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Occult renal failure in Primary Care. ¿A women's problem?

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SUMMARY

Background: *Chronic renal failure is becoming a public health problem. The estimation of glomerular filtration rate (GFR) using the MDRD-4 equation is important to find out patients with impaired renal function. The aim of this study was to determinate the rate of patients took care in Primary Care with «occult» renal failure, defined as a GFR less than 60 mL/min/1.73 m^2, and serum creatinine levels in the normal range of the laboratory (< 1.3 mg/dL for men, and < 1.2 mg/dL for women).* ***Methods:*** *Patients over 18 years-old took cared in Primary Care of the health area of Plasencia (Caceres), who were measured serum creatinine level between march to july 2006. We estimated GFR using MDRD-4 formula and classified the level of kidney function according to the NKF-DOQI guidelines.* ***Results:*** *We estimated GFR in 13.784 analyses. In 1.042 the GFR was less than 60 mL/min/1.73m^2, from 960 patients (6.96%). Mean age 76.8 years (range 40-98 years). 418 keep normal serum creatinine levels (43.5%).* ***Conclusion:*** *Renal impairment seems to be prevalent in the general population took care in Primary Care. An elevated rate of patients with renal failure present serum creatinine levels in the laboratory normal range, «occult» renal failure. The systematic estimation of GFR using MDRD formula is necessary to detect this patients with renal impairment.*

Key words: ***«Occult» renal failure. Glomerular filtration rate. MDRD-4. Primary care.***

INSUFICIENCIA RENAL OCULTA EN ATENCIÓN PRIMARIA. ¿UN PROBLEMA EXCLUSIVO DE MUERES?

RESUMEN

Introducción: *La insuficiencia renal crónica se está convirtiendo en un problema de salud pública. La estimación del filtrado glomerular (FG) mediante fórmulas permite detectar las personas con daño renal.* ***Objetivo:*** *Conocer el porcentaje de personas atendidas en atención primaria con insuficiencia renal (IR) oculta definida por presentar un FG estimado < 60 mL/min/1,73 m^2, con niveles de creatinina sérica dentro de los límites de referencia del laboratorio (< 1,3 mg/dL en hombres y < 1,2 mg/dL en mujeres), que hubiesen pasado desapercibidas.* ***Método:*** *Personas mayores de 18 años atendidas en Atención Primaria del Área de Salud de Plasencia (Cáceres) a las que su médico de atención primaria solicitó la medición de niveles de creatinina, entre el 1 de marzo y el 31 de julio de 2006 (5 meses). Se estimó el FG*

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usando la fórmula MDRD-4 y se clasificó el grado de IR de acuerdo con las guías DOQI de la NKF. ***Resultados:*** *Se realizaron 13.784 mediciones de creatinina sérica en mayores de 18 años. 1.042 presentaron FG < 60 mL/min/1,73 m^2, correspondientes a 960 personas (6,96%). Edad media 76,8 años (rango 40-98). De ellas, 418 (43,5%) presentaban IR «oculta», todas mujeres, con edad media 76,5 años y Cr media 1 mg/dL.* ***Conclusiones:*** *Existe un elevado porcentaje de pacientes atendidos en atención primaria con FG < 60 mL/min/1,73 m^2 que mantiene niveles de creatinina en los límites normales. La estimación del FG de forma sistemática permite detectar dichos pacientes, fundamentalmente mujeres mayores de 65 años, que pasarían desapercibidos, lo que se ha denominado IR «oculta».*

Palabras clave: ***Insuficiencia renal «oculta». Filtrado glomerular estimado. MDRD-4. Atención primaria.***

INTRODUCTION

Renal failure (RF) represents a public health care problem in developed countries.[1] The prevalence of the population on renal replacement therapy increases year by year,[2] arterial hypertension and diabetes mellitus being its main causes. It is estimate that in Spain about two million people have RF and are unaware of their condition. Since it is asymptomatic in its early stage, detecting it depends on the methods used to assess renal function, glomerular filtration rate (GFR) being the best index. However, serum creatinine level (Cr) has been used,[3] although given the hyperbolic relationship existing between both parameters serum Cr levels may be within the normal limits until advance advanced stages. For that reason, the use of formulas estimating GFR from Cr, and other demographical, anthropometrical, and biochemical parameters has been proposed. The most commonly used formulas have been the Cockcroft-Gault's,[4] and those derived from the study «Modification of Diet in Renal Disease (MDRD)».[5,6] Currently, the MDRD-4 equation[7,8] has been proposed due to the easiness for implementation in laboratory reports and its sensitivity in early detection of RF.

The main goal of this study was to assess the percentage of health care users older than 18 years with «occult» RF assisted at Primary Care. Secondary objectives were to know the total percentage of users with GFR < 60 mL/min/1.73 m^2 and their distribution by Basic Health Care Areas, and by RF stages according to K/DOQI guidelines from the National Kidney Foundation[9] (fig. 1).

MATERIAL AND METHODS

The Health Care Area of Plasencia (Cáceres) assists 114,005 users distributed in 14 Basic Health Care Areas. The Department of Clinical Analyses from the Virgen del Puerto Hospital receives samples from all areas but three; it is a reference center for 97,839 users (86% of the area), 84,897 older than 14 years.

A descriptive and cross-sectional study was undertaken in which GFR was calculated by the MDRD-4 formula in all people older than 18 years from the health care area of Plasencia, and to whom their primary care doctor would have ordered the measurement of serum Cr.

MDRD-4 = 186 x Cr (mg/dL)$^{-1.154}$ x age$^{-0.203}$ x (0.742 if female) x (1.212 if black race).

The data analyzed were: age, gender, Cr, RF stage, and Basic Health Care Area where the user came from. The technique used for determining serum Cr is the modified Jaffé's method (Modular Analytics, Roche Diagnostics S.L.). The software used for the automated calculation of GFR was Omega 2000 (Roche Diagnostics S.L.). The data required in the equation are automatically gathered by the system from the user's identification label. It was considered that patients presented «occult» RF when GFR < 60 mL/min/1.73m^2 and Cr was within the laboratory re-

STAGE	DESCRIPTION	GFR (mL./min./1.73 m^2)
1	Renal damage with normal GFR	> 90
2	Renal damage with slightly decreased GFR	60-89
3	Moderately decreased GFR	30-59
4	Severely decreased GFR	15-29
5	Renal failure	< 15 or dialysis

Fig. 1.—Chronic renal failure classification acording to the K/DOQI Guidelines of the National Kidney Foundation. GFR: glomerular filtration rate.

Table I. Characteristics of the patients with GFR < 60 mL/min/1.73 m^2

	High Cr (total)	High Cr (men)	High Cr (women)	Cr normal (total)
n = 960	542 (56.5%)	287 (29.9%)	255 (26.6%)	418 (43.5%)
Age (years)	77 ± 9.7	75.5 ± 9*	78.8 ± 10	76.5 ± 8.4*
Gender (% women)	48,2%	0%	100%	100%
Cr (mg/dL)	1.6 ± 0.7	1.6 ± 0.8+	1.5 ± 0.4	1 ± 0.05*
GFR	43.3 ± 10.7	48 ± 10.5*	38 ± 8.3	54.8 ± 3.7*

Data expressed as percentage or mean ± standard deviation.
* P < 0.001 as compared with the group of women with High Cr. + P = 0.014 as compared with the group of women with High Cr.

ference range (< 1.3 mg/dL form men and < 1.2 mg/dL for women).

The data were analyzed by the SPSS v. 13.0 software package (SSPS Inc. Chicago, Illinois). The results were considered to be statistically significant when p < 0.05.

RESULTS

Between March 1st and July 31st of 2006, 13,784 Cr determinations were ordered from Primary Health Care to patients older than 18 years (mean: 2,757/month). In 1042 determinations, the GFR was 60 mL/min/1.73m^2. We reviewed those analyses and when they corresponded to the same patient, we selected the lowest Cr value. Thus, we eliminated 82 analyses, remaining 960 patients (6.96%) with mean age of 76.8 years (range 40-98) and 70.1% were women. Of them, 418 (43.5%) had normal Cr levels, all of them being women. Compared with those women with "occult" RF with those with high Cr, we observed that women with «occult» RF are younger (table 1).

Table 2 shows the data corresponding to the different Basic Health Care areas. By RF stages, 887 (92.4%) were in stage 3, 68 (7.1%) in stage 4, and 5 (0.5%) in stage 5. All the patients with «occult» RF were in stage 3. Figure 2 shows how stages 3 and 4 predominantly affect those people older than 70 years. In women with stage 3 RF, «occult» RF represents more than 50% of the cases for any age

Table II. Characteristics by Primary Health care Center of the area of Plasencia

HC center	Adult population	> 65 years (%)	GFR done	GFR/100 pop.	% GFR < 60 mL/min/1.73 m^2	Age (years)	Gender (%♀)
Ahigal	3,431	36.7	65.3	19	8.1	76.2	63
Cabezuela del Valle	6,251	24.4	977	15.6	7.2	77.5	67.1
Mohedas de Granadilla	3,068	35.7	610	19.9	7.5	76.4	80.4
Casas del Castañar	3,682	31.9	646	17.5	7.9	75	66.7
Aldeanueva del Camino	4,419	31.1	779	17.6	7.5	77.2	81.7
Hervás	4,355	26.3	992	22.8	7.7	76.6	65.8
Jaraiz de la Vera	11,348	26	2,198	19.4	6.5	77.4	71.1
Serradilla	2,663	32.9	357	13.4	8.9	77.2	64.5
Plasencia I	18,082	22.7	2,303	12.7	6.3	76.9	71.9
Plasencia II	14,419	23.6	2,443	16.9	7.7	76.5	66.7
Plasencia III	13,079	16.2	1,826	14	5.3	77	72.9
Total	**84,897**	**25.4**	**13,784**	**16.2**	**6.96**	**76.8**	**70.1**

GFR: estimated glomerular filtration rate by the MDRD-4 equation.

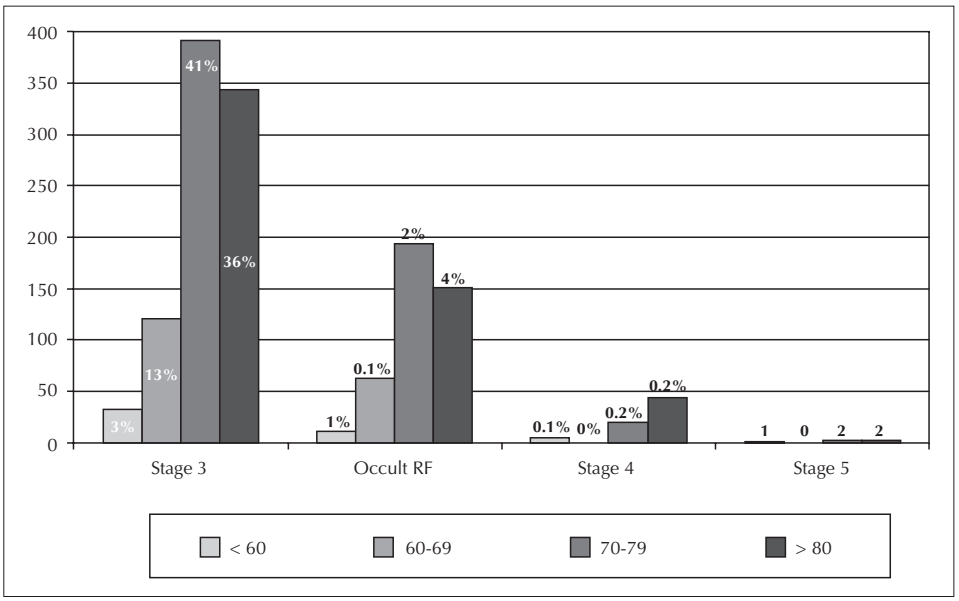

Fig. 2.—Distribution of individuals with GFR < 60 mL/min/1.73 m² by stage of renal failure and age.

group, especially between the age 60 and 79 years (fig. 3).

DISCUSSION

In this study, we observed that almost 7% of the people having a blood test done at the primary care level present a GFR < 60 mL/min/1.73m², and of them, more than 40% present serum Cr levels within the normality range , 3% of the whole sample. All the patients with «occult» RF were women, with mean age of 77 years. This datum is in agreement with that obtained in the «Study for the assessment of occult renal disease among the Spanish population attended at Primary Care (ERO-CAP)», [0] and may be explained by several reasons: firstly, men demand less medical assistance than women,[11] and since RF is an asymptomatic disease it does not require health care assistance until advanced stages; secondly, the SAPALDIA study[12] showed than women present higher prevalence of RF than men, independently of using MDRD-4 or Cockcroft-Gault's formulas; and thirdly, the limitations in the MDRD-4 equation.

The MDRD-4 formula depends on Cr levels, age, and gender. Thus, given the same age, men need higher Cr levels to present GFR < 60 mL/min/1.73m². Considering our criteria for «occult» RF, if we use the Cr value rounded-up to one decimal, men would have to be 94 years old, or older, whereas women would reach this values with only 36 years of age.

One of the main limitations of the study is not having performed a random sampling of the population, so that we are not able to speak about the prevalence of «occult» RF. There may be a selection bias since the laboratory work-up was ordered from the Primary Care level to users because of intercurrent pathological conditions that may be affecting their baseline renal function. So that, our data correspond to the percentage of patients attended at Primary Care to whom a laboratory check-up has been done during the study months. However, they are similar to those obtained by other prevalence studies done on the general population.[10, 12-15] Rodrigo and Andrés,[16] in their study done on 1000 patients assisted at the primary care, observed that 14.5% presented GFR < 60 mL/min/1.73m², of whom 72% had normal Cr levels. These data are higher than those from our patients since the Cr levels the authors used as normal were higher.

Another possible limitation of the study is derived from the GFR calculation since it uses Cr values rounded-up to one decimal. From the study carried out by the Department of Clinical Analyses, Cr values were adjusted to two decimals and the reference Cr levels were reduced being lower than 1 mg/dL for women and 1.2 mg/dL for men.

The importance of this study lies on the fact it collects all the laboratory work-ups coming from Primary Care of a health area with more than 100,000 population, representing the reality of patients attended at this level, without any kind of selection. It brings data better reflecting the increasing incidence of people with RF in primary care clinics, and it identifies a high percentage of individuals with decreased GFR that have normal Cr values («occult» RF) and are usually missed since GFR is not determined, particularly in women aged 70-80 years. The identification

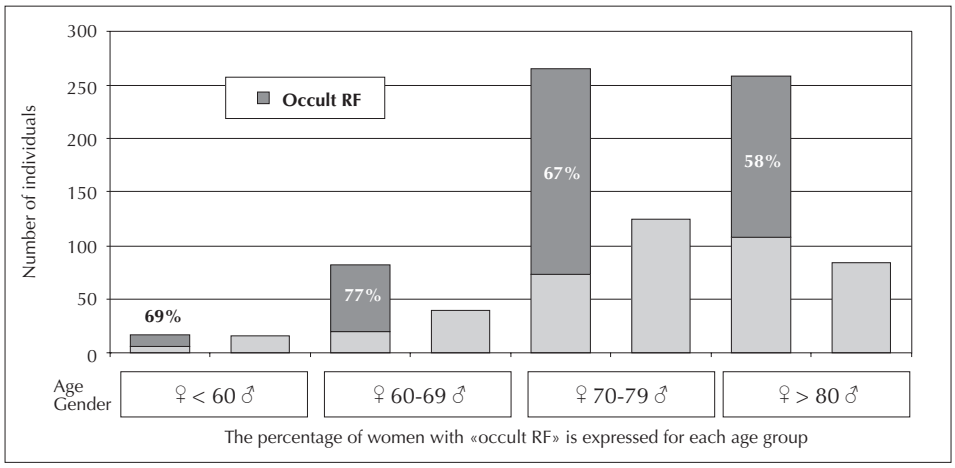

Fig. 3.—Distribution of stage 3 RF patients by gender and the presence of «occult RF».

of these individuals with RF brings the possibility to primary care physicians taking decisions aimed at controlling other risk factors, taking into account that the majority of these patients die from other causes different than renal disease, of generally cardiovascular origin,[17,18] and it prevents the use of nephrotoxic drugs that may favor progression of RF and the need for dialysis.

The differences in the different basic health care areas may be explained by the conjunction of three causes: a) the population aging, assessed as the percentage of people older than 65 years; b) the high percentage of women with GFR < 60 mL/min/1.73m^2; and c) larger analytical sampling, estimated by the rate of laboratory work-ups ordered per 100 population.

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