CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Gout in African Americans

Eswar Krishnan, MD, MPhil

Department of Medicine, Stanford University School of Medicine, Palo Alto, Calif.

ABSTRACT

PURPOSE: African Americans have a substantially higher prevalence of risk factors for gout than Caucasians. The aim of the present study was to compare the risk for incident gout among African Americans and Caucasians.

METHODS: Incidence rates of physician-diagnosed gout among 11,559 Caucasian men and 931 African American men aged 35 to 57 years and at high cardiovascular risk, observed for 7 years as a part of the Multiple Risk Factor Intervention Trial, were analyzed. Cox regression models were used to account for potential confounding by age, body mass index, diuretic use, hypertension and diabetes status, aspirin and alcohol consumption, and kidney disease.

RESULTS: At baseline, after accounting for risk factors, African Americans had a 14% lower prevalence of hyperuricemia than Caucasians. Incidence of gout increased with increasing prevalence of risk factors in both Caucasians and African Americans. Ethnic disparities in incidence rates were most apparent among those without other risk factors for gout. In separate Cox regression models, after accounting for risk factors, African American ethnicity was associated with a hazard ratio of 0.78 (95% confidence interval [CI], 0.66-0.93) for physician-diagnosed gout and 0.88 (95% CI, 0.85-0.90) for incident hyperuricemia. Significant interactions were observed; the association was the strongest (hazard ratio 0.47; 0.37-0.60). These associations were unaffected by addition of serum urate as a covariate or by using alternate case definitions for gout.

CONCLUSIONS: After accounting for the higher prevalence of risk factors, African American ethnicity is associated with a significantly lower risk for gout and hyperuricemia compared with Caucasian ethnicity.
 • *The American Journal of Medicine (2014) 127, 858-864*

KEYWORDS: African American; Disparities; Gout; Incidence; Uric acid

Little is known about the incidence of gouty arthritis (gout) among African Americans, an ethnic group that constitutes about 13% of the current US population. African Americans have a disproportionately higher frequency of risk factors for gout and hyperuricemia such as high intake of seafood, elevated blood lead levels, physical inactivity, obesity, alcohol, hypertension, diabetes, renal failure, and antihypertensive medications.[1-4] Despite these risk factors, the unadjusted mean serum urate and unadjusted prevalence of hyperuricemia and gout among African Americans are not significantly greater than among Caucasians.[5-7] Indeed, among those with no renal impairment, the age-standardized prevalence rate of gout among African Americans was nearly identical to that among Caucasians.[8] In a study that attempted to correlate incidence of gout with risk factors, Hochberg et al[9] observed higher crude incidence rates of gout in a cohort of 352 African American physicians (31 cases of gout) when compared with a separate cohort of 571 Caucasian physicians (29 cases of gout); this excess risk was explained by the higher prevalence of hypertension among

Funding: The Multiple Risk Factor Intervention Trial (MRFIT) was conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with the MRFIT investigators. The present study was performed using a limited-access data set obtained from the NHLBI and does not necessarily reflect the opinions or views of the MRFIT or the NHLBI. ClinicalTrials.Gov Identifier: NCT 00000487.

Conflict of Interest: EK has served as a consultant to Takeda Pharmaceuticals, Inc., URL Pharmaceuticals Inc., Metabolic, Inc., and UCB Pharmaceuticals, Inc., and has received grant support from URL, ARDEA Biosciences, and Takeda. However, these entities did not sponsor this study nor did they have access to the contents before publication.

Authorship: EK was responsible for all aspects of this manuscript from concept to finalizing the manuscript. He serves as the guarantor for this paper. There are no patents, products in development, or marketed products to declare with respect to this manuscript.

Requests for reprints should be addressed to Eswar Krishnan, MD, MPhil, Stanford University School of Medicine, 1000 Welch Road, Suite 203, Palo Alto, CA 94304.

E-mail address: e.krishnan@stanford.edu

0002-9343/$ -see front matter
http://dx.doi.org/10.1016/j.amjmed.2014.03.039

African Americans. Other potential explanatory factors such as kidney disease, blood pressure medications such as diuretics, weight gain, and alcohol and aspirin use were not accounted for in this analysis. Whether or how such adjustment would have impacted the conclusions of that study is unclear. The present study was undertaken to test the hypothesis that the risk for incident gout associated with African American ethnicity differs from that associated with Caucasian ethnicity using a large cohort of middle-aged men with high prevalence of risk factors for gout, including hypertension, obesity, alcohol use, and aspirin use.

CLINICAL SIGNIFICANCE

- We demonstrate that the incidence and prevalence of gout and hyperuricemia in African Americans are low despite the high prevalence of risk factors.
- We hypothesize that African ancestry provides a protective effect that mitigates the other effects of other risk factors for gout.
- Identifying the biological basis of this phenomenon can help devise ways to prevent and treat gout.

METHODS

Data Source

Data were made available through the National Heart, Lung, and Blood Institute limited-access program. The Multiple Risk Factor Intervention Trial (MRFIT) participants provided informed consent for data collection and analysis. The Stanford Institutional Review Board approved the present analyses. Dr Krishnan possesses the original data and statistical codes. This study was unsponsored.

Participant Enrollment and Follow-up

From 1973 to 1975, 361,662 men at high risk for coronary artery disease aged 35 to 57 years and free of a history of hospitalization for myocardial infarction were screened in 22 clinical centers in 18 cities in the United States through the MRFIT trial. Exclusion criteria were serum creatinine level >2.0 mg/dL, diastolic blood pressure ≥115 mm Hg, serum cholesterol >9.05 mmol/L (350 mg/dL), taking medication for diabetes or previous hospitalization for a heart attack for 2 weeks or more. Those with self-reported physician diagnosis of diabetes but not on medications were not excluded. Participants were assigned randomly to special intervention (n = 6428) or usual care (n = 6438) groups. Although the study was designed to encompass 6 examinations performed annually, some participants who entered the study early in the enrollment phase were followed-up for 7 visits. Interval medical history and cardiovascular events were assessed at these visits. Vital status was assessed throughout the trial for an average of 7 years. Additional information about the MRFIT design has been published.[10-12]

Exclusions

For the present analyses, only those who identified themselves as Caucasians or African Americans were included.

Study Assessments

Questionnaires. At the baseline and follow-up visits, participants completed questionnaires on medical history and alcohol consumption. The medical history questionnaire included a self-report of gouty arthritis, defined as an affirmative answer to the question: "During the past 12 months has a doctor told you that you have gout?" No case validation for this definition is available through the MRFIT study, although it was found to have good reliability in other epidemiologic settings.[13-15]

Medications. Information on frequency of current use of aspirin, diuretics, and other blood pressure medications, and gout medications were collected at all visits. Use of allopurinol, probenecid, or colchicine was collectively categorized as "anti-gout" medicine use. Blood pressure medications were of 2 categories: diuretics and nondiuretics. Information on individual gout medications and their dose information were not available. The diuretics utilized were triamterene, spironolactone, hydrochlorothiazide, and chlorthalidone.

Laboratory Testing. Fasting blood samples were collected at each visit. Serum creatinine, lipid, and urate analyses were performed in a central laboratory using auto analyzers.[10,16] Urine testing for proteinuria and hematuria was performed at the local study center using the urine dipstick (Ames Labstix) method.[16]

Physician Evaluation. The study physician reviewed the medical history and medication history with the participants. The physical examination component included anthropometry, blood pressure measurement, and a clinical evaluation.

Assessment of Gout. The study physician assessed all participants for gout and classified participants into one of the following categories: gout present, no evidence of gout, and suspicion of gout. The MRFIT study protocol did not specify any standard criteria for this clinical assessment, and the determination was left to the clinical judgment of the individual study physician. Patients seldom presented with acute swollen joints that might have been amenable to aspiration and verification of presence of urate crystals. The primary case definition for gout was MRFIT study physician diagnosis of gout. Participants with suspected gout were not counted as cases in the present study. To assess the impact of any systematic errors associated with this case definition, we reanalyzed the data using alternate definitions for incident gout (sensitivity analyses): a) self-reported diagnosis and b) initiation of any gout medication (allopurinol, colchicine, or probenecid).