Original Article

PREVALÊNCIA E FATORES ASSOCIADOS À DOENÇA ARTERIAL PERIFÉRICA EM INDIVÍDUOS COM DIABETES MELLITUS

PREVALENCE AND FACTORS ASSOCIATED WITH DISEASE PERIPHERAL BLOOD IN INDIVIDUALS WITH DIABETES MELLITUS

PREVALENCIA Y FACTORES ASOCIADOS CON LA ENFERMEDAD ARTERIAL PERIFÉRICA EN PACIENTES CON DIABETES MELLITUS

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RESUMO

Objetivo: estimar a prevalência e fatores associados à Doença Arterial Periférica (DAP) em pacientes com diagnóstico de Diabetes Mellitus do tipo 2 assistidos no Centro Hiperdia, Viçosa/MG. **Método:** estudo transversal, realizado a partir da análise de 249 prontuários, em 2012. A associação de DAP com cada variável foi avaliada pelo *Qui-quadrado de Pearson* ou Exato de *Fisher*. Regressão logística foi utilizada. **Resultados:** a amostra foi composta predominantemente por mulheres (71,1%), indivíduos acima de cinquenta anos (76,3%) e com diagnóstico de hipertensão (83,5%). Aproximadamente, 44,6% apresentaram obesidade e 14,9% úlcera prévia em membro inferior. A prevalência de DAP foi de 15,3%, sendo a chance da doença cinco vezes maior em indivíduos com 61 anos ou mais (*Odds Ratio* - OR=5,43; IC95%: 1,54 - 19,12) e com ausência de sensibilidade plantar (OR=3,17; IC95%: 1,01 - 10,06). **Conclusão:** esses resultados devem ser considerados no planejamento de ações preventivas e assistenciais a essa população.
Descritores: Doença arterial periférica; Diabetes mellitus; Estudos transversais.

ABSTRACT

Objective: to estimate the prevalence and factors associated with Peripheral Artery Disease (PAD) in patients with Diabetes Mellitus type 2 assisted at the Center Hiperdia, Viçosa-MG**. Method:** Cross-sectional study, based on the analysis of 249 records, in 2012. The PAD association with each variable was assessed using the chi-square Pearson or Fisher's exact. Logistic regression was used. **Results:** The sample was composed predominantly of women (71.1%), individuals over fifty years (76.3%) and diagnosed with hypertension (83.5%). Approximately 44.6% were obese and 14.9% prior ulcer in lower limb. The prevalence of PAD was 15.3%, the chance of disease five times higher in individuals with 61 years or more (OR=5.43; 95% CI: 1.54 - 19.12) and the absence of protective sensation plant (OR=3.17; 95% CI: 1.01 - 10.06). **Conclusion:** These results should be considered in the planning of preventive measures and assistance to this population.
Descriptors: Peripheral arterial disease; Diabetes mellitus; Cross-sectional studies.

RESUMEN

Objetivo: estimar la prevalencia y los factores asociados con la enfermedad arterial periférica (EAP) en pacientes con Diabetes Mellitus tipo 2 asistida en el Centro Hiperdia, Viçosa, MG. **Método:** Estudio transversal, basado en el análisis de 249 expedientes, en 2012. La asociación EAP con cada variable se evaluó mediante la chi-cuadrado de Pearson o exacta de Fisher. Se utilizó regresión logística. **Resultados:** La muestra se compone fundamentalmente de las mujeres (71,1%), las personas más de cincuenta años (76,3%) y diagnosticado con hipertensión (83,5%). Aproximadamente el 44,6% eran obesos y el 14,9% de la úlcera previa en el miembro inferior. La prevalencia de EAP fue del 15,3%, el riesgo de enfermedad cinco veces mayor en las personas con 61 años o más (OR =5,43; IC del 95%: 1,54 - 19,12) y la ausencia de plantas sensación (OR=3,17; IC del 95%: 1,01 - 10,06). **Conclusión:** Estos resultados deben ser considerados en la planificación de las medidas preventivas y de ayuda a esta población.
Descriptores: Enfermedad arterial periférica; Diabetes mellitus; Estudios transversales.

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INTRODUCTION

Peripheral Artery Disease (PAD) is one of the most prevalent complications in diabetic individuals and is characterized by a gradual reduction of blood flow due to occlusive factors in the arterial beds, triggered by an atherosclerotic process of the abdominal aorta and arteries of the lower limbs, causing reduction of the arterial lumen and consequent tissue ischemia. The most prevalent symptom in PAD is intermittent claudication, consisting of burning pain or cramp triggered by gait, accentuated by the continuation of the exertion and ceasing with rest[1-2].

Globally, there were 202 million people living with peripheral arterial disease in 2010, 69.7% of them in low-income or middle-income countries, including 54.8 million in Southeast Asia and 45.9 million in the Pacific Western region[3]. In Brazil, a cross-sectional population study evaluated 1,330 Japanese-Brazilians of both genders, aged ≥ 30, and found PAD in 21.1% of the patients, the same in both genders[4]. Epidemiological data showed a strong association between PAD and Diabetes Mellitus (DM)[3]. The Framingham's study, which based on questionnaire responses answered by the patients, found a 20% association of PAD and diabetes [5].

There are several risk factors for PAD, being DM and smoking the most important, followed by systemic arterial hypertension (SAH), dyslipidemia and advanced age[2]. In individuals diagnosed with DM, the longer the disease, the greater the risk of PAD, since the association of other factors such as smoking, sustained hyperglycemia, presence of peripheral neuropathy, dyslipidemia and SAH, predisposes to its onset[3]. In those individuals, the early detection of cases and the prevention and control of modifiable risk factors such as SAH, obesity, smoking, and others associated with PAD improve treatment efficacy, reduce the risk of complications such as ulcers and amputations, besides ensuring the quality of life of the assisted individuals[3].

The growing interest in early diagnosis of PAD has been occurring not only because of its increased prevalence associated with aging, but also because it relates to atherosclerotic disease in other territories, such as coronary and cerebral. The results of clinical studies have identified a substantial reduction in the risk of cardiovascular and cerebrovascular events, including death, myocardial infarction and cerebrovascular accident with appropriate pharmacological intervention in patients diagnosed with PAD[6].

This study aims to estimate the prevalence and factors associated with Peripheral Arterial Disease (PAD) in patients diagnosed with Type 2 Diabetes Mellitus assisted at the Hiperdia Center, Viçosa/MG.

METHODS

This is a cross-sectional study based on the medical records of individuals with type 2 DM who were followed up by the Hiperdia Center for Arterial Hypertension and Diabetes Mellitus Secondary Care between January and December 2012. The present study was prepared from the actions linked to the project: *"Health promotion and prevention of skin lesions in diabetic patients in the Health Care Center (Hiperdia), Viçosa, MG: an interlocution proposal between extension and research"*.

The Hiperdia Center for Hypertension and Diabetes Mellitus Secondary Care characterizes as a medium complexity reference center managed by the Municipal Health Department of Viçosa-MG, aimed at the care of people with a diagnosis of SAH and DM of referenced municipalities that make up the micro-region of Viçosa, MG.

The Viçosa micro-region is located in the region called *Zona da Mata mineira*. It has a total area of 1,898.6 km², an estimated population of 136,886 inhabitants in 2014, according to the IBGE, and is divided into nine municipalities: Araponga, Cajuri, Canaã, Porto Firme, Paula Cândido, Petra do Anta, São Miguel do Anta, Teixeiras and Viçosa. The municipality of Viçosa serves as a hub city of the micro-region. It has a population of 76,745 inhabitants and an HDI of 0.775.

The patient care at the Hiperdia Center is performed by a multidisciplinary team consisting of a nurse, psychologist, social worker, nutritionist and physician, who promote treatment, prevention of injuries and rehabilitation with the target audience that attends the service. People diagnosed with DM are referred from Primary Health Care (PHC) to that center, according to the following criteria: diagnosis of type 1 or 2 DM; using insulin or oral anti-diabetic in full dose

with bad metabolic control; people with recent diagnosis of DM with indication for insulinization and type 1 or 2 DM with changes in foot plantar protective sensitivity[7].

This study included all the records of individuals older than 18 years diagnosed with type 2 DM, referred to the Hiperdia Center according to the criteria mentioned above. There was exclusion of the records of individuals with brachial ankle index (BAI) greater than 1.40. Such values are compatible with non-compressible arteries and do not define the diagnosis of PAD[2,8].

Initially, 266 medical records were identified, of which 249 met the inclusion and exclusion criteria. Two previously trained researchers performed the data extraction from those records, which occurred in August and September 2013. The data were recorded in a form built for this purpose and later entered into a database in the Epi info 7.0 program. The demographic characteristics of the individuals investigated were: gender (male and female) and age grouped in age groups (19-50, 51-60, 61 years or more). The clinical characteristics included: presence of SAH (yes, no); Obesity (yes, no); Smoking (yes, no); Alcoholism (yes, no); History of previous ulcers (yes, no); Amputation of lower limbs (yes, no); Protective plantar sensitivity (absent, present); and BAI.

The identification of PAD was performed through the evaluation of the BAI with the vascular Doppler and the sphygmomanometer[3]. BAI is the relationship between systolic blood pressure in the posterior or pedis tibial artery and systolic pressure in the brachial artery. The study adopted the reference values of the BAI recommended by the VI Brazilian Guidelines on Hypertension[8] and the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines[2], which adopt the following interpretation criteria: PAD - less than or equal to 0.90 in one or both lower limbs; Normal - between 0.91 and 1.40; and Non-Compressible - values above 1.40. BAI characterizes as a good diagnostic test because it is fast, has easy reproducibility and low cost[8]. In normal situations, the systolic pressure is higher in the lower limbs than in the upper limbs, except in situations of cardiovascular diseases, in which that relationship reverses, suggesting the

presence of arterial obstructions, leading to the diagnosis of PAD[8].

The initial analysis included a description of the study population through absolute and relative frequency distribution. Subsequently, the prevalence of PAD was estimated and its association with each explanatory variable was assessed using Pearson's Chi-square test or Fisher's exact test with significance level of 5%.

The association between the presence of PAD and the explanatory variables was performed using the multiple logistic regression model. Considering the objectives of this research, for the selection of the final model of logistic regression, the backward elimination method was used by Likelihood Ratio (LR). This method starts with the inclusion of all significant explanatory variables in the model ($p < 0.20$) in the bivariate analysis. The variables are then removed one at a time, starting with that which reduces LR by the smallest amount. The equation is evaluated at each step and the procedure is repeated until each variable that remains in the model explains a significant portion of the variation observed in the response[9]. In the multivariate model, the variables that presented $p < 0.05$ were considered significant. The variable "gender" was maintained in the model independent of its statistical significance. All analyses were performed in the Epi info 7.0 program.

The study was approved by the Human Research Ethics Committee of the Federal University of Viçosa (UFV), under opinion No. 367.011, obeying the ethical precepts for researches involving human beings, in accordance with Resolution No. 466/12 of the National Council of Health. Prior authorization for this study was requested from the management of the Hiperdia Center for Hypertension and Diabetes Mellitus Secondary Care.

RESULTS AND DISCUSSION

There was evaluation of 249 medical records, which had a sample composed predominantly by women (71.1%) and patients with a diagnosis of SAH (83.5%). The age varied between 19 and 89 years, being individuals over 50 years more frequent (76.3%). About 44.6% were obese and 14.9% had a history of lower limb ulcer. Alcohol use

and smoking were observed in 4.0% and 7.6% of the medical records, respectively. Regarding the monofilament plantar sensitivity test, approximately 7.0% of the patients presented loss of sensitivity.

　　　The prevalence of PAD was 15.3% (95%CI: 11.0% - 20.3%) and was higher in individuals aged 61 years or more, with the presence of SAH, and in people with a loss of plantar protective sensitivity in the univariate analysis (Table 1).

Table 1 - Distribution of Peripheral Arterial Disease (PAD) frequency according to the demographic and clinical characteristics of people diagnosed with Diabetes, Viçosa/MG (2012).

Variables	Total	Peripheral Arterial Disease		p-value
	n(%)	Yes n(%)	No n(%)	
Total		38 (15.3)	211(84.7)	
Gender				
Female	177(71.1)	24(63.2)	153(72.5)	0.241
Male	72(28.9)	14(36.8)	58(27.5)	
Age group				
19-50 years	59(23.7)	3(7.9)	56(26.5)	
51-60 years	76(30.5)	5(13.3)	71(33.6)	<0.001
61 years or more	114(45.8)	30(78.9)	84(39.8)	
Hypertension †				
Yes	208(83.5)	36(94.7)	172(81.5)	0.054
No	41(16.5)	2(5.3)	39(18.5)	
Obesity				
Yes	111(44.6)	14(36.8)	97(46.0)	0.297
No	138(44.4)	24(63.2)	114(54.0)	
Smoking †				
Yes	19(7.6)	2(5.3)	17(8.1)	0.550
No	230(92.4)	36(94.7)	194(91.9)	
Alcohol use †				
Yes	10(4.0)	0(0.0)	10(4.7)	0.367
No	239(96.0)	38(100.0)	201(95.3)	
Previous amputation †				
Yes	4(1.6)	1(2.6)	3(1.4)	0.486
No	245(98.4)	37(97.4)	208(98.6)	
Previous ulcer				
Yes	37(14.9)	8(21.1)	29(13.7)	0.243
No	212(85.1)	30(78.9)	182(86.26)	
Plantar protective sensitivity				
Absent	17(6.8)	6(15.8)	11(5.2)	0.017
Present	232(93.2)	32(84.2)	200(94.8)	

† Fisher's exact;

　　　In the multivariate analysis, PAD remained associated with advanced age and absence of plantar protective sensitivity. Individuals aged 61 years or more were five times more likely to develop PAD when compared to individuals aged 19-50 years (OR = 5.43; 95%CI: 1.54 - 19.12). The absence of plantar sensitivity in the study subjects increased their chance to develop BAI by about three times (OR = 3.17; 95%CI: 1.01-10.06) (Table 2).

Table 2 - Multiple logistic regression model for the occurrence of Peripheral Arterial Disease (PAD) in patients with type 2 diabetes according to the independent variables surveyed, Viçosa/MG (2012).

Variable	Gross Analysis		Adjusted Analysis	
	OR(95%CI)	P-value†	OR(95%CI)	P-value†
Gender				
Female	1	-	1	-
Male	1.53(0.75-3.18)	0.244	1.41 (0.61-3.29)	0.416
Age group				
19-50 years	1	-	1	-
51-60 years	1.31(0.30-5.73)	0.715	1.27(0.28-5.54)	0.771
61 years or more	6.67(1.94-22.88)	0.002	5.45(1.59-19.19)	0.008
SAH[b]				
Yes	3.87(0.89-16.82)	0.070	2.90(0.66-13.65)	0.180
No	1	-	1	-
Obesity				
Yes	0.71(0.35-1.44)	0.341		
No	1	-		
Smoking				
Yes	0.63(0.14-2.84)	0.549		
No	1	-		
Alcohol use				
Yes	0.53(0.06-4.23)	0.850		
No	1	-		
Previous amputation				
Yes	1.91(0.193-18.79)	0.581		
No	1	-		
Previous ulcer				
Yes	1.74(0.72-4.20)	0.21		
No	1	-		
Plantar Protective Sensitivity				
Absent	3.48(1.20-10.10)	0.021	3.19(1.01-10.07)	0.049
Present		-	1	-

[a]OR= *odds ratio*; [b]Systemic Arterial Hypertension;†p-value of the Wald's test for heterogeneity.

There was a prevalence of 15.3% of PAD in patients diagnosed with type 2 DM followed by the Hiperdia Center for Hypertension and Diabetes Mellitus Secondary Care. The factors associated with PAD were age over 60 years and absence of plantar protective sensitivity.

One estimates that PAD is present in 12% to 16% of patients with DM when evaluated by the brachial ankle index. The duration of DM and hyperglycemia positively associates with the presence and severity of PAD[10]. The actual prevalence of PAD in people diagnosed with DM has been difficult to determine since most patients are asymptomatic and many of them do not report their symptoms. This study focused on the detection of PAD in type 2 diabetic patients and found a prevalence of 15.3%. This result was higher than the 5.2% found in patients with a diagnosis of type 2 DM in Beijing, China[11], 5.9% in the United States of America[12] and 14.4% in India[13], but lower than the frequency of 39.28% found in Pakistan[14].

Different sampling methods, differences in sample size, different distributions of risk factors in the studied populations, and techniques to identify PAD different from the Ankle-Brachial Index may be responsible for the variations occurring in the overall prevalence among the studies. Moreover, the development of PAD in diabetic individuals may vary in different ethnic groups or genders. A study conducted in Karachi, Pakistan, found that the prevalence of PAD in women was almost twice that found among men (46.71% vs. 24.22%)[14]. Observing that difference in the prevalence of PAD between men and women in the Karachi study[14], and considering that, in the sample of the present study, about two-thirds were women, the difference in the proportion of men and women in the sample of the present study may have elevated the overall prevalence of PAD in the studied group.

PAD in patients with DM has become an increasingly important concern for public health, both in the developed world and in developing countries. Epidemiological evidence suggests a strong association between DM and an increase in the prevalence of PAD, showing that people diagnosed with DM have a two to four times increased occurrence of PAD[10].

BAI values below or equal to 0.90 are strong predictors of diffuse atherosclerotic disease and demonstrate the presence of arterial stiffness due to the calcification of the middle layer and consequent stiffness of the vascular wall[4]. Generally, that situation occurs in individuals with high cardiovascular risk, who present with smoking, dyslipidemia, DM, advanced age and SAH as predictors to develop the disease[3]. People with altered BAI values should undergo further diagnostic evaluation for carotid and peripheral arterial disease [15].

In this study, there was no significant difference in the prevalence of PAD among men and women. Other studies also did not identify such association[1,4,13]. According to the PAD pathophysiology, men aged over 45 years and women after menopause are more susceptible to the development of that disease[2-3]. Differences in the prevalence of PAD among men and women may occur due to differences in the prevalence of other predisposing factors of PAD among women and men. One study pointed out that women presented a higher Body Mass Index (BMI) compared to men, and the duration of DM was higher for women[14]. In that sense, it justified the inclusion of the gender variable in the final

model, even though it remained not significantly associated with the outcome.

The main risk factors for PAD include SAH, smoking, DM and dyslipidemia, which may lead to the progressive and, sometimes, generalized development of atherosclerotic plaques in the arteries[2-3], isolated or associated. In the present study, only age and plantar protective sensitivity associated with PAD. In the literature review, only one study analyzed the relationship between the absence of plantar protective sensitivity and PAD, which did not find a significant association[16].

Studies have shown that the prevalence of PAD increases with age[2-3,17], rising above 10% among patients in their 60s and 70s[18]. Those patients are likely to develop complications from peripheral vascular occlusions; after five to 10 years, one-third of the limping progress to critical ischemia, approximately 20% require vascular procedure and 10% lower limb primary amputation[2].

On the other hand, there was no association between PAD and the presence of SAH, smoking and obesity, differently from other studies[3-4,12-13]. Researches have shown that SAH associates with lower BAI in patients with DM, although the association is generally weaker than that found in patients with coronary and cerebrovascular disease[18]. SAH increases the risk of developing PAD in some studies[3,12,14], but not in others[1,17].

Smoking is one of the major risk factors for vascular atherosclerosis, including PAD[2-3]. However, in this study, a history of smoking did not significantly associate with PAD, probably because the definition adopted in this study to assess the history of smoking did not differentiate current or former smokers, and the number of smokers was very small according to the information obtained from the medical records. Other studies with patients with type 2 DM[1] and with the general population[17] also did not identify an association between history of smoking and PAD.

There was no association between obesity and PAD in the studied population. In the literature, that association is controversial. Studies with patients with type 2 diabetes[13] and Japanese-Brazilians of both genders aged ≥ 30[4] did not identify an association of PAD with abdominal obesity and increased BMI. However, a study conducted in China found an association between PAD and obesity after controlling potential intermediate factors, such as

hypertension, dyslipidemia and hyperglycemia[19]. The present study used BMI to classify patients as obese, which may have limited the identification of association.

The presence of PAD has been reported as a risk factor for the development of lower limb ulcers and amputations in diabetic patients[20]. In the analyzed sample, only one individual with PAD suffered previous amputation and eight had previous ulcer, but those variables did not associate with that disease. The under-registration of that information in the medical records would be a possible explanation for the occurrence of that fact.

FINAL THOUGHTS

Given the prevalence of PAD found in patients diagnosed with DM and, since the morbidity and mortality from that disease associate, preventive measures such as PAD screening with foot evaluation (BAI, plantar sensitivity test, presence of lesions) and educational guidelines for patients at risk for the disease should help reduce the devastating effects of that disease. The results show us the need to reflect on the importance of individualized assessment of risk factors in order to subsidize action directed at possible events, being necessary to invest in prevention and training of all health personnel.

Although there is insufficient knowledge in the effectiveness of interventions to prevent PAD, more effective treatment of DM, hyperlipidemia and SAH, along with physical training and smoking control, can be effective strategies, contributing to reduce the associated cardiovascular morbidity and mortality.

From those considerations, in order to guarantee a better quality of life for the diabetic patient diagnosed with PAD, it is of the utmost importance that a multidisciplinary team, composed by nurses, doctors, psychologists, nutritionists and social workers, follows him/her up, since researches have pointed out the effectiveness of the multidisciplinary action in the prognosis of the disease. Therefore, it is necessary to stimulate the individual to develop an active participation in his/her health-disease process, being necessary not only to know his/her condition, but also to be able to intervene positively on his/her life and health.

Among the limitations of the present study, there is the fact that it took place at a Secondary Care Reference Center, with peculiar characteristics and with a clientele with certain profile, which prevents generalizing the results for the population with diagnosis of Type 2 DM. As PAD has a high mortality rate, the results of the present study may present survival bias. This would explain the reasons of not finding traditional risk factors (smoking, hypertension) for heart disease/stroke, which are the leading causes of death in patients with PAD, as risk factors for PAD survivors in this study.

Moreover, the data were obtained from a secondary source, restricting research only to the variables contained in the medical records. Finally, there was no measurement of the quality of the information obtained by the medical record, so it is important to take into account possible errors resulting from its completion.

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