# URINARY STONE RISK PROFILE IN STONE FORMER PATIENT

**[1]Tommie Prasetyo, [1]Ponco Birowo, [1]Nur Rasyid.**

[1]Department of Urology, Faculty of Medicine/Indonesia University, Cipto Mangunkusumo Hospital, Jakarta

***ABSTRACT***

***Objectives:*** *We were comparing the urinary stone risk profiles in stone former subjects group with normal population (non stone-former) group.* ***Material & method:*** *In this study, each group consist of 10 subjects. Urine samples used was a 24-hour-urine. All subjects in this study were previously informed and voluntarily participating. Inclusion criteria in this study were adult, stone free, residing in Jakarta. Measurement was performed in Department of Molecular Biology and Biochemistry Faculty of Medicine Indonesia University. Statistical analysis was performed using SPSS 20 (Chicago, USA) with Student's t-test or Mann-Whitney ($p < 0.05$ was considered significant).* ***Results:*** *There was a significant difference in the mean age of two groups with no significant difference in weight and height. Significant difference ($p < 0.05$) in urinary profile was found in urea, uric acid, chloride, potassium, phosphate, and ammonia. Conversely, we found no significant differences ($p > 0.05$) in sodium, creatinine, calcium, magnesium, oxalate, and citrate levels.* ***Conclusion:*** *There were no significant differences in urinary stone promoting and inhibiting factors between two groups. Bigger number of sample size with better sampling method must be conducted for future studies.*

***Keywords:*** *Urinary stone risk profile, stone former, non stone-former.*

***ABSTRAK***

***Tujuan:*** *Membandingkan profil mineral urine pembentuk batu pada kelompok stone former dengan populasi normal (non stone former).* ***Bahan & cara:*** *Pada penelitian ini, setiap kelompok terdiri atas 10 subjek. Sampel urine yang digunakan adalah urine 24 jam. Semua subjek dalam penelitian ini diberikan informasi sebelumnya dan berpartisipasi secara suka rela. Kriteria inklusi pada penelitian ini adalah dewasa, dalam keadaan bebas batu, dan tinggal di Jakarta. Pengukuran kadar mineral urine dilakukan di Departemen Biologi Molekuler dan Biokimia Fakultas Kedokteran Universitas Indonesia. Analisis statistik dilakukan dengan menggunakan SPSS 20 (Chicago, USA) dengan Student's t-test atau Mann-Whitney (dengan nilai $p < 0.05$ dianggap bermakna).* ***Hasil:*** *Terdapat perbedaan bermakna pada usia ($p > 0.05$) kedua kelompok, namun tidak didapatkan perbedaan bermakna pada tinggi dan berat badan ($p < 0.05$). Perbedaan bermakna didapatkan pada kadar urea, asam urat, klorida, kalium, fosfat, dan ammonia ($p < 0.05$). Sebaliknya, tidak ada perbedaan bermakna ditemukan pada kadar natrium, kreatinin, kalsium, magnesium, oksalat, dan sitrat.* ***Simpulan:*** *Tidak didapatkan perbedaan bermakna pada promotor dan inhibitor pembentukan batu saluran kemih. Jumlah sampel yang lebih besar dan metode yang lebih baik harus dilakukan pada penelitian berikutnya.*

***Kata kunci:*** *Profil mineral urine pembentuk batu, stone former, non stone-former.*

Correspondence: Tommie Prasetyo, c/o: Department of Urology, Faculty of Medicine/Indonesia University, Cipto Mangunkusumo Hospital, Jakarta. Jl. Diponegoro No. 71, Jakarta Pusat, Indonesia. Phone: +62 21 3152892, Fax: +62 21 3145592. E-mail: tommie.prasetyo@gmail.com.

## INTRODUCTION

Urolithiasis is one of the oldest disease in the world, first ever found in ancient Egypt. Based on the Indonesia guideline for urolithiasis, this disease still contribute the highest number of patients in urology clinic despite there is no large scale study of urolithiasis incidence and prevalence in Indonesia.[1] The incidence increases in many parts of the world, such as Germany (0.54-1.47% on 1979-2001) and Italy (6.8-10.1% of males on 1986-1998). In USA and Japan, the prevalence is getting higher on the last 20 years, 0.6% and 1.4% respectively.[2]

Urolithiasis formation is a complex process, multifactorial, and yet not fully understood. Promoting factors that favor formation of stones includes low water intake, low citrate levels, and an increase in solutes such as calcium, oxalate, uric acid, and phosphate.[3] Therefore, urinary minerals and volume in patients with history of urinary tract

stone becomes important parameters that have to be known in preventing urinary stone, both primarily or secondary (recurrence).[4] This study intends to see the difference in urinary mineral profile in patients with history of urinary tract stones while in urolithiasis-free-condition. Hopefully, primary and secondary prevention could be done with the knowledge of urinary profile that shows the potential of urinary stone formation.

## OBJECTIVE

We were comparing the urinary stone risk profiles in stone former subjects group with normal population (non stone-former) group.

## MATERIAL & METHOD

This is a preliminary study that is done before randomized controlled trial that sought the relationship between water intake and urinary forming stones mineral profile in subject with former urolithiasis.

In this study, we compared urinary mineral profile on subject with former urolithiasis (stone former group) with normal population (without former urolithiasis as control). We used 24-hour urine from both groups. Subjects and normal population were gathered voluntarily. Inclusion criteria used in this study are adults (above 18 years old) in free-stone conditions, lives in Jakarta, and willing to collect 24-hour urine. Exclusion criteria are person in long term medicine consumption and can not collect 24-hour urine.

Every subjects got two containers containing urine preservatives (HCl and toluene). Container containings HCl was used to collect urine for 16 hours while the one containing toluene was used to collect the rest 8 hours. The 24-hour urine collected from both groups then measured by its volume, pH, oxalate, calcium, magnesium, citrate, uric acid, creatinine, sodium, chloride, pottasium, ammonia, and phosphate in the Biochemistry and Molecular Biology Department Faculty of Medicine Indonesia University Laboratory. Thus, Tiselius Crystallization Risk Index (Tiselius CRI) were counted from the urinary mineral profile to estimate the risk of urinary supersaturation that initiates urinary stone formations.[5] Statistical analysis were done using SPSS 20 (Chicago, USA) with unpaired t-test or Mann-Whitney with p value $< 0.05$ considered as significant.

## RESULTS

There were 10 volunteers with history of urolithiasis (in stone-free condition) and 10 without former history. All subjects were males with average

**Table 1.** Subjects characteristic.

| Characteristic | Control | Stone Former | p |
|---|---|---|---|
| Age | 26.4 ± 1.58 y.o. | 47.90 ± 15.1 y.o. | < 0.05 |
| Body weight | 74.75 ± 5.98 kg | 73.8 ± 5.3 kg | > 0.05 |
| Body height | 170.8 ± 5.29 cm | 168.4 ± 5.1 cm | > 0.05 |

**Table 2.** Urine profile.

| Urine Profile | Control | Stone Former | p |
|---|---|---|---|
| Volume (mL/24 hours) | 1035.2 ± 577.81 | 1646.4 ± 1260.48 | > 0.05 |
| pH (24 hours) | 6.26 ± 1.11 | 5.66 ± 0.68 | > 0.05 |
| Creatinine (mmol/L) | 12.25 ± 7.12 | 8.46 ± 3.42 | > 0.05 |
| Urea (g/dL) | 1.89 ± 0.97 | 0.85 ± 0.33 | < 0.05 |
| Sodium (mmol/L) | 205 ± 103.76 | 144 ± 57.38 | > 0.05 |
| Potassium (mmol/L) | 31.92 ± 9.22 | 18.37 ± 3.89 | < 0.05 |
| Calcium (mmol/L) | 2.62 ± 2.01 | 3.97 ± 3.12 | > 0.05 |
| Phosphate (mmol/L) | 29.89 ± 8.2 | 22.03 ± 7.16 | < 0.05 |
| Magnesium (mmol/L) | 2.8 ± 2.1 | 2.2 ± 1.7 | > 0.05 |
| Chloride (mmol/L) | 136.8 ± 53.38 | 89.86 ± 45.53 | < 0.05 |
| Uric acid (mmol/L) | 123.7 ± 199.38 | 28.35 ± 11.51 | < 0.05 |
| Citrate (mmol/L) | 2.9 ± 2.6 | 1.8 ± 1.0 | > 0.05 |
| Oxalate (mmol/L) | 0.47 ± 0.28 | 0.59 ± 0.26 | > 0.05 |
| Ammonium (mmol/L) | 7.96 ± 6.16 | 14.4 ± 4.1 | > 0.05 |
| Tiselius cri | 1.09 ± 1.03 | 1.38 ± 1.44 | > 0.05 |

of 47.9 years old on stone former group and 26.4 years old on the other group ($p > 0.05$). There was no difference in weight and height average on both groups ($p > 0.05$), 73.8 kg and 74.75 kg respectively; 168.4 cm and 170.8 cm respectively (Table 1).

Significant differences ($p < 0.05$) were spotted on urea, uric acid, chloride, potassium, phosphate, and ammonia ($0.85 \pm 0.33$ vs $1.89 \pm 0.97$ g/dL, $28.35 \pm 11.51$ vs $123.7 \pm 199.38$ mg/dL, $89.86 \pm 45.53$ vs $136.8 \pm 53,38$ mmol/L, $18.37 \pm 3.89$ vs $31.92 \pm 9.22$ mmol/L, $22.03 \pm 7.16$ vs $29.89 \pm 8.2$ mmol/L, dan $14.4 \pm 4.1$ vs $7.96 \pm 6.16$ mmol/L) but on volume, pH, sodium, creatinine, calcium, magnesium, oxalate, and citrate ($1646.4 \pm 1260.48$ vs $1035.2 \pm 577.81$ mL/24 jam, $5.66 \pm 0,68$ vs $6.26 \pm 1.11$, $144 \pm 57.38$ vs $205 \pm 103.76$ mmol/L, $8.46 \pm 3.42$ vs $12.25 \pm 7.12$ mmol/L, $3.97 \pm 3.12$ vs $2.62 \pm 2.01$ mmol/L, $2.2 \pm 1.7$ vs $2.8 \pm 2.1$ mmol/L, $0.59 \pm 0.26$ vs $0.47 \pm 0.28$ mmol/L, $1.8 \pm 1.0$ vs $2.9 \pm 2.6$ mmol/L) there were no significant differences on both groups.

## DISCUSSION

The risk of once urolithiasis recurrence in someone with former urinary stone history is 50%.[6,7] The purpose of this study is to see if there are differences on promoters/inhibitors level between subject with former urinary stone in stone-free condition compared with normal population. Primary and secondary prevention could be done with the knowledge of urinary profile that shows the potential of urinary stone formation.

There were groups of cases and control that share similar physical characteristic ($p > 0.05$) but significant differences on ages ($p < 0.05$). The significant differences on ages are caused by the peak incidence of urolithiasis is between 40-60 years old,[4] but the volunteers in the control group were below 30 years on age. The results of this study will be better if the subjects were not so different on age. All subjects on this study was living on same geographical area so there were no climate and weather bias.

The stone promoters that were measured are calcium, oxalate, uric acid, phosphate, pH, and low urine volume. There were significant differences on uric acid and phosphate in both groups ($p < 0.05$). Despite no significant differences found on both groups, lower urinary pH and higher calcium were found on cases group. Higher urine volume and lower uric acid level on cases group could be affected by diet, where subjects with former urolithiasis history might have better knowledge and attitude on those factors. Similar study in Iran compared urinary minerals level on stone former and non stone former groups. There were no significant differences on urinary stone promoters.[8] One Randomized Control Trial (RCT) in Italy comparing urinary minerals on recurrent stone former and those who didn't, found significant differences on all promoters.[9] Other study in France comparing urinary minerals between high drinker and low drinker subjects, found significant differences on urine volume, phosphate, and uric acid level. There were no significant differences on calcium and oxalate level.[10]

The inhibitors measured in this study were citrate and magnesium. There were no significant differences on both groups ($p > 0.05$). Study by Mirzazadeh, et al., showed no significant differences on citrate and magnesium level on stone former groups compared with non stone former.[8] RCT done by Borghi, et al., found significant inhibitors level of citrate and magnesium on stone former groups that had recurrence if compared with no recurrence group.[9]

The risk of stone formation by Tiselius crystallization risk index in this study showed no significant differences on both groups. The study in Iran that compared urinary minerals level in stone former compared with non stone former showed no Tiselius CRI significant differences on both groups,[8] and also in France with high drinker and low drinker group.[10] Nevertheless, one RCT in Italy showed relative saturation levels that differ significantly on recurrent stone former compared to those who didn't.[9]

The weakness in this study is all subjects were males, but that was based on higher urolithiasis prevalence on males and easier 24-hour urine collection. Besides, there is no difference of stone formation patophysiology on both sexes. There are also no age, activity, and diet matching to prevent bias in results.

## CONCLUSION

There were no significant differences in urinary stone promoting and inhibiting factors between two groups. There were statistically significant differences on phosphate and uric acid level but with higher levels on control groups. Bigger sample size number with better sampling method must be conducted in future studies to prevent bias.

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