Prevalence and factors associated with microalbuminuria in type 2 diabetic patients at a diabetes clinic in northern Tanzania

S Ghosh, I Lyaruu, and K Yeates

Abstract
The aim of this study was to determine the prevalence and factors associated with microalbuminuria in patients with type 2 diabetes attending the diabetes clinic at Kilimanjaro Christian Medical Centre in northern Tanzania. We enrolled 149 patients aged over 19 years. Three morning urine samples separated by a gap of 1 month each were analysed within a 6-month period. Urinary albumin concentration was measured by an immunoturbidimetric assay and two positive tests (urinary albumin excretion 30–300 mg/L) were considered as positive for microalbuminuria. The overall prevalence of microalbuminuria was 29%. Presence of microalbuminuria was significantly related to age, systolic blood pressure, use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers, body mass index, fasting blood glucose, haemoglobin A₁c level, serum creatinine, and creatinine clearance (p<0.05). However after a multivariate logistic regression only haemoglobin A₁c, creatinine, and creatinine clearance were strongly associated with microalbuminuria. In conclusion, the study revealed a higher prevalence of microalbuminuria among people with type 2 diabetes, compared with another Tanzanian study in Dar es Salaam. Determination of the urinary albumin excretion is an easy method for screening of microalbuminuria, and is recommended for all diabetic patients even in low-resource settings, to provide optimum management to delay the progression to end-stage renal disease.

Introduction
Diabetes mellitus remains a tremendous challenge to public health worldwide. The estimated number of people living with diabetes in Africa is currently 12.1 million, but a recent projection showed that the number will reach 23.9 million by 2030.¹ More than 482,000 East Africans are now diagnosed with type 2 diabetes, Tanzania being the leading country with 201,000 among an estimated population of over 38 million.²

Diabetic nephropathy is the leading cause of end-stage renal disease (ESRD) worldwide.³ In Africa it is probably the third most common cause of chronic kidney disease after hypertension and glomerulonephritis. It also accounts for a third of all patients requiring renal replacement therapies, which are prohibitively expensive and not widely available in Africa due to cost and lack of expertise.⁴

Persistent urine albumin excretion of between 30 mg/day and 300 mg/day (which is equivalent to 30–300 mg/L of a spot urine sample or 20–200 µg/min of a timed urine sample is defined as microalbuminuria (MA). It is the earliest clinical manifestation of nephropathy.⁵ MA is also a predictor for cardiovascular disease, one of the components of metabolic syndrome. Nephropathy is also a strong risk factor for diabetic retinopathy.⁶⁻⁸ However, previous studies have shown that unlike macroalbuminuria, MA can revert to normoalbuminuria in patients with diabetes when they are treated with agents known to protect the kidneys and reduce proteinuria.⁹ Despite the availability of therapies to reduce MA, people with diabetes are not routinely evaluated for MA in most low-resource sub-Saharan African settings, including our centre. With this knowledge our study objective was to detect the prevalence of MA and utilise this knowledge to implement measures which may delay the progression to ESRD and have a future impact on clinical practice guidelines for the management of patients with type 2 diabetes in Tanzania as a whole.

Patients and methods
This cross-sectional analytical hospital-based study was conducted among consecutively enrolled adults (>19 years) with type 2 diabetes attending the Diabetes Clinic at the Kilimanjaro Christian Medical Centre (KCMC) between August 2010 and February 2011. KCMC is one of the four referral hospitals in Tanzania and it serves a population of 15 million people. Patients with urinary tract infections, active heart failure and HIV infection were excluded from the study. Those subjects found to have overt proteinuria >300 mg/day by using urine dipsticks were also excluded. A total of 149 individuals...
were included in the study after written consent. The study participants were interviewed using a structured questionnaire designed by the investigators. A thorough history including duration of diabetes from diagnosis was obtained. A trained nurse took the following measurements: height (m), body weight (kg), and blood pressure in the sitting position after 5 minutes rest. Fasting blood glucose (mmol/L) and random blood glucose (mmol/L) of patients was tested from capillary blood samples using a Glucoplus meter with gluco strips (code number 86).

Fasting blood samples were drawn for serum creatinine, serum cholesterol, and triglycerides and were analysed with the chemical analyser COBAS INTEGRA 400 Plus (serial NO 397672). Serology for HIV was tested by SDBioline. Haemoglobin A\textsubscript{1c} (HbA\textsubscript{1c}) was measured using DCA 2000+ analyser (manufactured by Bayer Elkhart, USA). All participants were referred to an ophthalmologist for dilated fundoscopic examination for diabetic retinopathy (DR). Three spot morning urine samples at 1 month intervals were analysed within a 6-month period. Albumin concentration was measured by HemoCue Albumin 201 (turbidimetric immunoassay) which provides quantitative determination of albuminuria. It measures urine albumin between 5 and 150 mg/L. Two or more positive test results were taken as microalbuminuria.

Data were coded and entered into a database using SPSS (Statistical Package for Social Sciences) Version 16.0 and were summarised into frequency tables, charts and cross tabulations. Statistical significance was tested using the Chi-square test at 5% tolerable error. Measures of association were expressed using odds ratios (ORs) with 95% confidence intervals (CI).

**Results**

Of the 149 patients, 92 were female (62%). Over-all, 43 subjects (29%) had microalbuminuria. There was a statistically significant mean age difference between the microalbuminuric group (61.3±10.5 years) and the normoalbuminuric group (57.1±10.7 years), as was the case for systolic blood pressure (p=0.04). Among 93 (62%) hypertensive patients, 78 (84%) were on angiotensin converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARBs). Among those on ACE-I or ARBs, 57 (73%) had normoalbuminuria while 21 (27%) had microalbuminuria. However, of those who were on other types of anti-hypertensive drugs, 7 (47%) had normoalbuminuria while 8 (53%) had microalbuminuria. Hence, those on ACE-I or ARBs were found to be three times more likely to have normoalbuminuria compared with those without these medications; OR of 3.1, CI 1.0–9.6. The mean body mass index (BMI) in the microalbuminuric group was statistically significantly lower (p=0.03) compared with the normoalbuminuric group. However, no statistically significant correlation was observed between microalbuminuria and duration of diabetes (p=0.14), smoking (p=0.12), or alcohol (p=0.32) – see Table 1.

Fasting blood glucose and HbA\textsubscript{1c} concentrations were significantly higher among microalbuminuric patients (p=0.04 and p=0.002, respectively). Likewise, the mean serum creatinine (79±18 µmol/l) was significantly higher (p<0.001) in the microalbuminuric group. Creatinine

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normoalbuminuria (mean ± SD)</th>
<th>Microalbuminuria (mean ± SD)</th>
<th>p value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n=57)</td>
<td>40 (70%)</td>
<td>17 (30%)</td>
<td>0.84</td>
<td>0.93 (0.45–1.92)</td>
</tr>
<tr>
<td>Female (n=92)</td>
<td>66 (72%)</td>
<td>26 (28%)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Alcohol</strong></td>
<td></td>
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</tr>
<tr>
<td>Yes (n=102)</td>
<td>70 (69%)</td>
<td>32 (31%)</td>
<td>0.32</td>
<td>0.67 (0.3–1.48)</td>
</tr>
<tr>
<td>No (n=47)</td>
<td>36 (77%)</td>
<td>11 (24%)</td>
<td></td>
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</tr>
<tr>
<td><strong>Smoking</strong></td>
<td></td>
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</tr>
<tr>
<td>Yes (n=42)</td>
<td>26 (62%)</td>
<td>16 (38%)</td>
<td>0.12</td>
<td>0.55 (0.26–1.17)</td>
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<tr>
<td>No (n=107)</td>
<td>80 (75%)</td>
<td>27 (25%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Type of anti-hypertensive</strong></td>
<td></td>
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</tr>
<tr>
<td>ACE-I or ARBs</td>
<td>57 (73%)</td>
<td>21 (27%)</td>
<td>0.04</td>
<td>3.1 (1–9.6)</td>
</tr>
<tr>
<td>Others</td>
<td>7 (47%)</td>
<td>8 (53%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>57±11</td>
<td>61±10</td>
<td>0.03</td>
<td>-4.13 (-7.9 to -0.3)</td>
</tr>
<tr>
<td><strong>Age at onset of diabetes (years)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>49±9</td>
<td>52±11</td>
<td>0.18</td>
<td>-2.4 (-5.9 to 1.1)</td>
</tr>
<tr>
<td><strong>Duration of diabetes (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8±7</td>
<td>10±6</td>
<td>0.14</td>
<td>-1.9 (-4.3 to 0.6)</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>28.9±5.5</td>
<td>26.8±5.2</td>
<td>0.03</td>
<td>2 (0.1–4)</td>
</tr>
<tr>
<td><strong>Blood pressure (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>131±20</td>
<td>139±27</td>
<td>0.04</td>
<td>-8.2 (-16.2 to -0.1)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>80±11</td>
<td>83±14</td>
<td>0.25</td>
<td>-2.6 (-0.4 to -0.1)</td>
</tr>
</tbody>
</table>

Notes:
SD = standard deviation, CI = confidence Interval, ACE-I = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, BMI = body mass index.
clearance was significantly lower in the microalbuminuric subjects compared with the normoalbuminuric group (p<0.001), see Table 2.

However, after the multiple logistic regression analysis using microalbuminuria as the dependent variable, only HbA1c (p=0.02), serum creatinine (p=0.03), and creatinine clearance (p=0.04) showed a significant association with microalbuminuria, see Table 3.

Among 149 enrolled diabetic patients, 111 subjects were examined for retinopathy. The remaining 38 participants either did not consent or did not turn up for the screening. Retinopathy was more frequent among the microalbuminuric patients than in the normoalbuminuric patients. However, this was not statistically significant (p=0.41).

### Table 3 Multiple logistic regression analysis using microalbuminuria as the dependent variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>SE β</th>
<th>p value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>0.05</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01–0.08</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.01</td>
<td>0.002</td>
<td>0.03</td>
<td>0.001–0.01</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>-0.002</td>
<td>0.001</td>
<td>0.04</td>
<td>-0.005–0.0</td>
</tr>
</tbody>
</table>

Note

- β = Unstandardised coefficients
- SE = Standard error
- CI = Confidence interval
- HbA1c = Haemoglobin A1c

### Discussion

In the present study, the overall prevalence of MA was 29%. Various epidemiological and cross-sectional studies have reported marked variation in the prevalence of MA. Studies in the white United Kingdom population revealed a prevalence of 7–9%,10,11 while in Mexican Americans it was 31%,12 Hispanic Americans 35%,13 northern Indians 27%,14 and sub-Saharan Africans 10–57%.15,16

This variation can be attributed to factors such as differences in the populations (difference in ethnicity), definitions of MA, method of urine collection, methods of measurement of MA, and sample size.

Genetic susceptibility linked to the angiotensin encoding gene as shown in Oji-Kkee Indians could also be an important determinant for development of renal disease in diabetes.17 The prevalence of MA across genders was not statistically different in the present study. Similar findings were found by Lutale et al15 and Afkhami et al.16,18 However, earlier studies have reported an increased prevalence of MA in men compared with women.19,20 This could be explained by the difference in the behavioural patterns, as males are more prone to risk factors like smoking and alcohol than females, possibly contributing to renal damage in males.

We found a statistically significant relationship between MA and age. Varghese et al also reported a similar finding.21 The possible explanation for this age effect could be either longer duration of hyperglycaemia and its adverse effects in an older age group, or the presence of age-related arteriosclerotic changes in the glomeruli. However some studies found no statistical correlation between age and MA.16,18 These discrepancies are probably related to differences in the distribution of age in the different study populations.

The present study showed no significant correlation between MA and duration of diabetes, similar to some earlier studies,16 though other studies have reported a significant correlation between MA and duration of diabetes.18,21 This conflicting observation may have occurred because of difficulty in dating the onset of diabetes. In many African countries diabetes goes undetected for long periods and newly diagnosed people with diabetes may present with well-established complications.

A statistical correlation was also found between MA and systolic blood pressure in our study. Similar findings were reported by Vijay et al.22 However, some studies15,23 found statistical correlation between MA and diastolic blood pressure. This variation could be due to our study population being older and more prone to isolated systolic hypertension.

In the present study there was a statistically significant correlation between microalbuminuria and BMI (lower BMI in the microalbuminuric group) similar to a study by Ruilope et al,24 whereas Afkhami et al failed to show any correlation between MA and BMI.19 The association between lower BMI and MA could be due to other confounding variables such as longer duration of diabetes and poor glycaemic control with relative insulin deficiency, which may induce weight loss. These patients with a lower BMI may be at a higher risk of developing diabetic complications.
The present study showed that those hypertensive patients who are on ACE-I or ARBs are three times more likely to have normoalbuminuria than those using other types of anti-hypertensive medications. Similarly Haller et al found olmesartan (an ARB) and Vora et al, foundtrandolapril (an ACE-I) to be associated with a delayed onset of MA in hypertensive type 2 diabetic patients. This could be explained by the fact that in addition to lowering blood pressure, ACE-I or ARBs also reduce the profibrotic effects of angiotensin 2 on glomeruli, thus preventing hypertrophy and hyperfiltration of the remaining healthy glomeruli and decreasing proteinuria.

Similar to the current study, poor glycaemic control is a well-known contributor to the development and progression of MA. In our study, serum creatinine values were significantly higher in the microalbuminuric group, which is similar to some previously published studies. However, Chowta et al did not observe any statistical correlation. This could be explained by the fact that asymptomatic diseases like hypertension and glomerulopathies (which were not excluded in our study) may account for MA and raised creatinine levels in the general population, some of whom may later develop diabetes.

We did not find any statistically significant correlation between MA and retinopathy, similar to earlier studies. Hence it is apparent that retinopathy is not a strong marker for MA, and may instead be a significant predictor for macroalbuminuria.

One of the limitations of the study is that it was a clinic based study and this could have introduced some degree of referral bias, making it difficult to extrapolate the results to the community.

Conclusion

In conclusion, the overall prevalence of MA at our diabetes clinic in Northern Tanzania was 29%. Poor glycaemic control, age, systolic hypertension, BMI, and serum creatinine were significantly associated with MA. Those with MA also showed some degree of renal impairment, illustrated by significantly higher serum creatinine levels compared with normoalbuminuric subjects. The study also revealed that use of ACE-I in hypertensive people with type 2 diabetes may be a protective factor for development of MA. Considering the increasing incidence of type 2 diabetes in Tanzania, we recommend screening for MA to reduce the future burden of diabetic renal disease.

References

28. Wanjohi FW, Otieno FCF, Ogola  EN et al. Nephropathy in patients with diabetes: a hospital based study and this could have introduced some degree of referral bias, making it difficult to extrapolate the results to the community.