

# Impact of Drinking Water and other Causative Factors for Nephrolithiasis

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## ABSTRACT

Impact of drinking water i.e., its hardness and calcium contents on urolithiasis was studied. Thirty adult patients, both males and females of nephrolithiasis (Group-1) compared with those of 34 age matched control (Group-11) were included in this study. Mean age of Group-1 was 30.63 and  $\pm$  SD 3.58 and of Group-11 was 28.62  $\pm$  SD 2.60. Mean serum calcium level of Group-1 was 9.56 mg/100ml and  $\pm$  SD 0.7 and of Group-11 was 8.8mg/100ml  $\pm$  SD 1.30, which was significant ( $p < 0.05$ ). Mean 24 hours urinary excretion of calcium in Group-1 had 287.79 ( $\pm$  SD181.29) and in Group-11 had 187mg ( $\pm$ SD 88.91), which is significant. Mean serum uric acid was 5.37mg/dl ( $\pm$  SD 1.66) in Group-1 and 5.40mg/dl ( $\pm$ SD1.52) in Group-11 which is non significant. Mean 24 hour urinary excretion of uric acid in stone patients was 424.31mg $\pm$ SD 142.16 and in normal subjects was 314.29mg  $\pm$  SD173.49 (significant at  $p < 0.05$ ). Stone formers had a mean 24-hour urinary out put of 1336.7ml  $\pm$ SD 773.83, while non-stone formers had a mean out put of 1129.41ml  $\pm$  SD 512.36, which is not significant. Mean pH of freshly voided urine of Group-1 had 6.24  $\pm$  SD 0.78, while in Group-11 had 6.12 $\pm$ SD 0.38 and was not significant. Economic status and family history of both group was also analysed. Mean $\pm$ SE.

**Key words:** Drinking water, causative factor, nephrolithiasis

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## INTRODUCTION

Over the past few decades, there has been little research into the relationship between hardness of drinking water and stone disease, but various epidemiological studies in different countries have shown an overall negative association. Most authors suggest that habitual low level of intake of fluids and water and subsequent low urine output has a definite role in the pathogenesis of stone disease<sup>1,32,33,34</sup>.

The concept is developed, that calcium stone formation in the urinary tract may be explained on the basis of set of urinary risk factors. The main risk factors are volume, pH, and the excretion of urinary calcium, oxalate, uric acid and the glycosaminoglycans, the inhibitors of crystallization<sup>2,35</sup>. It has been apparent for many years that calcium stone disease is a multifactorial disorder. In the recent years, however, it has been shown that there are two main chemical factors which seem to determine the risk of forming calcium stones, namely, the degree of saturation of urine with calcium oxalate and calcium phosphate and the level of protective inhibitory activity against the crystallizations of calcium stones<sup>3,4</sup>. Risk factors are different for the various chemical types of urinary lithiasis, which include uric acid, urinary calcium, and oxalate and for struvite stones too<sup>4</sup>. Epidemiological studies and metabolic investigations of chemical

composition of urine have suggested that number of nutrients may influence the formation stones in the upper urinary tract. These stones, which are predominantly calcium oxalate in composition, are more common in affluent countries where there is relatively high consumption of protein, fat and low consumption of carbohydrate.<sup>6</sup> Experimental studies have shown that decreases intake of dietary fibers and increases intake of animal protein and refined carbohydrates, ascorbic acid and oxalate increase excretion of calcium and/or oxalate -2 of the six "urinary risk factors" for stone formation<sup>7</sup>.

## PATIENTS AND METHODS

Samples of drinking water were collected from the different areas of Quetta division. Water samples were collected from ground sources (rivers, karezes, superficial and tube wells of different depth as well as kitchen tap water). These samples were then sent to PCSIR Laboratories Lahore. Analysis regarding calcium hardness, magnesium hardness, total hardness and of other important variables were carried out.

A Group-1, comprising of 60 adults patients of either sex having stone disease, as diagnosed by ultrasound/IVU, compared with Group-2, of 34 age and sex matched controls, attending out patients clinics from Quetta city were included. A detailed proforma was also filled regarding age, sex, residence, diarrhoeal episodes, hypertension, socio-economic status, dietary habits and presenting

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complaints. No prior counseling's were made regarding routine dietary and drinking habits during sample collection. A clinical history and detailed physical examinations of both Groups were also carried out. Blood and urinary specimens were taken as per instructions given to both Groups and all biochemical laboratory tests were performed.

**RESULTS**

Analysis of drinking water: Calcium hardness was defined as the water with a calcium concentration more that 50ppm or mg/litre as described by Thomas Water Authority in U.K. Total hardness is determined largely by the concentration of calcium and magnesium as defined by U.S. Environmental Pollution Control8. Calcium hardness (mean and ±SE) in Quetta district was estimated as 118.63±21.28mg/L, Pishin district 118.75±11.86 mg/L and Chaghi 124.16±7.80mg/L. Total hardness of drinking water was high in Quetta district, higher in Pishin district and highest in Chaghi district, whereas calcium hardness were higher in all districts almost in equal proportion. Approximately incidence of urinary stones operations in the population was estimated as 28 per 100,000 in Quetta District (547), 5 in Pishin (95) and 4 in Chaghi district (28)29. Incidence of stone operations was highest in Quetta district as opposed to lowest water hardness and equal concentration of calcium of drinking water as compared to other districts of Quetta division. In contrast Chaghi District (comprises of both mountains and desert plains with scarcely and scattered population) has both highest calcium and total hardness of drinking water but the incidence of stone operations was lowest (Table 1).

Age range of subjects was between 17 and 65 years. Mean age of Group-1 was 30.63 years and ±SD.3.53 and the peak age was between 26 and 35 years (36.66%) (Table.2) Group-2 had mean range of 28.62 and ±SD 2.60 and maximum number of patients (41.19%) were between 26-35 years of age. The mean age of non-stone formers was less as compared to stone formers, not significant(Table 3).

Serum calcium level: Mean serum calcium level of Group-1 was 9.56mg/dl and ±SD 0.7 (Table 4). Normal controls had mean serum level of 8.8mg/dl and ±SD 1.30. There was significant mean difference of serum calcium between two Groups (p<0.05).

Mean urinary calcium excretion in stone formers was 287.79 mg per 24 hour and ±SD 181.29 and 43.33% of these patients had urinary excretion in excess of 250mg per 24 hours. Controls had lower daily mean excretion (187.0mg and ±SD 88.91) and 17.64% subjects in Group-2 had urinary excretion more that upper limit of 250mg/24 hour. Among stone

patients high rate of excretion of calcium was observed which was statistically significant at p<0.05 (Table 5).

Mean serum uric acid level was 5.37mg per 100ml and ±SD 1.66 in Group-1. Six out of thirty (20%) subjects in this Group were hyperurecaemic (serum uric acid more than 7mg per 100ml). Group-2 had mean value of 5.40 ± SD 1.52. Comparison of mean of both groups showed non-significant difference statically (Table 4,7)

Mean 24 hours urinary excretion of uric acid in stone patients was 424.31mg±SD 142.16, while mean excretion in control subjects was 314.29mg ± SD 173.49 (Table.5). It is significant at p<0.05. Twenty subjects were hyperuricosurics, with excretion of more than 750mg/24 hours. 24-hours Urinary volume and pH of freshly voided samples: Group-1 had a mean 24 hours urinary volume of 1336.7ml±SD 773.83, while Group-2 had 1129.41ml±SD 512.36. Mean difference was not significant statistically (Table.12). Mean pH of freshly morning-voided urine in stone subjects was 6.24±SD 0.78, while in control subjects it came out to be 6.12±SD 0.384. Mean difference was not significant.

Economic status and family history of patients: Economic status of subjects of both Groups were analysed in Table.15. The assessment of total monthly income of joint family was done and divided per head. Seventy percent of the stone patients had income less than 200 rupees per month and between 200-250 Rupees in 58% of the control subjects. Family history of patients analysed in Table 16

Table.1: Mean and SE comparison of various variables of drinking water between the districts of Quetta division

Variables	Quetta (n=14)	Pishin (n=8)	Chaghi (n=12)
Calcium as Ca <sup>+2</sup>	54.92 ± 5.90	47.50± 4.2	99.40± 11.58
Total hardness	240.42± 17.55	349.50± 114.51	357.4± 33.87*
Ca hardness as CaCO <sub>3</sub>	118.63± 121.28	118.75± 11.86	124.16± 7.80
Magnesium hardness	101.42±9.59	230.75±68.42	233.33± 22.85**
Magnesium as Mg <sup>+2</sup>	24.12 ± 2.43	35.56±147.5	56.69± 5.55**
PH	7.81±0.12	7.82±0.15	8.36± 7.50**
Silica	1.40±0.36	1.30± 11.06	99.40± 1158
Incidence of urinary stones per 100,000 of population	28	5	4

SE: Standard error of the mean, \*Statistically significant at p<0.05, \*\*Statistically significant at <0.01

Table 2: Age distribution of stone patients, Group-1

Age in years	=n	%age
6-25	14	16.66
26-35	22	36.66
36-45	16	33.33
46-55	06	10.02
56-65	02	3.33

Mean age: 30.63 ± SD for Group ± 3.58

Table 3: Age distribution of normal controls. Group-2

Age in years	=n	%age
16-25	04	11.76
26-35	14	41.19
36-45	12	35.29
46-55	02	5.88
56-65	02	5.88

Mean age 28.62 ± 2.60 Group-2

Table 4: Comparison of serum level of stone patients (Group-1) and with normal subjects (Group-2). Values are mean ±SD.No; of subjects are given in parenthesis

Parameters	Stone patient (n=30)	Normal subject (n=17)
Calcium (mg/100ml)	9.56** ±0.7	8.8 ±1.3
Uric acid (mg/100ml)	5.37 ±1.66	5.40* ±1.52

\*NS. Non-significant, \*\*Significant at P<0.05

Table 5: Comparison of 24 hours urinary values of stone patients (Group-1) and normal controls (Group-2) Values are given as mean ± 1 SD.

Parameters	Stone patient (n=30)	Normal subject (n=17)
Calcium (mg/100ml)	278.79* ±181.29	187.68 ±88.91
Uric acid (mg/100ml)	424.31** ±142.16	314.29 ±173.49

\*Significant at P<0.01, \*\*Significant at P<0.05, Number are shown in parenthesis

Table 6: Percentage of subjects excreting calcium in excess of 250mg per 24 hours among stone patients (Group-1) and controls normal (Group-2)

Stone patients	No stone subjects	P value
43.33%*	17.64%	<0.05

\*P<0.05 statistically significant at 5% level

Table 7: Percentage of hyperurecaemic in stones patients and in normal controls

Stones formers (n=60)	Stone pts (n=34)	P value
20.00%*	5.88%	NS**

\*Normal values for serum uric acid taken as 5.8 mg To 7.00mg/100 ml, \*\*Statistically not significant

Table 8: Biochemical analysis of serum in stone patients (Group-1). Values given are mean (mg/100ml SD and SEM) (n=60)

Parameters	Mean	SD	SEM
Calcium	9.56	0.70	0.128
Uric acid	5.37	1.66	0.303

Table 9: Biochemical analysis of serum in Group-1 and Group-2 Values are given in mean (mg/100 ml SD and SEM (n=34)

Parameters	Mean	SD	SEM
Calcium	8.8	1.30	0.31
Uric acid	5.40	1.52	0.368

Table 10: Urinary excretion of different variables per 24-hours in stone patients (Group-1). Values given are mean, SD and SEM (n=60)

Parameters	Mean	SD	SEM
Calcium (mg/24hr)	278.79	181.29	33.14
Uric acid (mg/24hr)	423.31	142.16	25.98

Table 11: Urinary excretion of different parameters per 24 hours in Normal controls (Group-2). Values given are mean, SD and SEM (n=34)

Parameters	Mean	SD	SEM
Calcium (mg/24hr)	187.69	88.91	21.58
Uric acid (mg/24hr)	314.29	173.49	42.9

Table 12: Urinary volume in 24 hours and pH of one fresh morning Specimen of urine in stone formers (Group-1). Values given are Mean, SD & SEM (n=60)

Parameters	Mean	SD	SEM
Urinary volume (ml/24hr)	1336.7	773.83	134.15
PH	6.24	0.781	0.142

Table 13: Urine volume in 24 hours and pH of one fresh morning Sample of urine of normal controls (Group-2). Values given are mean, SD and SEM (n=34)

Parameters	Mean	SD	SEM
Urinary volume (ml/24hr)	1129.41	512.36	124.35
PH	6.12	0.385	0.093

Table.14: Comparison of 24 hours urinary volume in stone and non-stone Subjects. Values are given in mean.

Stone patients (n=60)	Normal control (n=34)	P value
1336.7±SD 773.83 (ml/24hours)	1129.41±SD512.36 (ml/24hours)	Non Significant

Table 15: Economic status of stone formers and non-stone formers

Income Rs/ month per head	Percentage of cases	
	Stone formers	Non stone formers
<200	70.00	35.29
201-250	23.00	58.00
251-500	6.60	5.88
500+	Nil	Nil

Table 16: Percentage of family history of calculus disease In 30 upper urinary tract stones patients

Presence of family history				Total	Absence of family history
Mother	Father	Sibling	1 <sup>st</sup> Cousin		
4	2	-	-	12	48
13.33%	6.66%	-	-	20%	80%

## DISCUSSION

A low urine flow rate is likely to be the major contributor to the high prevalence of stones in this region. Pakistan is a desert, supplied almost exclusively with water from the river Indus and its tributaries. The composition of drinking water varies markedly across the country, depending on the nature of rocks and soil from which the water drains, and depending on whether the water for drinking is obtained from rivers and wells. Certain areas (Balochistan) have extremely hard water, with in excess of 300 parts per million of calcium, but the importance of this relationship to the risk of stone is unclear<sup>29</sup> the climate is extremely hot and dry. Whether the present study has shown negative or positive association between hardness of drinking water and urolithiasis is debatable. Though there was increased incidence of stones operations in Quetta district as compared to other districts of division<sup>29</sup>. No convincing evidence however, exists showing which water parameters i.e., calcium and magnesium (total hardness) or calcium alone (calcium hardness or bulk minerals like silica, carbonate, bicarbonate, magnesium sulphate were responsible for association, is more likely risk factors<sup>29</sup>, Robertson (1978) could not observed the effects of trace elements and minerals of drinking water on stone disease<sup>2</sup>. Shuster (1982) conducted a study on 2295 patients from two regions of U.S. i.e., Caroline which had soft water and high stone disease and the Rockies which had hard water and low stone incidence<sup>31</sup>. Peak incidence of stone patients lies between 26-33 years (36.66). Many studies showed the similar age pattern<sup>9</sup>. The mean age of symptoms in one study was reported as 33.3% years<sup>10</sup>. Khanum (1981) reported age pattern between 20-39 years in a study carried out at JPMC, Karachi<sup>11</sup>. Khan (1975) reported the earlier peak age between 16-20 years from Lahore<sup>12</sup>. Mean serum calcium level in this study is higher than that of normal controls and the mean was in the lower range in both groups which is significant at  $p < 0.05$ . This can be attributed to lower calcium intake in diet, as assimilate less diary products in this region as compared to Punjab and Sindh<sup>29</sup>. The relationship between dietary calcium intake and stone formation is controversial. A recent prospective study by Curhan et al. in 49976 men

provides data on this relationship<sup>13</sup>. Various studies conducted abroad reported mean serum calcium level within normal limits with the exception of those having calculi due to primary hyperparathyroidism<sup>5,14-17</sup> but this is rare in Pakistan<sup>18</sup>. Role of urinary excretion of calcium is not the single responsible factor and its leading role in causation of lithiasis is highly debatable. Since many hypercalciuric may not develops stones<sup>19</sup> and it is therefore postulated that pH and calcium oxalate may also cumulatively control saturation with calcium salts<sup>20</sup>. Many studies conducted in Pakistan and abroad, showed higher excretion of urinary calcium<sup>12,21,22</sup>. In this study higher number of patients were hypercalciuric (43.35%), which is significant at  $0 < 0.05$ . Similar results were obtained by Robertson (1982)<sup>2</sup>, but he fixed the upper limit of urinary excretion of 300mg for male and 250mg for female. Other workers at abroad also reported the higher percentage of hypercalciuric among stone formers<sup>4,10,15,20,23</sup>. The mean serum uric acid level in our study is higher in stone patients as compared to non-stone subjects, though the mean level of both groups was within normal range. A similar study was conducted at Karachi, showed lower mean serum uric acid among stone formers<sup>11,18</sup>.

In different studies conducted in country and abroad, the stone formers have been shown to excrete on an average more uric acid in urine<sup>3,4,10,24</sup>. However Shahjehan (1971) observed lower uric acid excretion in stone formers at JPMC Karachi<sup>18</sup>. In our country purine rich diet is not consumed ordinarily. Stone disease is more common in socioeconomic groups with higher income<sup>24</sup> and in industrialized cities compared to areas, which rely on agriculture<sup>26</sup>. In this study about half of the all patients belonged to poor socio-economic class, which have hyperuricaemia and hyperuricosuria. Which might be due to the consumption of imbalanced diet leading to protein breakdown and thus increasing uric acid excretion in urine. It appears therefore that uric acid abnormalities may also contribute toward idiopathic stone formation through calcium precipitation<sup>27</sup>. Economic affluence and a diet rich in protein may increase the incidence stone<sup>28</sup>. Heredity factors cause cystinuria, renal tubular acidosis, familial xanthinuria and oxolosis<sup>30</sup>.

## CONCLUSION

The pathogenesis of urinary stones is multifactorial. A variety of epidemiological risk factors appear to interact with individual traits to trigger stone formation. Our study of risk factors including drinking water in this region has been so far inconclusive. Some factors i.e., calcium, oxalate and constituents

of drinking water did not appear to be to be more important in determining the incidence of stone disease. However in the developed countries, high incidence of upper urinary tract stones has been related to high nutritional and protein rich diet but not in our region.

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