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ORIGINAL ARTICLE

Effect of metabolic uncontrolled diabetes mellitus (DM) on the resistance index of renal (IR) Interlobar arteries assessed with pulsed Doppler

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Abstract

Background: *Diabetes mellitus is a chronic degenerative disease characterized by elevated hyperglycemia, triggering a series of processes and culminating in chronic, uncontrolled, cellular and vascular damage in different organs.* **Objective:** *To assess whether the elevated glycosylated hemoglobin, microalbuminuria, and the time evolution of more than 10 years of diabetes mellitus are associated with elevated resistance index of the interlobar renal arteries assessed with pulsed Doppler in patients with metabolic uncontrolled diabetes mellitus.* **Material and methods:** *Transversal-analytical, observational, prospective study that included diabetic patients attending UMAE abdominal ultrasound in 25 of IMSS, from October 15, 2014 to November 15, 2014, which was performed for pulsed Doppler index resistance of vascular interlobar renal arteries and was collected from electronic medical records: age, sex, glycated hemoglobin, and microalbuminuria. The association between metabolic uncontrolled diabetes mellitus was analyzed with the elevation of resistance index by c^2 test or Fisher, being significant with a value of $p < 0.05$, and to assess the magnitude of the association that was measured with a response magnitude of 95%.* **Results:** *63 patients with type 2 diabetes were examined, with an average age of 52.3 ± 14.2 years, 41 were older than 50 years (65.0%), 26 with hypertension (41.2%), 32 with higher levels of glycated hemoglobin 7 (50.8%), 35 with normoalbuminuria (55.6%), 28 with microalbuminuria (44.4%), and 39 with a time evolution of diabetes of more than 10 years (61.9%). We observed a statistically significant difference between microalbuminuria and increased duration of diabetes mellitus with high resistance index.* **Conclusion:** *The alterations in renal microvasculature conditioned by the occurrence of microalbuminuria in diabetic nephropathy and the duration of diabetes are strongly associated with higher resistance index.* (Gac Med Mex. 2016;152:190-3)
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KEY WORDS: *Diabetes. Microalbuminuria. Resistance index.*

Introduction

Diabetes is a systemic, chronic-degenerative condition with varying degrees of hereditary predisposition, since different gene combinations, together with environmental factors, participate in its development. It is characterized by chronic hyperglycemia due to a deficiency in the production or action of insulin, which affects the intermediate metabolism of carbohydrates, proteins and fats. Hyperglycemia main symptoms are: polyuria, polydipsia, weight loss, sometimes polyphagia and blurred vision[1].

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Table 1. Comparison of RI higher or lower than 0.7 with the clinical and biochemical data of 63 diabetic patients

	Total (n = 63)	RI > 0.7 (n = 28)	RI < 0.7 (n = 35)	OR (95% CI)	p
Age (years)	52.3 ± 14.2	53.8 ± 11.7	51.8 ± 12.3	–	0.521
Age > 50 years	41 (65.0%)	21 (75.0%)	20 (57.1%)	2.2 (0.9-3.8)	0.139
Gender:					
Male	31 (49.2%)	15 (53.5%)	16 (45.7%)	–	0.535
Female	32 (50.8%)	13 (46.5%)	19 (54.3%)		
HBP	26 (41.2%)	15 (53.5%)	11 (31.4%)	2.5 (0.8-3.5)	0.076
Hb1Ac	32 (50.8%)	17 (60.7%)	15 (42.8%)	2.0 (0.7-4.2)	0.158
Microalbuminuria	28 (44.4%)	17 (60.7%)	11 (31.4%)	3.3 (1.0-5.1)	0.020
TDE > 10 years	39 (61.9%)	22 (78.5%)	17 (48.5%)	3.8 (1.2-5.7)	0.014

The most common type of diabetes in the world, and especially in the Mexican population, is type 2 DM. Overall, type 1 diabetes frequency is 5-10%, whereas that of type 2 diabetes ranges from 80 to 90% (5-10% corresponds to the variety known as MODY, with another 5-10% being produced by different genetic disorders[2]).

According to data reported up to 2001, 150 million people in the world were affected that year, and an estimate of nearly 300 million persons will suffer from it by the year 2025[2,3]. Between 1991 and 2000, the number of adults with diabetes increased by 49% in the USA: currently, there are nearly 16 million people affected by the disease, with this number increasing by 800,000 cases per year and annual costs estimated in 105 billion dollars[3].

Diabetes is associated with damages to the microcirculation, which can manifest as nephropathy, neuropathy and retinopathy. Chronic hyperglycemia is associated with an increase in protein kinase C activity, sorbitol accumulation and formation and deposit of nonenzymatic protein glycosylation products[4]; these alterations generate chronic renal insufficiency in 40% of cases. In addition, up to 70% of diabetics are estimated to suffer some form of neuropathy, and subjects with a family history of high blood pressure (HBP) are likely to develop early microvascular complications. The above-mentioned complications are similar for type 1 and type 2 diabetes[5].

Microvascular anomalies are associated with a metabolic disorder originated by insulin resistance rather than by hyperglycemia; in this sense, insulin resistance has been found to account for the existence of 40% of patients with coronary diseases[6]. In general, cardiovascular disease is linked to an accelerated atherosclerosis state and an increased risk for thrombosis, which explains why diabetic patients have a myocardial infarction frequency 2 to 4-fold higher than normal population[7].

At the renal level, the initial damage produced by poorly controlled chronic hyperglycemia is known as diabetic nephropathy, a term initially proposed to designate lesions that could be found in the kidney of the diabetic subject, but that currently is used exclusively to indicate renal lesions originated by microangiopathic or small vessels involvement[8,9]. Thus, it is a chronic vascular complication, exclusive to diabetes mellitus (DM), where renal microcirculation is affected, originating a series of functional and structural alterations mainly at the glomerular level[9].

To date, laboratory findings such albuminuria and increased blood creatinine may indicate the level of functional damage to the kidney, but unfortunately this occurs at chronic stages, and final diagnosis is obtained by renal biopsy, which, in spite of being a quick, effective and relatively safe procedure, it is all the same invasive. To date, there are not many studies assessing renal function deterioration by pulse Doppler ultrasound of the interlobar and arcuate arteries.

Our purpose was to assess if elevated glycosylated hemoglobin (HbA1c), microalbuminuria and diabetes time of evolution (DTE) longer than 10 years are associated with renal interlobar arteries resistance index (RI) as assessed by pulsed Doppler in patients with metabolically uncontrolled DM.

Material and methods

A cross-sectional, analytic, observational, prospective study was conducted at the IMSS *Centro Médico*

Nacional del Noreste No. 25, with support of the Department of Diagnostic and Therapeutic Imaging, at the ultrasound area. All patients with a DM diagnosis attending for abdominal ultrasound in the period encompassed from October 15 to November 14, 2014, who underwent pulsed Doppler of the renal interlobar and arcuate arteries, were included.

For the descriptive analysis, absolute frequencies, percentages, means or medians and standard deviation or minimum and maximum values were measured. For inferential analysis, the chi-square test or Fisher's exact probability test were used, with a p-value < 0.05 considered to be significant. To assess the magnitude of association, the odds ratio (OR) was measured with a 95% confidence interval (CI). The statistical package SPSS (version 18.0) was used.

Results

Sixty three patients with type 2 DM who met the established selection criteria were examined; their ages ranged from 34 to 72 years (average: 52.3 ± 14.2 years) and there were 31 males (49.2%) and 32 females (50.8%). Of the selected patients, 41 (65.0%) were older than 50 years; 26 (41.2%) had HBP; 32 (50.8%) had HbA1c levels higher than 7; 35 (55.6%), normoalbuminuria; 28 (44.4%), microalbuminuria, and 39 (61.9%), DTE longer than 10 years. HbA1c average level was 7.6 ± 2.2 g/dl and average DTE, 11.0 ± 7.0 years (Table 1).

Of the 41 patients who were older than 50 years, 21 (75.5%) had a RI higher than 0.7, whereas 20 (57.1%) did not, with no statistically significant correlation being found ($p > 0.05$) between diabetic patients older than 50 years and elevated RI, but an elevation risk of 2.2 was found. In addition, among the 15 male (53.5%) and 13 female patients (46.5%) who had a RI higher than 0.7, no statistically significant difference was found ($p > 0.05$).

Only 15 patients (53.5%) of 26 (41.2%) with systemic HBP had a RI higher than 0.7, whereas 16 (45.7%) did not, with no statistically significant correlation being found ($p > 0.05$) between diabetic hypertensive patients and elevated RI, but an elevated risk of 2.5 was found.

Of the 32 patients (50.8%) who had HbA1c higher than 7, only 17 (60.7%) showed a RI greater than 0.7 and 15 (42.8%) had a RI lower than 0.7, with no statistically significant correlation being found ($p > 0.05$) between elevated RI and diabetic patients and elevated HbA1c, but an increased risk of 2.0 was found.

Microalbuminuria was present in 28 patients (44.4%), out of which only 17 (60.7%) had a RI greater than 0.7, while in 11 (31.4%), RI was lower than 0.7, with a statistically significant correlation being found between diabetic patients with microlabuminuria and elevated RI ($p = 0.02$), as well as an increased risk of 3.3.

DTE was, on average, 11.0 ± 7.0 years, and in 22 patients (78.5%), RI was found to be higher than 0.7, whereas in 17 (48.5%), RI was below 0.7, with a statistically significant correlation being found between patients with DTE longer than 10 years and increased RI ($p = 0.014$), as well as an increased risk of 3.8.

Discussion

Endothelial dysfunction and generalized vascular damage can be found at type 2 diabetes early stages, which are often accompanied by transitory microalbuminuria. Some investigations have indicated that the changes produced in the kidneys, predominantly at the vascular compartment, and the levels of microalbuminuria are related to elevated RI in the pulsed Doppler of the intra-renal arteries. In our study, there were 35 diabetic patients with normoalbuminuria and 28 with microalbuminuria; of the latter, 17 had an elevated RI, with a statistically significant difference very similar to that from other investigations being observed[10].

As in many other diseases, the longer the time of disease evolution, the greater the damage sustained. The kidneys of diabetic patients with longer time of evolution have more deterioration than those of patients with shorter time of evolution, and increased resistance of intra-renal arteries is indirectly observed, as reported by some publications; we found a statistically significant difference in diabetic patients with a diabetes duration average of 14 years in comparison with patients with diabetes duration of 8 years[11].

Atherosclerotic changes normally occur early in diabetic patients and are likely to contribute to blood pressure elevation. Blood pressure optimal regulation is known to be very important to prevent vascular compartments histopathological changes. Unlike to what some publications have suggested on HBP-induced vascular compartment changes eliciting a RI elevation, we found no statistically significant correlation between HBP and elevated RI, although an increased risk of 2.5 was observed[12].

Lately, the influence of age as a risk factor for the development or worsening of some conditions has been looked into, due to the implications of cell deterioration for each organ. Greater deterioration of the

renal function has been observed in diabetic patients older than 50 years, a fact that is closely associated with the time of disease evolution: the more the years of evolution, the higher the risk for structural and functional damage. Therefore, age plays an important role in many chronic-degenerative conditions, but no statistically significant correlation has been found. Thus, in different published investigations, an increased risk for nephropathy has been observed in diabetic patients older than 50 years, but no significant association has been demonstrated. Our study was not the exception: although 41 patients were older than 50 years, only 21 showed elevated RI[13].

In diabetic patients, the use of HbA1c as a laboratory test to monitor the stability of hyperglycemia caused by adequate or inadequate therapeutic management has been highly useful for treating physicians to emphasize on treatment adherence. Many published investigations agree that HbA1c values higher than 7 are associated with hyperglycemia instability; the higher it is, the greater its damage will be, which will result in greater deterioration of the renal function over time. Furthermore, the risk factor implied by HbA1c levels persistently higher than 7 for the development of diabetic nephropathy, which ultimately will end up in chronic nephropathy, has been addressed through the years[14]. Investigations have failed to demonstrate a statistically significant correlation between HbA1c levels and intra-renal arteries RI increase, although they have shown an increased risk for its occurrence. The findings of our research were very similar: although 32 patients had HbA1c higher than 7 and 17 of them had interlobar arteries elevated RI, no statistically significant difference was found[15].

Previous studies have demonstrated a significant correlation between intra-renal arteries RI, serum creatinine and creatinine clearance levels in patients who had clinical evidence of microalbuminuria and proteinuria[16]. In our study, no emphasis was put on creatinine levels and, therefore, it would be convenient to correlate them in the future. The control of blood glucose levels and type 2 DM complications has been shown to be beneficial for diabetic patients with regard to microvascular complications. When we looked into the influence of the previously mentioned variables, we observed that TDE and the presence of microalbuminuria were statistically significant covariables in interlobular arteries RI elevation[17].

Conclusions

Many factors have been implied as causes for the development of small alterations in kidney vessels as part of the generalized vascular damage in type 2 DM. The consequences of these anomalies can entail an elevation of intra-renal arteries RI on pulsed Doppler. As demonstrated in the present study, elevated RI might be observed in type 2 diabetic patients, even at diabetic nephropathy first stages. TDE and microalbuminuria are statistically significant covariables that influence on interlobar and arcuate renal arteries RI elevation.

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