Hyperuricemia and Gout in Hawai'i

Mika D. Thompson BSc

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Background

Acute gouty arthritis, or acute gout, is the most common inflammatory arthritis in the United States (US), with a lifetime prevalence of 39 per 1,000 individuals, or 8.3 million Americans, based on data from the 2007-2008 National Health and Nutrition Examination Survey (NHANES).[1] Hyperuricemia, elevated uric acid serum levels, is the well-established causal precursor in the development of gout, and may also lead to an array of chronic comorbidities.[2,3] In the 2007-2008 NHANES, over 43 million Americans had sex-specific hyperuricemia. The prevalence of gout and hyperuricemia in the US appears to be on the rise, with incidence cases of gout more than doubling between 1969 and 1996, and then doubling again between 1990 and 2010.[4-6]

Characteristics of acute gout include a sudden onset of joint pain, erythema (reddening of the skin), limited range of motion, and inflammation.[2] Acute gout most often affects the large toe, the insteps, ankles, heels, and other joints of the lower extremities.[2] Following a flare up, patients may experience an asymptomatic period that may last several months to several years.

Gout is clinically similar to rheumatoid arthritis with regards to the substantial societal and personal burden associated with long-term chronic pain and physical disability. However, while primary hospitalization rates for rheumatoid arthritis have steadily decreased, annual hospitalizations for gout in the US have doubled in the last ten years.[7] In addition to the sizeable growth in prevalence, increases in gout-related hospitalization may be a result of the intermittent and self-limiting nature of the disease, leading to inaccurate or under-diagnosis, and delaying the proper treatment of the underlying issue.[5,8] The impact of gout on patients' health-related quality of life leads to a considerable economic burden, with conservative estimates exceeding $6 billion a year in the US alone, or more than $3000 in additional annual cost of care for a patient with gout compared to one without.[9]

Gout disproportionately affects certain subgroups based on age, sex, and race/ethnicity, with those in the highest risk category often less likely to receive quality gout care.[10] For instance, individuals of Pacific Islander and Asian descent are at an increased risk of hyperuricemia and gout, which may be attributable to a genetic predisposition and historical change in dietary lifestyle.[11,12] These groups also have significant health disparities in access to high quality health care.[13]

Gout in Hawai'i

As individuals of Pacific Islander and Asian heritage contribute to the majority of Hawaii's population, this is likely an important topic for the state. Nearly every major ethnocultural group in Hawai'i is thought to have an increased risk of elevated serum uric acid levels, including Native Hawaiians, Filipinos, Micronesians, Japanese, and other Polynesian populations.[11,14,15] Data from the 2016 Hawai'i State Department of Health Behavioral Risk Factor Surveillance Survey (BRFSS) showed that 21.9% of the state's adult population, or over 200,000 individuals, have been told by a doctor that they have some form of rheumatic disease, including rheumatoid arthritis, gout, lupus, or fibromyalgia.[16] Native Hawaiians and Pacific Islanders were found to have a significantly higher prevalence of arthritis at a younger age, compared to White and Asian males in Hawai'i.[17] However, few researchers have examined gout using Hawai'i-based samples. Given the increasing national prevalence and significant impact on health-related quality of life, economic burden, and health disparities, understanding gout and hyperuricemia in Hawai'i is crucial in informing evidence-based health policies and practices. Thus, the aim of this article is to examine prior findings on gout in Hawai'i and discuss the existing gaps in the literature with specific relevance to Hawai'i.

Clinical Features of Gout

Gout is caused by the accumulation of monosodium urate (MSU) crystals within joints, and is associated with elevated uric acid in the blood, or hyperuricemia.[5] Unlike most animals, humans lack the enzyme uricase, which converts uric acid into a more soluble end-product, leading to higher levels of serum uric acid. Hyperuricemia may be attributable to either an overproduction of uric acid from purine metabolism, or an underexcretion of uric acid by the renal system. Most individuals who develop gout have issues with both overproduction and underexcretion, with underexcretion thought to be the more important contributor to the disease state.[2,18]

Clinical gout progresses through four phases: asymptomatic hyperuricemia, acute gouty arthritis, intercritical gout, and chronic tophaceous gout. The asymptomatic hyperuricemia phase is when serum urate levels are elevated, above 6.8 mg/dL, but gout symptomatology has yet to present.[2] While most individuals with asymptomatic hyperuricemia do not develop the disease, studies have found that patients with urate levels exceeding 9.0 mg/dL are six times more likely to progress into clinical gout.[19,20] Acute gouty arthritis, or acute gout, is characterized by the formation of needle-shaped MSU crystals on joints, which causes a sudden onset of pain, erythema, limited range of motion, and inflammation.[2] Following a flare up, patients enter the intercritical gout phase, an asymptomatic period that may last several months to several years. The final phase, chronic tophaceous gout, is when patients may no longer experience asymptomatic intercritical periods and begin to develop chalky deposits of MSU, called tophi, visible on radiographs.[21] In this phase, individuals often experience unremitting chronic pain.

Epidemiology of Hyperuricemia and Gout

Cases of asymptomatic hyperuricemia and acute gout may be difficult to identify in population-based studies due to the level of intervention required to establish a definitive diagnosis; as such, there have been few studies on the epidemiology of gout in any population.[22] While few studies examine the national prevalence of gout, there are even fewer studies focused on the incidence.[23] One 52-year prospective cohort study found that the incidence of gout was 4.0 per 1,000 person-years in men, and 1.4 per 1,000 person-year in women.[24] Another 12-year prospective cohort study found an incidence of gout to be 1.5 per 1,000 person-years in male health professionals.[25] Use of diuretics significantly decreases the incidence rate; among individuals not exposed to diuretics, gout incidence more than doubled from 1977 to 1996.[6]

From the existing studies, we do know some important facts. Men are significantly more likely to develop gout than women; this difference may be attributable to an increased renal excretion of urate by estrogen.[26] Consequently, while older individuals are at an increased risk of hyperuricemia in general, women are disproportionately affected by age due to decreased estrogen following menopause.[5,27] Behavioral risk factors play a major role in both the onset and management of gout. Particularly, consumption of purine-rich foods, such as red meat and seafood, can lead to an overproduction of uric acid, and as a result, an increase risk of gout.[25] Further, alcohol use, sugar-sweetened foods and beverages, and obesity have all been shown to increase serum uric acid levels and gout.[28]

Ethnocultural Disparities of Gout in Asian/Pacific Islander Populations

Several epidemiological studies have found disparities in the ethnocultural and geographical distribution of hyperuricemia, particularly in the Asian-Pacific regions. Māori and Taiwanese aborigines are reported to have the highest prevalence of gout in the world.[18] These findings lead some investigators to postulate that hyperuricemia may be associated with the evolution of Austronesian ancestry. Gosling, Matisoo-Smith, Merriman[11] suggested that endemic malaria in early Polynesian settlements may have selected for higher levels of serum urate, which plays an important role in the immunological response to malarial infections. As a result, indigenous ethno-racial groups throughout the Oceania region may be predisposed to hyperuricemia, and consequently, have an increased risk of gout.

While there is an expectation of high rates of gout in Hawai‘i, in a 1966 study, Healey, Caner, Bassett, Decker[14] found that despite prevalence of hyperuricemia and gout among other Pacific Islanders, a sample of 49 Polynesians in Hawai‘i showed unexpectedly low levels of serum urate and no cases of gouty disease; these findings have not been further investigated.[11,18]

Some studies have found that living in urban versus rural areas may further contribute to hyperuricemia in the Pacific region. For instance, Finau, Stanhope, Prior, Joseph, Puloka, Leslie[29] found that Tongans living in urbanized regions of Tonga had a higher mean serum urate level than those in rural areas, and similar trends have been observed in Papua New Guinea populations.[11] Conversely, studies out of the Philippines found an increased prevalence in gout among members of a remote village when compared to an urban community.[30,31] However, the validity of these findings have been called into question due to methodological issues, particularly involving the comparability of these two prevalence estimates.[15] Given Hawaii's significant rural populations, this may be an important topic to consider in our state.

Westernization of the Indigenous Lifestyle

Dietary and lifestyle factors are important predictors of the development and progression of hyperuricemia and gout. The westernization of the Pacific diet has led to significant changes in eating habits and lifestyle behaviors, and has often been attributed to morbidity in the region.[32,33] For example, it is widely accepted that the high rates of obesity and type II diabetes among Native Hawaiians are related to the dietary shift away from traditional foods after the rapid westernization of the Hawaiian Islands and introduction of imported foods.[34,35] Since both gout and diabetes share many of the same dietary risk factors, namely sugar-rich food/beverages and obesity, some researchers believe that westernization of dietary behaviors have also led to the high prevalence of gout in the Pacific region.[36]

Trends in environmental factors, such as urbanization and the consumption of imported meat and fish over local fruits and vegetables, appear to support the theory that the change towards a western diet has contributed to gout in the Pacific Islands.[5,37] However, other researchers suggest that a predisposition to hyperuricemia may have been prevalent before westernization, citing the evidence of gout in archaeological studies.[11] Similar conclusions have been drawn through a systematic review of Filipinos with elevated serum urate levels, noting several studies that challenge the degree of contribution from changing dietary behaviors, while also recognizing that the problem has likely been exacerbated by these changes in Pacific Islanders.[15]

Nevertheless, the progression and prognosis of the disease state is known to be influenced by purine intake, which is abundant in a western diet.[2]

Another risk factor highly associated with hyperuricemia and gout is alcohol consumption; this association appears to increase risk of gout in a dose-dependent manner.[28] While risky alcohol consumption in Asian and Pacific Islander communities remain somewhat lower or comparable to mainland US populations, rapid shifts towards westernized lifestyles may increase the risk of gout in an already at-risk population.[32,38] Furthermore, some findings have suggested that while certain Pacific Islander groups, including Native Hawaiians, are not necessarily at higher risk of alcohol consumption, those that do use alcohol are more likely to binge drink.[39,40] Given the dose-response relationship demonstrated between alcohol consumption and gout, high rates of risky drinking are cause for serious concern in the Hawai'i and Pacific Island region.

A Gap in the Literature on Gout in Hawai'i

A major challenge in assessing the disease burden of gout in the Pacific region has been the lack of follow-up investigation into the disease and associated risk factors. Despite the claim that many of these ethno-racial groups have the highest prevalence in the world, there has been almost no studies on Hawaii's unique Asian/Pacific Islander population. The bulk of the existing Hawai'i-based literature took place between the 1950s to the 1960s, with little to no follow-up.[11,15,41] While there is some research on the anthropological origins of gout in Pacific Islanders, along with some recent epidemiological studies with Māori and Taiwanese aboriginals,[5,11,23,42] literature on Native Hawaiians is severely lacking. Furthermore, while there are no existing reports on the current frequency or distribution of gout in Hawai'i, insights regarding the prevalence of risk factors strongly associated with hyperuricemia suggest that gout may be a significant cause of morbidity in the state. For example, obesity and diabetes has been on the rise since the 1990s in both Hawai'i and the US mainland, with the highest prevalence in Native Hawaiian and other Pacific Islander populations.[43] Given the recent and past health trends in known risk factors related to gout, hyperuricemia, and comorbidities among Native Hawaiian populations, there exists an urgent need for further investigation.

Aside from the need to establish the current prevalence and incidence of gout in Hawai'i-specific populations, cost analyses should be performed to ascertain the economic burden associated with hyperuricemia and gouty arthritis in the Pacific region. As acute gout presents as a painful, chronic, reoccurring condition, researchers should further investigate the impact of gout in Hawai'i, and, ideally, develop interventions that may prevent disease occurrence or mitigate the consequences for affected individuals.

Finally, given the convergence of ancient migratory patterns in the Pacific and current ethno-racial disparities within these populations, the lack of research on genetic influences needs to be addressed to better understand which population are at risk. As mentioned, findings from a small sample of Polynesians from Hawai'i by Healey, Caner, Bassett, Decker[14] suggested that Native Hawaiians may be unique in having only slightly elevated serum uric acid levels, and have a lower likelihood of developing gout. However, since 1966, there have been no further investigations into this unique finding; since the sample only consisted of 49 individuals of 'Polynesian ancestry,' the researchers were unable to ascertain the risk of gout among Native Hawaiians specifically.

Conclusion

While recent and comprehensive research into gout in Hawai'i is significantly lacking, investigation into other Pacific Island communities suggests an increased risk of hyperuricemia and gout compared to the United States mainland and with consequences for many communities in Hawai'i. Many researchers point to the effects of westernization and associated dietary changes as a contributing factor, while others suggest that a genetic predisposition may be at least adding to the prevalence of gout in these populations. The need for research and understanding on gout is likely to be very important in Hawaii's population. Without data on the distribution and other factors of disease burden, it is not possible to directly ascertain the impact of gout in Hawai'i, reduce its prevalence, and mitigate its consequences.

Given limited state-level resources and the need for spending prioritization, it is important to take advantage of funding opportunities that may help shed light on gout and other arthritic conditions that may be disproportionality affecting populations in Hawai'i. For instance, the Centers for Disease Control and Prevention recently posted a Notice of Funding Opportunity that would fund the implementation of state-based approaches to improving arthritis management and quality of life for those affected by arthritis.[44] Utilizing national-level resources may enable substantial steps towards adequately addressing gout and other arthritic conditions, and potentially reduce the long-term cost burden in Hawai'i.

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Author's Affiliation:
Office of Public Health Studies, University of Hawai'i at Manoa, Honolulu, HI

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