Occult renal failure and associated factors in patients with chronic conditions

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Abstract

Introduction: Timely diagnosis and early therapeutic intervention reduce premature mortality associated with chronic renal failure.

Objective: To identify the prevalence and factors associated with occult renal failure in patients with chronic diseases. **Method:** Cross-sectional study of 1268 patients with type 2 diabetes mellitus and systemic arterial hypertension. A measuring instrument with questions about associated factors such as osteoarthritis, treatment of chronic conditions, smoking, analgesic consumption, alcoholism, body mass index, physical activity and serum glucose, cholesterol and triglyceride levels was used. **Results:** The prevalence of occult renal failure was 13.2 % (167/1,268), 13.4 % in diabetic patients (117/876) and 14.9 % in hypertensive patients (150/1,010). In the multivariate analysis, the factors associated with occult renal failure were being older than 60 years (aOR = 1.96, 95 % CI = 1.22-2.49), belonging to the female gender (aOR = 2.17, 95 % CI = 1.30-2.82), suffering from systemic arterial hypertension (aOR = 1.96, 95 % CI = 1.22-2.50) and not having overweight/obesity (aOR = 0.49, 95 % CI = 0.41-0.8). **Conclusions:** The prevalence of occult renal failure was 13 %. Female patients older than 60 years with overweight/obesity and systemic arterial hypertension should be examined in detail by the family doctor for occult renal failure early detection.

KEY WORDS: Occult renal failure. Diabetes mellitus. Systemic arterial hypertension.

Insuficiencia renal oculta y factores asociados en pacientes con enfermedades crónicas

Resumen

Introducción: El diagnóstico oportuno y la intervención terapéutica temprana disminuyen la mortalidad prematura asociada con insuficiencia renal crónica. **Objetivo:** Identificar la prevalencia y factores asociados con insuficiencia renal oculta en pacientes con enfermedades crónicas. **Método:** Estudio transversal de 1268 pacientes con diabetes mellitus tipo 2 e hipertensión arterial sistémica. Se usó un instrumento de medición con preguntas sobre factores asociados como artrosis, tratamiento de padecimiento crónico, tabaquismo, ingesta de analgésicos, alcoholismo, índice de masa corporal, actividad física y niveles séricos de glucosa, colesterol y triglicéridos. **Resultados:** La prevalencia de insuficiencia renal oculta fue de 13.2 % (167/1268), 13.4 % en pacientes diabéticos (117/876) y 14.9 % en hipertensos (150/1010). En el análisis multivariado, los factores asociados con insuficiencia renal oculta fueron edad > 60 años (R_{Ma} = 1.96, IC 95 % = 1.22-2.49), sexo femenino (R_{Ma} = 2.17, IC 95 % = 1.30-2.82), padecer hipertensión arterial sistémica (R_{Ma} = 1.96, IC 95 % = 1.22-2.50) y no tener sobrepeso u obesidad (R_{Ma} = 0.49, IC 95 % = 0.41-0.8). **Conclusiones:** La prevalencia de insuficiencia renal oculta fue de 13 %. Los pacientes mayores de 60 años, con sobrepeso u obesidad e hipertensión arterial sistémica deben ser examinados detalladamente por el médico familiar para la detección temprana de insuficiencia renal oculta.

PALABRAS CLAVE: Insuficiencia renal oculta. Diabetes mellitus. Hipertensión arterial sistémica.

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Introduction

In 1990, chronic kidney disease ranked 27th in the list of global mortality causes, with an annualized age-standardized rate of 9.6 per 100,000 population, which was increased to 11.1 per 100,000 population by 2010.¹ Globally, the prevalence of chronic kidney disease is estimated to be 10 %, ² and it is a disease that together with other chronic comorbidities increases the risk of early death.^{3,4} In Mexico, premature death due to chronic kidney disease increased by almost 400 % from 1990 to 2010.⁵ Despite the above, the frequency of this condition is unknown; one study in subjects older than 18 years found a prevalence of 8 %.⁶

In Mexico, the 2012 National Health and Nutrition Survey identified 22.4 million adults with systemic arterial hypertension (SAH) and 6.4 million adults with type 2 diabetes mellitus (DM2). The figures are relevant because only half the people with hypertension are aware of it and only one quarter of diabetics have their disease under control.⁷ The combination of chronic conditions, with the resulting negative impact on individual health and high social cost, turns chronic renal failure into a catastrophic event.⁸⁻¹⁰

Renal function initial failure is the result of complex interactions, mainly of chronic and degenerative conditions. Progression factors that worsen and accelerate kidney damage are persistent proteinuria,¹¹ SAH,¹² poorly-controlled DM2,¹³ smoking,¹⁴ dyslipidemia,¹⁵ anemia,¹⁶ associated vascular disease and obesity.¹¹ There is a higher frequency of occult renal failure in women^{17,18} and in people older than 50 years.¹⁹ Body mass index > 25 has been associated with occult renal failure.²⁰ Some dietary restrictions modify the consumption of protein, sodium and phosphorus and stop renal damage,²¹ with higher benefit if they are established in a timely manner. The purpose of this study was to estimate the prevalence of occult renal failure and associated factors in patients with SAH or DM2 under the care of the Family Medicine Unit 29 of the Mexican Institute of Social Security in Acapulco, Guerrero, Mexico.

Method

Cross-sectional study conducted in users of the Family Medicine Unit 29 of the Mexican Institute of Social Security, from November 1, 2014 to January 31, 2015. The following criteria were used for patient selection:

- *Inclusion*: patients with clinical diagnosis of SAH (systolic blood pressure > 140 mm Hg and

diastolic blood pressure > 90 mm Hg) or DM2 (blood glucose > 126 mg/dL), and with no recorded diagnosis of chronic kidney disease.

- *Exclusion*: patients without recent laboratory tests (blood glucose, cholesterol, triglycerides and creatinine levels) or who had a single kidney, any type of cancer or systemic lupus erythematosus.

The sample size was calculated considering a prevalence of occult renal failure of 7.6 %, ²² a 95 % confidence level (alpha error), study power of 0.20 (beta error) and an odds ratio (OR) of 1.9 between SAH and occult renal failure. The resulting sample size was 1268 patients; five were excluded.

To measure the potential factors associated with occult renal failure, a 28-item questionnaire was used to directly collect data from the patients. The questionnaire was previously validated by a panel of experts:²³ one family doctor, one nephrology specialist and two epidemiologists. With the questionnaire, patient general data were confirmed: gender, age, ethnicity and chief complaint. Time of evolution and current treatment of the condition were verified, and patients were asked about the use of non-steroidal analgesics, tobacco and alcohol consumption, osteoarthritis and periodicity of physical activity (physical exercise for at least 30 minutes daily, including household chores). After the interview, body weight, height and blood pressure were measured in each patient. The body mass index was estimated with body weight and height.

Data on cholesterol and triglyceride plasma concentration levels were taken from the electronic medical record. With patient age, gender and ethnicity, as well as with the most recent serum creatinine level result, the glomerular filtration rate was calculated using the formula proposed by the Chronic Kidney Disease Epidemiology Collaboration group.²⁴

Occult renal failure operative definition was the following: a patient with glomerular filtration rate < 60 mL/minute for more than three months and who was unaware of having chronic kidney disease. With the glomerular filtration rate, the severity of chronic kidney disease was classified in the six stages proposed by the Kidney Disease Outcomes Quality Initiative guideline.²⁴

Data analysis was carried out with the statistical program CIETmap.²⁵ The association between study-included variables and occult renal failure was estimated with the Mantel-Haenszel procedure using the odds ratio (OR), both in the bivariate and multivariate analyses.²⁶ The 95 % confidence interval (CI) of the OR was estimated with Miettinen's proposal.²⁷

Table 1. Glomerular filtration rate staging, according to the Kidney Disease Outcomes Quality Initiative guidelines

Stage and definition	Glomerular filtration rate (mL/minute)	n = 1268	%
No kidney damage	> 91	677	53.4
1 Evidence of kidney damage and normal GFR	≥ 90	17	1.3
2 Evidence of kidney damage and slightly decreased GFR	60-89	407	32.1
3 Moderate GFR decrease	30-59	161	12.7
4 Severe GFR decrease	15-29	5	0.4
5 End-stage renal failure	< 15	1	0.1

GFR = Glomerular filtration rate.

Table 2. Bivariate analysis of factors associated with occult renal failure

Factor	Occult renal failure (%)		naOR*	95 % CI**
	n	%		
Gender				
Females	120/794	15.1	1.62	1.13-2.31
Males	47/474	9.9		
Age (years)				
> 60	118/624	18.1	2.83	2.01-3.99
< 60	49/644	7.6		
Type 2 diabetes mellitus				
With	117/876	13.4	1.05	0.74-1.50
Without	50/392	12.8		
Systemic arterial hypertension				
With	150/1 010	14.9	2.47	1.49-4.10
Without	17/258	6.6		
Glycemic control				
Controlled	63/424	14.9	1.28	0.88-1.85
Uncontrolled	67/558	12		
Systemic blood pressure control				
Controlled	146/1 096	13.3	1.11	0.68-1.80
Uncontrolled	21/172	12.2		
Dyslipidemia				
With	38/285	13.3	1.04	0.70-1.54
Without	119/926	12.9		
Smoking				
Yes	13/102	12.7	0.96	0.52-1.76
No	154/1 166	13.2		
Osteoarthritis				
With	23/173	13.8	1.01	0.63-1.63
Without	144/1 094	13.2		
Body mass index				
< 25	117/1 000	11.7	0.58	0.83-0.40
≥ 25	50/268	18.7		

*Non-adjusted odds ratio. **95 % confidence intervals.

All patients signed the informed consent. The information provided by the patients was confidential but not anonymous. The study was approved by the Local Research Committee 1101 of the Mexican Institute of Social Security, with authorization number R-2014-1101-15.

Results

A total of 1268 patients with a clinical diagnosis of DM2 or SAH and without a diagnosis of chronic kidney disease participated in the study; 31 % (392) had been

Table 3. Final model of the multivariate analysis of factors associated with occult renal failure

Factor	naOR*	aOR**	a95 % IC*	het _{χ²} ²*	p
Female gender	1.62	1.78	1.24-2.56	9.8	0.53
Age older than 60 years	2.83	2.63	1.84-3.76	28.4	0.57
Systemic arterial hypertension	2.47	2.03	1.18-3.47	6.6	0.67
Body mass index > 25	0.58	0.60	0.88-0.41	7.0	0.60

*Non-adjusted odds ratio. **Adjusted odds ratio. [‡]Adjusted odds ratio 95% confidence intervals. [§]Chi-square test for heterogeneity.

diagnosed with SAH, 20 % (258) had been diagnosed with DM2 and 49 % (618) had been diagnosed with both conditions; 63 % (794) were females, and average age was 60.1 ± 11.1 years, with a range of 22 to 91 years.

Forty-one (3 %) patients reported practicing daily physical exercise, 8 % (107) had a smoking history, 0.3 % (4) referred alcohol consumption and 14 % (173) reported suffering from some type of osteoarthritis. According to the level of blood lipids, the patients had the following distribution: normal 40 % (507), hypertriglyceridemia 26 % (325), hypercholesterolemia 12 % (151) and dyslipidemia 23 % (285).

One-hundred and sixty-seven patients (13.2 %) had occult renal failure; 53 % (677) had a glomerular filtration rate > 91 mL/minute. Patient glomerular filtration rate distribution is shown in Table 1. In those patients only with DM2, the occurrence of occult renal failure was 45 % (117/258), in those who only had SAH, it was 38 % (150/392) and in patients with both conditions, 16.2 % (100/618).

In the bivariate analysis, four factors were found to be significantly associated with occult renal failure: female gender, age older than 60 years, suffering from SAH and body mass index < 25. Table 2 shows the strength of association and the 95 % confidence intervals of the factors included in the bivariate analysis.

The multivariate analysis showed an independent effect of the four factors identified in the bivariate analysis. Age > 60 years had the highest strength of association (aOR = 2.63, a95 % CI = 1.84-3.76) and, in decreasing order, it was followed by suffering from HAS and being a female. Body mass index < 25 was shown to be a protective factor (aOR = 0.60, a95% CI = 0.88-0.41) against occult renal failure; Table 3 shows the multivariate analysis final model.

Discussion

In this study, a prevalence of occult renal failure of 13.2 % was found in patients with SAH or DM2. There was also evidence of four factors associated with occult renal failure: female gender, age > 60 years, presence of SAH and body mass index < 25.

In our study, we used the equation proposed by the Chronic Kidney Disease-Epidemiology Collaboration because it provides more advantages and greater accuracy in comparison with the formula proposed by the Modification of Diet in Renal Disease, in addition to improving the predictive power of glomerular filtration and being useful in the prediction of overall and cardiovascular mortality and of the risk for developing end-stage chronic kidney disease.²⁸

We found that 13.2 % of patients with DM2 or SAH had occult renal failure, a figure close to the 13.5 % reported by Peralta in the United States.⁸ Since prevalence in our study was estimated in patients with DM2 or HAS, the occurrence must have been overestimated, given that the entire population had risk factors for occult renal failure.

In our research, the female gender was the factor with the highest strength of association with occult renal failure, a finding that is not new.^{17,19} Various theories suggest that it is more common in women due to anatomical differences with regard to man's kidney size,²⁹ to a differentiated response to angiotensin,³⁰ to differences in lifestyles according to gender³¹ and hormonal changes in women.³² Being a woman and being older than 60 years are risk factors for developing occult renal failure.³³ We also found that age > 60 years was associated with occult renal failure. Other studies have found similar results.^{12,18}

SHA associated with occult renal failure has been reported by multiple observational studies that have identified it as a modifiable risk factor, both for the development of chronic kidney disease and for its progression.³⁴⁻³⁷

Our study revealed that a body mass index < 25 was a protective factor against occult renal failure. The same result was reported by Kalyesubula.¹⁷ Otero found a similar mean body mass index (< 27) to be a protective factor.¹⁵ Da Silva suggests that the relationship between obesity and kidney damage is due to an accumulation of adipose tissue, mainly in viscera, which causes kidney compression, with a consequent increase in intrarenal pressure. Obesity also increases inflammatory and adipocyte production processes.³⁸

Timing is one of the main limitations of cross-sectional studies. In our study, it is necessary to discern whether low body mass index is the result of the presence of DM2, SAH or occult renal failure, since in the context of these patients, following a diet and practicing physical exercise as part of the treatment and control of the disease lead to body weight reduction. We consider that high body mass index precedes occult renal failure. Our result is similar to that reported by other studies that also found a protective effect of a normal body mass index.^{15,17}

It is necessary to train and update health professionals as part of the improvements to the health system, so that primary care doctors have the ability to identify patients at kidney disease early stages.³⁹ Occult renal failure early detection implementation in patients with chronic diseases is feasible at primary care.

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