35.2 and 60.3%, respectively), $p < 0.0001$.

Patients with DM presented a more severe clinical picture when compared to those without DM. Shown in Table 3, diabetes seems to be a risk factor for patients with COVID-19 to present alterations related to a worse prognosis of A1c, ferritin, C-reactive protein (CRP), oxalacetic transaminase (TGO) and pyruvic transaminase (PGT). In addition, it is observed that patients with diabetes have a higher prevalence of coronary artery disease (CAD) and cerebrovascular arterial disease (CED) ($p < 0.0001$), table 3. Finally, Figure 2 shows that the presence of diabetes in COVID-19 is associated with a higher frequency of death, hospitalization and mechanical ventilation in this population ($p < 0.0001$).

**Table 2 -** Demographic characteristics of the population. Values expressed in N (%)

| Variables | Total (n= 762) | No diabetes (n=299) | Diabetes (n=533) | $X^2$ | Valor de P |
|---|---|---|---|---|---|
| **Sex** | | | | | |
| **Women** | 411 (53,9) | 289 (54,2) | 122 (53,3) | 0,058 | 0,81 |
| **Men** | 351 (46,1) | 244 (45,8) | 107 (46,7) | | |
| **Breed** | | | | | |
| **White** | 89 (11,7) | 65 (12,2) | 24 (10,5) | 9 | 0,054 |
| **Black** | 18 (2,4) | 14 (2,6) | 4 (1,7) | | |
| **Asian** | 11 (1,4) | 11 (2,1) | 0 | | |
| **Other** | 157 (20,6) | 117 (22) | 40 (17,5) | | |
| **Unkown** | 487 (63,9) | 326 (61,2) | 161 (70,3) | | |
| **Diabetes type** | | | | | |
| **DM1** | 6 (0,8) | 0 | 6 (2,6) | 762 | <0.0001 |
| **DM2** | 223 (29,3) | 0 | 223 (97,4) | | |
| **No diabetes** | 533 (69,9) | 533 (100) | 0 | | |
| **Obesity** | 55 (7,2) | 24 (4,5) | 31 (13,5) | 19,522 | <0.0001 |
| **Smoking** | 177 (23,2) | 94 (17,6) | 83 (36,2) | 31,104 | <0,0001 |
| **Insulin** | 138 (18,1) | 0 | 138 (60,3) | 392,23 | <0,0001 |
| **Oral antidiabetics** | 164 (21,5) | 2 (0,4) | 162 (70,7) | 469,58 | <0,0001 |

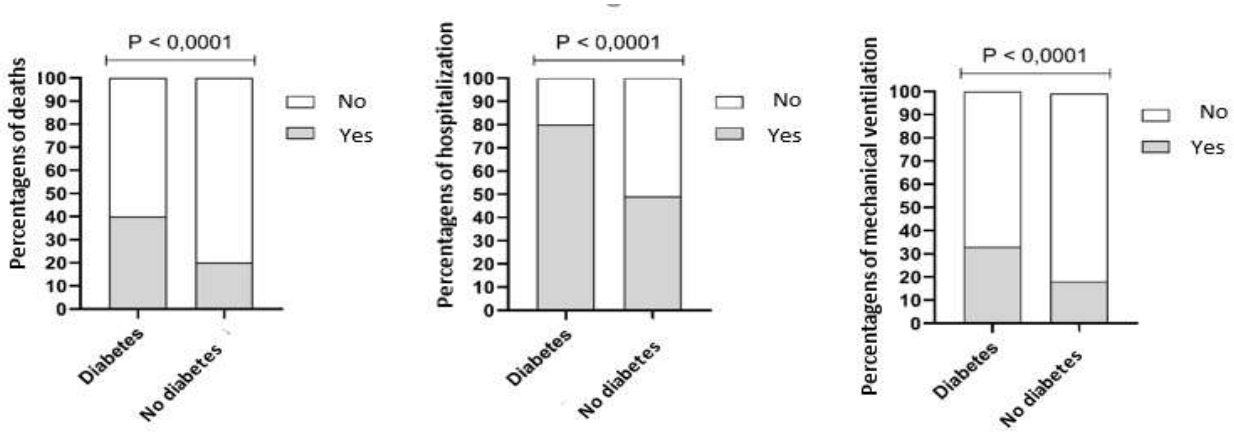
DM1: type 1 diabetes; DM2: type 2 diabetes.. Source: Authors.

**Table 3** - Clinical aspects. Values expressed in N (%)

| Variables | Total (n= 762) | No diabetes (n=299) | Diabetes (n=533) | $X^2$ | Valor de P |
|---|---|---|---|---|---|
| **High HbA1c** | 77 (10,1) | 9 (1,7) | 68 (29,7) | 138,932 | <0,0001 |
| **High Ferritin** | 122 (16) | 70 (13,1) | 52 (22,7) | 10,919 | <0,0001 |
| **High CRP** | 63 (8,3) | 38 (7,1) | 25 (10,9) | 3,03 | 0,082 |
| **High TGO** | 257 (33,7) | 177 (33,2) | 80 (34,9) | 55,25 | <0,0001 |
| **High TGP** | 131 (17,2) | 97 (18,2) | 34 (14,8) | 50,66 | <0,0001 |
| **Diabetic Retinopathy** | 19 (2,5) | 0 | 19 (8,3) | 45,35 | <0,0001 |
| **Diabetic Neuropathy** | 30 (3,9) | 0 | 30 (13,1) | 72,687 | <0,0001 |
| **Chronic Kidney Disease** | 102 (13,4) | 44 (8,3) | 58 (25,3) | 40,27 | <0,0001 |
| **High Blood Pressure** | 374 (49,1) | 181 (34) | 193 (84,6) | 164,18 | <0,0001 |
| **DAC or DACe** | 149 (19,6) | 70 (13,1) | 79 (34,6) | 49,95 | 0,0001 |
| **Pulmonar Disease** | 118 (15,5) | 69 (12,9) | 49 (21,4) | 8,74 | 0,003 |
| **Serious Medical Condition** | 176 (23,1) | 97 (18,2) | 79 (34,5) | 73,6 | <0,0001 |

CRP: C-reactive protein; TGO: oxaloacetic transaminase; TGP: pyruvic transaminase; CAD: coronary artery disease; CADe: cerebrovascular arterial disease. Source: Authors.

**Figure 2 -** Percentage of death (A), hospitalization (B) and mechanical ventilation (C) in patients with and without diabetes. Values expressed in N (%).




Source: Authors.

## 4. Discussion

The results of our study were in agreement with most clinical trials and studies involving the problem between diabetes and COVID-19, having statistical significance, when compared to people without DM in all studied variables. Among the different biochemical parameters evaluated as TGO, PGT, serum ferritin and CRP, higher markers were higher in individuals with diabetes when compared to those without diabetes and positively associated with worse outcomes(Guo et al., 2020). It was only notethat, in relation to gender, in our study, there were no differences in relation to the outcomes. According to a large population-based study including 264,390 individuals with type 1 DM and 2,874,020 patients with type 2 DM registered with a general practice in England showed that mortality related to DM COVID-19 was higher in men(Holman et al., 2020). Another systematic review of observational studies published in April 2021 confirms that males compared to females were associated with an increased risk of COVID-19-relateddeath (Schlesinger et al., 2021). A possible explanation would be attributed to the fact that we are a reference hospital for diabetes treatment, but not for COVID-19. Thus, more severe patients were transferred to other units where there was greater structure and support for more specialized interventions, creating a possible bias in our analyses.

Because it is a chronic and complex inflammatory disease, especially with regard to type 2 of the disease, with imbalance in the immunesystem(Berbudi et al., 2019; Guzmán & López, 2012), diabetes mellitus,far beyond hyperglycemia brings with it a series of triggers for the production of inflammatory cytokines produced in various organs, highlighted in the visceral adipose system. Interleukin-6, Tumor Necrosis Factor Alpha and Beta (TNF-α), adipocins are examples of inflammatory markers widely studied in metabolic syndrome, in which DM is inserted(Tanaka, 2016). However, with the advance of molecular medicine several other inflammatory substances have been discovered, some of which are even associated with specific complications of diabetes, and interleukin 18 can be cited, currently considered as amarker and prognostic factor in diabetes kidney disease (Satış et al., 2021; Hirooka & Nozaki, 2021). It should be noted here that this metainflammation or inflammatory storm as it is being termed does not lead to worse outcomes only in COVID-19, obviously. It is not new that diabetes has a much broader feedback and, it could be said, with complicating elements for several other diseases, favoring a higher prevalence not only of opportunistic infections or not, but also of cancer, depression, cardiovascular diseases, being also the main cause of blindness, end-stage kidney disease and non-traumatic amputations (Kautzky-Willer et al., 2016). Common denominator,the inflammatory "storm" and the vicious circle that reverberates and becomes more severe as the disease progresses in time and the worse its control, not only in relation to blood glucose itself, but involving glycemia, blood pressure, uric acid, emotional stateand many other variables(Hackett & Steptoe, 2016). Looking not only at the tip of the iceberg,it would not be difficult to presume, since the

beginning of the pandemic, that diabetes would be among the factors associated with worse outcomes, including mortality.

Since its inception, several studies, including multicentric meta-analyses have confirmed DM as a strong predictor of COVID-19-relatedmortality (Cariou et al., 2020). Nevertheless, despite the indisputable association with the state of metainflammation, we do not have, so far, a specific marker of worse or better prognosis in the diabetic population infected by COVID-19, which is the great challenge of the moment (Brito et al., 2020). We know that disease time is important, as well as associated comorbidities, metabolic control, socioeconomic condition, among others (Brito et al., 2020). But the current task force is looking for one or more factors that could be specifically associated with coronavirus infection (Kumar et al., 2020). The unveiling of this problem would bring many benefits, favoring more effective and specific approaches. However, until then, the results are only speculative (Schlesinger et al., 2021).

Several lines of evidence suggest a role for a homologue of the angiotensin-converter enzyme 2 (ECA2), a membrane protein that has high affinity when binding ectodomain of the Peak SARS-CoV-2. Sequence-based analyses released by SARS-CoV-2 infer that the host receptor for cell input of the virus is ACE2(Li, 2008).

It was found that the more expressed the ACE2 protein is in cell lines, the greater the susceptibility to infection and replication by SARS-CoV(Tanonaka & Marunouchi, 2016). Thus, identifying diseases and characteristics causally associated with altered expression of ACE2 may clarify why certain individuals are more susceptible to SARS-CoV-2 infection (or more severe infections) and the underlying mechanisms (Rao et al., 2020).

Studies propose a potential effect of diabetes on increased expression and activity of ACE2. Increased ace2 protein levels were found in both people with type 1 diabetes and type 2 diabetes (Gutta et al., 2018) and diabetic mice (Wysocki et al., 2006). A recent study of mendel randomization analysis highlighted the provisional relevance of diabetes-related characteristics is to ace2 expression, the most consistent finding of increased expression of ACE2 in the lung in diabetic individuals (Rao et al., 2020).

Notably, pro-inflammatory status, attenuation of innate immune response, possibly increased level of ACE2 in people with diabetes probably contribute to a worsening prognosis by SARS-CoV-2 and assistance for severe outcomes (Bonyek-Silva et al., 2021).

A clue to the search for these possible markers may be found in anatomoptologic studies of the pancreas, where it is known, that there is a viral tropism for this organ, causing in many affected, disdifferentiation of both β cellsand also α cells (M. Salazar, J. Barochiner, 2020). This process, although likely to occur in individuals without DM, is statistically much higher in those with DM and has led to one of the components of the so-called "post-COVID syndrome", as enigmatic as the disease itself, both worsening glycemic control in patients already affected and who recovered as pulling the trigger in those predisposed, with an insulin reserve already partially compromised (Müller et al., 2021).

Studies have shown that SARS-CoV-2 is capable of infecting and replicating human endocrine and exocrine cells of the pancreas and that human pancreatic alpha and beta cells derived from pluripotent stem cells may be permissive to SARS-CoV-2infection (Müller et al., 2021). Furthermore, the expression of ACE2 in the microvasculature component was observed in the adult human pancreas, both in the endocrine compartment and in the exocrine compartment. The presence of ACE2 corroborates an increased sensitivity of beta cells to SARS-CoV-2 during inflammatory conditions (Müller et al., 2021; Steenblock et al., 2021).

The evidence described, therefore, identified a link between inflammation and ace2 expression levels in islet β cells, since the supraregulation of ACE2 under pro-inflammatory conditions associated with tropism in pancreatic human β cells by SARS-CoV-2, is a major determinant for the entry, spread and transmissibility of the COVID-19 disease-relatedvirus (Müller et al., 2021; Cao et al., 2020).

Thus, it is imperative to clarify whether human pancreatic endocrine cells are permissive and affected by SARS-CoV-

2 infection and elucidate the mechanisms underlying a potential endocrine dysfunction associated with COVID-19.

## 5. Conclusion

Considering the epidemiological importance of diabetes, urgent research is made that elucidate the above-mentioned doubts, aiming at more appropriate therapeutic interventions and, therefore, improving outcomes in this population. In the case of a new and still little known disease, with several questions, probably many of the answers will only come over time, through more robust, prospective and randomized studies, with larger and more diverse populations.

Therefore, we suggest future analyzes and comparisons to assess clinical outcomes, glycemic control and sequelae related to post COVID syndrome 19 in individuals with and without diabetes.

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