Association between Gout-related characteristics, Level of Aggression and Depression among Individuals with gouty arthritis: a cross-sectional, multi-center study

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Abstract:

The elevated levels of serum uric acid (UA) have been implicated in the development of multiple health problems, including gout. Despite the importance of behavioral changes, there is limited literature to support the relationship between gout-related characteristics and aggressive and depressive behaviors of individuals with gouty arthritis. The study aims to determine the association between gout-related characteristics and severity of aggression and depression among individuals diagnosed with gouty arthritis. This paper utilized an observational, cross-sectional multi-center design. Additionally, the independent variables were gout-related characteristics and dependent variables were aggression and depression levels. Results revealed that from a total of 75 participants, with a mean age of 52.56 (+10.53) recruited for the study, 21 (28%) reported high levels of aggression while 24 (32%) have high level of depression. Using logistic regression (p≤0.05), findings showed that there were significant relationships between gout-related characteristics and aggression and depression. Moreover, gout duration of greater than five years showed association for aggression alone while presence of comorbidities, affectation of two or more joints, and the number of gout attacks showed significant relationship for depression. Clinicians may be confident that these are the characteristics that should be part of the holistic assessment of patients with gouty arthritis.

Keywords: aggression, depression, gouty arthritis, uric acid

INTRODUCTION

Hyperuricemia or elevated levels of uric acid (UA), has been linked with the development of multiple medical conditions, including cardiovascular diseases, metabolic syndrome, and gout (Feig at al., 2008; de Oliveira & Burini, 2012). Among these health problems, gout evidently shows a clinically significant increase in UA levels, resulting in precipitation of sodium urate monohydrate crystals within joints that causes pain and discomfort (Firestein et al., 2012)

Chandratre et al. (2013) examined studies concerning health-related quality of life among gouty arthritis individuals. Pieces of evidence were found between gout and poorer general psychological health especially those with comorbidities and gout characteristics, including frequency of attacks and degree of pain severity in joints. These gout characteristics are essential in determining patients who are more susceptible to psychological sickness. Also, there is a scarcity of studies concerning the prevalence of psychological comorbidities, such as aggression and depression in relation to specific gout characteristics (Prior et al., 2016). Interestingly, recent research evidenced the increased prevalence of depression among gout patients both in the United States secondary care (Khanna, Hagerty, Mischler, & Morlock, 2013) and United Kingdom primary care (Prior et al., 2016). In this light, conducting a similar study in the Philippine setting would be essential to determine similarities and differences in results, considering various influences, such as genetic, cultural, environmental, and dietary factors (Prasad & Krishnan, 2014).

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The primary aim of the study was to explore the association between gout-related characteristics and levels of aggression and depression among adults diagnosed with gouty arthritis. The 12 gout-related characteristics include: Body Mass Index (BMI), history of smoking, history of alcohol drinking, self-reported comorbidities, average gout pain within the past 30 days, number of joints with gout, serum UA levels, number of gout attacks in the last 12 months, gout duration, presence of tophi, family history of gout, and use of gout medications. Specifically, the study seeks to answer the following questions:

1.   What are the levels of aggression and depression of gouty-arthritis individuals?
2.   What is the profile of the participants in the gout-related characteristics?
3.   Which among the gout-related characteristics are predictors of aggression and depression?

METHODOLOGY

This study utilized an observational, cross-sectional design, employing a multi-center approach. The study sought ethical approval from the University of Santo Tomas, Graduate School-Ethics Review Committee (Reference no. GS-2016-PN 382-R1) and University of the Philippines Manila-Ethics Review Board (Reference no. UPMREB 2017-282-01). This cross-sectional study was reported in accordance with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.

Participants were diagnosed patients with gouty arthritis aged greater than 30 years old. They were selected from various healthcare facilities in the city of Manila who can read, write, and follow simple directions in both Filipino and English.

To avoid factors that may affect the results, individuals with a history of clinical depression and aggression prior to gout diagnosis and those handicapped by physical disabilities that negatively affect their ability to receive and follow instructions were excluded. The power calculations to estimate sample size using G*Power 3.1 indicated a need for 75 participants to acquire power = 0.95 at an alpha level of 0.05, using a small effect size of 0.05 for a two-tailed test (Polit & Beck, 2017).

Upon approval of the healthcare facilities, the research procedure was explained and Informed Consent Forms were given. The participants were also informed that they will be referred to a specialist (e.g., psychiatrist/ psychologist) in the nearest facility within the hospital should they feel distress or anxiety.

The socio-demographic profile of the participants was identified, such as age, gender, educational attainment, civil status, and employment status. The gout-related characteristics of the respondents were recorded in terms of lifestyle patterns (e.g. smoking history and alcohol drinking history); body mass index (BMI) by determining the participant's height and weight, self-reported disease-related comorbidities, which was adopted from the Self-Administered Comorbidity Questionnaire (Sangha et al., 2003); and the average gout pain level for the past 30 days, identified through the use of 1–10 Numeric Pain Rating Scale (one to three referred as mild pain, four to six as moderate pain, and seven to ten as severe pain) (Krebs, Carey & Weinberger, 2007). Moreover, this part also included questions pertaining to gout-specific features based on the American College of Rheumatology/ European Union League against Rheumatism Classification Criteria for Gout (Neogi et al., 2015): the number of joints with gout, serum UA level taken within the past 6 months, gout duration, presence of tophi, family history of gout, and use of gout medications.

Permission to use the Buss-Perry Aggression (BPA) Questionnaire and the Patient Health Questionnaire-9 (PHQ-9) was secured from the respective authors of the tools.

The frequency and proportions were used for history of smoking, alcohol drinking, presence of comorbidities, gout duration, history of gout, affected joints, presence of tophi, gout attacks, and use of gout medications. Mean scores and standard deviation values were calculated for aggression, depression, and continuous data, such as Body Mass Index (BMI), gout pain level, and serum UA level. Participants who obtained a score of 66

to 145 were regarded as high aggression, and those who garnered a score of 29 to 65 were deemed as low Aggression (Alves-Ferreira, Costa & Santos, 2012). Univariate analysis using logistic regression was also conducted to determine the association between gout-related characteristics and aggression and depression. The odd-ratio (OR) and its 95% confidence interval (CI) were reported to identify the magnitude and direction of the association. The IBM Social Packages for Social Sciences version 23.0 was employed to analyze the data.

RESULTS

A total of 75 patients diagnosed with gouty arthritis, 25 females and 50 males, were selected in this study, obtaining a mean age of 52.52 and 52.58 years old, respectively. Of the 75 participants with gouty arthritis, 21 (28%) had high levels of aggression and 24 (32%) had high levels of depression. Table 1 shows a summary of the aggression, depression, and gout-related characteristics of participants with gouty arthritis.

Table 1. A comparison of high and low aggression and depression scores of the characteristics of participants with gouty arthritis

Gout-related characteristics	Aggression*			Depression**	
	Low (n=54)	High (n=21)		Low (n=51)	High (n=24)
	Mean (SD) 50.13 (1.14)	Mean (SD) 78.29 (2.46)		Mean (SD) 3.25 (0.34)	Mean (SD) 15.46 (0.68)
Body Mass Index mean (SD)	25.21 (4.74)	25.30 (4.84)		25.71 (4.76)	24.23 (4.78)
Gout pain level mean (SD)	6.52 (2.84)	6.88 (2.79)		6.11 (2.84)	7.71 (2.83)
Serum Uric Acid level mean (SD)	8.53 (2.17)	7.60 (1.75)		8.21 (2.11)	9.43 (1.32)
History of Smoking n (%)	23 (42.59)	13 (61.90)		24 (47.06)	12 (50.00)
History of Alcohol drinking n (%)	36 (66.67)	15 (71.43)		36 (70.59)	15 (62.50)
Presence of comorbidities n (%)	46 (85.19)	18 (85.71)		41 (80.39)	18 (75.00)
Gout duration (>5 years) n (%)	24 (44.24)	3 (14.29)		20 (39.22)	7 (29.17)
Family History of gout n (%)	27 (50.00)	7 (33.33)		26 (50.98)	8 (33.33)

Affected joints (>2 joints) n (%)	42 (77.78)	16 (76.19)	37 (72.55)	21 (87.5)
Presence of Tophi n (%)	23 (42.59)	8 (38.10)	19 (37.25)	12 (50.00)
Gout attacks (>2 attacks) n (%)	45 (83.33)	19 (90.48)	42 (82.35)	22 (91.67)
Use of gout medications n (%)	43 (79.63)	15 (71.43)	39 (76.47)	19 (79.17)

*Aggression based on BPAQ
**Depression based on PHQ-9

Table 1 reveals that most of the participants with low levels of aggression and depression had histories of smoking and alcohol drinking. Furthermore, these participants with low levels of aggression have comorbidities, are experiencing gout for more than five years, and have history of gout in their families. Most also have more than two joints affected, experience more than two attacks in a month, and have tophi and are under medications.

Logistic regression showed associations between the independent and dependent variables. These univariate associations are presented in Table 2.

Table 2. Association between gout-related characteristics and aggression and depression.

Gout-related characteristics	Aggression*				Depression**		
	B-coefficient	OR	p-value		B-coefficient	OR	p-value
Body Mass Index	-0.650 (0.432)	0.522	0.133		-0.431 (0.407)	0.650	0.291
Gout pain level***	**0.233 (0.473)**	**1.263**	**0.013**		**0.466 (0.459)**	**1.593**	**0.032**
Serum Uric Acid level***	**-0.912 (0.691)**	**0.402**	**0.018**		**-0.597 (0.717)**	**0.550**	**0.045**
History of Smoking	-1.059 (0.693)	0.347	0.126		-0.432 (0.632)	0.649	0.495

History of Alcohol drinking	0.465 (0.763)	1.592	0.542		0.598 (0.680)	1.818	0.379
Presence of comorbidities	-0.345 (0.454)	0.708	0.448		**-0.046 (0.418)**	**0.955**	**0.020**
Gout duration (>5 years) ***	**-1.412 (0.757)**	**0.244**	**0.022**		-0.755 (0.646)	0.470	0.243
Family History of gout	0.517 (0.620)	1.677	0.405		0.356 (0.589)	1.428	0.545
Affected joints (>2 joints) ***	-0.006 (0.397)	0.994	0.987		**0.578 (0.411)**	**1.782**	**0.016**
Presence of Tophi	-0.279 (0.661)	0.757	0.673		-0.374 (0.629)	0.688	0.552
Gout attacks (>2 attacks) ***	0.286 (0.473)	1.331	0.546		**0.393 (0.468)**	**1.481**	**0.029**
Use of gout medications	-0.110 (0.486)	0.896	0.821		-0.043 (0.491)	0.958	0.930

*Aggression: Low= 29-65, High=66-145 based on BPAQ.
**Depression: Low= 0-10, High=11- 27 based on PHQ-9;
***mean value; Bold-significant at p≤0.05, OR= Odds Ratio

Results indicate that the average gout pain level (p=0.013) and serum UA (p=0.018) were significantly associated with aggression and depression among patients with gouty arthritis. Only gout duration (0.022) was significantly associated with aggression. On the other hand, self-reported comorbidities (p=0.020), number of joints with gout (p=0.016), and number of gout attacks (p=0.029) were more significantly associated with depression.

DISCUSSION

An observational, cross-sectional design was utilized in this study to address the research questions and match the objectives with the methodology. Mann (2003) claimed that through this design, prevalence and relationships between variables will be determined. The findings were then utilized to explain results from other similar research findings, and it helped address further studies (Hackshaw, 2014). The advantage of conducting this design was that the participants did not undergo any experimental treatment; thus, ethical difficulties were minimal. Also, only a single group was used, which means that the data were collected only once, and multiple outcomes could be studied (Mann, 2003). Furthermore, employing a multicenter approach in this kind of observational clinical research was beneficial for a better generalizability of the results, a larger sample size, and consequently, having an improved efficiency (Sprague, Matta, Bhandari & Anterior Total Hip Arthroplasty Collaborative Investigators, 2009).

In this study, gout-related characteristics and their association with aggression and depression level were better determined through cross-sectional, multi-center design, as it yielded a broad scope and accurate results.

This study highlighted the importance of the association of gout-related characteristics with aggression and depression levels among individuals with gouty arthritis. Significant relationships were found in gout pain and serum UA level for both aggression and depression. Moreover, gout duration of greater than five years showed association for aggression alone while presence of comorbidities, affectation of two or more joints, and the number of gout attacks showed a significant relationship with depression.

The results of this study concurred with other studies that stating that UA levels have a direct relationship with aggression (Lorenzi et al., 2010). The impairment of the purinergic system, which is common among gout patients, has been linked in the neurobiology of aggressive behavior (Lara et al., 2000). In the purinergic system, the metabolites and the associated purinergic receptors of the purine nucleotides and nucleosides including adenosine triphosphate (ATP), uridine triphosphate (UTP), and guanosine triphosphate (GTP), signal molecules to regulate cell to cell communication (Ulrich et al., 2012). Results further revealed a link between purinergic mechanisms or specific receptor subtypes and the facilitating aspects of mood and behavior. Thus, purinergic dysfunction can be speculated as the mechanism-based justification, which lead to an altered behaviour, such as impulsivity, aggression, locomotor activity changes, and sleep pattern disturbance, and mood (Ortiz et al., 2015).

Hyperuricemia also plays a major role in the linkage of gout-related characteristics and depression. The pain and discomfort in affected joints and frequency of gout attacks also contribute to a state of emotional distress, disability, and depression, as indicated in the multistage model of cognition, disability, and affect (Pincus & Williams, 1999). Given that gout-related characteristics and comorbidities contribute to poor health-related quality of life (Chandratre et al., 2013; Scirè, 2013), depression occurs with these individuals, who require close monitoring and assistance to cope with their suffering (Kang et al., 2015).

Results from this study were also consistent with the pathophysiology of the gout condition. As the serum UA level increases and physiological saturation exceeds, the threshold for UA in body fluids may lead to the formation and deposition of monosodium urate crystals, which occurs in and around joints, causing acute attacks of severe pain and inflammation (Roddy & Doherty, 2010). As depicted in the General Aggression Model, these situational factors, such as pain and discomfort due to gout duration, influence the aggression level of an individual (Anderson & Bushman, 2002).

One of the limitations of this study was the statistical treatment used. Multivariate logistic regression analysis may be employed to further generalize the data and to avoid confounding effects by analyzing the association of all variables together (Sperandei, 2014).

Clinically, determining these behavioral changes is important among health professional members, such as doctors, nurses, health psychologists, and physical therapists, since this would serve as a basis in the implementation of an effective approach on psychotherapeutic intervention and rehabilitation. These significant associations may also be considered as predictors of aggressive and depressive behaviors, which validates the necessity to address the biopsychosocial aspects in future studies.

Future researchers may also analyze other gout-related characteristics, such as the number of swollen and tender joints; and the socio-demographic variables, such as social stratification (upper, middle and lower classes), in order to have an in-depth correlation and evaluation of the level of behavioral symptoms affected by these factors. A larger sample size, considering the developmental age groups of the participants and focusing on participants with high aggression level and high depression level would be beneficial to ensure a greater degree of precision, representativeness of the population , and the generalizability of results. Lastly, future researchers may also design a psychotherapeutic prevention program for gout patients based on the results of the study in order to improve the quality of care provided by healthcare professionals, such as educating them about the nature of gout and how to prevent its occurrence.

CONCLUSION

Findings revealed that there were significant relationships between the aggression and gout-related characteristics, particularly the average gout pain level, gout duration and serum uric acid (UA) levels. Clinicians can be confident that these are the characteristics that should be part of the holistic assessment of patients with gouty arthritis. However, caution should be made in interpreting the results of the study given the limitation. The significant relationship between the depression and gout-related characteristics, such as self-reported comorbidities, average gout pain level, serum UA, number of joints with gout, and number of gout attacks, should be highlighted in the implementation of psychotherapeutic intervention. Therefore, allied health professionals should also take into account that high levels of aggression and depression among individuals with gouty arthritis are associated with gout-related characteristics.

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DISCLOSURE

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