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THE INFLUENCE OF INCREASED CARBONATED BEVERAGES CONSUMPTION ON THE RISK OF NEPHROLITHIASIS DEVELOPMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

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ABSTRACT

Nephrolithiasis, a frequent medical disorder, is affected by a variety of environmental factors, including food. Fluid consumption is an important dietary strategy for reducing kidney stone risk since it has a direct impact on nephrolithiasis. The primary goal of this study is to collect accurate and trustworthy data about the effect of carbonated beverages on the risk of developing nephrolithiasis in order to make evidence-based recommendations. To accomplish this purpose, we conducted a thorough and systematic review, followed by a meta-analysis. This enabled us to assess the link between increasing carbonated beverage consumption and nephrolithiasis risk. Our search included Medline, Web of Science, and PubMed databases up to April 2024, yielding 249 articles initially, 39 of which met eligibility requirements after title and abstract screening. The meta-analysis includes a total of 16 publications. A random-effects model was used to analyse the acquired data in order to account for differences in study design and population. We used the R programming language (version 4.3.1) to compute pooled relative risks (RRs) and 95% confidence intervals (CIs), as well as to quantitatively analyse heterogeneity using the I2 statistic. Our findings revealed a significant link between increasing carbonated beverage consumption and an increased risk of developing nephrolithiasis (RR: 1.855; 95% CI, 1.26–2.74). To reduce potential health hazards, we highly advise consumers to limit the intake of carbonated beverages. This reduction is crucial not only for minimising kidney problems and other chronic illnesses, but also for promoting nephrolithiasis prevention and encouraging people to adopt healthy eating habits.

Keywords: Nephrolithiasis, Carbonated beverages, Systematic review, Meta-analysis, Relative risk

INTRODUCTION

Nephrolithiasis, also known as kidney stone disease, is caused by the crystallisation of minerals and salts in the urinary tract, which often occurs when urine becomes oversaturated with lithogenic compounds like calcium, oxalate, and uric acid. This urological illness is becoming a major global health concern, affecting an increasing number of people in both industrialised and developing countries. The impact of nephrolithiasis is not limited to the acute pain and discomfort associated with stone passage, but also includes long-term complications such as chronic kidney disease (CKD), bone demineralisation, cardiovascular disease, and even increased mortality (Alexander et al., 2014; Taylor et al., 2015; Ferraro et al., 2013; Vande-Pol et al., 2019; Zakari et al., 2024). According to a recent economic analysis, the financial burden of nephrolithiasis is expected to rise significantly, with a projected cost of more than $3 billion USD by 2030, driven by rising incidence, recurrence rates, and healthcare utilisation (Antonelli et al., 2014; Ziemba et al., 2017; Liu et al., 2023).

Modifiable risk factors, particularly nutrition and lifestyle decisions, are significant contributors to the rising occurrence of kidney stones. A high consumption of animal protein, salt, and oxalate-rich meals, along with insufficient hydration, provides a metabolic milieu favourable to stone formation (Scales et al., 2012). Fluid consumption is particularly important in kidney stone prevention since low urine volume and high solute content increase the likelihood of crystal formation. While water remains the recommended fluid, more people are turning to sugar-sweetened beverages (SSBs), particularly carbonated soft drinks, which may increase the risk of stone development. Frequent consumption of carbonated beverages has been linked to an increased risk of nephrolithiasis, according to epidemiological studies. Some studies have even linked poor dietary and lifestyle choices to more than half of incident stone cases (Ferraro et al., 2017; Enas et al., 2022; Shabani et al., 2022; Constance et al., 2023; Alruwaili et al., 2023).

Carbonated soft drinks, particularly those sweetened with high-fructose corn syrup (HFCS), have become dietary staples in many nations, particularly the United States, where per capita consumption is still among the highest in the world (Bleich et al., 2009; CDC, 2023). These beverages not only contribute to caloric excess (about 150 calories per 12-ounce serving), but they also contain substances such as phosphoric acid, caffeine, and fructose, all of which have been linked to changes in urine composition. Several processes have been hypothesised, including increased urinary calcium and oxalate excretion, decreased citrate levels, and pH changes in urine, all of which lead to higher lithogenic potential (Al-Dabbagh et al., 2022; Taylor et al., 2008; Fox et al., 1972; Imran et al., 2023; Omoyajowo et al., 2024). Despite rising awareness, carbonated soft drink consumption remains high, particularly among teenagers and young people. Given this backdrop, it is critical to determine the extent to which carbonated beverages influence the formation of kidney stones. With recurrence rates predicted to be as high as 50% within 5 to 10 years of the first episode (Rule et al., 2014), effective dietary-based prevention interventions are critical. The emphasis on modifiable risk factors, particularly beverage choices, can help to lessen the personal, societal, and economic cost of nephrolithiasis.

As a result, the purpose of this study is to examine and quantify the association between carbonated beverage consumption and the risk of nephrolithiasis using a systematic review and meta-analysis. The study aims to inform public health guidelines and individual dietary decisions by synthesising available knowledge, ultimately contributing to a reduction in kidney stone incidence and recurrence through evidence-based preventative efforts.

MATERIALS AND METHODS

Methodology

We did a comprehensive literature search on the Medline, Web of Science, and PubMed databases from inception to April 2024. Our search focused on studies that investigated the association between increased consumption of carbonated beverages and the likelihood of developing nephrolithiasis.

The search terms "nephrolithiasis," "urinary calculi," "kidney stones," "kidney calculi," or "genitourinary disorder" combined with "carbonated beverage," "carbonated drinks," "beverages," "soft drinks," "sugary soda," "energy drinks," "sport drinks," or "carbonated water" were used to find pertinent articles. To find any more pertinent articles, we manually examined the bibliographies of the included studies and associated reviews in addition to the database searches.

Articles published in English with accessible full text and statistical measures measuring nephrolithiasis and carbonated beverages were included in the study. Given the heterogeneity in eligible age groups across research, there were no age restrictions imposed on study participants. We retrieved data from 16 papers after thoroughly evaluating their relevance and eligibility.

We used a random-effects model to analyse the obtained data, accounting for differences in study design and population. We conducted this research using the R programming language (version 4.3.1). The I^2 statistic was used to quantify heterogeneity, with values more than 50% and 75% indicating moderate and substantial heterogeneity, respectively. All statistical tests were two-sided, with a significance level of $P < 0.05$. Hedges' g (Hedges et al., 1985) was used to calculate the between-study effect sizes.

$$Hedges's(g) = Cohen's(d) \times \left(1 - \frac{3}{4(n_I + n_C) - 9}\right) \quad (1)$$

Where Cohen's (d) is given as;

$$Cohen's(d) = \frac{\overline{X_I} - \overline{X_C}}{\sqrt{\frac{(n_I - 1)S_I^2 + (n_C - 1)S_C^2}{n_I + n_C - 2}}}$$

And the variance of Hedges's (g) is given by;

$$V_g = [J(df)]^2 V_d \quad (2)$$

Random-Effects Model

The random-effects model makes the assumption that the effect size at the study level is a random sampling from an infinite number of similar studies (DerSimonian & Kacker, 2007). The impact size at the study level can fluctuate systematically as a result of differences in the research population, interventions, comparators, endpoint definitions, and designs.

Thus, the deviation (θ_i) between the individual study's effect size (y_i) and the true effect in the population (μ) is more than that expected due to sampling variation (ε_i) alone (Mona *et al.*, 2020). Consequently, the effect size of each particular study can be represented as follows:

$$y_i = \mu + \theta_i + \varepsilon_i \quad (3)$$

Here, θ_i depends on the between-study variance (τ^2), while ε_i depends on the within-study variance $(\sigma^2{}_i)$. As the random-effects model draws a random sample of effect sizes, the mean of the effect size deviation is zero. It assumes that θ_i is normally distributed with a mean of zero and a variance of (τ^2), represented as $\theta_i \sim N(0, \tau^2)$, and that the sampling error is also normally distributed as $\varepsilon_i \sim N(0, \sigma^2{}_i)$.

The weight (w_i) associated with each individual study is the inverse of the total variation, given by $w_i = 1/(\sigma^2{}_i + \tau^2)$.

The pooled effect estimate of y_i is calculated as:

$$\hat{\mu}_r = \frac{\sum y_i w_i}{\sum w_i} \quad (4)$$

Where y_i is distributed as; $y_i \sim N(\mu, \sigma_i{}^2 + \tau^2)$

This estimated effect size's variance can also be re-presented as:

$$V(\hat{\mu}_r) = \frac{1}{\sum w_i} \quad (5)$$

Restricted maximum likelihood (REML): The between-study variance was estimated using restricted maximum likelihood (REML) method (Raudenbush, 2009).

The estimate $\hat{\tau}^2_{REML}$(eqn. 7) is produced by setting the derivative of the restricted log-likelihood function of eqn. (6)

$$InL(\tau^2) = -\frac{k}{2}In(2\pi) - \frac{1}{2}\sum In(v_i + \tau^2) - \frac{1}{2}\sum \frac{\left(y_i - \hat{\mu}_{RE}(\hat{\tau}^2_{ML})\right)^2}{(v_i + \tau^2)} - \frac{1}{2}In\left(\sum \frac{1}{(v_i + \tau^2)}\right) \quad (6)$$

with respect to τ^2 equal to zero and solving the resulting equation for τ^2. This gives;

$$\hat{\tau}^2_{REML} = Max\left\{0, \frac{\sum W^2_{i,RE}\left(\left(y_i - \hat{\mu}_{RE}(\hat{\tau}^2_{ML})\right)^2 - v_i\right)}{\sum W^2_{i,RE}} + \frac{1}{\sum W_{i,RE}}\right\} \quad (7)$$

Where; $W_{i,RE} = \frac{1}{(v_i + \hat{\tau}^2_{REML})}$ and $\hat{\tau}^2_{REML}$ is calculated by a process of iteration with an initial estimate of $\hat{\tau}^2_{REML}$ greater than or equal to zero and each iteration step requires non-negativity (DerSimonian& Laird, 1986; Sidik& Jonkman, 2007).

RESULTS AND DISCUSSION

Results

Figure 1 shows the selection procedure along with the reasons for exclusion. After removing duplicates and reviewing the titles and abstracts, 39 of the 249 articles that the literature search initially produced were determined to be potentially eligible. After a comprehensive full-text examination, 16 publications were selected to be included in the meta-analysis.

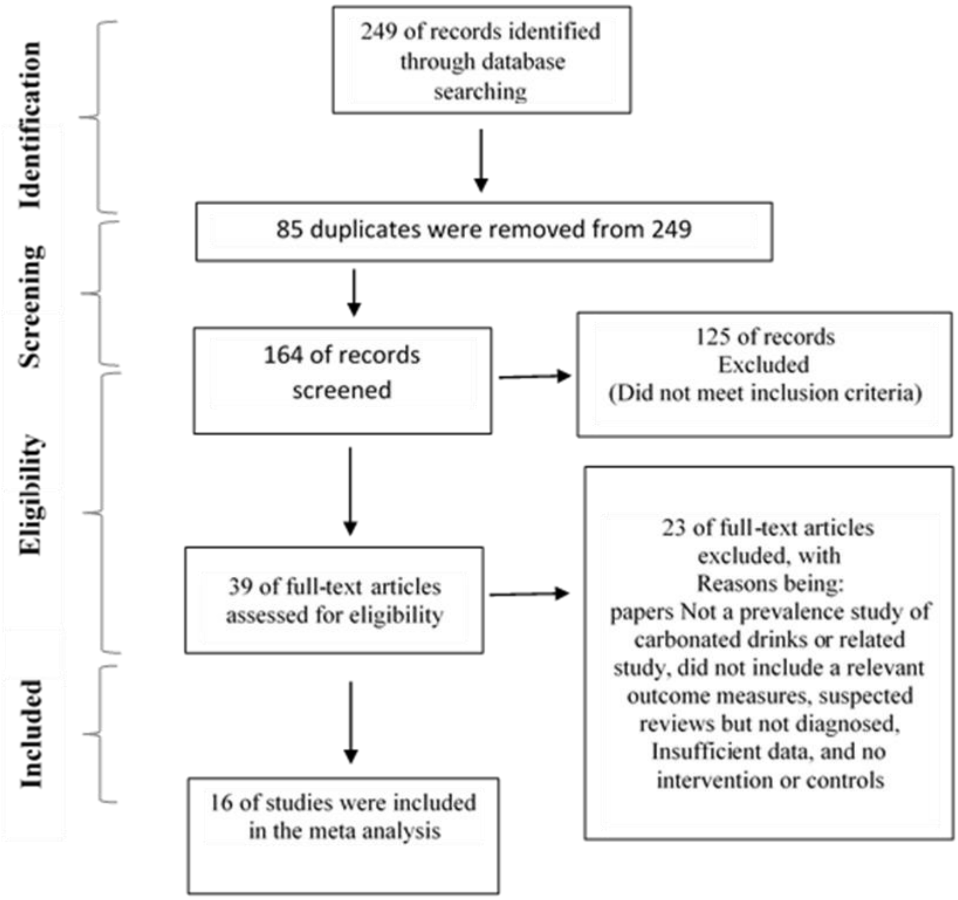
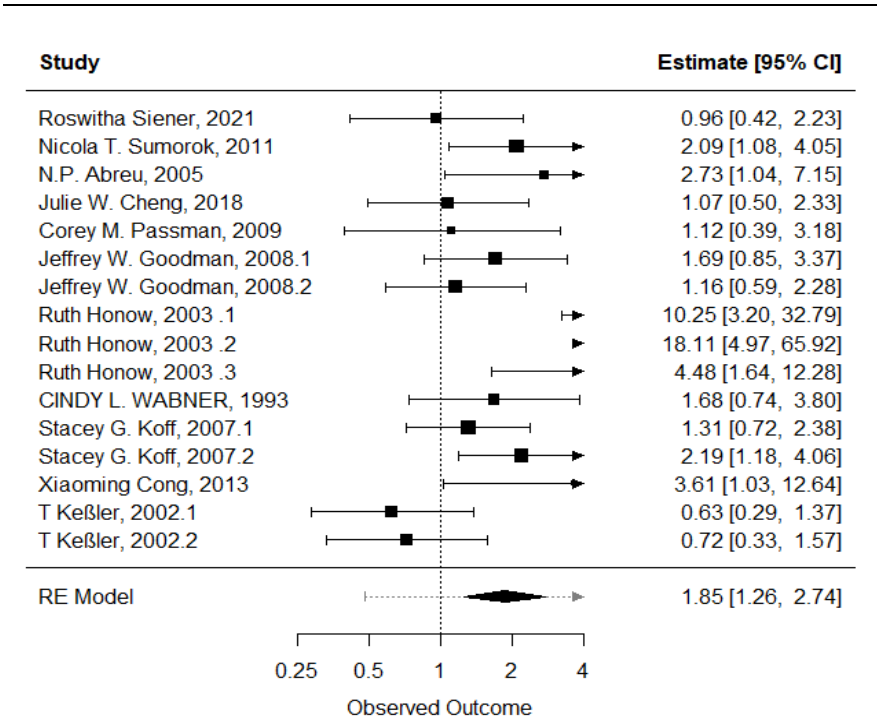


Figure 1: Flow of information through the different phases of included studies for systematic review and meta-analysis

Table 1: Heterogeneity Test

	Random-Effects Model
I^2– Statistic:	71.99%
Q – Statistic:	45.4668
P – Value	0.0001
tau^2– Statistic	0.4365

Table 1 shows the random-effects model's heterogeneity test findings. The I^2 statistic, which indicates how much total variation among research is due to heterogeneity rather than chance, is 71.99%. This implies that actual variations between the included studies account for roughly 71.99% of the variability in research findings, rather than random chance. The corresponding Q statistic, which quantifies the amount to which the observed diversity in effect sizes across the included studies exceeds what would be predicted by chance, is 45.4668, with a p-value of 0.0001. This shows that the Q statistic is statistically significant, providing strong evidence against the null hypothesis of homogeneity and indicating significant heterogeneity among the papers included in the study.



Decrease Risk *Increase Risk*

Figure 2: Forest plot of meta-analysis comparing highest vs controlled level of carbonated beverage intakes and risk of developing nephrolithiasis

The terms "Decrease Risk" and "Increase Risk" are used in Figure 2 to contextualise the possible health consequences of nephrolithiasis incidence that occur in relation to the intake of carbonated beverages. "Decrease Risk" denotes that consuming more carbonated drinks is linked to a lower chance of developing the condition or adverse event being studied (prevalence of developing nephrolithiasis incidence). In essence, it implies that people who consume more carbonated beverages are less likely than those who consume fewer to acquire nephrolithiasis. On the other hand, "Increase Risk" implies that a higher exposure to the factor is linked to a higher likelihood of encountering the condition or adverse event under study.

High carbonated beverage consumption was associated with a considerably higher risk of having nephrolithiasis (RR: 1.85; 95% CI, 1.26 – 2.74), as seen in Figure 2. Table 2 shows this estimate's significance along with the associated confidence interval.

Table 2: Pooled estimate and relative risk (RR)

Estimate	RR	Se	P-value	CI
0.6178	1.855	0.1986	0.0019	0.2285,1.0071

Table 2 shows that the predicted effect size is 0.6178, with a relative risk of 1.855. These figures show the relative risk of developing nephrolithiasis as a result of drinking more carbonated beverages. In this context, a relative risk of 1 shows no correlation, whereas a number greater than 1 implies increased risk and a value less than 1 indicates decreased risk. The related p-value of 0.0019 indicates that the relative risk estimate is statistically significant. The standard error, which measures the accuracy of the estimate, is 0.1986. With a 95% confidence level, the Confidence Intervals show that the true value of the estimate is between 0.2285 and 1.0071. Notably, the estimate of 0.6178 is within this range, demonstrating statistical validity.

To sum up, the table highlights a strong correlation between the prevalence risk of nephrolithiasis and higher carbonated beverage intake. A significant rise in the risk of nephrolithiasis is linked to the consumption of carbonated beverages, as indicated by the estimated relative risk of 1.855.

Key Findings and Public Health Implications

The results of this meta-analysis offer strong proof that consuming more carbonated drinks is substantially linked to an elevated risk of nephrolithiasis. Individuals who consume large amounts of carbonated beverages are about 86% more likely to develop kidney stones than those who consume them in moderation, according to the pooled relative risk (RR = 1.855; 95% CI: 1.26–2.74; p = 0.0019). Concerns expressed by previous epidemiological and clinical investigations are supported by this connection, which is still statistically significant and clinically significant.

The strength of relationship may differ by study population, geography, beverage types, and other lifestyle factors, despite the fact that the overall trend is robust, according to the high level of heterogeneity among included studies ($I^2 = 71.99\%$). The stability of results across several research, in spite of this heterogeneity, suggests a reliable pattern that cannot be written off as chance.

These findings emphasise the significance of dietary counselling and policy-level initiatives targeted at lowering the consumption of sugar-sweetened and carbonated beverages, particularly in high-risk populations, from the standpoint of public health. This evidence is a call to action for health authorities and clinicians to include beverage consumption patterns in preventive nephrolithiasis guidelines, especially in low- and middle-income countries, given the rising prevalence of kidney stones worldwide and the growing popularity of sugary drinks.

Additionally, these findings create new opportunities for patient-specific recommendations and focused health education efforts. As part of a larger lifestyle management strategy to address recurrent nephrolithiasis, clinicians and nutritionists may take into account customised risk assessments based on beverage consumption patterns.

Discussion

This meta-analysis provides compelling evidence that excessive carbonated beverage consumption is related with a significantly higher risk of developing nephrolithiasis. The pooled relative risk of 1.855 (95% CI: 1.26-2.74) implies that people who consume the most of these beverages are nearly twice as likely to get kidney stones as those who consume less. These findings are consistent with prior observational studies linking sugary beverages to negative renal outcomes such as changed urine composition, increased calcium excretion, and lower citrate levels—all of which contribute to stone formation.

Multiple pathways could be involved in the biochemical mechanisms that underlie this connection. Carbonated drinks, particularly those that are high in sugar and phosphoric acid, can increase the excretion of calcium and oxalate, two chemicals that promote stone formation, and lower the pH of the urine. Furthermore, sodas with a high fructose content have been linked to elevated serum uric acid levels, which may further raise the risk of uric acid stones. Additionally, drinking soft drinks frequently takes the place of drinking water, which lowers urine volumes, which is a known risk factor for nephrolithiasis.

The existence of heterogeneity (I^2 = 71.99%) must be recognised notwithstanding the strength of these findings. Differences in study design, geography, participant demographics, definitions of beverage exposure, and confounding variable adjustment are probably the causes of this discrepancy. For instance, because of increased vulnerability to dehydration, research carried out in areas with high ambient temperatures might find a stronger correlation. Similar to this, the effect magnitude can vary across artificially sweetened or carbonated water beverages and sugar-sweetened sodas, as several included research categorised them under broad exposure categories.

Given the broad availability and consumption of carbonated beverages worldwide, particularly among young people, these findings have important public health implications. Interventions that raise knowledge about the hazards of excessive carbonated beverage intake, together with support of improved hydration practices, may help to reduce the burden of nephrolithiasis. More research, particularly large-scale prospective cohort studies and controlled trials, is needed to explain causal processes and differentiate the impacts of various beverage kinds.

CONCLUSION

The results of this meta-analysis show a strong correlation between the risk of nephrolithiasis and higher carbonated beverage use. High-intake individuals are almost twice as likely to be at danger as those who consume less. These findings highlight the need for increased knowledge and vigilance about the regular intake of sugary and carbonated beverages, particularly in groups that are already at risk for kidney stones.

It is critical to recognise that nephrolithiasis, which frequently presents as a benign but painful illness, poses a substantial threat to both the healthcare system and human well-being. It has high treatment expenses and is increasingly recognised as a systemic disease linked to a variety of health issues, including bone fractures, chronic kidney disease, renal cell carcinoma, cardiovascular disease, and even death. To lower these risks and the related socioeconomic burden, preventative measures focussing on modifiable lifestyle factors can be extremely helpful for people who are at high risk of recurring or incident instances.

While further study is needed to understand the causative pathways and specific effects of different beverage types, the results clearly supports reducing carbonated beverage consumption as a preventive measure.

Policy Recommendations

The following suggestions are made in light of the observed risk of nephrolithiasis in order to promote healthier eating habits and prevent the emergence of the disease:

i. Public health campaigns to educate about carbonated drink risks
ii. Transparent labeling regulations for sugary beverages
iii. School/workplace guidelines promoting water intake
iv. Taxation on sugar-sweetened drinks to fund health initiatives
v. Healthcare counseling to reduce carbonated beverage consumption in high-risk individuals.

By following these suggestions, we can reduce the risk of nephrolithiasis and encourage improved kidney health among the general public. This may consequently lead to greater overall health and a decreased burden on health care providers.

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