Gout in black South Africans: a clinical and genetic study

Bilkish Cassim, Girish Mody, Vijay K Deenadayalu, Michael G Hammond

Abstract
Objective—To define the clinical characteristics of gout and determine if there were any genetic associations with gout in black South Africans.
Methods—The records of 107 patients with gout seen over a five year period were retrospectively analysed. The HLA class I and class II antigens were studied in a prospective survey of 46 patients.
Results—The male to female ratio was 6:6:1. The diagnosis of gout was based on identification of monosodium urate crystals from the synovial fluid, synovial tissue or tophaceous material in 62 patients (58%) and on clinical criteria in the remaining 45 patients (42%). The mode of presentation was monoarthritis in 40 patients (37-4%), pauciarticular in 30 (28%) and polyarthritis in 37 (34-6%). The joints which were most frequently involved were the knee in 91 patients (85%), the first metatarsophalangeal in 80 (74-8%) and the ankle in 66 (61-7%). A secondary cause was identified in 52 patients (48-6%) (diuretic therapy in 48 patients and chronic renal impairment in four); 55 patients (51-4%) had primary gout. The genetic study showed an increased frequency of HLA-B14 in patients with primary gout compared with controls.
Conclusions—Gout is more common in black Africans than previously recognised and frequently presents with involvement of more than one joint. There was an increased frequency of HLA-B14 in patients with primary gout but the clinical significance of this is uncertain.


Genetic and environmental factors influence the prevalence of hyperuricaemia and gout in various ethnic groups and urban and rural populations. Gout was reported to be uncommon in black Africans and this was confirmed in a previous survey from our hospital. More recent studies have reported a greater prevalence of gout in black Africans and a higher prevalence has also been reported in a black American population. Although a genetic predisposition to gout is well recognised, no association with HLA antigens has been reported. In view of the relative rarity of gout in black Africans, we studied the HLA class I and class II antigens to determine if these antigens were associated with the development of gout. In addition, we defined the clinical characteristics of gout in black Africans.

Patients and methods
The King Edward VIII Hospital is a 2000 bed State funded public hospital attached to the University of Natal Medical School in Durban, South Africa. A computer assisted search of the inpatient records over a five year period from 1984 to 1989 was undertaken and the results of synovial fluid analysis were reviewed to identify patients with gout. Patients were considered to have gout if monosodium urate crystals were identified in synovial fluid, synovial tissue or tophi or if they fulfilled the American Rheumatism Association (ARA) clinical criteria for gout. There were 107 patients who fulfilled these criteria. Their clinical records were reviewed and the age of onset, duration of disease, history of alcohol intake, mode of presentation, criteria for diagnosis, presence or absence of associated diseases and available biochemical data were recorded. The clinical characteristics of the subgroups of patients were compared using Student’s t test for equal and unequal variances.

HLA class I and class II antigens were determined in a prospective study of 46 patients with gout. HLA-A, B and C were identified using a two stage lymphocytotoxicity test and 180 antisera. HLA-DR and DQ were defined with 120 antisera on B cell enriched lymphocyte suspensions prepared by the use of straws packed with nylon wool. HLA-A, B and C were determined in all 46 patients (23 primary and 23 secondary gout), HLA-DR in 36 patients (20 primary and 16 secondary gout) and HLA-DQ in 34 patients (18 primary and 16 secondary gout). The control group comprised blood donors and staff of the Natal Institute of Immunology. HLA-A, B and C were tested in 2366 controls, HLA-DR in 534 and HLA-DQ in 517. The differences in frequency of the various antigens between patients and controls were tested for significance by means of the χ2 test and Fisher’s exact test (in the case of small cell sizes). The resulting probabilities were multiplied by the number of HLA specificities tested to obtain the corrected values.

Results
The mean age at onset of disease was 50-5 (11-5) years (range 32–85 years) and the mean...
duration of gout was 3·4 (4·4) years (range one month to 23 years). The male to female ratio was 6·6:1. Females were significantly older at onset of disease than males (57 years compared with 49·3 years (p < 0·01)) and secondary gout was more frequent in females (78·6%) than in males (44%) (p < 0·05). However, there was no significant difference in the duration of disease, mode of presentation or pattern of joint involvement between males and females (table 1).

The diagnosis of gout was based on identification of monosodium urate crystals in 62 patients (58%). The crystals were identified from the synovial fluid in 53 patients, mostly from the knee (43 patients), and from synovial biopsy tissue (three), and tophi (six). A clinical diagnosis of gout was made in the remaining 45 patients (42%) who fulfilled the ARA clinical criteria for gout.16 A history of recurrent acute attacks was obtained in 92 patients (86%) and 39 (36%) had suspected tophi. Tophi were present at the elbows in 63% of patients, ears in 30%, hands in 22%, and feet in 22%. There was no difference in the frequency or site of tophi in patients with primary or secondary gout. Hyperuricaemia at the time of presentation was noted in 103 patients (96%).

The pattern of presentation was monoarthritis in 40 (37·4%), pauciarticular in 30 (28%) and polyarthritis in 37 (34·6%). The joints most frequently involved were the knee (91 patients (85%)), first metatarsophalangeal (80 (74·8%)) and ankle (66 (61·7%)).

A secondary cause was identified in 52 patients (49·6%)—48 receiving diuretic therapy for either hypertension (43) or cardiomyopathy (five) and four who had chronic renal impairment alone. The four patients with chronic renal impairment included three who were over 60 years and one who was 49 years old. Two of these patients had hypertension alone, one had hypertension and diabetes, and the remaining patient did not have any coexisting disease. Urinary uric acid excretion was normal in the two patients in whom the test was performed. Renal impairment (increased blood concentrations of urea and creatinine) was also present in 14 of the 43 patients with hypertension who were receiving diuretic therapy. The possible contribution of non-steroidal anti-inflammatory drugs (NSAID) to renal impairment could not be determined from a review of the hospital records.

One patient had chronic myeloid leukaemia and another pulmonary tuberculosis; however, the diagnosis of gout preceded that of the two other conditions and these patients were classified as having primary gout. A history of alcohol intake was recorded in 92 patients. Seventy three patients (79%) gave a history of alcohol intake, but details as to the type and amount of alcohol consumed were not available.

Table 2 compares patients with primary gout and those with secondary gout. An older age at onset (53 years) was noted in secondary gout, compared with 48·3 years in primary gout (p = 0·05). Secondary gout was more common in females (78·6%) compared with males (44%) (p < 0·05). There was no significant difference in duration of disease, mode of presentation or pattern of joint involvement between the primary and secondary groups.

In the HLA study there was a significant increase in the frequencies of the A28, B14, Cw1, DR8 and DQw3 antigens in patients with primary gout and of A28, B17 and Cw3 antigens in patients with secondary gout compared with control subjects (table 3). After correction for the number of antigens tested, only B14 remained significantly increased in patients with primary gout (p(exact) = 0·005). Further correction for the two groups of patients also showed a significant increase for B14 (p < 0·01). Comparing primary and secondary gout (table 3), the B14 antigen was present in 26·1% of patients with primary gout and 4·4% of patients with secondary gout (χ² = 4·21; p(exact) = 0·048), whilst the B70 antigen was present in 43% of patients with secondary gout and 8·7% of patients with primary gout (χ² = 7·22; p(exact) = 0·0083). Corrected p values did not reach statistical significance.

**Discussion**

Gout has been recognised as an uncommon disease in black Africans. Small numbers of patients with gout were reported from

| Table 1 Comparison between male and female patients |
|-----------------|-----------------|-----------------|
|                  | Male            | Female          |
| Mean age at onset (yr) | 49·3 (12·4) | 56·9 (9·5) |
| Duration of disease (yr) | 3·4 (4·5) | 3·2 (3·9) |
| Mode of presentation Monoarticular (%) | 38 | 36 |
| Pauciarticular (%) | 28 | 29 |
| Polyarticular (%) | 32 | 36 |
| Secondary gout (%) | 44 | 78·6 |
| Joints involved Knee (%) | 87 | 71 |
| Metatarsophalangeal (%) | 77 | 77 |

| Table 2 Comparison between primary and secondary gout |
|-----------------|-----------------|-----------------|
|                  | Primary         | Secondary       |
| Mean age at onset (yr) | 49·3 (12·3) | 57 (11·4) |
| Duration of disease (yr) | 3·6 (4·6) | 3·2 (4·5) |
| Mode of presentation Monoarticular (%) | 42 | 33 |
| Pauciarticular (%) | 20 | 36 |
| Polyarticular (%) | 38 | 31 |
| Secondary gout (%) | 17·3:1 | 2·7:1 |
| Joints involved Knee (%) | 84 | 87 |
| Metatarsophalangeal (%) | 73 | 77 |

| Table 3 Comparison of HLA frequencies in control subjects and patients with primary or secondary gout |
|-----------------|-----------------|-----------------|
|                  | Controls (n = 2366) | Primary (n = 23) | Secondary (n = 23) |
| A28 | 21·1 | 39·3 | 43·5** |
| B14 | 6·1 | 6·1*** | 4·4 | 0·048 |
| B70 | 28·1 | 8·7* | 43·5 | 0·0083 |
| Cw1 | 0·5 | 4·3* | 0·0 | 0·0 |
| Cw3 | 12·1 | 13·0 | 30·4** |
| DR8 | 4·7 | 15·0* | 0·0 |
| DQw3 | 31·9 | 55·6* | 37·5 |

Comparisons with control: *p < 0·05; **p < 0·01; ***p < 0·0001. †Comparisons between primary and secondary gout.
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Uganda, Kenya, Zaire and Zimbabwe. During epidemiological surveys in South Africa a few cases of hyperuricaemia were detected but no patients with gout were seen. Lowenthal and Dymond reported 11 patients with gout seen over a 38 month period in Johannesburg and 19 patients with gout who were seen over a five year period were reported from our hospital. However, a recent study from Brazzaville showed that gout was the most frequent cause of inflammatory arthritis and was detected in 60 patients, while Miyajyawa et al reported 71 patients with gout from Togo.

Our study of 107 patients represents the largest series of gout in black Africans and confirms an increasing prevalence, which may be attributable to genetic or environmental factors and to a greater awareness of the disease and increased detection as a result of synovial fluid analysis for monosodium urate crystals in patients with pauciarticular polyarthritis. Among the risk factors for gout, a high prevalence of 25% for hypertension has been reported in our local urban population. We found an increased prevalence of HLA-B14 in patients with primary gout but the clinical significance of this finding is uncertain and may be the result of a sample bias. An increased prevalence of HLA-B14 antigen has also been reported in black South Africans with insulin dependent diabetes and Graves’ disease but none of our B14 positive patients had either of these diseases.

Conclusions
In this hospital based study we confirm that gout is more common in black Africans than previously recorded. This may be the result of environmental factors associated with increasing urbanization in a country undergoing socio-economic and political change, genetic factors, or an increased awareness of the disease. On the basis of this study we suggest that, among black Africans, gout must be included in the differential diagnosis of pauciarticular or polyarthritis in males and postmenopausal females. A weak association with HLA-B14 has been noted in patients with primary gout and further studies are needed to determine if this is of any clinical significance.

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doi: 10.1136/ard.53.11.759

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