Journal of Diabetes and Its Complications 29 (2015) 761–765

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Is there a difference in progression of renal disease between South Asian and white European diabetic adults with moderately reduced kidney function?

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ARTICLE INFO

Article history:
Received 13 April 2015
Received in revised form 20 May 2015
Accepted 21 May 2015
Available online 29 May 2015

Keywords:
Chronic kidney disease
Diabetes mellitus
Estimated glomerular filtration rate
Ethnicity
Glycated haemoglobin

ABSTRACT

Aims: We examined potential ethnicity-related differences in progression of chronic kidney disease (CKD) between South Asian and white European diabetic adults with CKD stage 3 over a 5-year period.
Methods: We analysed data collected from diabetic adults of white European and South Asian ethnicity who had attended diabetes and diabetes-renal outpatient clinics with baseline estimated glomerular filtration rate (eGFR) values ≥30 and <60 ml/min/1.73 m^2 over 5 years (2005–2010); 891 (76%) were white Europeans, 282 (24%) were South Asians.
Results: Despite similar baseline eGFR ($P = 0.103$), South Asians were younger [median (interquartile range) 68 (63–73) vs. 70 (64–77) years; $P < 0.001$] and had worse baseline glycated haemoglobin than white Europeans [8.0 (7.0–9.1) vs. 7.6 (6.8–8.7)%; $P = 0.004$]. The 5-year follow-up eGFR and the decline in eGFR did not differ between the two groups. Thirty-five (12.4%) South Asians and 82 (9.2%) white Europeans progressed to stages 4–5 CKD ($P = 0.112$). There was a trend towards higher follow-up glycated haemoglobin levels in South Asians ($P = 0.064$).
Conclusions: Despite worse glycaemic control, South Asian diabetic adults with CKD stage 3 did not show any difference in 5-year decline in eGFR compared with white Europeans. These data do not support ethnic differences in progression of CKD between the South Asian and white European patient populations.

1. Introduction

The prevalence of diabetes mellitus (DM) is increasing worldwide accompanied by serious vascular complications. Diabetic nephropathy (DN) is a major microvascular complication associated with end-stage renal disease (ESRD) requiring renal replacement therapy and transplantation. DN affects approximately 40% of patients with DM (Gross et al., 2005) and is the most common cause of chronic kidney disease (CKD) and incident ESRD in this patient population (Atkins & Zimmet, 2010; UK Renal Registry, 2014; United States Renal Data System, 2014).

Modifiable risk factors for DN include glycaemic control, hypertension, dyslipidaemia, smoking, and albuminuria. Intensive glycaemic control, in particular, is a major modifiable risk factor for the development and progression of DN in both type 1 and 2 DM (Microalbuminuria Collaborative Study Group, 1999; Stratton et al., 2000). Of importance, early and sustained improvements in glycaemic control may effectively delay the onset and slow the progression of DN (DCCT Research Group, 1993; UKPDS, 1998).

Non-modifiable risk factors for DN include genetic and ethnic background, age, gender, and DM duration. A growing body of literature has documented a strong association between various gene variants resulting from several allelic polymorphisms and increased susceptibility to DN (Ewens, George, Sharma, Ziyadeh, & Spielman, 2005; Rizvi, Raza, & Mahdi, 2014). While the individual's genetic makeup contributes to the risk of DN, several meta-analyses have further demonstrated a variable overall risk of the polymorphisms associated with DN in different ethnic groups (Sun et al., 2014; Wang

Conflict of Interest: M. Pallayova: Grant/Research support from: Slovakian Diabetes Association/Lilly Diabetes Clinical Research Initiative. H. Rayner: No competing interests. S. Taheri: S. Taheri is funded by the Biomedical Research Program at Weill Cornell Medical College in Qatar, supported by the Qatar Foundation. S. Taheri also received funding from the following grants from the Qatar National Research Fund: NPRP 4-1392-3-345 and NPRP 7-701-3-192. I. Dasgupta: No competing interests.

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http://dx.doi.org/10.1016/j.jdiacomp.2015.05.012
1056-8727/

et al., 2012; Zhao et al., 2013; Zhou, Jiang, Qin, & Drummen, 2014). Evidence mostly from nearly 2 decades ago suggests that South Asians (those originating from the Indian Subcontinent) with DM have an increased risk of DN, a more rapid progression of nephropathy, and a higher incidence of end-stage renal failure than white Europeans (Burden, McNally, Feehally, & Walls, 1992; Roderick, Raleigh, Hallam, & Mallick, 1996). Very little data are available regarding ethnic differences in DN in more contemporary populations, benefitting from more modern approaches to diabetes management. Recently, Dreyer, Hull, Mathur, Chesser, and Yaqoob (2013) examined differences in renal decline between South Asian and White European patients with DM in the primary care setting. They observed a 0.31 ml/min/1.73 m^2 greater decline in estimated glomerular filtration rate (eGFR) in the South Asian population. Using data from a large secondary care centre based in a region with a high South Asian population, we examined the potential ethnicity-related differences in progression of CKD between South Asian and white European adults with DM and stage 3 CKD at baseline over a 5-year period.

2. Subjects, materials and methods

This study used a cross-sequential design, analysing data collected from all adults with DM of white European and South Asian ethnicity who had attended diabetes and diabetes-renal outpatient clinics at the Heart of England NHS Foundation Trust, based in the West Midlands (UK), a region with one of largest congregation of South Asians in the UK. Adults with an estimated glomerular filtration rate (eGFR) of ≥ 30 and < 60 ml/min/1.73 m^2 at baseline over a 5-year period (2005–2010) were included. Demographic, and baseline and follow-up biochemical data for this study were extracted from the hospital electronic database. Ethnicity was self-reported. South Asian ethnicity included Indian, Pakistani, Bangladeshi and Asian from any other ethnic group. White European ethnicity included white British, white Irish and white from any other ethnic group.

The eGFR values were calculated using the original 4-variable Modification of Diet in Renal Disease Study formula (Levey et al., 1999);

For creatinine in mg/dl: eGFR = 186 × (Serum Creatinine) $^{-1.154}$ × (Age) $^{-0.203}$ × (0.742 if Female) × (1.210 if African American).

For creatinine in μmol/l: eGFR = 32788 × (Serum Creatinine) $^{-1.154}$ × (Age) $^{-0.203}$ × (0.742 if Female) × (1.210 if African American).

We did not apply any correction factors in the equation for the South Asian participants for lack of a validated equation at the time.

Glucose control was assessed by glycated haemoglobin (HbA1c), measured using methods calibrated according to the National Glycohemoglobin Standardization Program and reported in percentage units. The eGFR and HbA1c at baseline and at end of follow up, and change in eGFR over 5 years (delta eGFR) were compared between the groups.

2.1. Statistical analyses

The Shapiro–Wilk test was used to assess normality of data distribution. Since the data were not normally distributed, we used the Wilcoxon rank-sum test and the Wilcoxon-matched pairs signed-ranks test for univariate analyses. The Spearman's rank correlation coefficient (rho) and regression analyses were utilised to examine relationships between renal function and its potential predictors. Data are presented as medians and interquartile ranges (IQR). The follow-up absolute changes (Δ) in eGFR and in HbA1c were calculated by subtracting the baseline values from the 5-year follow-up values. The number in whom complete data were available is shown in the text/table/figures. Findings were considered to be statistically significant at the 5% level. Statistical analyses were performed using Stata 11.2 Special Edition (StataCorp LP, College Station, TX).

3. Results

Of the entire cohort of patients of 1173, 891 (76%) patients were white Europeans, and 282 (24%) were South Asians, 54% were female and the median (IQR) age was 70 (64–76) years. There was no significant difference in baseline eGFR between South Asian and white European adults. Compared to white Europeans, South Asians were younger ($P < 0.001$) and had worse baseline glucose control ($P = 0.004$; Table 1; Fig. 1). The baseline eGFR was negatively correlated with age both in South Asian (rho = −0.15; $P = 0.011$; Table 2) and in white European patients (rho = −0.1; $P = 0.002$; Table 2), as well as in the entire cohort (rho = −0.11; $P < 0.001$; Table 2).

Over 5-year follow-up, 122 (13.7%) white European and 39 (13.8%) South Asian patients were lost to follow-up. The 5-year follow-up eGFR, albumin/creatinine ratio (ACR), and protein/creatinine ratio (PCR) did not differ between South Asian and white European patients. Furthermore, there was no statistical difference in decline in eGFR over 5 years between the two groups (Table 1; Fig. 2). Thirty-five (12.4%) patients in South Asian group and 82 (9.2%) white European patients progressed to stage 4 or 5 CKD ($P = 0.112$). There was a trend towards higher 5-year follow-up HbA1c levels in South Asian than in white European patients ($P = 0.064$; Table 1; Fig. 1). We did not find any difference in an absolute change in HbA1c over the 5 years between the two groups. The follow-up eGFR was negatively correlated with the follow-up ACR only in South Asian patients (rho = −0.25; $P = 0.013$; $N = 99$). Through bivariate association analyses (Table 2; Fig. 3), we further found out that negative correlations of the follow-up eGFR with age observed in the entire cohort (rho = −0.09; $P = 0.004$; $N = 1012$) were driven by significant correlations found only in white European patients (rho = −0.1; $P = 0.006$; $N = 769$). In a similar way, we observed trends towards a greater decline in eGFR with both increasing age (rho = −0.06; $P = 0.085$; $N = 769$) and worse baseline long-term glucose control (rho = −0.07; $P = 0.082$; $N = 699$) only in white European patients (Table 2; Fig. 4). Although both increasing age and

Table 1
Clinical and biochemical characteristics by ethnic group ($N = 1173$).

	South Asians ($N = 282$)	White Europeans ($N = 891$)	N	P
Age [years]	**68 (63–73)**	**70 (64–77)**	**1173**	**<0.001**
Sex, females [%]	49.2	56.5	1173	0.645
Baseline serum creatinine [μmol/l]	112.5 (97–134)	110 (95–128)	1169	0.102
Baseline eGFR [ml/min/1.73 m^2]	49.7 (42.8–55.8)	51.7 (43.7–56.5)	1173	0.103
Baseline ACR [mg/mmol]	4.2 (1–19.4)	3.5 (1.9–7.6)	71	0.787
Baseline HbA1c [%]	**8.0 (7.0–9.1)**	**7.6 (6.8–8.7)**	**1044**	**0.004**
Baseline HbA1c [mmol/mol]	**64 (53–76)**	**60 (51–72)**	**1044**	**0.004**
Baseline total cholesterol [mmol/l]	4 (3.5–4.7)	4.1 (3.6–4.8)	1133	0.242
5-year follow-up serum creatinine [μmol/l]	121 (99–155)	118 (97–147)	989	0.191
5-year follow-up eGFR [ml/min/1.73 m^2]	46.8 (34.3–56.1)	45.9 (36.2–58.0)	1012	0.589
ΔeGFR over 5 years [ml/min/1.73 m^2]	−2.9 (−10.2, 5.9)	−3.2(−10.8, 5.9)	1012	0.659
5-year follow-up ACR [mg/mmol]	3 (1.2–9.4)	3 (1–9.6)	409	0.622
5-year follow-up PCR [mg/mmol]	21.5 (12–60.5)	18 (12–35)	461	0.156
5-year follow-up HbA1c [%]	**7.9 (7.1–8.9)**	**7.6 (6.9–8.8)**	**734**	**0.064**
ΔHbA1c over 5 years [%]	0 (−0.9, 1.1)	0.1 (−0.8, 1)	674	0.508

Data expressed as median (interquartile range). *ACR*, albumin/creatinine ratio; *eGFR*, glomerular filtration rate estimates; *ΔeGFR*, an absolute change in eGFR; *HbA1c*, glycated haemoglobin; *ΔHbA1c*, an absolute change in HbA1c; *PCR*, protein/creatinine ratio.