Increased prevalence of albuminuria among non-European peoples with type 2 diabetes

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Abstract

Background. A high incidence of albuminuria, varying by ethnicity, has been found in a number of populations worldwide. There have been few opportunities to explore the prevalence of albuminuria as a marker of chronic kidney disease while adjusting for other risk factors in the different ethnic groups in New Zealand.

Methods. We examined the association between albuminuria and ethnicity using cross-sectional data from a large cohort study of type 2 diabetes conducted in New Zealand.

Results. The study population was 65,171 adults in primary care with type 2 diabetes, not on renal replacement therapy; median age was 64.7 years, median diabetes duration 5.1 years and 48.5% were non-European. Microalbuminuria or greater was present in 50% of Maori, 49% of Pacific people, 31% of Indo- and East-Asians and 28% of Europeans. Regression analyses were used to examine the association between ethnicity and albuminuria—measured as albumin:creatinine ratio—after controlling for study site and other known risk variables: age, sex, duration of diabetes, smoking status, socioeconomic status, body mass index, systolic and diastolic blood pressure, triglyceride levels, HbA1c and being on an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker. After controlling for these risk factors and compared with Europeans, odds ratios for 'advanced' albuminuria (≥100 mg/mmol) were 3.9 (95% confidence interval: 3.2–4.6) in Maori, 4.7 (3.6–6.3) in Pacific people, 2.0 (1.5–2.7) in Indo-Asians and 4.1 (3.2–5.1) in East-Asians.

Conclusion. Non-European ethnicities appear to carry significantly higher risks of albuminuria in type 2 diabetes.

Keywords: albuminuria; epidemiology; ethnic disparities; type 2 diabetes

Introduction

End-stage renal disease (ESRD) is three to four times more common in Maori and Pacific populations than it is among those of European origin in New Zealand [1]. Type 2 diabetes is two to three times more common among Maori and Pacific people than non-Maori and non-Pacific people in New Zealand [2, 3]. In the years 2003–07, diabetes was the primary cause of new ESRD in New Zealand for 63 and 67% of cases among Maori and Pacific People, respectively, but only 16% among people of European origin [4]. A study conducted in the 1990s found that, compared with Europeans, the hazard ratio for Maori and Pacific people with diabetes dying over a 5-year period was 1.84 and 1.06, respectively; but the hazard ratio for death from renal disease (as recorded on death certificates) was 15.4 and 1.6, respectively [5]. These calculations were adjusted for age and gender, but not for other risk factors. Neither the data on primary cause of ESRD nor 5-year death rates were available for other ethnicities.

Albuminuria in people with type 2 diabetes is independently predictive of diabetic nephropathy leading to renal replacement therapy [6, 7] and separately predictive of cardiovascular disease (CVD) [6, 8] and premature mortality [9, 10]. Because of its prognostic significance, urine albumin:creatinine ratio (UACR) is assuming an important role in the staging of chronic kidney disease [11]. A high incidence of albuminuria, varying by ethnicity, has been found in a number of populations worldwide [12, 13]. In particular, some minority (African-American, US Hispanic) and indigenous populations (American Indian, Alaska Natives) appear to be at high risk of diabetes and renal disease, both separately and together [14–16]. Independent correlations with albuminuria have included poor blood sugar control in those with diabetes, hypertension, older age, obesity [17], smoking [18] and low personal income [19]. However, there have been few opportunities to explore the prevalence of albuminuria as a
marker of chronic kidney disease while adjusting for other risk factors in the different ethnic groups in New Zealand. The aim of this study was to assess the associations between ethnicity and albuminuria in a large population of people with type 2 diabetes.

Materials and methods

Study population

The study population included people with type 2 diabetes who had attended at least one diabetes annual review in primary health care as part of a national programme between 2000 and 2006 in New Zealand. Routine data collected during diabetes annual reviews were amalgamated from 24 regional organizations (Primary Health Organizations, Diabetes Trusts and one District Health Board) that collected individual-level data from general practices around New Zealand. This database formed the New Zealand Diabetes Cohort Study and details of the data collection are published elsewhere [8, 20]. These primary care data were linked by a unique identifier on each person (encrypted National Health Index) to the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) [4]. The study received multi-centre ethical approval in 2004 (WGT/04/09/077).

Outcome measures

The primary outcome was UACR categorized into ‘normal’ (<2.5 mg/mmol in men and ≤3.5 mg/mmol in women), ‘microalbuminuria’ (>2.5/3.5 to <30 mg/mmol), ‘macroalbuminuria’ (30 to <100 mg/mmol) and ‘advanced albuminuria’ (≥100 mg/mmol). Risk variables included ethnicity, socioeconomic status, age at diagnosis, duration of diabetes, gender, smoking status (current, previous or never), systolic and diastolic blood pressure, body mass index (BMI), glycated haemoglobin (HbA1c), serum total cholesterol and high-density lipoprotein and use of angiotensin-converting enzyme inhibitor or angiotensin II blocker medication (ACE/ARB). Ethnicity was self-assigned in primary care. Ethnic categories in the study included European, Maori, Pacific Islander, Indo-Asian, East-Asian and ‘other’, which includes Middle Eastern, Latin American/Hispanic, African and others [21]. Socioeconomic status was assessed using quintiles of the area-based New Zealand deprivation score [22].

Analyses

The last assessment made between 2000 and 2006 for each participant was used in the analyses. Those that were registered with ANZDATA prior to that date were excluded from the analysis, which effectively excluded those who were on dialysis or had a renal transplant prior to the assessment. Multiple logistic linear regression analyses were used to calculate odds ratios for micro-, macro- and advanced albuminuria comparing different ethnic groups after controlling for other risk factors and adjusting for study centre. For the regressions shown in Figures 1–4 and in Table 5, UACR concentrations were log transformed due to non-normality of data, and one unit was added prior to log transformation to avoid loss of data when log(0) is rendered as missing.

Results

There were 72,529 people with type 2 diabetes who had a routine diabetic assessment in primary care in New Zealand between 2000 and 2006. Of these, 257 had previously undergone dialysis or a renal transplant, a further 7033 had no recorded UACR and a further 68 had no ethnicity recorded, leaving a cohort of 65,171 who were the subjects for this analysis. The demographic and clinical characteristics of this cohort are presented in Table 1. The median age was 64.7 years (interquartile range 53.8–73.1), median duration of diabetes was 5.1 years (2.3–9.7) and 48.5% were non-European. The median age for Europeans was older than other groups, which reflects the fact that Maori, Pacific and Asian people tend to be diagnosed much younger than Europeans. Between half and two-thirds of Maori and Pacific people in the cohort were in the lowest national socioeconomic quintile compared with one-third of Indo-Asian and less than a quarter of East Asian and European people. The median BMI and HbA1c

Fig. 1. Association of age with log UACR, by ethnicity, unadjusted. N = 65 171.
were high in Maori and Pacific people and the highest rate of current smoking was among Maori (28%). Approximately 50% of all Maori and Pacific people had albuminuria (Table 2).

ACE/ARB medication was prescribed for 61.1% of all those with microalbuminuria or greater, including similar proportions of patients by ethnic group, except that rates for Asian groups with microalbuminuria were slightly lower (Table 3). After controlling for age and other risk factors including ACE/ARB treatment, the odds ratios for having microalbuminuria or greater, macroalbuminuria or greater and advanced albuminuria were all significantly raised for
Microalbuminuria = UACR > 2.5 (men) or > 3.5 (women) and <30; macroalbuminuria = UACR > 100 mg/mmol.

Table 3. People on ACE/ARB, by categories of albuminuria and ethnicity, N = 65 171*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>European (n = 33 650)</th>
<th>Maori (n = 10 622)</th>
<th>Pacific (n = 10 663)</th>
<th>Indo-Asian (n = 3 166)</th>
<th>East-Asian (n = 1 941)</th>
<th>Other ethnicity (n = 5 129)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None, N (%)</td>
<td>10 818 (44.7)</td>
<td>2563 (48.1)</td>
<td>2609 (48.0)</td>
<td>805 (36.6)</td>
<td>426 (31.6)</td>
<td>1521 (39.9)</td>
</tr>
<tr>
<td>Microalbuminuria, N (%)</td>
<td>4489 (58.2)</td>
<td>2148 (61.7)</td>
<td>2085 (60.9)</td>
<td>391 (51.3)</td>
<td>212 (49.1)</td>
<td>606 (55.6)</td>
</tr>
<tr>
<td>Macroalbuminuria, N (%)</td>
<td>755 (65.0)</td>
<td>636 (66.8)</td>
<td>630 (65.1)</td>
<td>83 (63.4)</td>
<td>60 (65.2)</td>
<td>96 (68.1)</td>
</tr>
<tr>
<td>Advanced albuminuria, N (%)</td>
<td>401 (70.6)</td>
<td>631 (73.8)</td>
<td>561 (67.4)</td>
<td>48 (67.6)</td>
<td>50 (71.4)</td>
<td>58 (72.5)</td>
</tr>
</tbody>
</table>

*It is assumed that the 4117 people with missing medication data were not on ACE/ARB. Microalbuminuria = UACR > 2.5 (men) or > 3.5 (women) and <30; macroalbuminuria = UACR > 100 mg/mmol.

Figures 1–3 show unadjusted associations, by ethnicity, between log UACR and age, duration of diabetes and BMI, respectively. The associations with age were strongest for European and weakest for Maori and Pacific peoples, the strongest associations with duration of diabetes were for Maori and Pacific peoples, while for BMI, the strongest associations were for East Asian, Pacific, Indian, Pacific and Maori. HbA1c showed an unadjusted J-shaped relationship with log UACR (Figure 4). Table 5 shows significant independent associations between log UACR and age, gender, duration of diabetes, BMI, HbA1c, systolic blood pressure, triglycerides, smoking, ACE/ARB treatment and deprivation score. There remained a significant independent effect of ethnicity (P < 0.0001). The confidence intervals suggest that all non-European patients except those of other ethnicity had significantly higher log UACR than did Europeans.
Discussion

The rates of albuminuria were very high in this large primary care population with type 2 diabetes. Maori, Pacific and East-Asian, followed by Indo-Asian participants, were more likely than Europeans to have albuminuria after controlling for traditional risk factors.

One limitation of the study is that a single UACR result was used in this analysis, and the coefficient of variation of measures of albuminuria can be up to 20% [23]. Although serial measures would increase precision, it is unlikely that they would move many individuals across categories of albuminuria or substantively change the findings. It has been suggested that UACR reference ranges should be adjusted by sex, age and race [24–26], perhaps in relation to differences in muscle mass [25, 27]. We are not aware of any validation studies of a single UACR compared to timed collections across our ethnic groups. We did not have a direct measure of renal function, such as serum creatinine, consistently available.

It is likely that factors not measured in this study contribute to the association of albuminuria with ethnicity. A genetic predisposition to renal disease is possible, such as that found in African-Americans with non-diabetic renal disease [28], but has yet to be demonstrated among other ethnic groups and for those with diabetes. A high rate of nephropathy, but not retinopathy, in Maori with newly diagnosed diabetes argues for a familial or environmental cause independent of diabetes [29]. The same conclusion may follow the observation that, in Maori and Pacific people with diabetic nephropathy, there is a stronger familial clustering of nephropathy than of diabetes [30]. Fetal programming—with subtle dietary deficiencies, stress and high rates of smoking during pregnancy—is considered to affect renal development in utero and may be associated with hypertension, proteinuria and decreased renal function later in life [31]. Rates of smoking during pregnancy, small-for-gestational-age and premature births are high among Maori [32]. Periodontal disease, associated with chronic kidney disease [33], is high among Maori [34].

Differential access to health care, delayed diagnosis of diabetes and differential rates of medication prescription and adherence are all potential contributors to ethnic variations in albuminuria. Maori and Pacific, but not Asian adults, have more unmet needs for general practice care than Europeans [35]. Ethnic differentials in access to health care have been suggested in various reports from New Zealand [36, 37], such that equitable access has become a national priority, with early evidence of success [38]. Within this cohort, Maori and Pacific patients were just as likely to be on ACE/ARB as were European patients. Delayed diagnosis of diabetes does not appear to be a

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**Table 4.** Odds ratios (and 95% confidence intervals) of albuminuria, compared to no albuminuria, by ethnic group, \(N = 55\,055^a\)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>European (N = 29,230)</th>
<th>Maori (N = 8,662)</th>
<th>Pacific (N = 8,560)</th>
<th>Indo-Asian (N = 2,515)</th>
<th>East-Asian (N = 1,706)</th>
<th>Other ethnicity (N = 4,382)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microalbuminuria or greater</td>
<td>1</td>
<td>2.4 (2.2–2.6)</td>
<td>2.4 (2.1–2.9)</td>
<td>1.4 (1.2–1.6)</td>
<td>1.7 (1.5–2.0)</td>
<td>1.0 (0.9–1.1)</td>
</tr>
<tr>
<td>Macroalbuminuria or greater</td>
<td>1</td>
<td>3.1 (2.7–3.6)</td>
<td>3.7 (3.0–4.5)</td>
<td>1.8 (1.5–2.0)</td>
<td>2.9 (2.4–3.4)</td>
<td>1.0 (0.8–1.1)</td>
</tr>
<tr>
<td>Advanced albuminuria</td>
<td>1</td>
<td>3.9 (3.2–4.6)</td>
<td>4.7 (3.6–6.3)</td>
<td>2.0 (1.5–2.7)</td>
<td>4.1 (3.2–5.1)</td>
<td>1.0 (0.7–1.5)</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, duration of diabetes, HbA1c, systolic blood pressure, triglyceride level, BMI, smoking, socioeconomic status, ACE/ARB and study site. Microalbuminuria = UACR > 2.5 (men) or > 3.5 (women) and < 30; macroalbuminuria = UACR 30 to < 100; advanced albuminuria = UACR ≥ 100 mg/mmol; 10 116 persons missing data on one or more adjusting variable.

**Table 5.** Association between log albumin:creatinine ratio and risk factors, multivariate regression, adjusted for study site, \(N = 55\,055^a\)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Coefficient</th>
<th>P</th>
<th>Lower CI</th>
<th>Upper CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity (reference European)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori</td>
<td>0.606</td>
<td></td>
<td>0.571</td>
<td>0.671</td>
</tr>
<tr>
<td>Pacific</td>
<td>0.654</td>
<td></td>
<td>0.498</td>
<td>0.810</td>
</tr>
<tr>
<td>Indo-Asian</td>
<td>0.405</td>
<td></td>
<td>0.307</td>
<td>0.504</td>
</tr>
<tr>
<td>East-Asian</td>
<td>&lt;0.001</td>
<td></td>
<td>0.138</td>
<td>0.262</td>
</tr>
<tr>
<td>Other</td>
<td>0.017</td>
<td></td>
<td>-0.041</td>
<td>0.077</td>
</tr>
<tr>
<td>Body mass index (kg m⁻²)</td>
<td>0.009</td>
<td>&lt;0.001</td>
<td>0.007</td>
<td>0.012</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.008</td>
<td>&lt;0.001</td>
<td>0.006</td>
<td>0.010</td>
</tr>
<tr>
<td>Female (reference male)</td>
<td>-0.143</td>
<td>&lt;0.001</td>
<td>-0.180</td>
<td>-0.105</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>0.023</td>
<td>&lt;0.001</td>
<td>0.016</td>
<td>0.029</td>
</tr>
<tr>
<td>Deprivation score (1 least to 10 most)</td>
<td>0.014</td>
<td>&lt;0.001</td>
<td>0.008</td>
<td>0.019</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>-0.086</td>
<td>&lt;0.001</td>
<td>-0.132</td>
<td>-0.040</td>
</tr>
<tr>
<td>HbA1c squared (%)</td>
<td>0.011</td>
<td>&lt;0.001</td>
<td>0.008</td>
<td>0.013</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>0.008</td>
<td>&lt;0.001</td>
<td>0.007</td>
<td>0.009</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>0.086</td>
<td>&lt;0.001</td>
<td>0.068</td>
<td>0.104</td>
</tr>
<tr>
<td>Smoker (0 never, 1 past, 2 current)</td>
<td>0.025</td>
<td>0.021</td>
<td>0.004</td>
<td>0.045</td>
</tr>
<tr>
<td>On ACE/ARB</td>
<td>0.332</td>
<td>&lt;0.001</td>
<td>0.302</td>
<td>0.551</td>
</tr>
</tbody>
</table>

*10 116 persons missing data for one or more variables.
current explanation—there are fewer Maori and Pacific people than Europeans with undiagnosed diabetes [3]. There are limited data available about Asians in New Zealand; however, all Asian groups are at increased CVD risk compared to Europeans, including those with newly diagnosed diabetes [39]. On the other hand, once adjusted for multiple risk factors, East Asians with diabetes have a lower risk of a first CVD event than do Europeans [8].

Low medication adherence among people with a long-term condition is a widespread problem [40]. There is evidence from one Pacific group of lower medication adherence than among Europeans [41], and differences in affordability and adherence may be an important contributor to ethnic disparities in diabetes control in the USA [42].

Poverty, itself recognized as having multiple relationships to renal disease and race or ethnicity [43], is also associated with many of the factors we have described above. Our measure of deprivation is significantly associated with log UACR (Table 5). Nevertheless, this measure lacks precision at the individual level (it assigns to the individual the average deprivation of his or her residential area), does not include education or occupation and reflects only current status rather than a life-course of accumulated disadvantage [22]. Therefore, we have probably underestimated the association of UACR and socioeconomic deprivation.

Figures 1–3 show considerably different relationships, by ethnicity, between UACR and age, duration of diabetes and BMI. Maori and Pacific show a limited relationship of UACR with age—but at young age their UACR is already higher than European at old age. Maori and Pacific show the strongest association between UACR and duration of diabetes, which would support prioritizing services to these groups to control risk factors. Similarly, rising BMI is associated with UACR in all non-European groups, which would support priority access to bariatric surgery for these groups.

Given the well-established links between albuminuria and end-stage renal failure and cardiovascular mortality, there must be concern that half of all Maori and Pacific people in the study cohort have microalbuminuria, compounded by relatively high levels of cigarette smoking. It must also be of concern that only 61% of those with microalbuminuria or greater, across the whole study cohort, have been prescribed an ACE/ARB, despite their being universally recommended [44, 45]. Further understanding the causes of the ethnic differences in albuminuria in people with type 2 diabetes requires investigation of factors present well before diabetes develops. Effective interventions will similarly need to occur well before diabetes develops. In the meantime, it is clear that we need to substantially improve rates of primary care therapy and continue to explore and implement ways to improve medication adherence [40].

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Conflict of interest statement. None declared.

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