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Letters to the Editor

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Prevalence and clinical factors associated with gout in patients with diabetes and prediabetes

SIR, The relationship between gout and diabetes is complex. Patients with gout have a high prevalence of type 2 diabetes [1]. Gout is also a risk factor for developing type 2 diabetes [2]. However, patients with diabetes have a lower risk of developing gout [3]. Although several studies have examined the clinical associations of diabetes in patients with gout, the prevalence and clinical associations of gout in patients with diabetes are not well documented. The aim of this study was to examine the prevalence of gout and the clinical factors associated with gout in a large community-based group of patients with diabetes.

We analysed data from 18 358 patients with diabetes, impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) from the Diabetes Care Support Service (DCSS) register collected by specialist nurses between May 2007 and November 2010. The DCSS register contains annually collected clinical information for all patients with diabetes and IFG/IGT attending participating primary health-care clinics within Auckland, New Zealand [4]. This study was approved by the Northern X Regional Ethics Committee. Diagnosis of diabetes mellitus, IFG and IGT were defined according to the World Health Organization criteria [5]. The presence of gout was determined by physician diagnosis as recorded in clinical notes. Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease formula [6]. Statistical analysis and modelling were performed using SAS 9.2 (SAS Institute, Cary, NC, USA) and GraphPad Prism 5.02 (GraphPad Software, La Jolla, CA, USA). Prevalence values were directly standardized to Segi's world population with 95% confidence intervals determined using www.openepi.com (accessed 17 December 2010). Multivariate logistic regression models were used to determine estimates for independent predictive contributions of each variable for each group. All *P*-values are two-sided, with $P < 0.05$ considered statistically significant.

There were 733 patients with type 1 diabetes, 14 066 with type 2 diabetes and 3559 with IFG and/or IGT (IFG/IGT). Mean (S.D.) age was 61 (14) years, diabetes disease duration 8.6 (7.8) years, BMI 32.4 (7.5) kg/m^2 and haemoglobin A1c (HbA1c) 7.4 (1.6)%. There were 9473 (52.6%) men; 9515 (51.8%) were European. In the entire study group, there were 2778/18 358 (15.1%) patients with gout. The direct age- and sex-standardized prevalence (95% CI) of gout was 1.2% (0.5%, 1.9%) in patients with type 1 diabetes, 16.0% (15.4%, 16.5%) in type 2 diabetes and 14.2% (13.1%, 15.4%) in IFG/IGT ($P < 0.0001$ for type 1 *vs* both the other groups). Gout affected >20% of men with type 2 diabetes or IFG/IGT. Ethnicity-specific prevalence rates of gout varied considerably in patients with type 2 diabetes; age- and sex-adjusted prevalence (95% CI) was 5.0% (3.7%, 6.4%) in Indian, 12.5% (11.6%, 13.3%) in European and 28.5% (26.8%, 30.3%) in Māori.

No clinical factors were independently associated with gout in patients with type 1 diabetes (data not shown). The following clinical factors were independently associated with a diagnosis of gout in patients with type 2 diabetes: age, male sex, Māori or Pacific ethnicity, lower eGFR, BMI, lower HbA1c, higher triglycerides, diuretic use and non-use of insulin and metformin (Table 1). In patients with IFG/IGT, the clinical factors independently associated with a diagnosis of gout were male sex, Māori or Pacific ethnicity, and lower eGFR (Table 1).

This large community-based study has identified a high prevalence of gout in patients with type 2 diabetes and IFG/IGT, affecting one in five men. In contrast, the prevalence of gout in patients with type 1 diabetes was considerably lower. The prevalence of gout in patients with type 2 diabetes and IFG/IGT is high compared with the estimated 2009 national prevalence of gout in New Zealand of 2.7% [7]. Risk factors for gout in the general population such as age, male sex and renal impairment [1] were also associated with gout in this study of patients with type 2 diabetes. In addition, we have identified several diabetes-specific factors including low HbA1c and lack of hypoglycaemic medication that are associated with gout in this population. These findings are consistent with previous research that has demonstrated an inverse relationship between serum urate and HbA1c in the general population, particularly in men [8].

We acknowledge the potential limitations of our study. The cross-sectional design does not allow analysis of the direction of the relationships between gout and diabetes. The New Zealand setting may limit the international applicability due to high rates of gout in the indigenous Māori population [9]. However, the regression analyses identified a number of clinical factors associated with gout, independent of ethnicity. Although misclassification of gout may have occurred, physician diagnosis is standard in large epidemiological studies of gout [1].

Gout may have implications for diabetes management: active arthritis restricts exercise, gout may provide additional complexity to dietary management, medications for acute gout may contribute to diabetes complications and severe gout may lead to more complex foot disease. Gout

TABLE 1 Clinical factors associated with gout in patients with type 2 diabetes and IFG/IGT: multivariate logistic regression analysis

Variable	Type 2 diabetes, $R^2 = 0.15$				IFG/IGT, $R^2 = 0.19$			
	Gout ($n = 2248$)	No gout ($n = 11830$)	Adjusted odds ratios (95% CI)	P	Gout ($n = 509$)	No gout ($n = 3058$)	Adjusted odds ratios (95% CI)	P
Age (per year)	64.6 (12.7)	60.8 (13.6)	1.03 (1.02, 1.03)	<0.0001	64.2 (12.5)	61.4 (13.5)	1.03 (1.00, 1.06)	0.051
Sex (male *vs* female), *n* (%)	1563 (70)	5714 (48)	0.47 (0.40, 0.56)	<0.0001	397 (78)	1392 (46)	0.25 (0.11, 0.53)	0.0003
Ethnicity (Māori or Pacific *vs* non-Polynesian), *n* (%)	397 (78)	3756 (32)	3.18 (2.68, 3.78)	<0.0001	177 (35)	558 (18)	4.00 (2.15, 7.43)	<0.0001
Smoking (yes *vs* no), *n* (%)	1140 (54)	5530 (50)	1.15 (0.99, 1.35)	0.067	266 (58)	1194 (47)	0.71 (0.41, 1.23)	0.22
eGFR (per every 10 ml/min decrease)	72.4 (28.2)	96.3 (31.1)	0.98 (0.98, 0.98)	<0.0001	78.9 (23.5)	96.5 (27.7)	0.98 (0.97, 0.99)	0.0067
Duration of diabetes (per year)	8.8 (7.3)	8.0 (7.0)	0.99 (0.98, 1.00)	0.11	–	–	–	
BMI (per every kg/m^2 increase)	34.9 (7.8)	32.3 (7.4)	1.06 (1.04, 1.07)	<0.0001	33.8 (7.2)	32.2 (7.3)	1.04 (1.00, 1.08)	0.078
HbA1c (per every 1% increase)	7.4 (1.6)	7.6 (1.7)	0.88 (0.83, 0.93)	<0.0001	6.2 (0.5)	6.1 (0.5)	1.34 (0.75, 2.42)	0.33
Systolic blood pressure (per every mmHg)	133.4 (17.9)	132.6 (16.9)	1.00 (1.00, 1.00)	0.70	134.4 (16.4)	134.1 (16.4)	1.01 (0.99, 1.03)	0.24
Diuretic use (yes *vs* no), *n* (%)	987 (44)	3429 (29)	1.26 (1.08, 1.48)	0.0042	160 (31)	791 (26)	1.47 (0.80, 2.73)	0.22
Aspirin use (yes *vs* no), *n* (%)	1471 (65)	7298 (62)	0.88 (0.75, 1.04)	0.14	233 (46)	1130 (37)	1.07 (0.61, 1.87)	0.83
Metformin use (yes *vs* no), *n* (%)	1257 (56)	7862 (66)	0.84 (0.71, 0.99)	0.043	36 (7.1)	221 (7.2)	1.30 (0.60, 2.82)	0.51
Insulin use (yes *vs* no), *n* (%)	392 (17)	1931 (16)	0.73 (0.58, 0.92)	0.008	–	–	–	
Total cholesterol (per every mmol/l)	4.5 (1.1)	4.6 (1.1)	0.88 (0.57, 1.36)	0.57	4.8 (1.1)	5 (1.0)	0.21 (0.01, 3.94)	0.30
LDL cholesterol (per every mmol/l)	2.3 (0.9)	2.5 (0.9)	1.02 (0.66, 1.58)	0.69	2.7 (0.9)	2.9 (0.9)	3.50 (0.19, 63.50)	0.40
HDL cholesterol (per every mmol/l)	1.2 (0.3)	1.3 (1.0)	0.89 (0.54, 1.45)	0.63	1.2 (0.4)	1.3 (0.4)	3.20 (0.18, 57.17)	0.43
Triglycerides (per every mmol/l)	2.3 (2.4)	1.9 (1.6)	1.47 (1.19, 1.82)	0.0004	2.1 (2.2)	1.8 (1.0)	1.41 (0.36, 5.59)	0.62

Data are presented as mean (S.D.), unless otherwise mentioned. Percentage reflects the number with available data. LDL: low density lipoprotein; HDL: high density lipoprotein.

management should be carefully considered in the routine clinical care of patients with type 2 diabetes and pre-diabetes.

Rheumatology key message

- Lower HbA1c and hypoglycaemic medication non-use are associated with gout in type 2 diabetes.

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Goal-directed therapy for RA in routine practice is associated with improved function in patients with disease duration up to 15 years

SIR, Improved therapies have dramatically increased our ability to suppress RA disease activity. Short-term goal-directed therapy or treat-to-target, central to the management of hypertension and diabetes, may be the next step to increase effectiveness of RA therapy, although recent recommendations for treat-to-target strategies acknowledge the limited data from routine care (RC) [1]. Nevertheless, inducing remission is a logical short-term goal in RA [2, 3]. Patients receiving DMARDs and achieving low disease states have less joint damage progression [4, 5]. Patient preferences for therapy outcomes consistently identify their priorities as reduced pain and maintenance of function [6, 7]. Our RA Centre service routinely uses goal-directed therapy (GDT) strategy, short-term goal DAS-28 remission (DAS-28 < 2.6). After 2 years, we tested if this strategy improved patient function, comparing RA Centre outcomes with those of clinics in the same hospital not using this strategy.

An RC group of consecutive patients recruited from clinics where treatment aimed to reduce signs and symptoms with no precise goal, was compared with a matched sample of RA Centre patients, the GDT group. The Guy's Hospital Research Ethics Committee approved the study and patients gave informed consent. Patients with RA (ACR 1987 revised criteria) [8] over the age of 18 years were recruited for assessment, with no disease- or comorbidity-related exclusion criteria. Groups were matched within disease duration ± 2 years, age ± 5 years and sex. Rheumatologists treating the RC group were not aware of the patient DAS-28 score. HAQ-Disability Index (DI) was not used to guide treatment in either clinic. RC patients were assessed on a single occasion with joint counts and global disease activity performed by a research nurse not involved in therapy decisions. Fisher's exact tests were used for categorical data, and Wilcoxon signed rank sum tests for paired continuous data, almost all non-normally distributed. Multiple logistic regression assessed clinical factor contributions to achieving remission, and multivariable linear regression assessed influences on HAQ. Analyses were performed using SPSS 15.0 and Graph Pad Prism 5.

Ninety patients were recruited to the RC group and data compared with that collected contemporaneously from matched GDT patients. More GDT patients received combination DMARDs (12 *vs* 3%, $P = 0.048$) but not biologics (20 *vs* 13%, $P = 0.32$). Multiple regression analysis identified DAS-28, age, disease duration and pain VAS as independent predictors of HAQ-DI, with the highest contribution from DAS-28. Patients in the GDT group with disease duration up to 15 years showed significantly improved function compared with RC, with increasingly large differences in patients with shorter disease duration (Fig. 1A). Significantly more GDT patients achieved remission at all disease duration periods (Fig. 1B). Multiple logistic regression including all patients (disease duration up to 30 years) showed males were less likely to achieve remission [odds ratio (OR) 0.3; 95% CI 0.1, 0.8], and patients without erosions were more likely to achieve

FIG. 1 Goal-directed therapy increases the numbers of patients in remission and reduces HAQ in patients up to disease duration of 15 years. (**A**) Median HAQ is significantly lower in the GDT group at a range of disease durations. (**B**) Remission was defined by DAS-28 < 2.6; increased numbers of patients were in remission at all disease durations in the GDT group. $^*P < 0.05$, $^{**}P < 0.01$.