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Association of nephrolithiasis with the intake of carbonated drinks.

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ABSTRACT… Objective: To determine the association between the consumption of carbonated drinks and development of kidney stones. **Study Design:** Matched Case-control study. **Setting:** Liaquat National Hospital Karachi, Pakistan. **Period:** June 2017 to December 2017. **Material & Methods:** We recruited patients of nephrolithiasis admitted in Nephrology ward at Liaquat National Hospital as cases and controls from General Surgery ward. The sample size calculated was 186, with 93 cases and 93 controls, matched for age. Descriptive statistics of socio-demographic variables were computed. Multivariate logistic regression analysis was applied to determine the association between predictor and outcome variables. **Results:** A total of 186 patients participated in the study. Mean ages of the cases and controls were 34.92 (SD: 16.81) years and 31.76 (SD: 14.49) years, respectively. Around 66% of the cases and 75% of the controls had formal education. Approximately 16% of the cases and 10% of the controls were consuming soft drinks daily. Of them 77% were taking for more than 5 years. In multivariate analysis, we were unable to find significant associations between intake of carbonated drinks and kidney stones. However, the adjusted matched odds ratio (adj. mOR) for calcium intake was 6.36 (CI: 1.81- 22.33) and for caffeine intake was 7.9 (CI: 2.12 – 30.04). Those who had a past history of kidney diseases were at higher risk of developing kidney stones (mOR14.5; CI: 3.20- 65.76). **Conclusion:** The Study did not show any significant association of kidney stones with the intake of carbonated drinks. However, further longitudinal studies are required in order to confirm or refute any association between intake of carbonated drinks and nephrolithiasis.

Key words: Cold Drinks, Carbonated Drinks, Nephrolithiasis, Renal Stones, Risk Factors.

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INTRODUCTION

Estimated prevalence rate of uric acid stones is >0.75% in Pakistan.[1] About 5-10% of all kidney stones is composed of uric acid, however the prevalence of uric acid stones significantly increases among patients with obesity, diabetes or metabolic syndrome.[2] The formation of kidney stones, according to some studies is significantly associated with increased consumption of carbonated drinks.[1,3] Various other risk factors like magnesium and oxalate excretion, changes in pH and obesity are also linked with the intake of carbonated drinks.[5]

Nephrolithiasis is a very highly prevalent disease with rates ranging from 7 to 13% in North America, 5-9% in Europe, and 1-5% in Asia[4] There can be various factors which can lead to the formation of kidney stones like obesity, gender, intake of water and caffeine, age, smoking habits and diet. Once formed they can lead to complications and can cause and end organ damange as well.

Carbonated drinks increases the risk factor of stone formation because they contain phosphoric acid.[1,3] A number of other diseases can be caused by a high intake of soda and other carbonated drinks like diabetes, hypertension and chronic kidney diseases.[1] According to a study carried out in 2012, 28.3% of students were overweight and one of the cause of this obesity in children was intake of soft drinks.[5] These carbonated drinks are artificially sweetened and their regular consumption can increase the chance of heart attacks in men[6] and of gout in females.[7] There is a 26% higher chances of developing type 2

diabetes mellitus in people who consume the sugary soft drinks.[8] An incidence of 1116 per 100,000 was reported for 18 to 64 year old people in the year 2000[9] across all ages, sex and race.[10] High intake of soda and inefficient water intake can also lead to nephrolithiasis as the urinary volume should be more than 2 litres in a day.[11]

The purpose of this research is to collect valid and reliable information regarding the prevalence of kidney stones associated with the intake of carbonated drinks. By limiting the use of soft drinks the risk of kidney stone formation can be attenuate. And this will play a part in preventing the loss of a kidney and developing other chronic kidney diseases.

OBJECTIVE

To determine the association between the consumption of carbonated drinks and development of kidney stones

MATERIAL & METHODS

It was a matched case control study. The study was conducted from June 2017 to September 2017 for total of six months, at Liaquat National Hospital Karachi, Pakistan. The study participants were the patients admitted in wards of the Liaquat National Hospital. The cases were the patients admitted in urology ward with the diagnosis of kidney stones and the controls were the patients admitted in other wards without the diagnosis of kidney stones. The patients who refused to participate in the study were excluded. A structured questionnaire was developed in order to collect the information from the patients. It was a case control study and data was matched according to the age of the cases and controls.

The Sample size was calculated by OpenEpi software version 3.01. At Odds Ratio of 2.3[1] and proportion of exposure among cases and controls as 56.2% and 35.7% respectively, the final sample size calculated was 186, with 93 cases and 93 controls. The confidence level was 95% and power was 80% for sample size calculation.

Data was analyzed using software SPSS version 22. Descriptive statistics of socio-demographic variables were computed as frequency with percentages and mean with standard deviation or median with interquartile range (incase if data was not symmetrically distributed). Univariate and multivariate analysis was done using logistic regression to determine the unadjusted and adjusted relationship between predictor variables (age, gender, education, beverages use etc) and outcome (kidney stones). Adjusted Odds ratios with their confidence intervals were obtained of the different categories of independent variables. A p-value of <0.05 was considered as statistically significant.

The ethical approval and endorsement of the anticipated study was taken from ethical review committee (ERC) of the LNH. Fully Informed Consent on a structured consent form was required from all participants. The duration of interview was approximately 10 to 15 minutes. The participants in no way were subjected to unjustifiable discomfort during questionnaire filling.

RESULTS

A total of 200 patients (100 cases and 100 controls) matched on age participated in the study. Mean ages of the cases and controls were 34.92 (standard deviation (SD): 16.81) years and 31.76 (SD: 14.49) years, respectively. There were more male participants (58%) in sample than females (42%). Around 66% of the cases and 85% of the controls had formal education, of them 13% of controls and 6% of cases had postgraduate qualification. There was insignificant difference of body weight among the cases [mean (SD) = 66.93 (21.77) kg] and controls [mean (SD) = 65.25 (20.26) kg]. Approximately 16% of the cases and 10% of the controls consumed carbonated drinks every day. Almost 60% of cases and 70% of controls consumed carbonated drinks for more than 10 years. More than 60% wanted it with their meals, while less than 30% consumed is as refreshment. Merely 14% of cases and 13% of controls were smokers (p-value = 0.5). Around 17% of the cases and 21% of controls drank less than 3 glasses of water per day. About 30% of cases and 23% of controls frequently used

analgesics (p-value 0.07).

In univariate logistic regression analysis (Table-I) the patients who were less educated, matched odds ratio (mOR) 1.68 (95% CI: 0.90 -3.13), had co-morbid diseases mOR 2.6 (95% CI: 1.25-5.39) and had past history of kidney diseases mOR 9.25 (95% CI: 3.25-25.59) were at higher risk of developing kidney stones. The association was also significant when the family history was positive for kidney diseases, mOR 2 (95% CI: 1.09-3.64). In our sample, kidney diseases were found in fathers and siblings of 15% of the cases each, while 6% of fathers and 9% of siblings of the control group had a history of kidney diseases. Intake of calcium supplements was significantly associated with kidney stones, mOR 2.41 (95% CI: 1.23-4.73). Similarly we found strong associations between carbonated drink intake and kidney stone formation, mOR 4.8 (95% CI: 2-11.63). In our sample we were unable to find any significant associations between intake of carbonated drink and kidney stones. Apart from this, associations between quantity of daily water consumption and stone formation were also insignificant.

In multivariate logistic regression analysis (Table-II), adjusted matched odds ratio (adj. mOR) for calcium intake was 6.36 (95% CI: 1.81- 22.33) and for caffeine intake was 7.9 (95% CI: 2.12 – 30.04). Those who had a past history of kidney diseases were at higher risk of developing kidney stones, adj.mOR 14.5 (3.20- 65.76).

Characteristics	Cases (n)	Controls (n)	mOR (95% CI)
Gender			
Female	37	47	1 (reference)
Male	63	53	1.68 (0.90-3.13)
Education			
Educated	66	85	1 (reference)
Uneducated	34	15	3 (1.41-6.37)
Co-morbid			
Yes	34	18	1 (reference)
No	66	82	2.6 (1.25- 5.39)
Past history of kidney diseases			
No	60	93	1 (reference)
Yes	40	7	9.25 (3.25- 25.95)
Family history of kidney disease			
No	62	78	1 (reference)
Yes	38	22	2 (1.09- 3.64)
Caffeine intake			
No	63	47	1 (reference)
Yes	17	48	4.8 (2 – 11.64)
Calcium intake			
Yes	22	38	1 (reference)
No	78	62	2.41 (1.23- 4.73)
Carbonated drinks use			
No	14	15	1 (reference)
Yes	86	85	1.66 (0.79- 3.8)
Daily water intake			
≤ 8 glasses	49	61	1 (reference)
>8 glasses	51	39	1.68 (0.95 – 2.97)

Table-I. Univariate conditional logistic regression for association of carbonated drinks and other covariates with the formation of kidney stones.
Abbreviations: mOR, matched odds ratio, CI, confidence interval.

Characteristics	mOR (95% CI)
Education	
Educated	1 (reference)
Uneducated	1.53 (0.36 -6.4)
Co-morbids	
Yes	1 (reference)
No	0.32 (0.08 – 1.29)
Past history of kidney diseases	
No	1 (reference)
Yes	14.5 (3.20- 65.76)
Family history of kidney disease	
No	1 (reference)
Yes	1.42 (0.45- 4.49)
caffeine intake	
No	1 (reference)
Yes	7.9 (2.12 – 30.04)
Calcium intake	
Yes	1 (reference)
No	6.36 (1.81- 22.33)

Table-II. Multivariate conditional logistic regression for association of carbonated drinks and other covariates with the formation of kidney stones Abbreviations: mOR, matched odds ratio, CI, confidence interval.

DISCUSSION

In previous research by Saldana et al, the risk of chronic kidney disease increased by the intake of two or more colas per day.[12] In our sample 16% of the cases consumed carbonated drinks every day, compared to only 10% of the controls. However, we were unable to find any significant associations between the intake of carbonated drinks and kidney stones. Earlier meta-analysis also shows inconsistent results, where the risk of kidney stones was not significantly related to intake of juice (RR=1.02, 95% CI: 0.95, 1.10; P=0.64), soda (RR=1.03; 95% CI: 0.90, 1.17; P=0.65), or milk (RR=0.96; 95% CI: 0.88, 1.03; P=0.21). We could also not find significant associations between intake of water quantity and formation of kidney stones. There may be several explanations of the insignificance of results. One reason is the in-built respondent bias in cases and controls, leading the cases to recall consumption of soft drinks along with the frequency of consumption more accurately compared to that of controls. Wish bias could also have occurred with cases deliberately quoting lesser consumption compared to controls. The authors also suggest a larger sample size and probably a different study design in order to find more accurate associations. A cohort study design, with those who consumed soft drinks and maintained a diary could be more helpful in ascertaining true consumption as well as associations.[13]

On univariate logistic regression analysis we found significant associations of kidney stone formation with educational status, where lack of education made the person more likely to develop kidney stones compared to those who were educated. These associations of socio-economic status in terms of education and occupation with chronic diseases have been explored previously by researchers. Patients with lower education levels and from regions are found to be more likely to present to our tertiary care center with stone burden greater than 2 cm[14] Similarly univaritae analysis showed significant inverse associations between presence of co-morbidities and kidney stone formation. However, several factors namely educational status, co-morbidities and family history of kidney disease were insignificant when adjusted for confounders on multivariate analysis.

Our study also found significant associations of kidney stones with past history of kidney diseases. A study of cross-sectional data looking at the association of age, gender and race on health related quality of life of stone formers was performed and on multivariable analysis older patients had a significantly higher total health related quality of life score than younger patients (per 10-year increase OR 1.25, p <0.0001).[15]

The suggested connection between caffeine and calcium is that caffeine intake is linked with increased urinary calcium excretion which increases the risk of developing kidney stones.[16]

In the present research, increase in caffeine and calcium intake was significantly associated with kidney stone formation when adjusted for confounders. On the contrary, past studies have shown varying results, where caffeine intake

has also been independently associated with a reduced risk of kidney stones.[17] The effect of calcium supplementation on stone formation is controversial as large doses of calcium supplements may lead to stone formation, if taken apart from meals.[18]

CONCLUSION

Several studies have observed associations between kidney stone formation and intake of carbonated drinks. Those studies were, however, cross-sectional in design. Our study had a comparison group and cases were known hospital patients where they were included in the study through their laboratory diagnosis. This added to the strength of the study. It did not show any significant association of kidney stones with the intake of carbonated drinks but other factors were measured and are discussed above.

It is further suggested to design studies where larger sample sizes can be used with more in-depth assessments employing Food Frequency Questionnaires. These could help ascertain various associations and confounders that could have been overlooked by our study.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Maira Adeel	Conceptualization of study design, collection of data and literature search, assembling and entry of data, drafting of the article.	
2	Saima Zainab	Analysis and interpretation of data, Critical revision of the article for important intellectual content, statistical expertise, final approval of the article.	
3	Saima Athar	Proof reading and manuscript revision.	
4	Aneeta Khoso	Statistical expertise, final approval of the article.