

Gout management and outcomes during established COVID-19 pandemic in 2020–2021: a cross-sectional Internet survey

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Abstract

Objective: To assess the management of gout in established COVID-19 pandemic.

Methods: We assessed medication use, health care utilization, gout-specific health-related quality of life (HRQOL), psychological distress using Patient Health Questionnaire-4 (PHQ-4), resilience, illness perception, and health literacy in people with physician-diagnosed self-reported gout in established COVID-19 pandemic in a cross-sectional Internet survey.

Results: Among the 130 survey respondents with gout, the mean age was 62.8 years, 65% were male, 83% were White, 59% were prescribed urate-lowering therapy (ULT), and health literacy was adequate in 80%. A third of survey respondents reported more difficulty with their gout management since September 2020. Gout-specific HRQOL deficits were evident. Moderate-severe psychological distress was seen in 22%, and resilience score was 6.5 [standard deviation (SD), 1.9; range, 0–8]. Adjusted for age and sex, compared with no/mild psychological distress, moderate-severe psychological distress was associated with significantly higher odds ratio (OR; 95% confidence interval) of more difficulty with (1) getting health care for gout in clinic, 3.7 (1.0, 13.2); emergency room/urgent care, 8.1 (1.4, 45.0); and in the hospital, 9.8 (1.6, 59.6); (2) getting gout flares treated, 6.6 (1.6, 26.8); (3) avoiding gout complications, 4.5 (1.2, 16.7); and (4) daily activities at home, 4.2 (1.3, 14.1), and performing work, 4.1 (1.2, 13.6).

Conclusion: Respondents with gout reported health care gaps, low rates of ULT prescription, high psychological distress, and HRQOL deficits during established COVID-19 pandemic. Moderate-severe psychological distress was associated with difficulties in health care access and gout management. Interventions to address these challenges in gout management are needed.

Keywords: COVID-19, disease management, gout, Internet survey, medication use, psychological distress, quality of life, resilience

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Introduction

The corona virus disease 2019 (COVID-19) has significantly impacted the health care delivery in the United States.¹ In a recent Internet survey, we found that health care gaps, psychological distress, and health-related quality of life (HRQOL) deficits were commonly reported by people with gout during the COVID-19 pandemic.² Conversely, rheumatoid arthritis, but not gout, was associated with a higher risk of COVID-19 infection, and neither was associated with the

risk of COVID-19 death in a recent UK biobank study.³ With these exceptions, limited data are available regarding the impact of COVID-19 on people with gout.

A recent international survey reported substantial employment status changes in people with rheumatic diseases during the COVID-19 pandemic, which can lead to challenges with health care access, medication affordability, mental health, and disease activity.⁴ Given the continuing

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COVID-19 pandemic in the United States and under-recognition of the risk in people with gout,⁵ it was prudent to do a follow-up survey to assess the current issues faced by patients with gout during the second wave of the COVID-19 pandemic, that is, the established phase of the pandemic. In a recent study of predominantly low-socioeconomic-strata people with gout receiving health care at a public health gout clinic in Mexico, compared with those in the pre-pandemic period, an eight-time higher proportion with gout flares and higher serum urate levels were reported during the COVID-19 pandemic. Surprisingly, HRQOL and functional ability were better during the COVID-19 pandemic.⁶ These findings of increased flares *versus* improved HRQOL/function are contradictory. Although not directly comparable, HRQOL findings are inconsistent with our recent cross-sectional Internet survey that showed poor gout-specific HRQOL.²

Therefore, we aimed to assess the current patterns of gout care including health care access, HRQOL, psychological distress, and patient resilience in people with gout during the established COVID-19 pandemic in a cross-sectional survey study. We hypothesized that people with gout will report HRQOL deficits and psychological distress, and that high psychological distress and lower resilience would be associated with poorer HRQOL, due to the COVID-19 pandemic.

Methods

We evaluated the impact of COVID-19 pandemic on gout care by performing an online cross-sectional COVID-19 gout survey to examine the experiences of people with gout since September 2020. In September 2000, the United States passed a sad milestone of 200,000 deaths related to COVID-19 pandemic, according to the data from Johns Hopkins University.⁷ We invited the people visiting the Gout Education Society website (GES, a non-profit organization; <http://gout-education.org>), dedicated to gout education, to participate in a brief anonymized cross-sectional Internet survey on a voluntary basis between 24 November 2020 and 12 June 2021, which roughly corresponds to the second wave of the COVID-19 pandemic in the United States. This study was approved by the human ethics committee at the University of Alabama at Birmingham (UAB). People were eligible for this study if they responded affirmative to the question regarding

self-reported physician-diagnosed gout. We describe the study in accordance with the STROBE checklist for cross-sectional studies (Supplemental Appendix 1).

We collected data on demographics, use of gout medications including urate-lowering therapy (ULT; allopurinol, febuxostat, and probenecid) and other medications, difficulty with gout care and health care access, gout flares, gout-specific HRQOL, psychological distress, resilience, medication adherence, illness perception, and health literacy. Gout-specific HRQOL was assessed by the Gout Assessment Questionnaire–Gout Impact scale (GAQ-GIS).^{8,9} It has 24 items that are summed to provide the five subscales – gout concern overall, unmet need, medication side effects, concern during gout attack, and well-being during attack scale, each with a 0–100 score (higher score indicating more concern/need). The minimally clinically important difference (MCID) threshold on four of the five GIS subscales is 5–8 points.⁹ We used the Patient Health Questionnaire–4 (PHQ-4), a brief validated measure, to assess psychological distress with scores ranging 0–12, higher scores indicating more psychological distress; moderate (scores, 6–8) and severe (scores 9–12) psychological distress categories were combined for analyses.¹⁰

We measured resilience with a validated two-item Connor–Davidson Resilience Scale (CD-RISC2), scored from 0 to 8, and categorized a score of 6–8 as high resilience *as they were* at par with the general population scores.¹¹ We used the Brief Illness Perception Questionnaire (Brief-IPQ), a nine-item validated scale, where a higher item score indicates higher illness perception; total score is transformed onto 0–100.¹² Health literacy was measured with BRIEF, a validated four-item measure, with scores ranging 4–20: 4–12 (low literacy), 13–16 (may need assistance), and 17–20 (can read and comprehend education materials).¹³ Medication adherence with ULT was measured using the brief validated three-item measure by Voils *et al.*,¹⁴ scores ranging 1 (*perfect adherence*) to 5 (*perfect non-adherence*). The overall score is an average of scores on three items.

For patients who self-reported a physician-diagnosis of gout, we assessed bivariate correlations between PHQ-4, GAQ-GIS subscales, Brief-IPQ, and CD-RISC2 resilience scores with non-parametric Spearman's coefficients. Logistic

regression analyses examined the association of moderate-severe psychological distress with difficulty in gout management. Sensitivity analyses were done using anxiety and depression subscale scores instead of the total distress score. As an exploratory analysis, we compared the current with the baseline survey, using chi-square test for categorical or *t*-test for continuous variables. We attempted to reduce selection bias, by making the survey available to anyone with access to the Internet, rather than a study limited to a single medical center, geographical region, or country. A *p* value <0.05 was considered statistically significant.

Results

Of the 312 visitors to the website during the 6 months from November 2020 to June 2021 who clicked on the survey and reported any data, 130 survey respondents reported physician-diagnosed gout with a mean age of 62.8 years (SD, 12.8), 65% male, 83% White, 8% Black or African American, and 3% were Hispanic or Latino (Table 1). The remaining people reported a different type of arthritis/immune disease than gout/calcium pyrophosphate deposition disease (CPPD) or osteoarthritis (*n*=50), no immune disease/arthritis (*n*=95), or provided no response to the question (*n*=32). Among people with physician-diagnosed gout, 59% had been prescribed ULT by their provider; 27% had concomitant osteoarthritis, and 2% had concomitant pseudogout.

Gout medication use, gout flares, and health care access during the ongoing COVID-19

The proportion of the survey respondents with self-reported physician-diagnosed gout who never took each gout medication was as follows (medication-naïve; Supplemental Appendix 2): allopurinol, 40%; febuxostat, 88%; probenecid, 98%; colchicine, 45%; non-steroidal anti-inflammatory drugs (NSAIDs), 10%; and glucocorticoids, 38%. These proportions were higher than those reported at the baseline survey in April–June 2020, 20% (*p*=0.0008), 73% (*p*=0.011), 95% (*p*=0.28), 28% (*p*<0.0001), 3% (*p*=0.05), and 25% (*p*=0.06), respectively.

Gout flares were common in people during the established COVID-19 pandemic: 87% reported one or more gout flares since September 2020; 23% went to the urgent care or emergency room for gout flares; and 5% were hospitalized with

gout flares (Supplemental Appendix 3). A third of survey respondents reported more difficulty with their gout management related to the COVID-19 pandemic (Supplemental Appendix 4). Roughly, 8–19% respondents reported difficulty in getting health care and medication for gout since September 2020.

Gout-specific HRQOL, psychological distress, resilience, illness perception, and health literacy in people with gout and their correlation

The mean GAQ-GIS subscale scores were as follows: gout concern overall, 72.7 (SD, 21.9); unmet gout treatment need, 54.7 (SD, 24.2); gout medication side effects, 58.8 (SD, 25.3); gout concern during flare, 55.2 (SD, 24.2); and well-being during flare, 55.2 (SD, 23.3; Supplemental Appendix 5).

Mean scores on PHQ-2 depression, PHQ-2 anxiety, and PHQ-4 psychological distress scores were 1.7, 1.5, and 3.2, respectively (Supplemental Appendix 6), numerically slightly lower, but not significantly different than the baseline survey scores (*p*>0.05 for all). Psychological distress on PHQ-4 was rated as normal in 52%, mild in 27%, moderate in 9%, and severe in 13% (Supplemental Appendix 6).

The Brief-IPQ Illness perception total score was 49.5 (SD, 12.4) and patient health literacy score was adequate in 80% (Supplemental Appendix 6).

During the COVID-19 pandemic, PHQ-4 psychological distress was significantly positively correlated with GIS subscales and illness perception, and significantly negatively correlated with resilience score (Supplemental Appendix 7). Illness perception was significantly positively correlated with all GIS subscales (Supplemental Appendix 7).

Association of psychological distress with difficulty with gout management

Moderate-severe psychological distress was significantly associated with more difficulty with getting health care for gout in various settings (clinic, emergency room, urgent care, hospital), getting gout flares treated, avoiding gout complications, and performing work and daily activities at home during the COVID-19 pandemic (Table 2). In sensitivity analyses, similar associations were noted for depression and anxiety, that constituted PHQ-4 measure of psychological distress (Supplemental Appendix 8).

Table 1. Characteristics of study participants with doctor-diagnosed gout^a (*n* = 130).

	<i>n</i> (%) ^b (<i>n</i> = 130)
Age in years, mean (standard deviation)	62.8 (12.8)
Male sex	84 (65%)
Race/ethnicity	
White	107 (82%)
Black or African American	10 (8%)
Asian	2 (2%)
American Indian or Alaskan Native	2 (2%)
Native Hawaiian or other Pacific Islander	4 (3%)
Other	2 (2%)
Hispanic ethnicity	3 (2%)
Urate-lowering therapy (ULT) ^c prescribed by doctor	100 (82%)
Concomitant additional doctor-diagnosed arthritic conditions ^d	
Osteoarthritis	37 (30%)
Calcium pyrophosphate deposition disease (CPPD)	9 (7%)
Number of gout flares since September 2020 ^e	
0	14 (13%)
1	41 (37%)
2	22 (20%)
3	16 (14%)
4 or more	18 (16%)
Visits to urgent care or emergency room with gout flare ^f since September 2020	
0	82 (77%)
1	16 (15%)
2	6 (6%)
3 or more	2 (2%)
Hospitalized with gout flare ^g since September 2020	1 (1%)
^a Have you been told by a doctor that you have gout, calcium pyrophosphate disease (also called pseudogout) or osteoarthritis (wear and tear or cartilage loss or old-age arthritis)? Yes, No ^b <i>n</i> (%), unless specified otherwise. ^c ULT includes allopurinol, febuxostat or probenecid: Has your doctor prescribed allopurinol (also called Zyloprim or Alopripr), or febuxostat (also called Uloric), or probenecid (also called benemid) for you? Yes, No; Missing, <i>n</i> = 1. ^d Please check all of the diagnosis you have received from a health care provider (you can select more than one answer): Gout. Calcium pyrophosphate disease (also called pseudogout). Osteoarthritis (wear and tear or cartilage loss or old-age arthritis). ^e Missing, <i>n</i> = 19 (15%). ^f Missing, <i>n</i> = 23 (18%). ^g Missing, <i>n</i> = 24 (18%).	

Table 2. Multivariable-adjusted association of moderate-severe psychological distress with the difficulty with gout management.

	Moderate-severe psychological distress	
	Odds ratio (95% CI)	p value
Since September 2020, due to the corona virus epidemic, I have had more difficulty in ...		
Getting health care for my gout in the clinic	3.7 (1.0, 13.2)	0.047
Getting health care for my gout in the emergency room or urgent care	8.1 (1.4, 45.0)	0.02
Getting health care for my gout in the hospital	9.8 (1.6, 59.6)	0.01
Getting my gout medication refills from the doctor	1.4 (0.2, 9.3)	0.74
Getting my gout medication filled at the pharmacy	3.3 (0.7, 16.1)	0.15
Getting my gout flares treated	6.6 (1.6, 26.8)	0.008
Avoiding my gout flares	3.6 (0.9, 14.7)	0.08
Avoiding complications of my gout	4.5 (1.2, 16.7)	0.025
Getting information and education about how to keep gout under control	1.7 (0.3, 8.3)	0.50
Since September 2020, compared with before the coronavirus epidemic, I have had more difficulty during this epidemic with ...		
Gout overall	3.1 (0.9, 10.2)	0.06
Gout flares	5.9 (1.7, 20.7)	0.005
Chronic pain issues related to gout/arthritis	2.1 (0.7, 6.9)	0.20
Performing my daily activities at home	4.2 (1.3, 14.1)	0.02
Performing my work	4.1 (1.2, 13.6)	0.02
Participating in social activities	2.3 (0.7, 7.7)	0.19
CI, confidence interval. Bold Font indicates statistically significant estimates with a p-value < 0.05		

Exploratory analyses: comparison with baseline survey

Compared with our baseline Internet survey, except for NSAIDs, a lower proportion of respondents were taking gout medications more regularly since September 2020: allopurinol, 26% *versus* 44% ($p=0.048$); febuxostat, 0% *versus* 15% ($p=0.07$); probenecid, 0% *versus* 5% ($p=0.35$); colchicine, 15% *versus* 37% ($p=0.03$); NSAIDs, 77% *versus* 36% ($p<0.0001$); and glucocorticoids, 10% *versus* 15% ($p=0.53$) (Supplemental Appendix 1). Compared with the baseline survey in April–June 2020, some proportions were lower: the effect of gout on work, 32% *versus* 49% ($p=0.04$), and

difficulty getting health care for gout in the clinic, 19% *versus* 37% ($p=0.02$; Supplemental Appendix 3). GAQ-GIS scores were a statistically significantly and clinically meaningful lower (better) compared with the baseline survey scores for two GAQ-GIS subscales, unmet gout treatment need and gout concern during flare (Supplemental Appendix 4). Resilience score on CD-RISC2 scale was 6.5 (SD, 1.9), and 76% of the survey respondents had a CD-RISC2 score 6 or higher; both the mean resilience score [*versus* 5.6 (SD, 1.8); $p=0.005$] and the resilient proportion were higher than that at the baseline survey (76% *versus* 56%; $p=0.008$, Supplemental Appendix 5).

Discussion

Our cross-sectional Internet gout survey assessed the impact of the ongoing COVID-19 pandemic on gout care and gout management since September 2020. We explored differences from our previous cross-sectional survey, and these differences may be related to sampling (participant characteristic), rather than represent actual time-trends. Our survey results add to the current knowledge similar to the recent global rheumatology alliance survey of general rheumatology patients⁴ and a single-center gout clinic evaluation from Mexico.⁶ Several study findings merit further discussion.

The total PHQ-4 psychological distress score of 3.2 in our study was slightly higher than that reported at 2.1–3.0 in community-based samples or college students.^{15,16} Increased psychological distress has been noted in people with chronic diseases in the COVID-19 era.¹⁷ The patient health literacy score on BRIEF was adequate in 80%. The Brief-IPQ eight-item scores for this gout population are similar to recently published scores for gout and rheumatoid arthritis cohorts.^{18,19}

The mean resilience score (stress coping ability) was slightly lower than the 6–6.9 reported for general populations, but higher than 4.7–5.1 reported for patients with depression, anxiety disorder, or post-traumatic stress disorder.¹¹ We noted a low to moderate association of psychological distress, gout-specific HRQOL, and resilience. The increase in resilience score from April–June 2020² to the current survey (November 2020–June 2021) may be a sampling issue or be possibly related to the evolving COVID-19 pandemic and the recent availability of COVID-19 vaccine, at least partially.

We found an independent association of psychological distress with difficulty in getting health care for gout (clinic, emergency room, urgent care, hospital), getting gout flares treated, avoiding gout complications, and performing work and daily activities at home, since September 2020. The odds ratios ranged from 3.7 to 9.8, some with wide confidence intervals, due to a low rate of some outcomes. These are interesting findings and add to the current knowledge. Similar associations were noted for depression and anxiety, which constitute the PHQ-4 measure. Health care systems and providers need to develop interventions to address the health care access issues and psychological distress faced by people with gout. These might include tele-psychiatry, nurse

visits, patient navigator support, and a more efficient use of technology for better patient–provider team communication. This may help to improve gout management during the COVID-19 pandemic, which seems worse compared with that at the beginning of the pandemic. Many survey respondents were COVID-19 positive and several reported a family member or friend testing positive for COVID-19.

Gout-specific HRQOL assessed on GAQ-GIS subscale scores were worse/higher compared with a community-based sample of people with gout in a previous study⁸: gout concern overall, 72.7 (current) *versus* 63.1 (community-based sample); unmet gout treatment need, 54.7 *versus* 38.2; gout medication side effects, 55.8 *versus* 48.3; gout concern during flare, 55.2 *versus* 50.2; and well-being during flare, 55.2 *versus* 50.2, respectively. Gout-specific HRQOL on two of the four GIS subscale scores (unmet gout treatment need and gout concern during flare) were clinically meaningfully (5–8 points) worse than the community samples, previously reported.^{8,9,20}

Interestingly, 40% and 88% of respondents with physician-diagnosed gout had never taken allopurinol or febuxostat, respectively, the two most used long-term ULTs. This is in contrast to the recent Mexican gout clinic study that reported ULT use by 90% during the COVID-19 pandemic.⁶ Differences in setting (Mexican gout clinic *versus* all-comer gout Internet study), socio-demographics (95% men with a mean age of 55 years *versus* 65% men with mean age of 63 years), and time-period of study (March–June 2020 *versus* November 2020–June 2021) may explain some of these differences.

The regular use of NSAIDs reported at 77% in current survey is high, and likely indicates ongoing symptoms. A more regular intake of allopurinol since the COVID-19 pandemic compared with pre-COVID-19 was reported by 26% respondents. Overall, 39% respondents were taking their ULT (allopurinol, febuxostat) daily/regularly currently, similar to the 30–55% range reported in previous studies,^{21–23} but lower than 77% in the baseline COVID-19 gout survey.² The low rate of ULT use correlates well with the high rate of gout flares and NSAID use reported in the current survey and is very concerning. This rate of adherence to medications is lower than the 82% of respondents continuing their antirheumatic medications as prescribed in the global rheumatology alliance survey.⁴

Our study has several strengths and limitations. Strengths included a focus on key questions related to gout management during COVID-19. Our survey is at the risk of selection bias due to patient self-selection for participation and skills/resources for Internet use, that is, most likely people with Internet access, computer-literacy, and willingness to respond to a survey likely participated. Therefore, our study findings are generalizable only to gout patients who use the Internet and choose to answer a gout survey. The proportion of survey responders who were of White race/ethnicity was 80%, higher than the proportion of Whites (60%) in the United States, further impacting the generalizability of study findings. Due to the cross-sectional nature of the study, we were unable to determine the direction of associations of psychological distress with gout management. We examined associations, not causation. Non-responder characteristics are not available, due to the anonymized nature of the survey. The self-reported physician-diagnosis of gout used a valid question from population-based surveys by the Centers for Disease Control and Prevention (CDC)²⁴; however, its concordance with a physician-diagnosis of gout in the health record could not be tested. Due to anonymized nature of the survey, we cannot determine if some respondents participated in both baseline and follow-up surveys. For the sake of simplicity, and as a conservative approach, we treated the baseline and follow-up samples as independent. Therefore, our findings of comparison with the baseline survey need to be interpreted very cautiously, as differences we noted may be attributable to sampling differences between our two surveys. No imputation was done for missing data, as decided *a priori*.

In conclusion, we performed a cross-sectional follow-up Internet gout survey to assess the impact of COVID-19 on gout management. More difficulty with gout overall, the management of gout flares, and other aspects of gout were reported by the survey respondents, compared with the respondents' recollections from before the pandemic. Poor gout-specific HRQOL, psychological distress, but high resilience was reported by study participants. We found low rates of ULT use for gout since September 2020, which decreased since the first COVID-19 survey, indicating potential negative impact of the ongoing pandemic. The association of psychological distress with difficulty in getting health care for gout indicates the need for interventions to improve gout management in the ongoing COVID-19 pandemic.

Ethics/IRB approval and consent to participate

The University of Alabama at Birmingham's Institutional Review Board approved this study and all investigations were conducted in conformity with ethical principles of research (UAB X120207004). The IRB waived the need for a signed informed consent for this anonymized study.

Author contribution(s)

Jasvinder A. Singh: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Supervision; Validation; Writing – original draft; Writing – review & editing.

N. Lawrence Edwards: Investigation; Resources; Writing – review & editing.

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Availability of data and materials

These data are available from the authors after permissions have been obtained from the University of Alabama at Birmingham Institutional Review Board and the Gout Education Society (GES).

Supplemental material

Supplemental material for this article is available online.

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