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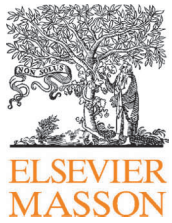

The Human and Economic Burden of Difficult-to-Treat Gouty Arthritis

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ABSTRACT

Gouty arthritis, one of the most painful and common forms of adult arthritis, is caused by monosodium urate crystal deposits in joints, most often in the lower extremities. Crystals trigger an inflammatory response leading to acute flares characterized by a rapid onset of pain, warmth, swelling, and redness in involved joints. Over time, continued monosodium urate crystal deposits and inflammation can lead to chronic tophaceous gout that result in bone erosion, progressing to joint destruction and significant disability. The goal of therapy in an acute gout flare is prompt and safe termination of pain and inflammation. Acute gouty arthritis is usually treated with nonsteroidal anti-inflammatory drugs, colchicine, or corticosteroids. However, for a growing number of patients, current standard treatments are ineffective or are contraindicated, largely due to the presence of comorbidities. Gouty arthritis can have a major negative impact of health-related quality of life, especially in patients with difficult-to-treat disease, as revealed by recent studies comparing health-related quality of life with that of the general population. Additionally, gouty arthritis also constitutes an important economic burden through absence from work and medical costs. This burden is even greater in patients with difficult-to-treat disease.

1. Introduction

Gouty arthritis, the most common inflammatory arthritis in adults, results from an elevated body uric acid pool, which leads to deposition of monosodium urate (MSU) crystals in joints and soft tissue. The crystal formation is caused by persistent urate levels in extracellular fluids above the saturation point of MSU. Typically, gouty arthritis initially presents with intermittent episodes of inflammation characterized by acute pain, erythema, and joint swelling. If left untreated, a more chronic course may develop, characterized by persistent inflammation and visible MSU deposits called tophi , resulting in bone erosion, irreversible joint damage, and significant disability [1,2].

The long-term therapeutic goal in the management of gouty arthritis is to promote crystal dissolution and prevent new crystal formation. This is achieved with the use of urate-lowering therapy (ULT) aimed at maintaining the serum uric acid below the saturation point for monosodium urate [3]. Symptoms of acute gouty arthritis are generally controlled with anti-inflammatory therapy, including nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, and corticosteroids [3]. Although the recommended treatment strategies are frequently effective, many patients with gouty arthritis have multiple comorbidities and associated contraindications to the standard available medications [4,5]. Moreover, a number of patients fail to respond and/or are intolerant to standard anti-inflammatory

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treatment, adding to the complexity of managing gouty flares (eg, nonresponse ranged from 27% to 62% after 36 hours in the 2 available clinical trials [6,7]). In recent studies, patients with frequent gout flares (ie, ≥3 gout flares per year) who cannot be successfully treated with colchicine, NSAIDs, and corticosteroids are referred to as having "difficult-to treat" gouty arthritis [8-10]. The frequent and uncontrolled flares in this growing subpopulation has been shown to have a significant impact on patient quality of life and productivity, and reflects the shortcomings of current standard therapies [2,11,12]. The objective of this paper is to review the literature on the human and economic burden associated with difficult-to-treat gouty arthritis.

2. Search Strategy

Systematic literature searches were performed in the PubMed database to identify papers describing the prevalence, comorbidities, health-related quality of life (HRQOL), and economic burden of gouty arthritis. The exact search strings that were used are presented in (Table 1). Papers were included in the review if the main objective was to describe the prevalence, comorbidities, HRQOL, and economic burden of gouty arthritis. Reference lists of included studies were screened for relevant additional papers. Gouty arthritis studies were excluded from the review if they were written in languages other than English or studied in the context of other chronic diseases. Studies specifically focusing on gouty arthritis and associated comorbidities were excluded if their sample size was fewer than 1000. Studies describing the prevalence of gouty arthritis were excluded if they reported only on prevalence in specific ethnic groups or regions.

3. Prevalence of Gouty Arthritis

Ten papers on the national prevalence of gout met the criteria for inclusion. Currie et al [13] were the first to report on the prevalence of gout and found that in Great Britain from 1971 to 1975, 0.26% of the population had gouty arthritis. Harris et al [14] reported a substantially higher prevalence in England in the early 1990s — 0.95%. More recently, data from the United Kingdom (UK) General Practice Research database showed that the prevalence of gouty arthritis in England was 1.4% from 1990 to 2005 [15,16]. Kuo et al [17] observed a higher prevalence of 2.5% in 2012 in their analysis of medical records contained in the UK Clinical Practice Research database and reported that the prevalence of gouty arthritis had risen by 63.9% since 1997. A rising prevalence of gouty arthritis has been reported in other geographic locations as well. For example, a study in Taiwan showed that the prevalence of self-reported gouty arthritis increased from 4.7% to 8.2% in men over the periods 1993 to 1996 and 2005 to 2008, respectively [4]. Physician-diagnosed gouty arthritis was observed in 2.9% of the Hanese population in Taiwan from 2004 to 2006 in a study in southern Taiwan [18]. Similar observations have been made regarding the increasing prevalence of gouty arthritis in the United States (US) [19,20], New Zealand [21,22], and Australia [23].

The rising prevalence of gouty arthritis is often attributed to the increasing prevalence of established risk factors for the condition, such as hypertension, diabetes, and the use of diuretics and cyclosporine [21,24-26]. Moreover, it is well known that the prevalence of gouty arthritis increases with age, likely reflecting the accumulation of hyperuricemia risk factors in old age, leading to a higher incidence of new cases of gouty arthritis in older populations [17,20]. In addition to a higher incidence among the elderly, some authors have speculated that increasing longevity may contribute to the rising prevalence of gouty arthritis by increasing the years lived with gout, based on the observation that that increases in prevalence could not be accounted for by increased incidence of disease alone [15,16]. Currently, gouty arthritis is the most prevalent inflammatory arthritis [18,27] and data suggest that its prevalence is likely to increase even further in the near future.

4. Comorbidity Burden in Gouty Arthritis

Gout is characterized by a substantial comorbidity burden, and is particularly interconnected with other diseases associated with hyperuricemia such as diabetes, hypertension, obesity, heart failure, and metabolic syndrome [28]. In a study conducted in a managed care setting, patients with gouty arthritis had a mean of 5 comorbid disorders; less than 5% of patients had no comorbidities [29]. Compared with patients with osteoarthritis, patients with gouty arthritis were significantly more likely to have cardiovascular disease, hypertension, diabetes, and chronic

Table 1
PubMed Search Strings

Topic	Search Strings	Number of Search Results	Included in Review
Prevalence of gout	(Prevalence [title] AND gout[title]	49	10
Comorbidities	Gout [title] AND co-morbid [title] OR comorbid [title]	25	8
Health-related quality of life	Gout [title] AND quality of life[title]	17	9
Economic burden	Gout [title] AND (direct costs "OR" indirect costs OR productivity OR economic) [title/abstract]	193	15