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Types of hyperuricemia in Toraja tribe: A cross-sectional study

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Abstract. *Background and aim:* The study investigates the incidence and types of hyperuricemia among the Toraja ethnic group. It aims to understand the relationship between their dietary habits and the risk factors associated with hyperuricemia. *Methods:* This research employed a cross-sectional design, collecting primary data through random uric acid level examinations and history taking in Makassar, Indonesia. We classified hyperuricemia into overproduction, underexcretion, or a combination of both. *Results:* Most participants were male (59%) and predominantly aged around 40 years, with most having good nutritional status. The most common type of hyperuricemia identified in the Toraja population was underexcretion. *Conclusions:* The findings of this study indicate that the most common type of hyperuricemia among the Toraja population is the under-excretion type. This suggests that most individuals in this population have difficulty excreting uric acid, which a purine-rich diet, such as red meat and alcoholic beverages, may influence. These findings highlight the importance of understanding dietary and lifestyle factors that contribute to elevated uric acid levels and the need for special attention to the health of the Toraja community.

Key words: Hyperuricemia, uric acid, underexcretion, overproduction

Introduction

Tana Toraja is one of the areas in South Sulawesi Province in Indonesia which has a unique culture, one of which is the funeral ceremony. The funeral ceremony of the Toraja tribe involves the slaughter of buffalo and the consumption of buffalo meat in relatively large quantities which has become part of the culture and customs in Tana Toraja (1). Apart from that, the Toraja people are also accustomed to consuming palm wine, a traditional Toraja alcoholic drink, which is also It has become part of the habits and culture of the Torajan people in welcoming guests and in various traditional ceremonies and in everyday life. Tuak is one of the honorary drinks in Toraja. Meanwhile, the habit of consuming foods high in purine and alcohol is a risk factor for hyperuricemia (2).

Hyperuricemia is a condition in which uric acid levels in the blood exceed the normal threshold of 6.8 mg/dL. At uric acid levels above 7 mg/dL, the risk of symptoms related to uric acid increases, and this condition can be diagnosed by measuring blood uric acid levels and urinary excretion, with excretion limits of over 800 mg/dL per day for men and over 750 mg/dL per day for women (3). This condition is quite common, with approximately 8.9% to 24.4% of the global population experiencing hyperuricemia (4).

Uric acid metabolism in the body involves the breakdown of adenosine monophosphate (AMP) and guanosine monophosphate (GMP), which are converted into hypoxanthine by the enzyme xanthine oxidase. The elimination process of uric acid primarily occurs through the kidneys and gastrointestinal system, with about two-thirds of uric acid excreted

by the kidneys (5). Initial filtration takes place in the glomerulus, where most of the uric acid is reabsorbed back into the bloodstream, with the remainder excreted in the urine. Under normal conditions, uric acid metabolism remains constant at a range of 300–400 mg per day. However, certain conditions, such as malignancy, enzyme disorders, or a diet high in purines, can increase uric acid production. Hyperuricemia may also occur due to decreased uric acid excretion, which is triggered by conditions like diabetes, renal insufficiency, and dehydration (6).

There are three main types of hyperuricemia: overproduction, underexcretion, and mixed. These types are categorized based on serum uric acid levels and 24-hour urine excretion. If urine uric acid levels are <600 mg/dL on a purine-free diet, hyperuricemia of the underexcretion type can be diagnosed, whereas levels >1000 mg/dL indicate overproduction. Additionally, on a regular diet, 24-hour urine uric acid levels <800 mg/dL suggest underexcretion, while levels >1000 mg/dL indicate overproduction. Mixed-type hyperuricemia is identified if urine uric acid levels are >1000 mg/dL with a fractional excretion of uric acid (FEUA) <50%. Hyperuricemia often presents without clinical symptoms but can develop into gouty arthritis in the joints and nephrolithiasis in the kidneys (7).

The study investigates the incidence and types of hyperuricemia among the Toraja ethnic group, aiming to understand the relationship between their dietary habits and the risk factors associated with hyperuricemia.

Materials and methods

This study uses a descriptive observational design to describe the incidence rate and types of hyperuricemia in the Toraja tribe. The research was conducted in Makassar city, South Sulawesi, beginning in August 2023 until completion. The target population of the study is adult Toraja residents living in Makassar city.

The study sample was selected from subjects who met the inclusion criteria, adults aged 18 years and older with serum uric acid levels above 7 mg/dL for men and above 6 mg/dL for women. Exclusion criteria included individuals with malignancies, kidney disorders, metabolic diseases, or those taking medications that affect uric acid excretion. All participants were interviewed using a questionnaire to collect clinical characteristics and demographic data. The patients have given their written informed consent on admission to use their prospective data base and files for research work. This study was approved by the Ethics Committee of the Faculty of Medicine, Hasanuddin University (615/UN4.6.4.5.31/PP36/2024.), on August 13, 2024.

Hyperuricemia

Hyperuricemia is an increase in uric acid level in the blood of more than 7 mg/dL.

Classification of hyperuricemia

It is an increase in uric acid level caused by excessive production (overproduction), decreased uric acid excretion (underexcretion), or a combination of both. Measurement of the uric acid to creatinine ratio in the first-morning urine. The classification results for underexcretion (uric acid to creatinine ratio in urine < 0.342), overproduction (uric acid to creatinine ratio in urine > 0.63), and mixed (uric acid to creatinine ratio in urine 0.3.63).

Laboratory examination

Serum uric acid is measured with the ABX Pentra Uric Acid CP reagent with Catalog No. A11A01670. Urine uric acid is measured with Roche Cobas C501 (Roche Diagnostic GmbH, Mannheim, German) with a reagent Roche Cobas Integra (Roche Diagnostic GmbH, Mannheim, German) Catalog number 03183807190. Urine creatinine is measured with Roche Cobas C501 (Roche Diagnostic GmbH, Mannheim, German) with a reagent Roche Cobas Integra (Roche Diagnostic GmbH, Mannheim, German) Catalog number 03263991190. Serum creatinine is measured with Pentra C400 Clinical Chemistry Analyzer (Horiba Medical, Montpellier France) with reagen ABX Pentra Creatinine 120 CP Catalog number A1101933. Serum random blood sugar is measured with Pentra C400 Clinical Chemistry Analyzer

Table 1. Participant characteristics.

Variable	Mean ± SD	Min	Max
Age (years)	40.6 ± 11.51	19	60
BMI (kg/m^2)	21.5 ± 1.55	19	25
Random blood sugar (mg/dL)	97.7 ± 13.53	73	150
Urine uric acid (mg/dL)	36.9 ± 20.49	6	90
Serum uric acid (mg/dL)	8.01 ± 0.89	6.6	10.4
Urine creatinine (mg/dL)	132.2 ± 77.64	13.7	350.3
Serum creatinine (mg/dL)	0.91 ± 0.18	0.6	1.3
Ratio urine Uric Acid/Creatinine	0.322 ± 0.12	0.055	0.665

Note: BMI, body mass index; mg, milligrams; kg, kilogram; dL, deciliter; SD, standard deviation.

(Horiba Medical, Montpellier, France) with reagen ABX Pentra Glucose PAP CP Catalog number A1101668.

Statistical analysis

Data analyses were performed using SPSS version 25 (IBM Corp; Armonk, NY, USA). The data are presented as means ± standard deviations (range).

Results

The study included 100 subjects with an average age of 40.64 ± 11.51 years. The average body mass index (BMI) was 21.5 ± 1.55 kg/m², and the random blood sugar was 97.7 ± 13.53 mg/dL. Urinary uric acid and creatinine averaged 36.9 ± 20.49 mg and 132.2 ± 77.64 mg, respectively. Serum uric acid and creatinine levels averaged 8.01 ± 0.89 mg/dL and 0.91 ± 0.18 mg/dL. The mean uric acid-to-creatinine ratio was 0.322 ± 0.310 mg. General characteristics are detailed in (Table 1).

Based on hyperuricemia types in this study, 64 subjects (64%) were classified as under-excreters, 5 (5%) as over-producers, and 31 (31%) as mixed-type hyperuricemia, as shown in (Table 2).

The clinical characteristics and laboratory results by hyperuricemia type are shown in Table 3. Among 100 study subjects, 64 had under-excretion hyperuricemia, 5 had overproduction, and 31 had the mixed type. The urinary uric acid/creatinine ratio averaged 0.253 ± 0.062 mg for under-excretion, 0.654 ± 0.009 mg for overproduction, and 0.409 ± 0.061 mg for mixed. Based on the uric acid/creatinine ratio cutoff values, under-excretion was the most common type of hyperuricemia observed, followed by the mixed and overproduction types (Table 3).

Table 2. Type of hyperuricemia.

Variable	n (100)	%
Underexcretion	64	64
Overproduction	5	5
Mixed type	31	31

Discussion

This study found a wide age range, with a mean of 40.64 years, a normal average body mass index (BMI) of 21.5 kg/m², and varied blood glucose levels averaging 97.7 mg/dL. Biochemical analysis showed a mean urinary uric acid level of 36.9 mg and serum uric acid at 8.01 mg/dL, indicating generally elevated levels. The average serum creatinine was 0.91 mg/dL, suggesting normal kidney function. The average uric acid-to-creatinine ratio in the study was 0.322, which provides insight into the balance of uric acid production and excretion among the subjects.

Of the total 100 subjects, the majority, 64 subjects (64%), fell into the under-excretion category. This means that most subjects have problems excreting uric

Table 3. Clinical characteristics and laboratory examinations.

	Underexcretion (n=64)		Overproduction (n=5)		Mixed type (n=31)	
Variable	**Mean**	**SD (min-max)**	**Mean**	**SD (min-max)**	**Mean**	**SD (min-max)**
Age (years)	39.3	11.64 (19-60)	43.2	12.008 (25-55)	42.9	11.10 (24-60)
BMI (kg/m^2)	21.89	1.52 (19-25)	21.2	0.83 (20-22)	20.92	1.50 (19-24)
Random blood sugar (mg/dL)	99.67	13.47 (83-130)	92.2	1.48 (90-94)	94.61	14.13 (73-150)
Urine uric acid (mg/dL)	8.13	0.87 (6.7-10.4)	7.12	0.216 (6.9-7.4)	7.916	0.907 (6.6-10.1)
Serum uric acid (mg/dL)	0.9	0.17 (0.56-1.22)	0.918	0.173 (0.76 - 1.19)	0.92	0.187 (0.56-1.32)
Urine creatinine (mg/dL)	0.253	0.062 (0.055-0.341)	0.654	0.009 (0.645-0.665)	0.409	0.061 (0.343-0.533)

Note: BMI, body mass index; mg, milligrams; kg, kilogram; dL, deciliter; SD, standard deviation.

acid through urine, so that uric acid levels in their bodies tend to increase. There are several conditions that can cause under-excretion type hyperuricemia, one of which can be seen in research results which show differences in uric acid levels. Patients with under-excretion have a higher average serum uric acid level (8.13 mg/dL) compared to those with under-excretion. which experienced overproduction (7.12 mg/dL) and mixed type (7.92 mg/dL) (8,9).

This is in line with research by Qi et al. Of the 644 patients registered, 80 (12.4%) had overproduction type, 390 (60.6%) had underexcretion type, and 174 (27.0%) had a combination of both (8). This is also in line with research by Yanai et al. that there were 1,684 cases (74.1%) of the uric acid underexcretion type, 309 cases (13.6%) of the renal overproduction type, 224 cases (9.9%) of the mixed type, and 55 cases (2.4%) of the normal type (9).

Most studies indicate that the primary cause of hyperuricemia is reduced uric acid excretion. In a study by Kurniari et al. in Bali, all hyperuricemia cases were due to under-excretion based on Fraction Uric Acid Clearance (FUAC) levels (10). Elevated serum uric acid in under-excretion cases reflects kidney inefficiency, leading to buildup in the blood. Normally, kidneys excrete 60-70% of uric acid, but dysfunction increases reabsorption, potentially causing gout and kidney stones. For managing hyperuricemia without kidney dysfunction or uric acid stones, xanthine oxidase inhibitors, like allopurinol or febuxostat, are ideal therapies as they reduce uric acid production. Allopurinol is often the first-line treatment due to its efficacy and cost, starting at 100 mg daily, and adjusted up to 300 mg if necessary. In cases of chronic kidney failure, lower doses (100 mg or below) are recommended. Uricosuric agents are less effective for this condition, while colchicine or NSAIDs may prevent gout attacks but don't address the underlying hyperuricemia causes (11,12).

Overproduction hyperuricemia is less common, found in only 5% of cases. It is often associated with older age, purine-rich diets (e.g., red meat, seafood, and alcohol), and specific cultural dietary practices, such as those seen in Toraja, Indonesia, where traditional celebrations involve foods high in purines. Aside from serum uric acid levels, another factor in under-excretion hyperuricemia can be assessed through the urinary uric acid-to-creatinine (UA/Cr) ratio, a key indicator of uric acid excretion efficiency or overproduction. A cutoff of 0.342 distinguishes under-excretion (<0.342) from other types. In this study, the average UA/Cr ratio for under-excretion patients was 0.253, below the threshold, confirming excretion impairment. This aligns with Choi et al.'s findings, which suggest that a random urinary UA/Cr ratio of 0.2 can predict gout patients excreting less than 600 mg/day, recommending uricosuric treatment (7).

Mixed hyperuricemia combines under-excretion and overproduction mechanisms, affected by factors like diabetes, obesity, hypertension, kidney disease, genetic predispositions, and high-purine diets. Patients in this category often have elevated uric acid due to combined dietary and metabolic influences (13).

Management of under-excretion hyperuricemia includes xanthine oxidase inhibitors like allopurinol, which reduce uric acid production, particularly

effective in patients with normal renal function. These inhibitors help prevent gout flares without significantly impacting kidney health, with initial doses typically at 100 mg/day.

Uricosuric agents, less suited for under-excretion, may be combined with xanthine oxidase inhibitors in mixed cases to enhance uric acid elimination via the kidneys. This dual approach addresses both overproduction and excretion deficits, promoting comprehensive uric acid reduction (14).

For mixed hyperuricemia, dietary and lifestyle changes are crucial. Limiting high-purine foods, increasing complex carbohydrates, avoiding sugars and alcohol, and staying hydrated are recommended. These adjustments support kidney function and mitigate uric acid build-up. Pharmacological treatment for mixed hyperuricemia often combines xanthine oxidase inhibitors and uricosuric agents, reducing both production and improving excretion. NSAIDs or colchicine may relieve gout-related pain but do not address underlying hyperuricemia (13,15).

Monitoring the uric acid-to-creatinine (UA/Cr) ratio aids in differentiating under-excretion from other hyperuricemia types. In this study, an average UA/Cr ratio of 0.253 among under-excretion cases reinforced impaired excretion as a key factor. Kidney function directly influences hyperuricemia management strategies. As impaired kidneys limit uric acid clearance, monitoring and adjusting treatment for renal status are essential to prevent kidney stones and other complications (16).

Finally, the study recommends further research to explore other risk factors that may contribute to hyperuricemia, such as genetic and environmental factors. By gaining a deeper understanding of the causes and underlying mechanisms of hyperuricemia within the Toraja community, it is hoped that more effective interventions can be developed to prevent and manage this condition. This research is expected to serve as a valuable data source for future studies and as a reference in developing better health policies for the Toraja population.

The limitation of the study is the limited sample size, which may not adequately represent the entire Toraja population, particularly in terms of gender and age diversity, which could affect the generalizability of the findings. Also, the current study did not explore these genetic aspects, which could provide a more holistic understanding of the condition. Finally, the study recommends further research to explore other risk factors that may contribute to hyperuricemia, such as genetic and environmental factors. By gaining a deeper understanding of the causes and underlying mechanisms of hyperuricemia within the Toraja community, it is hoped that more effective interventions can be developed to prevent and manage this condition. This research is expected to serve as a valuable data source for future studies and as a reference in developing better health policies for the Toraja population.

Conclusion

The findings of this study indicate that the most common type of hyperuricemia among the Toraja population is the under-excretion type. This suggests that a majority of individuals in this population have difficulty excreting uric acid, which may be influenced by a purine-rich diet, such as the consumption of red meat and alcoholic beverages. These findings highlight the importance of understanding dietary and lifestyle factors that contribute to elevated uric acid levels, as well as the need for special attention to the health of the Toraja community.

Additionally, the study emphasizes the need for a multidisciplinary approach in the management of hyperuricemia. Collaboration among general practitioners, internal medicine specialists, and rheumatologists is essential for early screening and providing appropriate management for patients. A holistic approach that includes medical intervention, education, and lifestyle modifications can help reduce the risk of hyperuricemia and potential complications. Education on a balanced diet and the importance of physical activity are also key elements in preventing this condition.

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Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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