

## Differences The Incidence of Hyperuricemia in Families with Gouty Arthritis and Families Without Gouty Arthritis in Buleleng Regional General Hospital, Bali, Indonesian

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### ABSTRACT

**Keywords:**

Hyperuricemia, Gouty Arthritis, History of gout.

The most common manifestation of hyperuricemia is gout. Hyperuricemia is the leading cause of gout. It is about five times more common than gout. The heritability of hyperuricemia and gout is about 73%, and 40-50% of patients have a family history of gout. Indonesia, especially Bali, has a high prevalence of hyperuricemia in families with gout at 26.6%. Therefore, we performed this study to look for differences in the incidence of hyperuricemia in families with gouty arthritis and families without gouty arthritis.

In an unpaired case-control study, which is the target population is Balinese, the target population is Balinese individuals with gouty arthritis who come to the Internal Medicine Polyclinic of Buleleng Regional General Hospital. The controls in this study were Balinese individuals without gouty arthritis; there were 41 samples who made a pedigree and checked serum uric acid at one time. Of the total 41 case-control samples used, the incidence of hyperuricemia in families with gouty arthritis is 65.9%, and in families without gouty arthritis, is 29.3%, with an Odd Ratio (OR) value of 2.25 with a 95% confidence interval, p-value = 0.002. There were differences in hyperuricemia incidence in families with gouty arthritis and families without gouty arthritis, with a p-value = 0.002. Hyperuricemia in families with gouty arthritis is 2.25 times (OR) higher than in families without gouty arthritis.



### Introduction

Hyperuricemia is an elevated serum uric acid level, usually greater than 6 mg/dL in women and 7 mg/dL in men. Hyperuricemia results from increased uric acid production, decreased excretion, or a combination of both processes<sup>10</sup> (Topolyanskaya, Vakulenko, Semashkova, Kupina, & Dvoretzkiy, 2020). Previously, hyperuricemia was more prevalent in developed countries than in developing countries. The prevalence of hyperuricemia in the US was 21.4%; in Bangladesh, the prevalence was 9.3% (men vs women; 8.4% vs 10.2%). However, this presented the fact that hyperuricemia was also

common not only in advanced countries but also in developing countries. However, there was no actual prevalence of hyperuricemia in Indonesia. Several studies were conducted in urban areas of Indonesia. In Depok City, West Java, the prevalence of hyperuricemia was 18.6%, while in Bali, the prevalence was 18.2%<sup>7</sup> (Dewi & Rini, 2020).

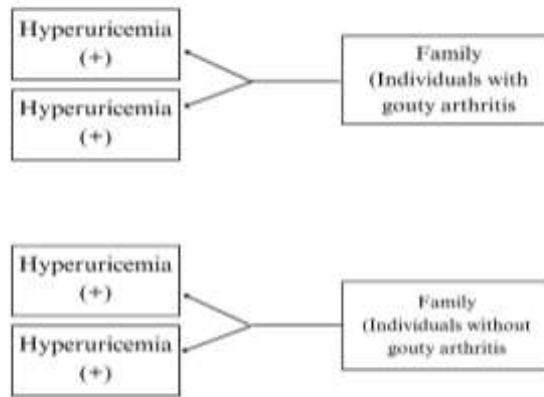
The most common manifestation of hyperuricemia is gout<sup>10</sup>. Gout is the most common inflammatory joint disease, impacting morbidity and premature mortality (Nian & You, 2022). The disease is heritable, as suggested by familial clustering of the disease; however, the existence of many known risk factors, such as male gender, increasing age, obesity, chronic renal impairment, hypertension, long-term use of diuretics and specific diets with high purine and alcohol, also supports a strong environmental contribution<sup>8</sup> (ERWIN, 2021). Whatever the cause, the result is elevated serum uric acid, which in some patients ultimately causes clinical gout<sup>9</sup>. Hyperuricemia is the leading cause of gout; it is about five times more common than gout, affecting 43.3 million (21.4%) U.S. 6. Adults people with higher serum urate levels are at an increased risk for incident gout. They will also have more frequent flare-ups over time<sup>6,10</sup> (Usman, Darmawan, Hamijoyo, & Wachjudi, 2019).

The heritability of hyperuricemia and gout is about 73%, and 40-50% of patients have a family history of gout<sup>9</sup> (Firsty & Putri, 2021). High heritability of hyperuricaemia, the main driver of urate crystal deposition and the development of gout, has led to efforts to identify susceptibility genes<sup>8</sup>. Several replicated loci are for genes encoding renal urate transporters or related proteins, whereas others may be involved in metabolic pathways<sup>6</sup> (Kuo et al., 2015).

Indonesia, especially Bali, has a high prevalence of hyperuricemia in families with gout at 26.6%. In previous studies in Bali, there was a high prevalence of hyperuricemia in families with a history of gout, particularly among men<sup>12</sup> (Sety, 2018). From the literature which states that hyperuricemia is the leading cause of gouty arthritis and the role of genes and family history influences gouty arthritis, it is estimated that there are differences in the incidence of hyperuricemia in families with gouty arthritis and families without gouty arthritis.

## Research Methods

The research design used an unpaired case-control, the target population of Balinese individuals with gouty arthritis who come to the Internal Medicine Polyclinic of Buleleng Regional General Hospital. The controls in this study were Balinese individuals without gouty arthritis. Research to look for differences in the incidence of hyperuricemia in families with gouty arthritis and families without gouty arthritis.

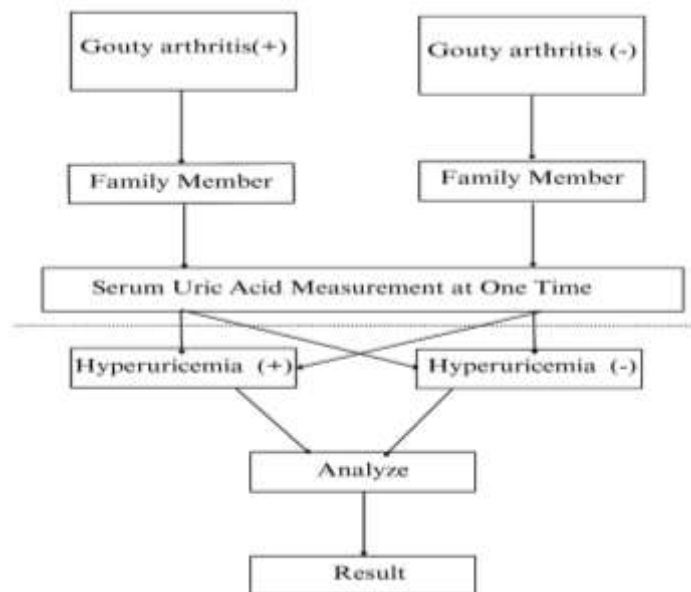


**Figure 1 The flow of sampling**

Sample selection using consecutive random sampling, sample size using the formula:

$$n_1 = n_2 = \frac{(z_{\alpha} \sqrt{2PQ} + z_{\beta} \sqrt{(P_1Q_1 + P_2Q_2)})^2}{(P_1 - P_2)^2} = 41 \text{ sample}$$

The research procedure is that individuals with gouty arthritis are made pedigree with identity data and addresses of family members, giving informed consent, and checking serum uric acid at once. The same procedure was also carried out on family members of individuals without gouty arthritis. Hyperuricemia was defined as serum uric acid  $\geq 7$  mg/dL for male subjects and  $\geq 6$  mg/dL for female subjects. Results were analyzed using the Statistical Program for Social Science (SPSS), and the data will be presented in a figure.



**Figure 2 Schematic of Research**

## Results and Discussion

Of the total 41 case-control samples used, the results of the incidence of hyperuricemia in families with gouty arthritis were 27 people (65.9%), and as many as 14 people (34.1%) did not experience hyperuricemia. Individuals with families without gouty arthritis experienced hyperuricemia in as many as 12 people (29.3%), and those who did not experience hyperuricemia in 29 people (70.7%). The incidence of hyperuricemia in families with gouty arthritis is 65.9%, and in families without gouty arthritis is 29.3%, with an Odd Ratio (OR) value of 2.25 with a 95% confidence interval, p-value = 0.002, which is statistically significant (Hati, 2022).

**Table 1**  
**Results of the analyzed differences in the incidence of hyperuricemia in families with gouty arthritis and families without gouty arthritis.**

	Hyperuricemia (+)	Hyperuricemia (-)	Total	P
Family With Gouty Arthritis	27 (65,9%)	14 (34,1%)	41 (100%)	0,002
Family Without Gouty Arthritis	12 (29,3%)	29 (70,7%)	41 (100%)	
Total	39 (47,6%)	43 (52,4%)	82 (100%)	

Gout is a common disease caused by purine metabolism disorder, primarily caused by the accumulation of uric acid crystals in joints and other tissues<sup>9</sup>. The occurrence of gout is often significantly correlated with the increase in serum uric acid levels. Genetic factors can contribute to the high prevalence of hyperuricemia in certain ethnic groups. Gout can be suffered due to genetic factors<sup>4,5</sup>. The history of gout in one's family tree can be a risk factor for gout. Gout is caused by genetics called primary gout. This is because the gene factor derived from parents who also suffer from gout is genetically inherited from its predecessor (MAUPE, 2019). Genetic factors in patients with gout usually begin with a disorder of purine metabolism, which causes excessive gout in the blood<sup>3</sup>.

Genes associated with gout fall into four categories: production of uric acid, reabsorption of uric acid in renal tubule, excretion of uric acid in renal tubule, and others<sup>9</sup>. Several common genetic variants are associated with serum urate and gout genome-wide association studies, such as SLC2A9, ABCG2, SLC22A12, GCKR, and PDZK1, among

others<sup>5</sup>. Therefore, genetic variants associated with serum urate levels require testing for association with gout, preferably in sample sets where gout is ascertained by the American Rheumatology Association clinical classification criteria or the gold-standard method of microscopic demonstration of MSU crystals<sup>4</sup>. The result of this study is that the incidence of hyperuricemia in families with gouty arthritis is 65.9%, and in families without gouty arthritis is 29.3%. A study in Northern Sulawesi, Indonesia, presented that genetics is considered as one of the prominent risk factors (OR 14.42 (8.01–26.23)  $p < 0.0001$ ). Another heritability analytical study for hyperuricemia and gout showed that hyperuricemia had more vital genetic traits than gout (UTAMA, 2021). The concordance of hyperuricemia was 53% in monozygotic twin pairs and 24% in dizygotic twin pairs ( $p < 0.001$ )<sup>3</sup>. Based on a survey by Feti Kumala Dewi (2020), there was a relationship between genetic and gout arthritis with chi-square results  $p = 0.0029$ . Research by Mei Fransyah (2021) the results showed that of the 40 respondents who suffered from Gout Arthritis, the majority of respondents who had family members who suffered from Gout Arthritis were 26 people (65.5%), and those who did not have family members who suffered from Gout Arthritis were 14 people (35.0%)<sup>3</sup>. From the results of the research obtained, researchers assume that gout arthritis sufferers are more dominant in families who have gouty arthritis because gout arthritis can be inherited from the genes of the patient's family<sup>13</sup>. The risk of gout is increased more by having affected first-degree relatives than by having affected second-degree relatives, and it appears 'dose-dependent' in that the risk increases with the number of affected relatives. These results confirm the long-held belief that gout clusters within families and supports an essential contribution of common familial factors in predisposing to the development of gout<sup>8</sup>.

In addition to the genetic factors outlined herein, several environmental risk factors contribute to the development of gout, including high intake of purine-rich beverages such as beer, purine-rich foods such as red meat and seafood, and sugar-sweetened beverages, including those sweetened with high-fructose corn syrup<sup>1,2</sup>. These dietary factors lead to increased purine synthesis through the hepatic salvage pathways, leading to increased urate production. High circulating insulin levels in individuals with metabolic syndrome also promote renal underexcretion of uric acid. Diuretic agents are a further meaningful environmental; acute urate increases accompanying therapies such as diuretics may also increase flare risk<sup>4</sup>.

This study regarding differences in the incidence of hyperuricemia in families with gouty arthritis and families without gouty arthritis has some limitations; we only measured serum uric acid at a given point in time. In contrast, the serum uric acid level in the body may fluctuate over hours. Transient hyperuricemia sometimes occurs in healthy individuals<sup>11</sup>; the authors did not examine other family risk factors that could affect the incidence of hyperuricemia or gouty arthritis.

## Conclusion

The study results showed differences in the incidence of hyperuricemia in families with gouty arthritis and families without gouty arthritis with  $p$ -value = 0.002.

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Hyperuricemia in families with gouty arthritis is 2.25 times (OR) higher than in families without gouty arthritis.

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