



HYPERURICEMIA IN FEMALE POPULATION AND ITS RELATION WITH AGE, MENOPAUSE, OBESITY, OSTEOARTHRITIS AND DIETARY HABITS

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ABSTRACT

Background: Hyperuricemia in females is often misdiagnosed thinking that it is a clinical entity common among males. In this study we want to report that hyperuricemia is also on increasing trend in the female population in relation to diet and age.

Material and methods: Serum uric acid levels of 47 patients that presented with joint pain to our OPD between February 2017 to February 2018 was tested. Other inflammatory arthritic conditions were ruled out. The correlation with age and other factors were then seen.

Results: Correlation of uric acid with other variables was done and it was found that age and menopause had a strong correlation with uric acid using Spearman's Rho of .709 ($p < 0.01$) and .755 ($p < 0.05$) respectively.

Conclusion: Hyperuricemia is a common problem misdiagnosed in females and is seen to increase significantly with age and in post menopausal period.

KEYWORDS :Hyperuricemia, age, post menopausal, high protein diet

INTRODUCTION

Gout/ Hyperuricemia is one of the most common reason leading to joint pain which predominantly attacks males. We have seen that hyperuricemia in females is the one of the most under diagnosed reason for joint pain in females.

The clinical disorder was known to Hippocrates and its association with hyperuricemia was recognized well over 100 years ago.¹One important difference between women and men with gout is the change in urate levels that occurs in women after menopause.²Gout is a frequent form of arthritis, presenting as a severe and painful inflammatory arthritis, mostly of the first metatarsophalangeal joint (podagra). It occurs suddenly, and in most patients it disappears completely within 5 to 14 days.³

Physiological daily amount of endogenous and exogenous uric acid is about 700 mg, which is balanced by an equal output via faeces and urine. As previously stated, 30% of uric acid is broken down by intestinal flora and expelled through the stool, while the remaining 70% (approximately 500 mg per day) is excreted unchanged through the kidneys.⁴

Gout is not rare in women. Although women comprise approximately 5% of all gout patients, the incidence has risen. According to Arromdee et al, the incidence of gout in men and women has doubled over the past 20 years.²

MATERIAL AND METHODS:

The study was conducted in the department of Orthopaedics, Central Referral Hospital, Sikkim during a period of 12 months i.e. from Feb 2017 to Feb 2018. The aim of the study was to see the occurrence of hyperuricemia in the hilly areas of Sikkim especially in female population and its correlation with age, menopause, pre-existing osteoarthritis, obesity and high protein intake. All patients who presented in the Orthopaedic department OPD with complaint of large joint pain was asked about the duration of the pain, dietary habits and whether they have attained menopause or not. Skiagram of the Knee joint was taken and empty stomach morning sample of blood for serum uric acid levels was sent for investigation. BMI was calculated to measure obesity. All other causes of inflammatory arthritis were ruled out before including them in the study.

The reference values were taken from the kit (Uric Acid Reagent, Uricase- POD) which is being used in Central Referral Hospital, Sikkim. The expected values for Adult males are 3.5 -7.2 mg/dl and females are 2.6-6.0mg/dl. The instrument used for analysis is EM-200

Auto analyzer and the calibration is being done on daily basis.

Statistical analysis: Descriptive statistics for demographic data was done using Spearman's Rank Correlation Coefficient to find out the correlation between uric acid and other variables

RESULTS:

In the present study, the average age was found to be 51.06 ± 17.17 and uric acid was 8.56 ± 2.91 (Table 1). Correlation of uric acid with other variables was done and was found that age and menopause had a strong correlation with uric acid with Spearman's Rho of .709 ($p < 0.01$) and .755 ($p < 0.05$) respectively. Correlation with other variables is shown in Table 2.

Table 1. Descriptive statistics for Age and Uric Acid

Variable	Mean	SD
Age	51.06	17.174
Uric Acid	8.56	2.91

Table 2. Correlation of Uric acid with other variables

Variable	Age	Osteoarthritis	Obesity
Uric acid	.709**	.428**	.566**
Level of Significance	.004	.003	.001

Variable	Alcohol with high protein diet	Menopause
Uric acid	.408**	.755*
Level of significance	.004	.014

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION:

Clinically, gout is often considered a preferential male disease. The condition is more common in men than in women. In women, it mainly becomes manifest in the postmenopausal period. Hippocrates was the first who stated that it was a sex-related disease. Among patients younger than 65 years, men have a fourfold greater prevalence than women.²

In several studies, the mean age at diagnosis of gout was 7-12 years greater in women than in men.^{6,7,8,9,10} In patients older than 60 years with newly diagnosed gout, approximately half were women. The incidence of females with gout peaks at age 80 years and older.²

The difference in age between men and women at the onset of gout is remarkable. After menopause, the incidence of gout is high compared to the reproductive age.^{6,9,11,12} Kim et al. suggested a possible role of 17-

beta-estradiol in the regulation of purine biosynthesis and uric acid metabolism and lowered serum urate.¹³ Also, Hak et al. found in a recent large prospective study that menopause increases the risk of gout.¹⁴

Pui et al. found further evidence of the role of estrogens in regulating serum uric acid, they found early onset hyperuricemia and gout following hormone treatment given for the purpose of female to male gender reassignment.¹⁵ Estrogen may enhance renal uric acid excretion. During gender reassignment, testosterone treatment likely dampens the effect of estrogen, and causes increased serum urate concentrations by reducing renal excretion of uric acid.²

A widely observed association in female gout is the presence of pre-existing joint disease, in particular, osteoarthritis (OA). Ally et al. found pre-existing joint disease in 70% of women and in only 37% of men. Similarly, Puiget et al. reported 76% of women with gout had OA compared to 40% of men.⁹ The latter study also found a relationship between nodal OA and mono- sodium urate crystal deposition in women with gout and nodal disease in the hands. The presentation of acute or subacute gout in the fingers of a woman with nodal OA may contribute to a delayed or incorrect diagnosis.²

Several articles on risk factors for hyperuricemia and gout have noted the association of obesity and alcohol consumption; however, these associations are not as strong in women as they are in men. Puig reported the incidence of obesity seen in his gout population was approximately 10% less in women, compared with the men in the study. And, in the comparison between women and men with gouty arthritis in Lally's study, that less than 9% of the women had associated alcoholism, compared to 45% of men.²

As already mentioned, hyperuricemia (both with and without urate deposition) and metabolic syndrome (defined as the coexistence of abnormal blood pressure, visceral obesity, dyslipidemia, and dysglycemia) are strongly associated.⁴

Study findings have indicated that heart disease, diabetes, hypertension, hyperuricemia, obesity, renal disease including renal insufficiency, elevated triglyceride and cholesterol levels, menopause, surgery, and elevated creatinine levels were all associated with the risk of gout.

Hyperuricemia is perhaps the most common and well-studied risk factor for developing gout; it is also one of the causal pathways of gout, so some may argue that it is the common channel to gout and, therefore, not a risk factor. Hypertension was consistently associated with higher risk of incident gout and more flares in those with prevalent gout. Higher body mass index was a risk factor for gout and overweight and obese patients were at significantly higher risk of incident gout.²⁶

Uric acid is the final product of purine nucleotide catabolism. In particular, purine nucleotides are derived from both endogenous (de novo molecule synthesis and nucleic acid breakdown) and exogenous sources (alimentary intake).¹⁶⁻¹⁸

Hyperuricemia is a very common condition, being usually caused by an unhealthy lifestyle that is mainly represented by a poor diet exceeding in purine nucleotides, protein, alcohol, and carbohydrates intake.¹⁶⁻²¹

In a study, Choi et al. (2004) showed that increasing alcohol intake is associated with higher risk of incident gout,²² similar to findings from other studies.²³⁻²⁵ The consumption of hard liquor, or having the equivalent of one shot per day, was also significantly associated with the risk of gout. Consumption of beer, but not wine, was significantly associated with incident gout.²² Thus, the risk of developing gout varies greatly and is dependent on the type and amount of the alcoholic beverage that is consumed.²⁶

Choi et al. reported that consumption of two or more sugar sweetened soft drinks a day was strongly associated with an increased risk of gout in men (RR=1.85, 95% CI: 1.08–3.16).²⁷ Moreover, it was also found that those fruits which are high in fructose, as well as fruit juices are also a contributing factor to an increased risk of gout in men.²⁷

Choi et al. found that increasing daily servings of meat and seafood were associated with significantly increased risk of incident gout, while dairy products were protective.²²

In one study, greater intake of fruits was associated with significantly lower risk of incident gout,²⁸ while in another study consumption of an apple or orange a day or more was associated with higher risk of incident gout with relative risk of 1.64 [95% CI: 1.05–2.56], compared to those with <1 apple or orange /day.²⁷

One study indicated that intake of folate was associated with lower risk of incident gout,²⁵ while higher intake of total Vitamin C was associated with lower risk of incident gout in two studies.^{25,29}

CONCLUSION

We have always seen that hyperuricemia is common in the male population leaving us to misdiagnose females coming to us with joint pain. In our study we have seen that it definitely does not occur only in males. We conclude that Hyperuricemia is common in females but it shows that the onset is in later part of life especially after reaching menopause, with a weak relation to dietary habits.

REFERENCES:

- Louis Solomon. Crystal deposition disorders. In :Apley's and Solomon, editors. Apley's System of Orthopaedics and Fractures. 9th ed. London: Butterworth-Heinemann, 2010. p.77-80.
- McClory J, Said N, MD. Gout In Women. Medicine and Health/Rhode island. Nov 2009; 92 : 363-68.
- Dirken-Heukensfeldt KJMJ, Teunissen TAM, Van de Lisdonk EH, Lagro-Janssen ALM . Clinical features of women with gout arthritis: A systematic review. Clin Rheumatol. 2010; 29:575–582.
- Grassi D, Ferri L, Desideri G, et al. Chronic Hyperuricemia, Uric Acid Deposit and Cardiovascular Risk. Current Pharmaceutical Design. 2013; 19: 2432-2438.
- Wallace KL, Riedel AA, Joseph-Ridge N, Wortmann R. Increasing prevalence of gout and hyperuricemia over 10 years among older adults in a managed care population. J Rheumatol. 2004; 31(8):1582–87.
- Lally EV, Ho Jr G, Kaplan SR. The clinical spectrum of gouty arthritis in women. Arch Intern Med 1986; 146:2221-5.
- De Souza AWS, Fernandes V, Ferrari AJL. Female gout. J Rheumatol. 2005; 32:2186–8.
- Harrold LR, Yood RA, et al. Sex differences in gout epidemiology. Ann Rheum Dis. 2006;65:1368-72.
- Puig JG, Michan AD, et al. Female gout. Arch Intern Med. 1991; 151:726-32.
- Meyers OL, Monteagudo FS. A comparison of gout in men and women. Safr Med J. 1986; 70:721-3.
- Deesomchok U, Tumrasvin T. A clinical comparison of females and males with gouty arthritis. J Med Assoc Thai. 1989; 72(9):510–15
- Chang SJ, Chen CJ, Hung HP, Ou TT, Ko YC. (2004)Community-based study in Taiwan aborigines concerning renal dysfunction in gout patients. Scand J Rheumatol. 2004; 33(4):233–38
- Kim KY, Schumacher HR, Hunsche E, Wertheimer A, Kong S. A literature review of epidemiology and treatment in acute gout. Clin Ther. 2003;25:1593–1617
- Hak AE, Curhan G, Grodstein FD, Choi HK. (2009) Menopause, postmenopausal hormone use and risk of incident gout. Ann Rheum Dis. 2009; 1: 109884
- Pui K, Waddell C, Dalbeth N. Early onset of hyperuricaemia and gout following treatment for female to male gender reassignment. Rheumatol (Oxford). 2008;47:1840-1.
- Richette P, Bardin T. Gout. Lancet. 2010; 375 (9711): 318-28.
- Choi HK, Mount DB, Reginato AM. Pathogenesis of gout. Ann Intern Med. 2005; 143: 499-516.
- Johnson RJ, Rideout BA. Uric acid and diet - insights into the epidemic of cardiovascular disease. N Engl J Med. 2004; 350:1071-4.
- Eggebeen AT. Gout: an update. Am Fam Physician. 2007; 76(6):801-8.
- Wu XW, Lee CC, Muzny DM, Caskey CT. Urate oxidase: primary structure and evolutionary implications. Proc Natl Acad Sci USA. 1989; 86: 9412-6.
- Eggebeen AT. Gout: an update. Am Fam Physician. 2007; 76(6):801-8.
- Choi HK, Atkinson K, Karlson EW, Willett W, Curhan G. Alcohol intake and risk of incident gout in men: a prospective study. Lancet. 2004 Apr 17;363(9417):1277–1281.
- Lin KC, Lin HY, Chou P. The interaction between uric acid level and other risk factors on the development of gout among asymptomatic hyperuricemic men in a prospective study. J Rheumatol. 2000 Jun; 27(6):1501–1505.
- Lin KC, Lin HY, Chou P. Community based epidemiological study on hyperuricemia and gout in Kin-Hu, Kinmen. J Rheumatol. 2000 Apr; 27(4):1045–1050.
- Lyu L-C, Hsu C-Y, Yeh C-Y, Lee M-S, Huang S-H, Chen C-L. A case-control study of the association of diet and obesity with gout in Taiwan. Am J Clin Nutr. 2003 Oct; 78(4):690–701.
- Singh JA, Reddy SG, Kundukulam J. Risk Factors for Gout and Prevention: A Systematic Review of the Literature. Curr Opin Rheumatol. 2011 March ;23(2): 192-202.
- Choi HK, Curhan G. Soft drinks, fructose consumption, and the risk of gout in men: prospective cohort study. Bmj. 2008 Feb 9; 336(7639):309–312.
- Williams PT. Effects of diet, physical activity and performance, and body weight on incident gout in ostensibly healthy, vigorously active men. Am J Clin Nutr. 2008 May; 87(5):1480–1487.
- Choi HK, Gao X, Curhan G. Vitamin C intake and the risk of gout in men: a prospective study. Arch Intern Med. 2009 Mar 9; 169(5):502–507.