Disproportionately high incidence of diabetes-related end-stage renal disease in the Canary Islands. An analysis based on estimated population at risk

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Abstract

Background. An exceptionally high incidence of diabetes-related end-stage renal disease (DM-ESRD) has been reported in the Canary Islands. This phenomenon was attributed to an increased prevalence of diabetes in this community. We compared the incidence of DM-ESRD in the Canary Islands with the rest of Spain among the estimated number of individuals at risk (people with diabetes in the population).

Methods. The population-at-risk was calculated using census population figures and estimates of self-reported diabetes prevalence from the Spanish National Health Survey in the years 2003 and 2006. The incidence of DM-ESRD for the same years was obtained through Spanish regional registries. The independent effect of age, community of residence and calendar year was estimated with a Poisson regression model. Age-standardized acceptance rate ratios were calculated for each community.

Results. Overall DM-ESRD incidence in the Canary Islands population-at-risk was 1209.9 per million population (pmp) in 2003 and 1477.3 pmp in 2006. Rates for the remaining Spanish regions ranged from 177.3–984.9 pmp. The incidence was higher in the Canary Islands across all age groups, but was most striking for patients ≥75 years. Diabetes prevalence in the general population was greater in the two youngest age strata and diminished from 75 years on in the Canary Islands, in comparison with other areas of Spain. Using a cluster of three communities with the lowest incidence as a reference, the relative risk of DM-ESRD in the Canary Islands population-at-risk was 3.88 [95% confidence interval (CI): 3.07–4.89]. Age-standardized acceptance rate ratios (95% CI) in the Canary Islands were 2.21 (1.85–2.61) in 2003 and 2.73 (2.34–3.17) in 2006.

Conclusions. Individuals with diabetes in the Canary Islands present a disproportionately high incidence of ESRD. Diabetic Canary inhabitants are exposed to the disease for a longer time and therefore, may be more vulnerable to the development of chronic diabetes complications, including ESRD.

Keywords: diabetes; diabetic nephropathy; end-stage renal disease; epidemiology

Introduction

The epidemiology of end-stage renal disease (ESRD) varies considerably worldwide [1]. Diabetes is the leading cause of ESRD in developed countries, where substantial increases in the prevalence of and reduced mortality from diabetes has paralleled an increase in the incidence of diabetes-related ESRD (DM-ESRD). In the United States, the annual incidence of DM-ESRD increased from 62.5 to 134 patients per million population (pmp) over the past decade [2]. In Europe, the incidence increased from 14.8 pmp in 1991–92 to 26.9 pmp in 1999–00 [3].

Incidence rates of DM-ESRD [4] in Spain range in the middle, in comparison with other European countries. According to the most recent data (2007), new cases of DM-
ESRD among those >15 years of age ranged between 9.6 and 37.8 pmp across different Spanish political regions (‘autonomous communities’) with the exception of the Canary Islands where the incidence was 103 pmp [4]. These data confirm previous reports that the incidence of DM-ESRD is more than 2-fold higher in this territory than in the rest of Spain [4–6]. The Canary archipelago is an Atlantic region of Spain with a population of about 2 million, who are mostly of European origin.

Although the high incidence of DM-ESRD in the Canary Islands could be mainly explained by a proportionately increased diabetes prevalence in this community [7], the influence of diabetes prevalence on DM-ESRD epidemiology has not been quantified, because renal data registries do not refer to the true population-at-risk, i.e. the total number of diabetic persons, but to the general population.

As an alternative to this traditional approach, the United States Renal Data System (USRDS) [8] has, since 2007, computed incident rates of DM-ESRD among the population-at-risk using a method proposed by the Centers for Disease Control and Prevention (CDC) [9]. The CDC estimates the prevalence of known diabetes using data from the National Health Interview Survey (NHIS), a cross-sectional household interview survey performed annually. Although interview-based surveys similar to the NHIS are regularly conducted in most Western countries, no data on the incidence of DM-ESRD in the population-at-risk have been reported outside the USA.

We estimated the incidence of DM-ESRD among diabetic subjects in the Canary Islands and the rest of Spain. Our goal was to clarify whether the increased incidence of DM-ESRD is a consequence of a higher prevalence of diabetes in our region.

Subjects and methods

Prevalence of diabetes

The prevalence of known diabetes in the adult Spanish population was obtained from the 2003 and 2006 National Health Survey (NHIS) [10]. The NHS is periodically conducted by the Ministry of Health to provide health information about the entire population, including the prevalence of common chronic diseases. Participants are selected following a stratified multistage procedure. The 2003 and 2006 NHS had 21 650 and 29 478 adult participants, respectively. Information, including self-reported diabetes, was recorded by direct personal interviews.

Incidence of diabetes-related end-stage renal disease

The number of new patients >15 years with DM-ESRD in the years 2003 and 2006 in the Canary Islands and in 14 of the 16 remaining Spanish autonomous communities was obtained through information from the national renal registry of patients [4]. Data from two communities were not available, and were excluded from the analyses.

For the total population >15 years of age for the 2003 and 2006 census were downloaded from the National Institute of Statistics [11], and used to calculate the annual incidence of DM-ESRD among the general population in each community. For calculation of the corresponding annual incidence rates in the population-at-risk, we used the number of persons with diabetes in each community as the denominator, assuming the prevalence rates observed in the 2003 and 2006 Spanish NHIS.

Standardized rate ratios of acceptance

Because comparisons of crude incidence rates are hampered by demographic differences between communities, age-standardized rate ratios of acceptance with 95% confidence intervals were also calculated for each region [12]. Briefly, age-specific rates were first calculated using the registry data on the number of incident patients for the different autonomous communities. The age distribution of the population in each community was also extracted from the 2003 and 2006 census data [11] and used to calculate the expected age-specific incidences for each region. The age-standardized acceptance rate ratio is the observed incidence divided by the expected incidence. A ratio >1 indicates that the rates are greater than expected given the area’s population structure.

Statistical analysis

To estimate relative risks between subgroups, we used a Poisson regression model with the number of DM-ESRD cases among the population-at-risk as the dependent variable and the number of diabetic people as the offset term, and age group (16–44, 45–64, 65–74 and ≥75 years), year of first ESRD treatment (2003 or 2006) and autonomous community of residence as predictors. To avoid over-parameterization, autonomous communities were clustered according to similar DM-ESRD incidence rates in the population-at-risk in the year 2006 as follows: Group 0, Basque Country, Balearic Islands and Extremadura; Group 1, Andalusia, Aragon, Castile-La Mancha, Navarre and Valencia; Group 2, Asturias, Cantabria, Castile-Leon, Catalonia, Galicia and La Rioja; Group 3, Canary Islands. Group 0 showed the lowest incidence of DM-ESRD and was used as the reference category. Interaction terms between groups of communities and age groups were tested and incorporated as necessary. Goodness of fit was assessed by the over dispersion coefficient and by comparisons between the observed incidence rates and the incidence rates predicted by the model. Data were analysed with the R statistical package (version 2.7.1).

Results

Figures for the overall population, crude prevalence of self-reported diabetes (population-at-risk) and the crude DM-ESRD incidence rate in the population-at-risk are shown in Table 1. The number of incident DM-ESRD cases was not available in three autonomous communities in 2003. Although incidence rates varied widely across the country, the greatest difference was observed between the Canary Islands and the remaining communities.

Incidence rates were higher in the Canary Islands than in any other community for all age groups in both 2003 (data not shown) and 2006 (Figure 1), but particularly higher in the oldest age groups. Notably, for patients aged ≥74 years, the proportion of incident DM-ESRD subjects in the Canary Islands was 7-fold higher than the average incidence for the rest of Spain. Additionally, the prevalence of self-reported diabetes in the Canary Islands was remarkably higher in the two youngest age groups, and was the only community where the prevalence of self-reported diabetes diminished from 75 years of age and older (Figure 1).

Using the three-community cluster with the lowest crude incidence rates in 2006 (Group 0) as a reference, incidence rate ratios of DM-ESRD among the diabetic population were modelled with a Poisson regression (Table 2). After adjusting for age and year of diagnosis, the rate ratios increased significantly across pre-established community groups. However, as compared with the reference group, the second and third groups presented a 33% and 100% greater risk for DM-ESRD, but the risk for diabetics in the Canary Islands was 288% higher. Age also affected the risk of DM-ESRD. A significant increment was found for the age group 65–74 years when compared with the 16–44 years reference group. In addition, an interaction
was found between the ≥75 years age group and residence in the Canary Islands. Using the 16–44 years old group as the reference, the relative risk of DM-ESRD among diabetic Canary persons ≥75 years was 1.384 (\(P = 0.023\)), whereas the corresponding risk among their coetaneous non-Canary counterparts was 0.832 (\(P = 0.047\)); i.e. for the age group ≥75 years, the incidence of DM-ESRD was increased by 38.4% in the Canary Islands, whereas it decreased by 16.8% in the rest of Spain.

Corresponding age-standardized acceptance ratios [95% confidence interval (CI)] in the Canary Islands were 2.21 (1.85–2.61) in 2003 and 2.73 (2.34–3.17) in 2006 (Figure 2). These values are statistically significant at the 5% level if the lower confidence limit is >1. The Canary Islands were the only community with significantly increased standardized acceptance rate ratios in both 2003 and 2006.

**Discussion**

The high incidence of DM-ESRD in the Canary Islands has been attributed to a high prevalence of type 2 diabetes [7,13]. However, two recent population-based studies in...
Table 2. Incidence rate ratios of diabetes-related end-stage renal disease among the diabetic population modelled with a Poisson regression

<table>
<thead>
<tr>
<th></th>
<th>Estimation (SE)</th>
<th>Relative risk (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calendar year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>0</td>
<td>1</td>
<td>0.762</td>
</tr>
<tr>
<td>2006</td>
<td>0.013 (0.152)</td>
<td>1.014 (0.929–1.106)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–44</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>45–64</td>
<td>0.063 (0.084)</td>
<td>1.065 (0.902–1.256)</td>
<td>0.458</td>
</tr>
<tr>
<td>65–74</td>
<td>0.332 (0.084)</td>
<td>1.393 (1.182–1.642)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥75</td>
<td>−0.184 (0.093)</td>
<td>0.832 (0.694–0.998)</td>
<td>0.047</td>
</tr>
<tr>
<td>Age ≥75 Canary Islands(^a)</td>
<td>0.325 (0.155)</td>
<td>1.384 (1.022–1.875)</td>
<td>0.023</td>
</tr>
<tr>
<td>Autonomous community(^b)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 0</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>0.288 (0.106)</td>
<td>1.33 (1.08–1.63)</td>
<td>0.007</td>
</tr>
<tr>
<td>Group 2</td>
<td>0.695 (0.105)</td>
<td>2.00 (1.63–2.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Canary Islands</td>
<td>1.355 (0.119)</td>
<td>3.88 (3.07–4.89)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The cluster of three communities with the lowest crude incidence rates in 2006 (Group 0) was used as a reference.
\(^a\)This line shows an interaction between age group ≥75 and Canary Island. For explanation see the text.
\(^b\)Group 0: Basque Country, Balearic Islands and Extremadura.
Group 1: Andalusia, Aragon, Castile-La Mancha, Valencia and Navarre.
Group 2: Asturias, Cantabria, Castile-Leon, Catalonia, Galicia and La Rioja.

Fig. 2. Age-standardized acceptance ratios and 95% confidence interval in autonomous communities for the years 2003 and 2006. The Canary Islands were the only community with significantly increased standardized acceptance rate ratios (>2-fold) in both 2003 and 2006.
the Canary Islands [14,15] found prevalence rates in the upper part of the range observed for other Spanish regions. According to our analysis, the information provided by the NHS seems to be congruent with these latter findings.

Our analysis rules out the hypothesis that the exceptionally high incidence of DM-ESRD in the Canary Islands is merely the result of a proportionally higher prevalence of diabetes. According to the NHS estimates of the population exposed to diabetes, the risk of DM-ESRD in the Canary Islands would be 3.1 to 4.9 times greater than for diabetic persons from other autonomous Spanish communities. To our knowledge, a difference of this magnitude between regions within the same country is without precedent. Consequently, it is notable that data from the NHS suggests that diabetes prevalence in the youngest age strata tends to be greater in the Canary Islands than in other Spanish areas (Figure 1). If true, diabetic Canary inhabitants would have longer exposure to the disease and therefore, be more vulnerable to developing of chronic diabetes complications, including ESRD.

Some methodological limitations of our study could have influenced the results. One is the use of self-reported diabetes to estimate the population-at-risk. The NHS was the only data source supplying a homogeneous and concurrent estimate of diabetes prevalence in all communities, but it unavoidably misses an unknown proportion of diabetic subjects that are not aware of their condition. Another potential source of error could be related to the fact that renal registries do not employ standard criteria to establish the cause of ESRD. Discrepant diagnostic criteria may have led to a greater trend towards ascribing the cause of ESRD to diabetes in the Canary Islands than in other Spanish regions. Overall, the results of our study are striking and cannot be considered the consequence of methodological pitfalls. Therefore, identifying the possible causes of the increased incidence of DM-ESRD in the Canary Islands becomes crucial for health planning in this community. A predisposing genetic background, the availability of health services and a lower socioeconomic status all deserve consideration.

The Canary population is mainly Caucasian, descended from the Iberian Peninsula (mainland Spain) inhabitants, although North African genetic contribution is also reported [16]. Although speculative, genetic background could be a factor contributing to the increased DM-ESRD incidence in the Canary population. Identification of genes that confer susceptibility to type 2 diabetes and nephropathy [17] and their interaction with environmental risk factors could yield important insights to clarify this possibility.

Regarding health services availability, the public healthcare system is free, providing universal coverage. Therefore, it is improbable that the greater incidence of treated ESRD in the Canary Islands can be explained by healthcare inequalities between communities.

Thirdly, the mean socioeconomic status in the Canary Islands, reportedly among the lowest of Spanish communities, may contribute [18]. Low socioeconomic status is associated with a greater ESRD risk, particularly when diabetes is the cause of chronic kidney disease [19]. Other recent investigations confirmed that obesity [20] and mortality due to coronary heart disease [21] and diabetes [22], whose geographical variations in Spain are also explained by socioeconomic variables [23], are markedly elevated in the Canary Islands. The reasons for this association are not entirely understood, but lesser utilization of health services, poorer adherence to medical treatments and unhealthy lifestyle habits could be involved. It is conceivable that low socioeconomic status could be a seminal underlying factor for all of these issues in the Canary Islands.

Other factors are implicated in the incidence of ESRD, such as survival from competing causes of death among patients with chronic kidney disease and variations in the acceptance of patients into dialysis treatment programmes [24]. Both variables would be expected to impact primarily the oldest age group, and deserve consideration since we found a positive association between the DM-ESRD risk and the interaction term ‘Canary Islands*age ≥75 years’. Longer survival is not a plausible cause for this association. As mentioned above, mortality from cardiovascular diseases in the Canary Islands is among the highest in Spain. In fact, life expectancy in the Canaries ranks near the bottom of Spanish communities [25]. In contrast, rate of diabetes-associated mortality rate [21] would tend to reduce the total number of people at risk in the oldest age groups. This might explain the disproportionately high rate of DM-ESRD in the elderly Canary population. On the other hand, the incidence of DM-ESRD may be higher because of increased acceptance of older people with diabetes. It is difficult to determine the extent to which the increasing access and acceptance of renal replacement therapy affects the higher incidence of ESRD. Specific analyses must be conducted in order to investigate whether the criteria for acceptance to dialysis are more liberal in the Canary Islands than in other Spanish communities.

In conclusion, our analysis presents a depressing scenario for our region, where DM-ESRD is probably the most serious and resource-consuming health problem in the community. If, as expected, the number of newly diagnosed diabetic patients is growing, the burden of chronic kidney disease attributable to diabetes will also continue to grow. Urgent response from governments, health-care authorities and organizations involved in diabetes care is imperative to attenuate or prevent progression of renal complications in diabetic patients.

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Conflict of interest statement. None declared.

References

Low-GDP fluid (Gambrosol trio®) attenuates decline of residual renal function in PD patients: a prospective randomized study

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Abstract

Background. Residual renal function (RRF) impacts outcome of peritoneal dialysis (PD) patients. Some PD fluids contain glucose degradation products (GDPs) which have been shown to affect cell systems and tissues. They may also act as precursors of advanced glycosylation products.

Methods. A randomized double-blind trial was conducted in 48 PD patients on Gambrosol trio® fluid or low-GDP fluid. The primary endpoint was RRF changes. Secondary endpoints included proteinuria, C-reactive protein, creatinine, and glucose levels.

Results. RRF increased significantly more in the low-GDP fluid group (mean ± SD: 2.1 ± 1.3 vs. 0.4 ± 1.6 mL/min/1.73 m², respectively; P < 0.001). Proteinuria and C-reactive protein levels were also significantly lower in the low-GDP fluid group (P = 0.03 and 0.02, respectively).

Conclusion. Low-GDP fluid attenuates the decline of RRF, accompanied by a reduction in proteinuria and C-reactive protein levels. This suggests that low-GDP fluids may have a beneficial effect on cell systems and tissues in PD patients.