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Rising Global Burden of Gout: Time to Act

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Gout is the most common inflammatory arthritis in the world. According to the Global Burden of Disease Study 2017 (GBD 2017), there are 41 million adults with gout worldwide (1), over twice of the 19 million living with rheumatoid arthritis (RA). Yet, in contrast to the remarkable progress made in the treatment of RA, gout management remains poor despite treatment recommendations by various medical societies including the ACR 2020 guideline (2). About 70% of patients continue to experience frequent flares (3) and only 27% of patients with incident gout are ultimately started on urate lowering therapy (ULT) within 12 months of diagnosis (4). Further, less than 50% of patients remain adherent to ULT beyond a year (5). Patients may also trivialize their symptoms to avoid shame and embarrassment due to the stigma associated with gout, contributing to under-diagnosis and under-treatment. Gout adds considerably to healthcare costs related to frequent emergency room visits, hospitalizations, loss of work productivity and disability (6). Clearly, the burden of 41 million patients with poorly controlled gout is substantially greater than that of 41 million with well controlled gout.

The burden of gout is compounded by the additional impact of comorbidities that are prevalent in gout patients including hypertension (75%), CKD (70%), obesity (53%) and CVD (10% to 14%), each of which are associated with increased morbidity and mortality risk. Gout itself is associated with increased risk of death from cardiovascular diseases (7), as well as non-cardiac causes (8). Further, the overall higher risk of premature mortality in gout has remained unimproved over 2 decades in contrast to the improved mortality rates in RA over a similar timeframe (9).

Ability to make rational policy decisions to address the burden of gout requires an in-depth understanding of its current epidemiology. In this issue, Safiri, et al. have used data from the Global Burden of Diseases, Injuries, and Risk Factors Study 2017 (GBD 2017) to examine the epidemiology of gout, associated disability, and attributable risk factors in 195 countries

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and territories from 1990 to 2017. The GBD is a comprehensive epidemiologic study led by the Institute for Health Metrics and Evaluation (IHME) that aims to quantify levels and trends for hundreds of diseases, injuries, and risk factors. Based on the data from GBD 2017, there were 41.2 million prevalent cases and 7.4 million incident cases of gout globally (1). The prevalence of gout doubled from 20.2 million in 1990 to 41.2 million in 2017, and its incidence also doubled from 3.6 million to 7.4 million. Every region/country experienced an increase in prevalence over the time. The highest percentage increases in age-standardized prevalence rates were observed in high-income North America (34%), Australasia (19%) and tropical Latin America (16%).

An important examination in this study is the Years Lived with Disability (YLD) due to gout, a metric that reflects burden of disease related to prevalence and loss of health due to disease-related disability. The authors did not calculate Disability-Adjusted Life Years (DALYs) on the assumption that gout does not cause mortality directly itself. This assumption may be debatable given the established increased risk of mortality in gout, even though direct attribution to gout versus associated comorbidities is not clear. To compute YLDs, the authors considered three prespecified disease severity levels (asymptomatic, likely referring to intercritical gout; gout flare; and polyarticular gout reflecting the same severity as severe RA) that were assigned specific disability weights. Lack of clarity about derivation of the disability weights makes it difficult to discern how accurately they capture the true gout experience. Nonetheless, the authors estimated that gout was associated with 1.3 million YLDs in 2017. Mirroring the prevalence and incidence estimates, YLDs were highest in males and older adults. Interestingly, age-standardized YLDs also increased with increasing Socio-Demographic Index (SDI), suggesting higher gout burden in developed countries as compared to developing countries. Body mass index accounted for more YLDs due to gout than impaired kidney function (32.4% vs. 15.3%). In general, obesity contributed to 120 million DALYs, representing 5% of DALYs from any causes, with a prevalence of 603 million in 2015 (10), and in 2017, the prevalence of CKD was 698 million and YLDs were 7.3 million (1). These data highlight the added burden of highly prevalent comorbidities that exist in patients with gout.

While there may be some inaccuracies and underestimation of the trends due to lack of uniform data across the regions/countries and the need for modeling prevalence estimates, these data provide a clear portrait of gout as a global disease, rising in every corner of the planet. A key question arising from these data is why the prevalence and incidence of gout has doubled in less than 30 years. While physicians may have improved recognition and diagnosis of gout, that alone would not explain this finding. A 42% increase in the world population, from 5.28 billion in 1990 to 7.5 billion in 2017, combined with an increased life expectancy of 5.8 years in men and 6.6 years in women and a 4% increase in proportion of adults >60 years could be pertinent contributors (11, 12). However, these factors alone are insufficient to explain a 100% increase in <30 years.

The rise in obesity may also be an important contributor to the marked increase in gout prevalence globally. For example, in the US, the prevalence of obesity doubled from 18.7% in 1990 to 36.7% in 2016 (13), and globally, the age-standardized prevalence of obesity increased by at least 2-fold in 13 of the 20 most populous countries (10). Similar to gout, the

rise in obesity tracks with SDI. Obesity is strongly associated with hyperuricemia, a necessary, but not sufficient, risk factor for gout. While there are dietary and genetic influences on hyperuricemia, these may not be sufficient to fully explain the markedly increased prevalence of gout in 27 years. There may be additional societal level factors to consider in the context of obesity and impact on other comorbidities and gout, such as physical activity. Indeed, the rise in prevalence being tied to SDI suggests the need for a close examination of the social determinants of health that are likely contributing to gout burden in such a compressed timeframe.

In addition to providing an impetus to understand reasons for the increased prevalence of gout, the study by Safiri, et al. also provides compelling urgency to address important management issues in gout. Education of medical students and primary care physicians is of paramount importance since the majority of gout is managed in primary care. A major hurdle to education about gout management is the contrary opinion of primary care publications, such as the ACP 2016 gout guidelines (14) which questions the treat-to-target strategy advocated by rheumatology societies. The burden of gout is magnified when appropriate management is not offered early in the course of disease, when adequate control of hyperuricemia can prevent joint damage and tophi. Unfortunately, rheumatologists are often witness to the consequences of inadequate management that results in unnecessarily worsening the gout burden. Doherty and colleagues demonstrated the superiority of the treat-to-target approach involving education and patient engagement by nurses compared with usual care by general practitioners (15). Their findings clearly suggest that a proactive approach with individualized education and close communication with patients leads to improved outcomes and medication adherence.

In summary, Safiri, et al. have highlighted an alarming trend in the rise of gout worldwide over a mere 27-year period. Efforts to understand this trend are needed to halt the burden of gout. Beyond education, physicians and patients also need more therapeutic options. There are only 5 approved ULT medications in the US (though one is no longer available on the market), and fewer options in many other countries. This paucity of options is particularly challenging for patients with contraindications or intolerance to the few available medications. In parallel with treatment development efforts, dissemination and implementation of evidence-based treatment guidelines is urgently needed. Optimizing management of gout with the currently available therapies will certainly lessen the burden of this disease for the 41 million worldwide currently living with gout.

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