

## Chronic pain, obesity and inflammation in diabetic patients assisted in primary care: a cross-section study

*Dor crônica, obesidade e inflamação de pacientes diabéticos atendidos na atenção primária: um estudo transversal*

*Dolor crónico, obesidad e inflamación de pacientes diabéticos atendidos en atención primaria: estudio transversal*

### ABSTRACT

**Objective:** to compare chronic pain, obesity and inflammation in patients with and without type 2 diabetes mellitus treated in primary care. **Method:** cross-sectional study with a quantitative approach carried out in primary care in the Federal District. Data collection took place between 2017 and 2018 with 269 participants divided into two groups: with diabetes (n=142) and without diabetes (n = 127). The instruments adopted were: socio-demographic and clinical questionnaire, anthropometry, visual analogue scale for pain assessment, inflammation by the levels of the cytokines tumor necrosis factor and Interleukin 6. Descriptive statistical analysis was performed using SPSS®20.0. **Results:** age from 60 to 69 years, low education, retirement, smoking, high blood pressure, high blood glucose, and high glycosylated hemoglobin were significantly related to DM2. Cytokine levels were higher in patients with diabetes ( $p \leq 0.000$ ). There was a high prevalence of chronic pain in the lower limbs and obesity, which were significantly associated with higher levels of tumor necrosis factor and Interleukin 6. **Conclusion:** the relationship between chronic pain, obesity, and inflammation in diabetic patients was demonstrated. Nursing must consider them in nursing interventions, aimed at controlling diabetes and preventing complications.

**Descriptors:** Nursing; Primary Health Care; Diabetes Mellitus; Obesity; Cytokines.

### RESUMO

**Objetivo:** comparar dor crônica, obesidade e inflamação de pacientes com e sem diabetes mellitus do tipo 2 atendidos na atenção primária. **Método:** estudo transversal de abordagem quantitativa realizado na atenção primária do Distrito Federal. A coleta de dados ocorreu entre 2017 e 2018 com 269 participantes divididos em dois grupos: com diabetes (n=142) e sem diabetes (n=127). Os instrumentos adotados foram: questionário sócio demográfico, clínico, antropometria, escala visual analógica para avaliação da dor, inflamação pela dosagem de citocinas fator de necrose tumoral e Interleucina 6. A análise estatística descritiva foi realizada no SPSS®20.0. **Resultados:** a idade de 60 a 69 anos, baixa escolaridade, aposentadoria, tabagismo, hipertensão arterial, glicemia, hemoglobina glicada elevados foram significativamente relacionados ao DM2. Os níveis das citocinas foram maiores naqueles com diabetes ( $p \leq 0,000$ ). Observou-se elevada prevalência de dor crônica nos membros inferiores e obesidade, que foram significativamente associados aos maiores níveis do fator de necrose tumoral e Interleucina 6. **Conclusão:** foi demonstrada a relação entre dor crônica, obesidade e inflamação nos diabéticos. A enfermagem deve considerá-los nas intervenções de enfermagem, visando controle do diabetes e prevenção de complicações.

**Descritores:** Enfermagem; Atenção Primária à Saúde; Diabetes Mellitus; Obesidade; Citocinas.

### RESUMEN

**Objetivo:** comparar el dolor crónico, la obesidad y la inflamación en pacientes con y sin diabetes mellitus tipo 2 (DM2) tratados en atención primaria. **Método:** estudio transversal con abordaje cuantitativo realizado en atención primaria en el Distrito Federal. Se produjo una cola de datos entre 2017 y 2018 con 269 participantes divididos en dos grupos: con diabetes (n = 142) y sin diabetes (n = 127). Los instrumentos están equipados con: cuestionario sociodemográfico, clínico, antropométrico, escala visual analógica para evaluación del dolor, inflamación de la dosis de citocinas para necrosis tumoral e interleucina 6. Se realizó análisis estadístico descriptivo sin SPSS®20.0. **Resultados:** la edad de 60 a 69 años, baja escolaridad, jubilación, tabaquismo, hipertensión arterial, glucemia, niveles elevados de hemoglobina glucosilada significativamente relacionados con DM2. Hay nueve citocinas que fueron más altas en las personas con diabetes ( $p \leq 0,000$ ). Hubo una alta prevalencia de entumecimiento crónico en miembros inferiores y obesidad, asociado significativamente con niveles más altos de necrosis tumoral e interleucina 6. **Conclusión:** se ha demostrado una relación entre entumecimiento crónico, obesidad e inflamación en diabéticos. El paciente debe considerar nuevas intervenciones para la enfermedad, con el objetivo de controlar la diabetes y prevenir complicaciones.

**Descritores:** Enfermería; Atención Primaria de Salud; Diabetes Mellitus; Obesidad; Citocinas.

Luciano Ramos de Lima<sup>1</sup>

 [0000-0002-2709-6335](https://orcid.org/0000-0002-2709-6335)

Ananda Goncalves Menezes<sup>1</sup>

 [0000-0001-8629-0843](https://orcid.org/0000-0001-8629-0843)

Marina Morato Stival<sup>1</sup>

 [0000-0001-6830-4914](https://orcid.org/0000-0001-6830-4914)

Silvana Schwerz Funghetto<sup>1</sup>

 [0000-0002-9332-9029](https://orcid.org/0000-0002-9332-9029)

Cris Renata Grou Volpe<sup>1</sup>

 [0000-0002-3901-0914](https://orcid.org/0000-0002-3901-0914)

Izabel Cristina Rodrigues da Silva<sup>1</sup>

 [0000-0002-6836-3583](https://orcid.org/0000-0002-6836-3583)

Mani Indiana Funez<sup>1</sup>

 [0000-0002-4315-7185](https://orcid.org/0000-0002-4315-7185)

<sup>1</sup>University of Brasília, Brasil

**Corresponding author:**

Luciano Ramos de Lima

**E-mail:** [ramosll@unb.br](mailto:ramosll@unb.br)

### How to cite this article:

Lima LR, Menezes AG, Stival MM, et al. Chronic pain, obesity and inflammation in diabetic patients assisted in primary care: a cross-section study. Revista de Enfermagem do Centro-Oeste Mineiro. 2021;11:e4153. [Access \_\_\_\_]; Available in: \_\_\_\_\_. DOI: <http://doi.org/10.19175/recom.v11i0.4153>

## INTRODUCTION

Diabetes mellitus (DM) affects about 422 million people worldwide and about 1.6 million annual deaths are related to DM<sup>(1)</sup>. In Brazil, more than 13 million people live with DM<sup>(2-3)</sup>. Type 2 diabetes mellitus (DM2) is especially caused by an interaction of genetic and environmental factors, and most patients with DM2 are overweight or obese, conditions considered to be among the main causal factors of DM2<sup>(2,4)</sup>.

In order to prevent complications in these patients, it is necessary to control glucose, triglycerides, dyslipidemia, and obesity, as they are considered factors that favor the progression of complications, such as diabetic neuropathy. Thus, obesity has an important role that, when added to the lack of glycemic control, reduces the cellular capacity to eliminate free radicals and triggers the metabolic impairment of several cells such as neurons, which will result in inflammatory processes and the presence of pain<sup>(2-3)</sup>.

When DM2 evolves with the association of chronic inflammation, it is usually related to the activation of the innate immune system. It is known that inflammation can occur early in the development of DM2 and in the presence of additional risk factors, such as increased adiposity and insulin resistance, which contribute to further deterioration and metabolic imbalance, in addition to the development of painful processes<sup>(5)</sup>.

Thus, in this process, there is an increase in the levels of inflammatory mediators expressed by inflammatory cytokines, such as tumor necrosis factor alpha (TNF- $\alpha$ ), interleukin-1 beta (IL-1 $\beta$ ), IL-2, IL-6 and IL-8, among other cytokines that are markers of inflammation and may, therefore, be related to the painful process<sup>(5)</sup>. It is worth emphasizing the relationship that has been investigated between pain, inflammation and oxidative stress on nervous, endocrine and immune system dysfunctions arising in conjunction with DM2. Associations between obesity, waist circumference, body fat and muscle mass in diabetics were investigated in England, and it was observed that fat mass and body mass index (BMI) were related to DM<sup>(6)</sup>. In France, 766 patients with DM2 were stratified and among those with high BMI, 20% had pain<sup>(7)</sup>. In Japan, pain was related to obesity, demonstrating that individuals with pain had higher BMI<sup>(8)</sup>. Based on the above, it is observed that there are few investigations in the Brazilian literature on the

relationships between obesity, pain, especially chronic pain, and inflammation in individuals with DM.

Nursing has developed research on this theme<sup>(9-10)</sup>, however, with a more theoretical approach, with literature review studies. It is, therefore, necessary to develop research addressing these factors in the population of diabetics, especially when assisted in primary care, an important scenario for nurses to monitor patients with DM2. Thus, the objective of this study was to compare chronic pain, obesity and inflammation in patients with and without DM2 treated in primary care.

## METHODOLOGY

This is a cross-sectional study with a quantitative approach carried out in a Basic Health Unit (BHU) in the Federal District, which has three Family Health Strategy (FHS). For the sample calculation, the number of adult patients registered in an FHS (N=900) of the respective BHU was considered, with a confidence level of 95% and a statistical error of 5%, which resulted in 269 individuals as the final sample. Patients were divided into two groups with DM2 (n=142) and without DM (n=127). The sampling was for convenience and the group with DM2 included: patients diagnosed with DM2 for 06 months, age  $\geq 18$  years old, registered at the BHU and monitored at the service and being able to understand, verbalize and answer the proposed questions. In the group without DM, the inclusion criteria were the same, but they could not have a diagnosis of DM2. The research exclusion criteria were: pregnant women, people with mental illnesses and patients with cancer undergoing treatment. Data collection was carried out at the selected FHS at BHU, between August 2017 and June 2018.

For data collection, undergraduate students from the nursing and pharmacy courses were trained by professors from the Research Group. Participants were instructed to appear fasting at the BHU for blood collection in order to measure the biochemical parameters. Samples of 15 ml of blood were collected from the antecubital vein, in vacuum tubes, to investigate fasting blood glucose, glycated hemoglobin, total cholesterol, HDL, LDL, triglycerides, levels of inflammatory cytokines TNF- $\alpha$  and IL-6. The analyses were performed at the Clinical Analysis Laboratory of the University of Brasília. Values considered

normal were: fasting glucose  $\leq 126$  mg/dl, glycated hemoglobin (%), total cholesterol  $\leq 160$  mmol/L, HDL  $> 40$  mmol/L, LDL  $\leq 160$  mmol/L and triglycerides  $\leq 150$  mmol/L<sup>(3,11)</sup>.

Then, the participants answered a structured instrument for characterization of sociodemographic variables, lifestyle habits and clinical profile. An instrument was used to assess pain in terms of prevalence, location and duration, while pain intensity was measured using the visual analogue scale (VAS)<sup>(4)</sup>. Pain duration longer than 3 months was considered chronic pain<sup>4</sup>. Anthropometric measurements of weight and height were made in order to establish the BMI. Nutritional status was assessed and classified into eutrophic ( $18.5 \text{ kg/m}^2$  to  $24.9 \text{ kg/m}^2$ ), overweight ( $25 \text{ kg/m}^2$  to  $29.9 \text{ kg/m}^2$ ), and obesity ( $\geq 30 \text{ kg/m}^2$ )<sup>(2)</sup>.

Blood pressure (BP) was measured following all the steps recommended in the VII Brazilian Guidelines on Arterial Hypertension. BP was measured using the auscultatory technique, with a calibrated sphygmomanometer, with a cuff adapted to the patient's left arm and a stethoscope positioned over the line of the brachial artery.

Data analysis was done by creating a database in the Software Package for the Social Sciences (SPSS®) version 20.0. Initially, descriptive measures were calculated. To verify the

differences between proportions, the Chi-Square test was used. In the analysis of the normality of the variables, the Kolmogorov Smirnov test was adopted. As the variables were normally distributed, the t test and ANOVA with Bonferroni adjustment were used to compare the means between the study groups. A significance level of 5% was adopted for all tests.

This study was approved by the Research Ethics Committee of the State Health Department of the Federal District (CEPSES/DF) under opinion number 1.355.211/2015. All participants signed the Informed Consent Form.

## RESULTS

Two hundred and sixty-nine (269) individuals participated in this research and were divided into two groups: with DM2 (n=142) and without DM (n=127). Regarding sociodemographic data, most participants in the two groups were female, aged between 60 and 69 years, married, had completed elementary school, had an income of 2 to 3 minimum wages, did not smoke, did not drink alcohol, were sedentary, had normal sleep, were hypertensive and had chronic pain mainly in the lower limbs (LL). Most DM2 patients were retired, while non-DM patients were active (Table 1).

Table 1 - Comparison of the sociodemographic profile, life habits, comorbidities and pain of the participants according to the study groups (n=269), Brasília-DF, 2019.

		Study groups					P*
		Total (n=269)	With DM2 (n=142)		Without DM (n=127)		
		n (%)	N	%	n	%	
<b>Sex</b>	Female	220 (81.8)	112	78.9	108	85.0	0.125
	Male	49 (18.2)	30	21.1	19	15.0	
<b>Age (years)</b>	30 to 39	10 (3.7)	3	2.1	7	5.5	0.007
	40 to 49	34(12.6)	15	10.6	19	15.0	
	50 to 59	50(18.6)	22	15.5	28	22.0	
	60 to 69	103(38.3)	59	41.5	44	34.6	
	70 to 79	60(22.3)	33	23.2	27	21.3	
	$\geq 80$	12(4.5)	10	7.0	2	1.6	
<b>Marital status</b>	Single	36(13.4)	24	16.9	12	9.4	0.688
	Married	156(58.0)	76	53.5	80	63.0	
	Divorced	25(9.3)	14	9.9	11	8.7	
	Widowed	52(19.3)	28	19.7	24	18.9	
<b>Schooling</b>	Illiterate	19(7.1)	13	9.2	6	4.7	0.003
	Elementary	153(56.9)	90	63.4	63	49.6	

(continua)

		Study groups					P*
		Total (n=269)	With DM2 (n=142)		Without DM (n=127)		
		n (%)	n	%	n	%	
Family income	High school	92(34.2)	35	24.6	57	44.9	0.501
	University	59(21.9)	4	2.8	1	0.8	
	≤ 1 MW	101(37.5)	56	39.4	45	35.4	
Occupation	2 to 3 MW	128(47.6)	66	46.5	62	48.8	0.007
	≥ 4 MW	40(14.9)	20	14.1	20	15.7	
	Active	104(38.7)	47	33.1	57	44.9	
Smoking	Retired	82(30.5)	55	38.7	27	21.3	0.023
	Inactive	83(30.9)	40	28.2	43	33.9	
Drinker (alcohol)	Yes	18(6.7)	14	9.9	4	3.1	0.398
	No	251(93.3)	128	90.1	123	96.9	
Perform physical exercises	Yes	17(6.3)	10	7.0	7	5.5	0.112
	No	252(93.7)	132	93.0	120	94.5	
Sleep	Yes	85(31.6)	50	35.2	35	27.6	0.274
	No	184(68.4)	92	64.8	92	72.4	
SAH <sup>†</sup>	Normal	142(52.8)	72	50.7	70	55.1	0.000
	Difficulty sleeping	127(47.2)	70	49.3	57	44.9	
Chronic pain	Yes	191(71.0)	114	80.3	77	60.6	0.076
	No	78(29.0)	28	19.7	50	39.4	
	Yes	232(86.2)	127	89.4	105	82.7	
Pain site	No	37(13.6)	15	10.6	22	17.3	0.418
	LL <sup>§</sup>	169(62.8)	92	64.8	77	60.6	
	UL	30(11.2)	15	10.6	15	11.8	
	Dorsal region	45(16.7)	24	16.9	21	16.5	
	Other sites	25(9.3)	11	7.7	14	11.0	

Legend: \*chi-square test ( $\chi^2$ ); †SAH: Systemic Arterial Hypertension; ‡MW: minimum wage; §LL: lower limbs; ||UL: upper limbs.

Source: Prepared by the authors.

It was found that age, education, occupation, smoking and being hypertensive were significantly related to the presence of DM2, that is, patients aged between 60 and 69 years ( $p=0.007$ ), with elementary education ( $p=0.003$ ), retired ( $p=0.007$ ), smokers ( $p=0.023$ ), and hypertensive ( $p=0.000$ ) had a higher prevalence of DM (Table 1).

In the assessment of pain in the feet/calf using the VAS, it was observed that in both groups

the mean pain was 7.0, that is, most described it as severe. The mean amount of medication, fasting blood glucose and glycated hemoglobin was significantly higher in patients in the DM2 group. On the other hand, those in the group without DM had higher mean diastolic blood pressure (DBP), total cholesterol and LDL ( $p<0.05$ ) (Table 2).

Table 2 - Comparison of pain intensity in the feet/calf (VAS), blood pressure levels, anthropometry, biochemical profile and chronic pain of participants according to study groups (n=269), Brasília-DF, 2019.

	Study groups				p*
	With DM2 (n=142)		Without DM (n=127)		
	Mean	SD	Mean	SD	
Foot/calf pain intensity (VAS <sup>†</sup> )	7.5	2.06	7.2	2.19	0.197
Quantity of Medication/day	4.5	2.60	2.9	1.94	0.000
Systolic blood pressure/SBP (mmHg)	134.2	20.14	136.2	18.79	0.470
Diastolic blood pressure/DBP (mmHg)	81.0	13.50	85.2	13.45	0.014
Body Mass Index (BMI) (kg/m <sup>2</sup> )	30.9	5.04	32.7	28.77	0.491
Fasting blood glucose (mg/dl)	146.64	65.26	90.81	13.49	0.000
Glycated Hemoglobin (%)	6.99	1.85	5.61	0.53	0.000
Total Cholesterol (mmol/L)	188.15	42.10	208.63	46.80	0.000
Triglycerides (mmol/L)	164.53	90.39	152.89	94.60	0.147
HDL (mmol/L)	46.65	9.89	49.36	11.45	0.109
LDL (mmol/L)	107.19	36.73	129.77	40.91	0.000

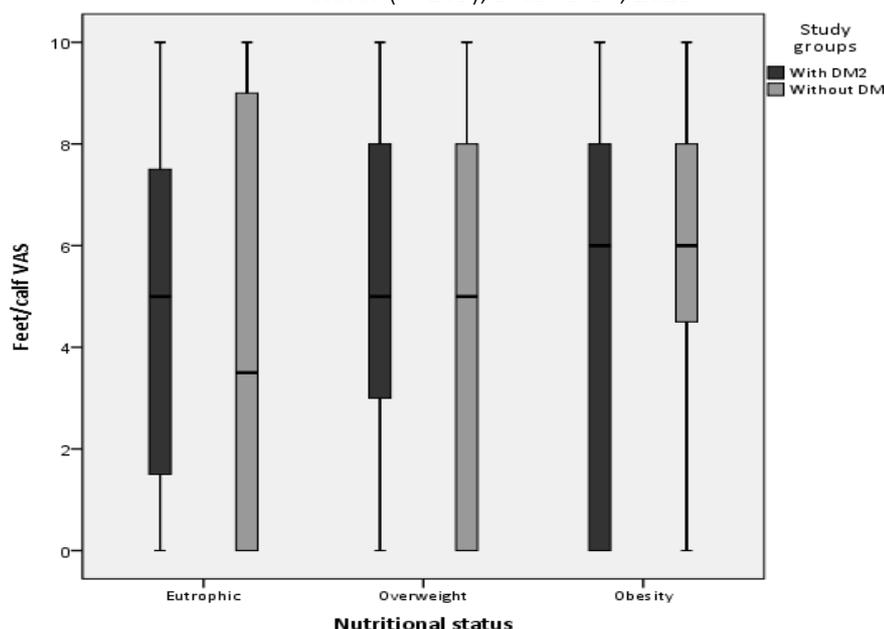
Legend: \*t test; SD: standard deviation; † VAS: visual analog scale.

Source: Prepared by the authors.

In the classification of nutritional status, it was observed that obesity prevailed in both study groups, with 52.8% in patients with DM2 and 48.0% in those without DM. When comparing the intensity of pain in the feet/calf of the study groups according to nutritional status, it was possible to observe a significant difference

between groups. It was found that when comparing eutrophics, those in the group without DM had lower pain intensity than those with DM2 ( $p=0.019$ ). Obese patients showed greater intensity of pain in the feet/calf when compared to eutrophic patients ( $p=0.042$ ) (Figure 1).

Figure 1 - Comparison of pain intensity in the feet/calf (VAS) of the study groups according to nutritional status (n=269), Brasília-DF, 2019.

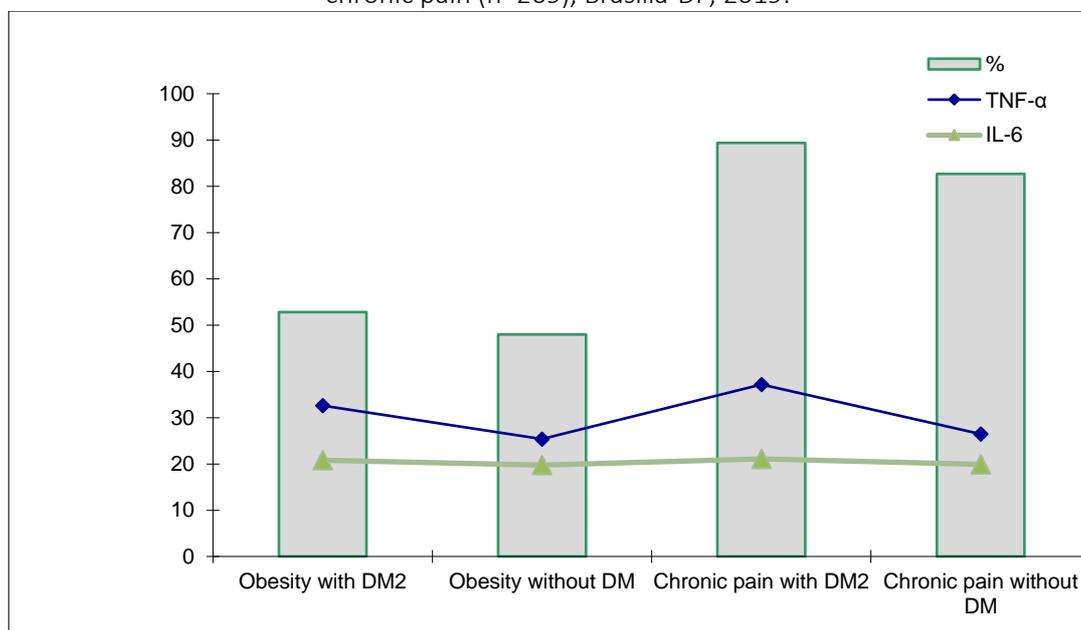


Source: Prepared by the authors.

Finally, analyses of the concentrations of the inflammatory cytokines IL-6 and TNF- $\alpha$  were performed and compared between the study groups. IL-6 and TNF- $\alpha$  levels were significantly higher in the group with DM2 compared to the group without DM. Patients in the DM2 group had a mean TNF- $\alpha$  of 36.12 pg/ml ( $\pm$ 18.18) while those without DM had a mean TNF- $\alpha$  of 26.33 pg/ml ( $\pm$ 18.00) ( $p$ <0.000). Regarding IL-6, those with DM2 had a mean of 21.49 ( $\pm$ 8.23) and those without DM had a mean of 19.69 pg/ml ( $\pm$ 5.67) ( $p$ <0.000).

When comparing the levels of inflammatory cytokines in the study groups according to the presence of obesity, there was a higher mean of TNF- $\alpha$  ( $p$ =0.024) and IL-6 ( $p$ <0.000) in obese patients with DM2 (M= 32.61 pg/ml; M=20.79 pg/ml, respectively) than in those obese without DM (M=25.38 pg/ml; M=19.74 pg/ml, respectively). Regarding chronic pain, higher levels of TNF- $\alpha$  (M=37.16 pg/ml;  $p$ <0.000) and IL-6 (M=21.09 pg/ml;  $p$ <0.000) were observed in those patients with DM2 who had chronic pain when compared to those without DM (TNF- $\alpha$ =26.49 pg/ml; IL-6=19.91 pg/ml) (Figure 2).

Figure 2 - Comparison of TNF- $\alpha$  and IL-6 levels in the study groups according to the presence of obesity and chronic pain (n=269), Brasília-DF, 2019.



Source: Prepared by the authors.

## DISCUSSION

The sociodemographic profile of patients with DM2 in this research is similar to that observed in other studies carried out in Brazil<sup>(9-10)</sup> and international<sup>(5-6,12)</sup>, which described samples of diabetic patients, mostly women, married, with mean 64 years old, few years of schooling and sedentary. In the present study, there was a higher prevalence of DM2 in individuals aged between 60 and 69 years, with little schooling and retired people. Other studies found a sample profile similar to that observed in the present study<sup>(13-15)</sup>.

The results of this study revealed a higher prevalence of smoking in the group of patients with DM2, in addition to presenting SAH as an associated comorbidity. A study carried out in

Thailand that compared individuals with and without DM also observed the prevalence of smoking among diabetics<sup>(15)</sup>, corroborating the results of other studies in this regard<sup>(14,16-17)</sup>. It is known that smoking added to the presence of DM increases the patient's risk of having cardiovascular disease<sup>(3)</sup>.

In addition, this study identified a greater use of medications in the DM2 group, with a mean of 4.5 medications/day. It should be considered that the World Health Organization (WHO) considers polypharmacy as the routine use of  $\geq 5$  simultaneous medications per patient, whether prescribed, over-the-counter or other traditional medications<sup>(18)</sup>. Other studies carried out with diabetic patients also found similar

results<sup>(17,19-20)</sup>. This result was expected, since an increase in the consumption of medication by the elderly was observed, in addition to the treatment of other comorbidities associated with DM, such as SAH. In this context, the role of nursing is important, especially when there is a need to use two or more medications, a situation continuously common with increasing life expectancy, so that medication interactions and side effects do not become dangerous and cause damage to the health of the individual<sup>(10,18)</sup>.

In this study, the group with DM2 had higher mean fasting glucose and glycated hemoglobin than those without DM, demonstrating the lack of glycemic control in these individuals. An international study also demonstrated this increase in glycemic indexes in patients with DM<sup>(16)</sup>. It is noteworthy that glycated hemoglobin is an important marker of glycemic control and should be used by health professionals to monitor the control of DM2, since glycemic variations need to be considered in the control goals, in order to alleviate complications arising from lack of glycemic control, like diabetic neuropathy, visual and vascular alterations<sup>(3-4)</sup>.

In this sense, it is evident that the proper treatment of SAH in diabetic patients aims to prevent the development of comorbidities and complications arising from DM, as altered blood pressure increases the risk of heart and vascular diseases, myocardial infarction, angina and ischemia, besides to contribute to the process of renal and retinal damage<sup>(13)</sup>.

The results of the present study showed that diabetic patients had lower mean values of total cholesterol and LDL. Based on this finding, it can be inferred that these patients were using medication for the treatment of dyslipidemia, a variable that was not collected in this study. However, despite the values being lower than the group without DM, the mean total cholesterol presented was considered high, according to the classification adopted in this study. Similar findings were observed in other studies, which emphasize the importance of controlling dyslipidemia in individuals with DM<sup>(15,21)</sup>.

Regarding the nutritional status of the participants, most were obese. It is known that obesity is a factor that contributes to changes in the lipid and glycemic profile and in blood pressure levels, a fact observed in this sample. It is noteworthy that the maintenance of this nutritional status in the group without DM can

lead to individuals becoming carriers of the disease in the future<sup>(3,5)</sup>.

Regarding pain, most participants had chronic pain and obese patients showed greater intensity of pain in the feet/calf when compared to eutrophic patients. A study conducted with 766 patients in France estimated the prevalence of chronic pain in diabetic individuals, noting that, similarly to the present study, patients with DM2 were obese and had a higher prevalence of pain, referred to as numbness or burning sensation. It is worth mentioning that these pain descriptors are frequently used by patients with diabetic neuropathy<sup>(7)</sup>.

A high prevalence of chronic pain has also been observed in other studies. A study evaluated 129 patients with DM2 in primary care in Santarém-Pará, of which 67% reported pain and 34% of these were detected as having moderate pain in the lower limbs, described as tingling, needling and numbness<sup>(9)</sup>. In Africa, it was found that out of 961 diabetics, 52% reported chronic pain<sup>(16)</sup>.

When comparing pain intensity according to nutritional status, the fact that obese patients report greater pain intensity deserves to be highlighted for the health team, given the control of obesity and its damage to these patients' lives. Also, obese diabetics can experience worse health conditions, negatively impacting their quality of life.

It is known that diabetic patients with chronic pain have inflammatory changes. In the assessment of inflammation, it was observed that the levels of IL-6 and TNF- $\alpha$  were significantly higher in the group with DM2 compared to the group without DM, which increases in the presence of obesity and chronic pain. Other studies have shown that patients with DM and overweight had higher levels of TNF- $\alpha$ <sup>(15,21)</sup>. In a meta-analysis, 34 articles were reviewed to show that the concentration of TNF- $\alpha$  significantly increased in obese individuals compared to non-obese individuals, while IL-6 showed no difference between groups<sup>(22)</sup>. However, in a Brazilian study, higher concentrations of IL-6 were identified in obese diabetic patients, suggesting that the higher the BMI, the higher the concentration of IL-6<sup>(23)</sup>.

In a study carried out in Mexico with diabetic patients, pain was associated with IL-6 levels in neuropathy patients<sup>(24)</sup>. Still, in a study with women with abdominal obesity, a higher concentration of IL-6 was found, when compared

to those without obesity<sup>(25)</sup>. It is important to emphasize that the adipose tissue is considered an organ with endocrine function that releases in the body some pro-inflammatory cytokines such as TNF- $\alpha$ <sup>(4,5,27-28)</sup>. This cytokine, for decades, has been studied as a factor that induces insulin resistance<sup>(7-8)</sup> and also reaffirmed by the Brazilian Society of Diabetes<sup>(3)</sup>. On the other hand, IL-6 can be expressed in response to infection or nervous tissue damage, as it occurs mainly in diabetic individuals with neuropathy<sup>(9,19,22)</sup>.

This study showed the relationship between chronic pain, obesity and inflammation in patients with DM2. It is recommended that the identification of these factors is essential when approaching these patients. Studies have identified that the main nursing actions for patients with DM involve nursing interventions against the risk of ineffective peripheral tissue perfusion, risk of impaired cardiovascular function, ineffective health control, risk of unstable blood glucose, sedentary lifestyle, obesity, risk of impaired skin integrity and risk of falls. In this context, nursing interventions should be aimed at preventing heart disease, nutritional counseling, controlling prescribed medications, treating obesity and teaching about foot self-care<sup>(10,18,26-28)</sup>.

Therefore, it is considered that the presence of pain in this population is a very important finding for the nursing team, which should guide the patient to recognize that obesity can accelerate the process of complications arising from DM2, which can lead to insensitivity of the LL and risk for wound formation. In addition, pain can compromise the performance of DM2 patients in their daily activities.

Finally, this study presented as a limitation its cross-sectional design, which did not allow establishing causes and effects. In addition, no results regarding diabetic complications were presented. In this sense, it is recommended to carry out studies that aim to assess the influence of diabetic neuropathy on inflammation in these patients. Despite this, it is considered that the results found in this study can contribute to a direction of preventive health actions that should be prioritized in primary care, the best place to approach patients with DM2.

## CONCLUSION

The results of this study allow us to conclude that age from 60 to 69 years, low

schooling, retirement, smoking, high blood glucose, and high glycated hemoglobin were significantly related to DM2. There was a high prevalence of obesity and chronic pain. TNF- $\alpha$  and IL-6 levels were higher in patients with DM2, obese and chronic lower limb pain. It is emphasized that the observed characteristics need more attention in the context of health care, which involves education, lifestyle and presence of comorbidities. In nursing guidelines, these findings should be considered in order to be able to establish actions that enhance and improve the monitoring of patients with DM2, especially in primary care.

In this sense, nursing has a prominent role in primary care as a leading member of a team that offers care to patients with DM2. Actions should be specific in the assessment and control of obesity and pain, especially in the LL. It is recommended to evaluate the feet in these patients with pain, as they can progress to diabetic feet. Thus, these findings can support nursing care in the recognition of risk factors to design interventions and goals for DM2 control in individualized care.

## REFERENCES

- 1 - World Health Organization. Global Report on Diabetes. 2016;978:88. Disponível em: [http://www.who.int/about/licensing/%5Cnhttp://apps.who.int/iris/bitstream/10665/204871/1/9789241565257\\_eng.pdf](http://www.who.int/about/licensing/%5Cnhttp://apps.who.int/iris/bitstream/10665/204871/1/9789241565257_eng.pdf)
- 2 - Brasil Ministério da Saúde. Manual do pé diabético: estratégias para o cuidado da pessoa com doença crônica 2016. 62p. Disponível em: [http://189.28.128.100/dab/docs/portaldab/publicacoes/manual\\_do\\_pe\\_diabetico.pdf](http://189.28.128.100/dab/docs/portaldab/publicacoes/manual_do_pe_diabetico.pdf)
- 3 - Diretrizes da Sociedade Brasileira de Diabetes (2019-2020). Organização Adriana Costa e Forti et al. São Paulo: Editora Clammad, 2019. Disponível em: <https://www.diabetes.org.br/profissionais/images/DIRETRIZES-COMPLETA-2019-2020.pdf>
- 4 - American Diabetes Association. Obesity Management for the Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes-2019. Diabetes Care. 2019;42(Suppl.1):S81-89.

Disponível em: <https://doi.org/10.2337/dc19-S008>

5 - Rivero A, Martín IE, Marín DC, Rodríguez MA, Navarro GJF. Cytokines in Diabetes and Diabetic Complications. In: Foti M, Locati M. Cytokine Effector Functions in Tissues. Italy: Elsevier, 2017.

6 - Han TS, Al-Gindan YY, Govan L, Hankey CR, Lean MEJ. Associations of BMI, waist circumference, body fat, and skeletal muscle with type 2 diabetes in adults. *Acta Diabetol.* 2019;56(8):947-954. Disponível em: <https://doi.org/10.1007/s00592-019-01328-3>

7 - Bouhassira D, Letanoux M, Hartemann A. Chronic pain with neuropathic characteristics in diabetic patients: a French cross-sectional study. *PLoS One.* 2013;8(9):e74195. Disponível em: <https://doi.org/10.1371/journal.pone.0074195>

8 - Hozumi J, Sumitani M, Matsubayashi Y, Abe H, Oshima Y, Chikuda H, et al. Relationship between Neuropathic Pain and Obesity. *Pain Res Manag.* 2016;16(16):2487924. Disponível em: <https://doi.org/10.1155/2016/2487924>

9 - Aguiar FLXS, Ramos LFP, Bichara CNC. Detection of pain with neuropathic characteristics in patients with diabetes mellitus assisted in primary care units. *BrJP.* 2018;1(1):15-20. Disponível em: <https://doi.org/10.5935/2595-0118.20180005>

10 - Vieira VAS, Azevedo C, Sampaio FC, Oliveira PP, Moraes JT, Mata LRF. Cuidados de enfermagem para pessoas com diabetes mellitus e hipertensão arterial: mapeamento cruzado. *Rev. baiana enferm.* 2017;31(4):e21498. Disponível em: <https://doi.org/10.18471/rbe.v31i4.21498>

11 - Faludi AA, Izar MCO, Saraiva JFK, Chacra APM, Bianco HT, Afiune Neto A, et al. Atualização da Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose—2017. *Arq. bras. cardiol.* 2017;109(Suppl1):1–76. Disponível em: <https://doi.org/10.5935/abc.20170121>

12 - Herder C, Bongaerts BW, Rathmann W, Heier M, Kowall B, Koenig W, et al. Differential association between biomarkers of subclinical inflammation and painful polyneuropathy: results

from the KORA F4 study. *Diabetes Care.* 2015;38(1):91-6. Disponível em: <https://doi.org/10.2337/dc14-1403>

13 - Stojanović M, Cvetanović G, Anđelković M, Stojanović D, Rančić N. Impact of socio-demographic characteristics and long-term complications on quality of life in patients with diabetes mellitus. *Cent Eur J Public Health.* 2018;26(2):104-110. Disponível em: <https://doi.org/10.21101/cejph.a5022>

14 - Zhang Y, Wu J, Chen Y, Shi L. EQ-5D-3L Decrements by Diabetes Complications and Comorbidities in China. *Diabetes Ther.* 2020;11(4):939-950. Disponível em: <https://doi.org/10.1007/s13300-020-00788-z>

15 - Lainampetch J, Panprathip P, Phosat C, Chumpathat N, Prangthip P, Soonthornworasiri N, et al. Association of Tumor Necrosis Factor Alpha, Interleukin 6, and C-Reactive Protein with the Risk of Developing Type 2 Diabetes: A Retrospective Cohort Study of Rural Thais. *J Diabetes Res.* 2019;(8):2019:9051929. Disponível em: <https://doi.org/10.1155/2019/9051929>

16 - Jacovides A, Bogoshi M, Distiller LA, Mahgoub EY, Omar MK, Tarek IA, et al. An epidemiological study to assess the prevalence of diabetic peripheral neuropathic pain among adults with diabetes attending private and institutional outpatient clinics in South Africa. *J Int Med Res.* 2014;42(4):1018-28. Disponível em: <https://doi.org/10.1177/0300060514525759>

17 - Prado MAMB, Francisco PMSB, Barros MBA. Diabetes em idosos: uso de medicamentos e risco de interação medicamentosa. *Ciênc. Saúde Colet.* 2016;21(11):3447-3458. <https://doi.org/10.1590/1413-812320152111.24462015>

18 - World Health Organization. Medication Without Harm – Global Patient Safety Challenge on Medication Safety. Geneva: World Health Organization, 2017. Disponível em: <https://www.who.int/initiatives/medication-without-harm>

19 - Silva MRR, Diniz LM, Santos JBR, Reis EA, Mata AR, Araújo VE, et al. Uso de medicamentos e fatores associados à polifarmácia em indivíduos com diabetes mellitus em Minas Gerais, Brasil. *Ciênc. Saúde Colet.* 2018; 23(8):2565-2574. Disponível em:

<https://doi.org/10.1590/1413-81232018238.10222016>

20 - Penaforte KL, Araújo ST, Fernandes VO, Barbosa IS, Cestari VRF, Júnior RMM. Associação entre polifarmácia e adesão ao tratamento farmacológico em pacientes com diabetes. Rev RENE. 2017;18(5):631-8. Disponível em: <https://doi.org/10.15253/2175-6783.2017000500010>

21 - Cho NH, Ku EJ, Jung KY, Oh TJ, Kwak SH, Moon JH, et al. Estimated Association Between Cytokines and the Progression to Diabetes: 10-year Follow-Up From a Community-Based Cohort. J Clin Endocrinol Metab. 2020;105(3):e381-9. Disponível em: <https://doi.org/10.1210/clinem/dgz171>

22 - Duffles LF, Hermont AP, Abreu LG, Pordeus IA, Silva TA. Association between obesity and adipokines levels in saliva and gingival crevicular fluid: A systematic review and meta-analysis. J Evid Based Med. 2019;12(4):313-324. Disponível em: <https://doi.org/10.1111/jebm.12363>

23 - Rodrigues KF, Pietrani NT, Bosco AA, Campos FMF, Sandrim VC, Gomes KB. IL-6, TNF- $\alpha$ , and IL-10 levels/polymorphisms and their association with type 2 diabetes mellitus and obesity in Brazilian individuals. Arch Endocrinol Metab. 2017 Sept-Oct;61(5):438-446. Disponível em: <https://doi.org/10.1590/2359-3997000000254>

24 - Ramírez AC., Macedo RG, García CMD, Soto CS, Pádrón AM, Penã JE, et al. Neuropathy-specific alterations in a Mexican population of diabetic patients. BMC Neurology. 2017;17(161):e. Disponível em: <https://doi.org/10.1186/s12883-017-0939-6>

25 - Tangvarasittichai S, Pongthaisong S, Tangvarasittichai O. Tumor Necrosis Factor- $\alpha$ , Interleukin-6, C-Reactive Protein Levels and Insulin Resistance Associated with Type 2 Diabetes in Abdominal Obesity Women. Indian J Clin Biochem. 2016;31(1):68-74. Disponível em: <https://doi.org/10.1007/s12291-015-0514-0>

26 - Lima LR, Stival MM, Funghetto SS, Volpe CRG, Rehem TCMSB, Santos WS, et al. Lower quality of life, lower limb pain with neuropathic characteristics, female sex, and ineffective metabolic control are predictors of

depressive symptoms in patients with type 2 diabetes mellitus treated in primary care. Int J Diabetes Dev Ctries 2018; 8(38):1-8. Disponível em: <https://doi.org/10.1007/s13410-018-0667-5>

27 - Lima LR, Stival MM, Funghetto SS, Silva ICR, Rehem TCMSB, Santos WS, et al. Neuropatia e dor nos membros inferiores: sinais percussores do pé diabético. In: Parisi MCR, Leite CR, Rosa MFF. Interdisciplinaridade no contexto das doenças dos pés no diabetes: tratamento clínicos, políticas públicas e tecnologias em saúde. 1ª ed. Mossoró: EDUERN. 2021.

28 - Silva ACG, Stival MM, Funghetto SS, Volpe CRG, Funez MI, Lima LR. Comparação da dor e qualidade de vida entre indivíduos com e sem neuropatia diabética. Rev. Enferm. UFSM. 2021;(11): e1-10. Disponível em: <https://doi.org/10.5902/2179769263722>

#### Responsible editors:

Patrícia Pinto Braga

Daniel Nogueira Cortez

**Note:** This work is part of a scientific initiation research and PhD thesis linked to PPTCTS/UNB (Graduate Program in Health Sciences and Technologies/University of Brasília), "Analysis of clinical, inflammatory and genetic factors associated with painful diabetic neuropathy in Primary Care", financed by the Federal District Development Agency -FAP/DF. We thank the members of the Health, Care and Aging Research Group - GEPSSEN/UNB.

**Received in: 12/10/2020**

**Approved in: 17/05/2021**