The positive effect of the pH and volume of fluid intake on kidney stones in adult men

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Abstract

Purpose – The purpose of this study is to investigate the relationship between pH of water or other daily fluid intake and risk of kidney stones in adult men.

Design/methodology/approach – This case–control study included 120 adult men with kidney stones and 240 healthy controls matched by age. Participants were selected from the Urmia Imam Khomeini Educational Hospital in the northwest of Iran by the available sampling method between 2017 and 2018. The mean total daily fluid intake of the subjects over the past one year period was collected using a validated 139-item Food Frequency Questionnaire, and the pH of drinking water samples consumed over the past six months was determined using an electrochemical pH meter. Information on physical activity level and socio-demographic characteristics of all participants was collected.

Findings – The mean pH of daily water consumption was 7.1 ± 250.3 and 7.4% ± 250.3 in case and control groups, respectively. In multivariate logistic regression analysis after adjusting for the covariates 25 a significant relationship was detected between the pH of drinking water (not for other fluid intake26) and kidney stone disease (OR = 0.15, CI 0.06–0.4, P > 1. Moreover, no association was found between the volume of total fluid intake and risk of kidney stones.

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Informed consent: the study was approved by the Ethics Committee of the Urmia University of Medical Sciences and written informed consent was obtained from all individual participants after explaining the aims of the study to them.

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Originality/value – These findings support potential protective effects of drinking water intake with higher pH level on preventing kidney stones.

Keywords Volume, pH, Drinking water, Alkaline water, Kidney stone

Paper type Research paper

Abbreviations

DBP = diastolic blood pressure;
KSD = kidney stone disease;
MET = metabolic equivalent task;
OR = odd ratio; and
SBP = systolic blood pressure.

1. Introduction

Kidney stones are considered one of the most painful and costly diseases (Mayans, 2019). The prevalence of kidney stone diseases (KSD) was increasing globally over the past two decades (Romero *et al.*, 2010), and it is higher among men especially after the age of 40 with a prevalence rate of approximately 1.7% to 8.8% around the world (Jiang *et al.*, 2017). The mechanism of stone formation in urinary tract is a complex process resulting from several biochemical interactions including supersaturation, nucleation, growth, aggregation and retention of urine in kidney and ureter (Cunningham *et al.*, 2016; Littlejohns *et al.*, 2019). According to the recent studies, apart from genetics and history of urinary infections, a variety of other risk factors including increased excretion of water, decreased fluids intake, higher intake of animal proteins, calcium and oxalate and low intake of potassium can also contribute to the development of kidney stones (Alelign and Petros, 2018; Yongzhi *et al.*, 2018).

The relationship between some properties of fluid intakes such as volume and hardness of water and the development of KSD have been previously investigated (Gao *et al.*, 2019; Jayasumana *et al.*, 2014; Wright, 2015; Sengupta, 2013). Recently, researchers have focused on the role of increased fluid acid loads in forming kidney stones, and it seems that evidence on the protective effect of consuming alkaline fluids on kidney stones is dominant (Schwalfenberg, 2012; Magro *et al.*, 2016). The most common type of kidney stone in Iranian population mainly contain 60% calcium oxalate (Shahnani *et al.*, 2014). Moreover, the consumption of alkaline fluids can increase the pH of urine which in turn reduces the amount of its calcium, and in addition, the citrate of alkaline fluids blocks the adhesion of calcium oxalate crystals to renal epithelial cells; therefore, increasing urinary excretion of citrate can control calcium oxalate stones formation (Xu *et al.*, 2015; Tarplin *et al.*, 2016). Other beneficial effects of consuming alkaline water such as its anti-aging properties (via liquid antioxidants) and improved cardiovascular and bone health have been also observed in some studies (Schwalfenberg, 2012; Wynn *et al.*, 2010).

Considering the high prevalence of KSD in the northwest of Iran (Safarinejad, 2007) and the several sources of drinking water available for the citizens in the region like tap water, mineral water, boiled water, underground water, spring water, purified water and water purifier with alkaline filter, the current study was designed to assess the effect of the pH and volume of consumed fluids on kidney stones.

2. Materials and methods

2.1 Study population and data collection

This case–control study was conducted on 360 participants aged ≥ 40 (120 cases and 240 controls). The cases were kidney stone subjects recruited from the urology clinic of Urmia

Imam Khomeini Educational Hospital, and the controls with no kidney stone were recruited from the same educational hospital and a primary health center in the city during February 2017–June 2018. The controls were matched with cases by age. All participants were male (kidney stones are most common across men and the risk increases with age). The diagnosis of stones in the urinary tract was confirmed by a sonographist for stones > 5 mm and a radiographist using CT scan for stones < 5 mm (sonography may not detect stones smaller than 5 mm and CT scans are used for higher accuracy). Cases and controls with history of renal failure, cardiovascular disorders, hyperparathyroidism, urinary tract infections, hypertension (SBP/DBP $\geq$140/90 mmHg), gout, subjects with special diet or those taking any medicine like diuretics and who had chemotherapy drugs or history of radiation therapy were excluded. Cases and controls were selected through available sampling method. The study was approved by the Ethics Committee of the Urmia University of Medical Sciences and written informed consent was obtained from all individual participants after explaining the aims of the study to them. The participants were free to withdraw from the study at any time (no one left the study). The weight and height of each case and control were measured after removal of heavy clothes and shoes. Body mass index (BMI) of all participants was calculated as the ratio of weight (kg) to squared height (m^2). Additional covariate information regarding smoking habits, hookah use, educational level, place of residence, parents' kidney stone history, personal medical history, use of calcium supplements, alcohol consumption were collected using a self-administered questionnaire. Physical activity level of participants was obtained through MET-minutes/week (Craig *et al.*, 2003). Daily intakes of animal proteins, oxalate, calcium and potassium were obtained using a validated Food Frequency Questionnaire (FFQ) (Hulshof *et al.*, 2019; Mirmiran *et al.*, 2010).

2.2 Assessment of fluid consumption

Daily fluid intakes of subjects over the past one year period was obtained using a validated FFQ. Participants reported their consumption frequency of each fluid item over a one year period. For example, the calculation of a glass of milk three times a week was done as: $3 \times 300/7 = 128.6$ mL/day. Participants' consumed water samples were collected in 500-mL clean and plastic bottles. All the water samples were stored and analyzed for pH in a nutrition laboratory within 24 h. The pH of the collected samples was measured using an electrochemical pH meter (HORIBA brand) (electrochemical pH meter is a standard method for measuring the pH of water). The calibration of pH meter was performed using three buffers with pH (4, 7 and 9); then 100 mL of each water sample was taken in a beaker and pH of the water is determined by pH meter, the pH was read after waiting two minutes for its stability.

2.3 Statistical analysis

Statistical analyses were performed using IBM SPSS software. Continuous variables were expressed as mean $\pm$ standard deviation (SD) and categorical variables were expressed as numbers (percentages). The variables with normal distribution including age, BMI, daily water volume, other liquid volume, total volume, pH of daily water, pH of other liquids and total pH were compared by Independent *t*-test between cases and controls. Mann–Whitney *U* test was used for comparing the non-normal distribution variables including daily animal protein, oxalate, potassium and calcium intakes. Smoking, hookah use, use of salt at the table, education status, place of residence and physical activity level were compared by chi-square between two groups. Fisher's exact test was used for comparison of frequency variables including source of drinking water and use of salt in cooking. Odds ratio (OR) and the 95% confidence interval (CI) were calculated for the association between volume and pH of fluid intakes and the risk of kidney stones. The ORs were calculated for the tertiles of consumed water and other liquids volume and their pH by logistic regression in crude and three adjusted models. In all regression models, Model 1 was adjusted for education level and history of kidney stones in parents. Model 2 was adjusted for consumption of smoke and hookah, physical activity level in addition to variables in Model 1. Model 3 was adjusted for consumption of daily animal protein and potassium intake and place of residence (urban/rural), in addition to variables in Model 2. Throughout the analyses, a p-value < 0.05 was considered statistically significant.

3. Results

There was a significant association between alkaline water intake and risk of KSD. The baseline characteristics of participants are summarized in the Table 1. All participants were male and their mean average age was 49.3 years. The controls (1.3%), had significantly higher level of education (25 %) in comparison to cases ($P < 0.001$). In spite of control group (23.8%), most subjects in the case group were current smokers (32.5%) ($P < 0.001$). The number of hookah consumers was significantly higher in the controls (29.2%) than the cases (17.5%) ($P < 0.05$). The number of subjects with vigorous physical activity was significantly higher in control group (37.5%) than case group (21.4%) ($P < 0.05$). Among both cases and controls, the tap water use had the highest frequency (55 % in cases and 33.8% in controls), and the difference was significant between two groups ($P < 0.001$). The frequency of alkaline ionized water consumption was higher in the controls (0.8%) than the cases ($P < 0.001$). As seen in the Table 2, both daily animal protein and potassium intakes (obtained from FFQ) in cases were significantly lower than controls. The daily animal protein mean was (36.5 ± 12.2 g) in cases and (40.1 ± 10.9 g) in controls, whereas the mean of daily potassium intake was (1,571 ± 490 mg) and (1,733 ± 432 mg) in cases and controls respectively ($P < 0.05$). As seen in the Table 2, the daily consumed water pH mean in cases (7.1 ± 0.3) was significantly lower than controls (7.4 ± 0.3) ($P < 0.001$). The mean of daily total fluid volume (consumed water and other liquids) in controls (2574 ± 770 mL) was higher than cases (2,453 ± 1,036 mL), but this difference was not statistically significant. Table 3 shows the relationship between the pH level of water and fluids intake and kidney stones risk. There was a significant inverse association between the pH of daily drinking water and kidney stone risk in crude and all three adjusted models, as the OR in the last model was (OR = 0.15, CI 0.06–0.4, $P < 0.001$). Multiple logistic regression model was used to assess how much the pH of the consumed water is independent of other nutritional aspects for the risk of kidney stones formation. In the multivariate logistic regression analysis, there was no significant relationship between the consumed water volume, other liquid volume and total volume (consumed water + other liquid) and kidney stones among case and control groups.

4. Discussion

The incidence of KSDs increases day by day. Previous studies show that a low intake of fluids, especially water is associated with higher risk of kidney stone formation (Pubali M *et al.*, 2018). The result of current study demonstrates that alkaline water consumption have a protective effect on KSDs. The mechanism may be related to the effect of higher pH level liquids on transformation of a solid phase to liquid substances; furthermore, alkali load increases urinary pH and citrate excretion and higher amount of citrate intake in alkaline fluids by binding to calcium ions can prevents the calcium oxalate crystal deposition in kidneys and stone formation (Chen H-Y *et al.*, 2018).

Characteristic	Case group (n = 120) N (%)	Control group (n = 240) N (%)	p-value
Age (a)	49.3 ± 9.7	49.3 ± 9.7	1[b]
BMI (kg/m^2) (a)	26.9 ± 4.5	26.4 ± 3.8	0.31[b]
Level of education			
No education	30 (25)	3 (1.3)	–
High school diploma	49 (40.8)	92 (38.3)	<0.001*
Diploma and under graduate degree	22 (18.3)	85 (35.4)	–
Source of drinking water			
Tap water (pH = 7.1)	66 (55)	80 (33.8)	<0.001**
Mineral water (pH = 7.5)	4 (3.3)	3 (1.3)	–
Well water (pH = 6.8)	7 (5.8)	3 (1.3)	–
Boiled water (pH = 7.3)	9 (7.5)	5 (2.1)	–
Spring water (pH = 6.6)	5 (4.2)	5 (2.1)	–
Purified water (pH = 7.6)	3 (2.5)	5 (2.1)	–
Water purifier with alkaline filter (pH = 8.2)	0	2 (0.8)	–
Place of residence			
Urban	90 (75)	218 (90.8)	<0.001*
Rural	30 (25)	22 (9.2)	–
History of kidney stones in parents			
Yes	19 (15.8)	20 (8.3)	0.031*
No	101 (84.2)	220 (91.7)	–
Smoking status			
Non-smoker	75 (62.5)	154 (64.2)	–
Ex-smoker	6 (5)	29 (12.1)	0.04*
Current-smoker	39 (32.5)	57 (23.8)	–
Hookah use			
Yes	21 (17.5)	70 (29.2)	0.016*
No	99 (82.5)	170 (70.8)	–
Salt in cooking			
Yes	120 (100)	238 (99.2)	0.55**
No	0	2 (0.8)	–
Salt at tde table			
Yes	49 (40.8)	89 (37.1)	0.49*
No	71 (59.2)	151 (62.9)	–
Physical activity (met-min/week)			
Walking 4522<	48 (41)	71 (29.6)	–
Moderate 4,522–5,880	44 (37.6)	79 (32.9)	0.007*
Vigorous 5,880≥	25 (21.4)	90 (37.5)	–

Notes: Abbreviation: BMI, body mass index; [a]p-values are presented as mean ± SD; [b]p-values are for independent t-test to compare continuous variables; *p-values are for chi-square test to compare categorical variables; and **p-values are for Fisher's exact test to compare categorical variables. Compute of physical activity done with IPAQ questionnaire based on met-min/week (Craig *et al.* 2003)

Table 1. Baseline characteristics of participants and the distribution of demographic variables

Table 2. Comparison of the characteristics of all participants in case and control groups

	Case group (n = 120) Mean ± SD	Control group (n = 240) Mean ± SD	p-value
Animal protein intake (g/day)	36.5 ± 12.2	40.1 ± 10.9	0.002*
Potassium intake (mg/day)	1,571 ± 490	1,733 ± 432	<0.001*
Calcium intake (mg/day)	538 ± 223	530 ± 203	0.73*
Oxalate intake (mg/day)	1,377 ± 429	1,356 ± 405	0.64*
Volume of daily consumed water (mL)	1,244 ± 772	1,256 ± 683	0.88**
*** Volume of other liquid (mL)	1,209 ± 557	1,318 ± 612	0.10**
Total volume (water + other liquid) (mL)	2,453 ± 1,036	2,574 ± 770	0.26**
pH of daily consumed water	7.1 ± 0.3	7.4 ± 0.3	<0.001**
*** pH of other liquids	5.2 ± 0.6	5.1 ± 0.4	0.06**
Total pH (water + other liquid)	6.1 ± 0.3	6.2 ± 0.3	0.25**

Notes: *p-values are for Mann–Whitney U test to compare continuous variables; **p-values are for independent t-test to compare continuous variables. Daily dietary intake of animal protein, potassium, calcium and oxalate were obtained from FFQ and using Nutritionist IV Diet Analysis software and food composition table (Hulshof *et al.*, 2019; Mirmiran *et al.*, 2010); ***other liquids, including milk, tea, coffee, cola, lemonade, fruit juice, syrups, soft drinks and herbal essences

Table 3. Multiple logistic regression models for evaluating the relationship between pH and kidney stone

	Model	OR	95% CI	$\beta \pm$ SE	p-value
Daily consumed water pH	Crud model	0.09	0.04–0.2	−2.2 ± 0.5	<0.001
	Model 1	0.11	0.04–0.3	−2.3 ± 0.4	<0.001
	Model 2	0.14	0.05–0.4	−2.0 ± 0.5	<0.001
	Model 3	0.15	0.06–0.4	−1.9 ± 0.5	<0.001

Notes: Abbreviation: CI, confidence interval; OR, odds ratio; SE, standard error; and β, regression coefficient. Model 1: adjusted for education level and history of kidney stones in parents. Model 2: adjusted for consumption of smoke and hookah, physical activity level in addition to variables in Model 1. Model 3: adjusted for intake of daily animal protein and potassium and place of residence in addition to variables in Model 2. *The pH of other and total pH variables are not significantly related in the models that is reason why the data has not been included*

Several studies agree with the results from current study on the association between intake of alkaline water and kidney stones, Khan MM *et al.* and Siener *et al.* demonstrated that bicarbonate content of the alkaline water increases the urinary pH and citrate excretion into urine which inhibits the formation of kidney stone (Khan MM *et al.*, 2015; Siener *et al.*, 2004). Karagülle *et al.*(Karagülle *et al.*, 2007) have also reported that bicarbonate water can be recommended for preventing calcium oxalate stone formation owing to the inhibitory effect of citrate. Goodman *et al.*(Goodman *et al.*, 2009) have also reported that sport drinks containing more citrate and a higher pH level can be replaced with drinking water to reduce the risk of kidney stone formation.

The pH values of collected water samples in this study ranged between 6.5 and 8.3, meaning that there is a lot of variation in pH levels among different sources of consumed water. These pH values were within permissible limits as recommended by the World Health Organization (WHO, 2017).

A significant relationship was found between education level and risk of kidney stone formation, as education can influence individual's lifestyle and food choices. The achieved significant relationship between level of physical activity and kidney stone can be attributed to the sedentary life of cases and increased risk for KSD. The findings of this study were similar to the study conducted by Jiang *et al.* (2017), which has also showed a positive association between the risk of KSDs and male gender (a hormonal factor may be one of the key reasons for the higher prevalence in men), genetics, low educational level, amount of exercise, consumed water source and low intake of potassium. Smoking and hookah use is also significantly associated with the increased risk of KSDs in the current study, as the nicotine content of cigarettes, hookah and other tobacco products may gradually speed up the progression of kidney failure.

In this study, dietary intake of animal protein in the control group was significantly higher than the case group. Although animal protein is considered as a risk factor for kidney stone formation, the average daily consumption of animal protein in the both groups (40.1 ± 10.9 g vs 36.5 ± 12.2 g) were even less than the RDA recommendation (56 grams for an adult male).

A higher intake of dietary calcium and limitation of oxalate-rich foods were associated with a reduced risk of kidney stones, as a reduced intake of calcium-rich foods leads to an increased intestinal absorption of oxalate, that may itself rise the risk of stone formation (Alelign and Petros, 2018). The consumption of water with a higher pH level also would further reduce the risk.

The results of the current study are in contrast to some other studies such as the study conducted by Pubali *et al.* (2018), which showed that there is no statistically significant association between pH of drinking water and kidney stone incidence. Sumorok *et al.* (2012) have reported that despite high citrate and alkali content of orange soda, there was no significant alter in pH level of urine and citrate excretion between intervention and control groups. Passman *et al.* (2009) have also demonstrated that there were no differences in pH of urine and citrate excretion between individuals who consumed Fresca (citrate containing drink) and bottled water with respect to stone formation. The differences between the results of the current study and the above-mentioned studies can be attributed to the age range and health status of the subjects (nonstone-forming).

This study has some limitations. First, the case–control nature of the study is limited in defining causality. Second, KSD is a disease occurring over a long period of time, whereas in the current study, the diet and fluid intakes over that period were overlooked (using FFQ is the preferred method in nutritional studies).

Third, owing to the retrospective nature of case–control studies, the results are susceptible to recall bias. Fourth, the available information on stone composition was lacking. Fifth, impossibility of 24-h urine collection to test its pH (because most of the subjects with kidney stones referred to Urmia Imam Khomeini Educational Hospital were treated on an outpatient basis with painkillers and left the hospital and did not cooperate in 24-h urine collection).

5. Conclusion

The results of this case–control study in the northwest of Iran provide some evidence of the potentially beneficial effect of having drinking water with higher pH level on kidney stone formation and suggest that a daily fluid intake especially water consumption > 2,500 mL is related to lower risk of KSD in adult men. Moreover, as epidemiological evidence on this topic is extremely limited, and further investigations with well-designed prospective cohort and RCT studies with a larger sample size are required and participants' 24-h urine analyses is recommended to investigate the study process more accurately.

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