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## **A chemical odyssey: Exploring renal stone diversity by age and sex in Punjab, Pakistan**

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## A chemical odyssey: Exploring renal stone diversity by age and sex in Punjab, Pakistan

Dear Editor,

Renal calculosis is one of the most common urological disorders worldwide with a prevalence ranging from 1% to 13% in different regions<sup>[1]</sup>. Renal stones are crystal concretions formed on the inner surface of the kidney, resulting from disruptions in both the metabolism or the excretion of stone constituents, or attributable to the Randall's plaques and plugs. These stones are a result of various endogenous factors, such as age, sex, and genetic makeup as well as various exogenous factors like geography, weather conditions, and dietary factors<sup>[2]</sup>. Numerous epidemiological studies have documented variations in the incidence of renal calculosis geographically. These studies provide a piece of substantiating evidence for the proposition that individuals residing in warmer climates exhibit a greater lifetime prevalence of urolithiasis, attributable to the effects of dehydration<sup>[3]</sup>. Our country, Pakistan resides in the Afro-Asian stone-forming belt with a prevalence of renal stones at approximately 16%<sup>[4]</sup>. The treatment of these stones whether in the form of medical expulsive therapy or surgical intervention leads to a significant burden on the hospitals as well as the economy.

Stone analysis has a pivotal role in the preliminary understanding of the underlying causes, aiding in formulating treatment strategies and preventive measures. Both the European and American urological societies recommend stone analysis at least once for each patient<sup>[5-6]</sup>. The present study aimed to analyze the chemical composition of renal stone disease in Punjab Pakistan and to determine the age and sex-correlated prevalence of these stones.

For the present study, we retrieved the data from Nexus Pro Laboratory Information Management

System of Chughtai Lab, Lahore, spanning over one year between July 2018 and June 2019. The lab received a total of 2956 stone specimens from Lahore and its neighboring cities. After pre-treatment to form pellets, all analyses were done on the Perkin-Elmer Fourier Transformer Infrared Spectrophotometer. Pure stones were characterized by a predominant component constituting 80%–100% of the composition, while mixed stones exhibited a major component comprising less than 80%. Patients who sought stone composition analysis from the laboratory, encompassing those with spontaneously passed or surgically removed urinary system stones, were included in the present study. Their urinary stone samples underwent chemical analysis upon receipt at the Clinical Biochemistry section. However, individuals whose stone chemical analysis data were either missing or incomplete were excluded from the present study.

The demographic information and continuous variables were presented as mean  $\pm$  standard deviation. Categorical variables were described with frequencies and percentages. The statistical analysis was conducted using Microsoft Excel version 13 and IBM SPSS version 26.

Out of the 2956 stone analysis results, 65.2% (1928) were males and 34.8% (1028) were females. The male-to-female ratio was 1.9 : 1. The mean age of the study population was 36.83 ( $\pm$  15.51) years, ranging from one to 90 years old. The chemical composition of all analyzed renal stones with their respective frequencies is shown in [Table 1](#). Calcium oxalate stones (pure) had the highest prevalence with their presence in 1335 patients. Pure stones had a higher rate of occurrence, compared with mixed stones. The prevalence of stones in males and females

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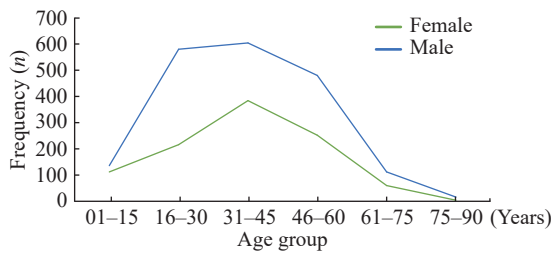
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**Table 1 Chemical composition of renal stones in study participants**

Type of stones	Number of the patients (n=2956)	Frequency (%)
Calcium oxalate (pure)	1335	45.16
Calcium oxalate (mix)	565	19.11
Uric acid (pure)	336	11.37
Uric acid (mix)	167	5.65
Carbonate apatite	223	7.54
Carbonate apatite (mix)	163	5.51
Ammonium urate	101	3.42
Struvite	46	1.56
Cystine	20	0.68



**Fig. 1 Age and sex distribution of renal stones in study participants.**

is shown in *Fig. 1*, in which the male population showed a higher incidence of stones, compared with females in all age groups. However, their pattern of distribution across these age groups was the same and found to be statistically significant ( $P$ -value = 0.00). The patient age group 31–45 years showed the highest frequency of renal stones with 33.4% of the reported cases, as compared with other age groups. However, the lowest frequency is observed in the 76–90 age group being with only 0.7% of the whole study population.

The outcomes derived from epidemiological investigations have broadened our comprehension of kidney stone diseases. Nevertheless, the analysis of stones is infrequently pursued, particularly in our geographic region, due to financial constraints and a prevailing skepticism regarding its utility. Currently, multiple modalities are available for stone analysis. However, we have chosen Fourier transform infrared spectroscopy (FTIR) spectroscopy because of its quick examination, moderate cost, and ability to identify organic components or non-crystalline substances.

Urinary stone composition varies worldwide with calcium oxalate stones identified as the predominant

type in numerous studies<sup>[7-8]</sup>, including our investigation, where they accounted for a prevalence of 45.16%. Although the majority of the cases are generally considered idiopathic, urinary oxalate excretion plays an important role in the formation of calcium oxalate stones, which acts as a continuous variable when correlated with the urinary stone risk in robust epidemiological cohort studies<sup>[9]</sup>. Additionally, the present study corroborates previous research, highlighting uric acid as the second most prevalent stone type and cystine stones as among the least common, consistent with findings from our geographic region<sup>[10]</sup>. This underscores the influence of diet and environmental factors on stone composition, which may further help us to study the mechanisms of urine stone formation and focus on preventative strategies.

Urinary stone disease not only directly affects individual well-being but also bears indirect consequences for the national economic scenario. Given that the highest rates of occurrence manifest among people with age between 21–40 years, a subpopulation generally associated with an elevated economic productivity, the proficient management of the disease becomes particularly salient. In the present study, the mean age was  $36 \pm 15$  years with the highest prevalence observed in the 31–45 year age group, which is similar to a study showing the maximum frequency of patients between the 3<sup>rd</sup> and the 5<sup>th</sup> decade<sup>[11]</sup>.

In the present study, a higher preponderance of renal calculus disease was found in males than in females. The male-to-female ratio in the present study was 1.9 : 1, which is in accordance with similar studies done in our geographic region, for example, Bibi *et al*<sup>[10]</sup> and Rafique *et al*<sup>[12]</sup> reported the ratios of 3.8 : 1 and 3 : 1, respectively. Nonetheless, the ratios observed in other studies surpass those found in the present study, indicating a rising trend in the prevalence of urinary stones among women in recent years. This phenomenon may be attributed to the escalating rates of obesity or alterations in dietary patterns. The aforementioned observation aligns with the studies investigating the prevalence of the disease across sexes. These studies focus on the concentration of biomolecules present in the urine, which act as potent inhibitors of *in vitro* mineralization, highlighting that the level of urinary inhibitors was three times higher in female than in male patients with renal stones<sup>[13]</sup>.

The present study possesses certain limitations. Firstly, it was a single-center cross-sectional design. Although the findings of the study are substantial on

their own, additional prospective studies are required to yield definitive insights. Secondly, the study data is driven from a commercial lab where we had a limited access to the patient history, so the factors promoting the stone formation could not be delineated. Third, analyzer constraints at the time of the study prevented a detailed differentiation of mineralogical variants (e.g., whewellite and weddellite) and a comprehensive reporting of mixed stone components.

In conclusion, the present retrospective cross-sectional study sheds light on the nuanced prevalence of kidney stone compositions in the population of Lahore and its surrounding areas, with an emphasis on the dominance of pure stones and the age group of 31–45 years. These results may have important implications for reducing economic burdens by guiding more efficient preventive and therapeutic strategies. Ultimately, this will contribute to the improved patient care and cost-effective healthcare outcomes.

Yours sincerely,

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