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ORIGINAL RESEARCH ARTICLE

A Quantitative Synthesis to Assess the Influence of Carbonated Beverage Consumption on the Occurrence of Abnormally Low Calcium Levels in the Bloodstream

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ABSTRACT

This research looks into how drinking carbonated beverages (CB) relates to hypocalcemia. Hypocalcemia is a condition where people have low calcium levels in their blood, which can be serious to a healthy life. We reviewed past studies using databases such as Medline, Web of Science, PubMed, and Google Scholar to capture older articles, screening up to April 2023 for relevant publications. Out of 198 articles identified, after closely examining titles and abstracts, 25 were deemed relevant. In the end, we included six studies in our detailed analysis. To understand the data, we calculated pooled relative risks (RRs) along with 95% confidence intervals (CIs) using a random effects model. This helped us deal with differences in results across the studies. We assessed variability using the I^2 statistic. The analysis revealed a moderate association between higher CB consumption and an increased risk of hypocalcemia, with a pooled RR of 1.34 (95% CI: 0.93–1.92). Variability across studies was moderate (I^2 = 51.46%). These findings suggest that regular consumption of carbonated beverages may moderately increase the risk of developing hypocalcemia. Clinically, this underscores the importance of reducing CB intake to prevent potential adverse effects on calcium metabolism and overall bone health.

INTRODUCTION

Calcium is a necessary electrolyte that is involved in many body processes. Calcium acquires an electric charge when it dissolves in biological fluids like blood, which helps with functions like neurone transmission and muscle contraction. A considerable amount of calcium is in the bloodstream, with over 40% of it coupled to proteins like albumin, even though the majority is stored in bones. Although it does not take part in immediate physiological activities, this bound calcium acts as a store for cellular functions (James, 2023).

When the body's calcium levels drop too low, it can cause hypocalcaemia, which can lead to a number of health problems. A number of things can cause this syndrome, such as parathyroid gland malfunction, insufficient calcium intake from food or drink, problems with renal function, or side effects from drugs. Severe hypocalcaemia can cause muscle cramps, sadness, tingling in the limbs, and stiffness in the muscles. This disorder is frequently detected by routine blood tests (James, 2023).

Carbonated drinks, especially soft drinks, are a major cause of hypocalcaemia, especially in people with hypoparathyroidism (Guarnotta et al., 2017). Postoperative hypoparathyroidism, which can result in chronically low calcium levels, can occur in certain patients after total thyroid surgery. Although 60–70% of cases recover in 4–6 weeks, 2–10% of patients may experience chronic hypoparathyroidism with persistent calcium shortage (Lorente-Poch et al., 2015).

A higher risk of hypocalcaemia and bone fractures has been linked to high cola drink intake, according to research (Docimo et al., 2012; Mazariegos-Ramos et al., 1995; Amato et al., 1998; Wyshak et al., 1994; Moran et al., 2013). Phosphoric acid, a frequent constituent in many carbonated drinks, is the main cause of concern since it can disrupt the metabolism of calcium. By either boosting renal excretion or decreasing intestinal absorption of calcium, phosphate consumption from food or drink can lower blood calcium levels. For those who have impaired parathyroid function after surgery, this effect is especially

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harmful, increasing their vulnerability to the negative effects of carbonated beverages (Tucker et al., 2006).

To sum up, excessive carbonated beverage consumption greatly increases the chance of developing hypocalcaemia and associated health issues, particularly in people with hypoparathyroidism. Comprehending this correlation is essential for formulating dietary guidelines and reducing the hazards linked to use of carbonated beverages.

This study's main goal is to collect precise and trustworthy data on the prevalence of hypocalcaemia associated with drinking carbonated beverages. We accomplished this goal by carrying out a comprehensive systematic review and meta-analysis with the intention of establishing evidence-based conclusions that measure the association between higher intake of carbonated beverages and the risk of hypocalcaemia. Not only can these insights help people avoid developing this condition, but they can also help them make better nutritional choices.

MATERIALS AND METHODS

We searched four databases (Medline, Web of Science, PubMed, and Google Scholar) extensively in April 2023 for pertinent English-language papers. In order to ensure a thorough evaluation of the literature, Google Scholar was purposefully included to capture older works that might not be indexed in the other databases. These databases were selected because they offer access to high-quality, peer-reviewed research and are often used in health-related research.

We concentrated on experimental research investigating the connection between the incidence of hypocalcaemia and the intake of carbonated drinks. In addition to "Hypocalcaemia" and "Calcium deficiency disease," we used important search terms like "Carbonated drinks," "Sugary soda," and "Energy drinks." We also used Medical Subject Headings (MeSH) terms, such as "Caffeine," "Osteoporosis," "Bone Density," and "Phosphoric Acid," in order to refine our search.

The English-language publications that included statistical measures for evaluating hypocalcaemia, or low calcium levels, were included in the inclusion criteria. Since the qualifying age ranges in different research vary greatly, we did not place age-based restrictions on study participants. After carefully reviewing each article for eligibility and relevance, we selected and extracted data from six of them. We used precise inclusion criteria to guarantee the calibre of the included studies, concentrating on peer-reviewed publications that investigated the connection between calcium levels and carbonated beverage intake. Additionally, we evaluated each study's quality using the Newcastle-Ottawa Scale (NOS), which rates research according to criteria like outcome assessment, comparability, and participant selection.

To analyze the collected data, we performed a random-effects meta-analysis using the R programming language (version 4.3.1). All statistical tests employed were two-sided, with a significance threshold set at $P < 0.05$. Hedges' g (Hedges *et al.*, 1985) was used to estimate the between study effects sizes. Additionally, we conducted a sensitivity analysis to determine how the exclusion of individual studies impacted the overall effect size, particularly given the moderate heterogeneity observed ($I^2 = 51.46\%$). This analysis allowed us to assess the robustness of our findings.

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

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 operates under the assumption that the effect size see in a study is just one random sample from countless similar studies (DerSimonian & Kacker, 2007). There are many reasons why the effect size can change. These include differences in study populations, the intervention used, the comparator, how endpoints are defined, and even the overall study design. All these factors can lead to systematic variations in effect size at the study level. So, the difference between a specific study's effect size and the population's true effect size (μ) tends to be more than what you could expect from simple sampling variation alone (Mona et al., 2020).

As a result, we can express each individual study's effect size like this:

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

In this expression, we have the observed effect size, along with terms: θ_i that account for between-study variance (τ^2) and ε_i that account for the within-study variance (${\sigma^2}_i$).

Since this model uses a random selection of effect sizes, it assumes that the mean deviation of effect sizes equals zero. It is also considered that; it is normally distributed and centered around zero with variance (τ^2), plus that the sampling error (ε_i) is also distributed normally. Each individual study gets a weight (w_i) based on the total variation's inverse: $w_i = 1/({\sigma^2}_i + \tau^2)$.

Next, we get the pooled effect estimate ($\hat{\mu}_r$) represented as:

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

Where y_i can be seen to be distributed as;

$$y_i \sim N(\mu, {\sigma_i}^2 + \tau^2)$$

Finally, we describe the variance of this estimated effect size as follows:

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

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),

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

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

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

Where; $W_{i,RE} = 1 \Big/ \left(v_i + \hat{\tau}^2_{REML}\right)$ 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).

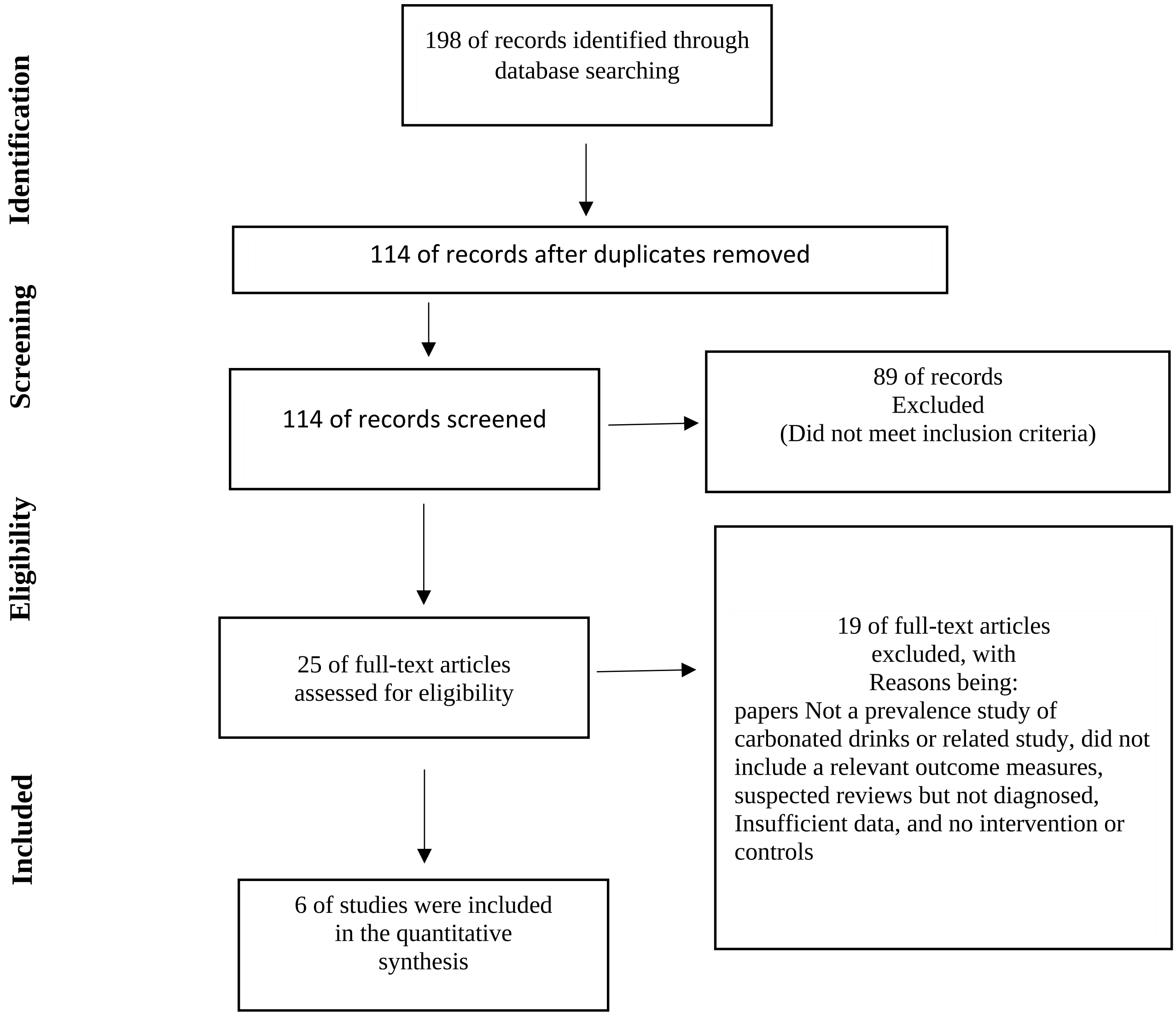

Figure 1: Flow of Information Through the Different Phases of Included Studies for Systematic Review and Meta-Analysis.

Figure 1 illustrates how we choose the study. We also provide explanations for those that were left out. A total of 198 articles were found during our literature search. We identified 25 that appeared to be suitable for our review after reviewing the abstracts and titles. Six articles that truly met our criteria and made it into the final analysis were then selected following a thorough review of the complete texts.

Now, let's talk about the results from a heterogeneity test in Table 1. The I^2 statistic tells us how much variation between studies is due to actual differences and not just random luck. Here, it's 51.46%. So, this means that about half of the differences in study outcomes come from real differences between the studies – not just chance. The Q statistic was calculated too – It came out to be 10.4527.

Next is the P-value. It's all tied to the Q statistic and it is 0.0634, which is more than 0.05. This means we do not have strong proof of significant differences among these studies. Lastly, we looked at the tau-squared statistic, which tells us how much variability in effect sizes isn't explained by random error. This value is 0.0851, showing us a bit of variance between studies, but it is not huge.

Table 1: Heterogeneity test

	Random-Effects Model
I^2 – Statistic:	51.46%
Q – Statistic:	10.4527
P – Value	0.0634
tau^2 – Statistic	0.0851

In summary, the results suggest that there is some level of heterogeneity (as indicated by the I^2 statistic) in the included studies, but it is not statistically significant (as indicated by the P-value). The tau^2 statistic (51.46%) indicates moderate heterogeneity among the studies.

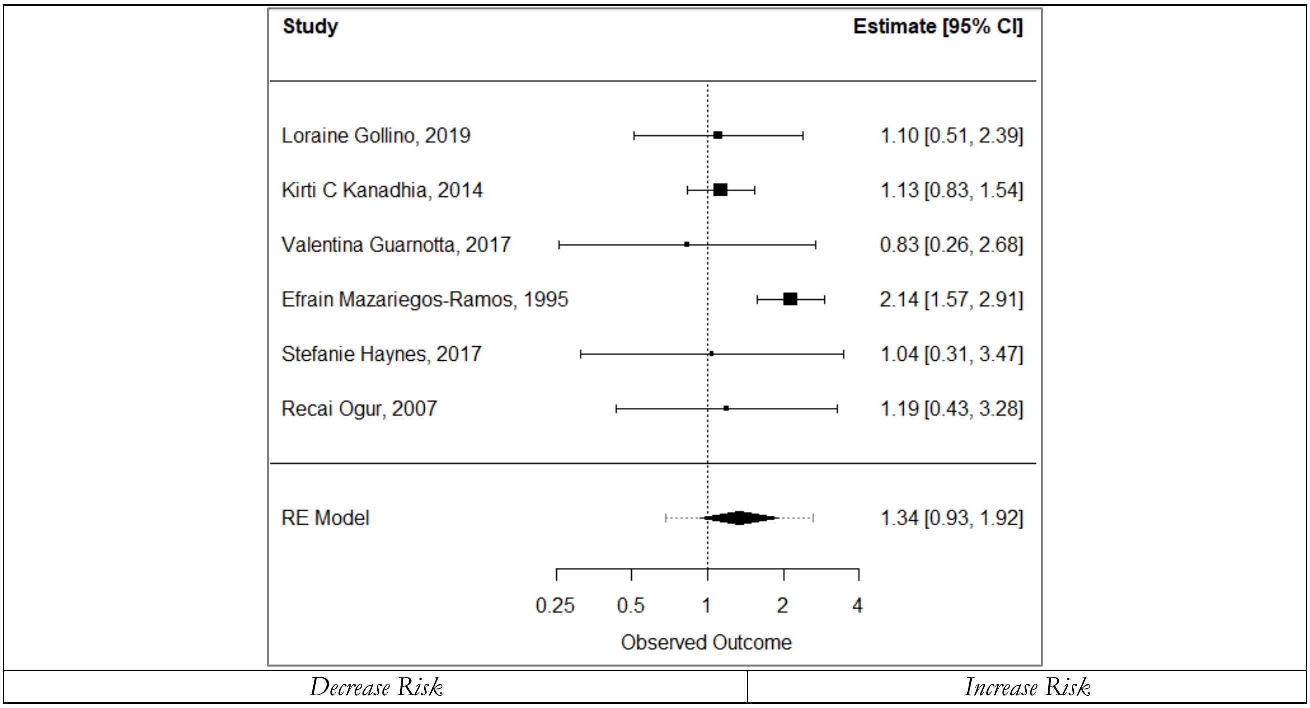

Figure 2: Forest plot of meta-analysis comparing highest vs. controlled level of carbonated beverage intakes and risk of Hypocalcemia incident.

The terms "Decrease Risk" & "Increase Risk," shown in Figure 2, help explain how health outcomes can be affected by hypocalcemia. So, when we say "Decrease Risk," it means that drinking more carbonated drinks is linked to a lower chance of having hypocalcemia. This suggests that folks who drink a lot of these fizzy beverages are less likely to have really low calcium levels compared to those who do not drink much. Now, on the flip side, "Increase Risk" means that consuming more carbonated drinks could lead to a higher chance of getting hypocalcemia. In simple words, if you drink more of those bubbly drinks, your risk goes up.

People who consumed a lot of carbonated drinks were much more likely to develop hypocalcaemia, as seen in Figure 2. A relative risk (RR) of 1.34 and a confidence interval (CI) of 0.93 to 1.92 were used to highlight this. Table 2 provides additional information regarding these figures and their meanings. Given that it can help prevent hypocalcaemia, this elevated risk highlights how crucial it is to watch what we eat and drink, particularly carbonated beverages. The results should inspire us to consider public health initiatives that could educate the public about the negative effects of excessive use of carbonated beverages on calcium levels and general health.

Table 2: Pooled estimate and relative risk (RR)

Estimate	RR	Se	P-value	CI
0.2913	1.338	0.1836	0.1127	-0.0687, 0.6512

Dietary Interventions

Let us examine a few figures from Table 2. The combined estimate is 0.2913. This figure aids in quantifying the subject of our research. Since 0.1127 is bigger than 0.05, the P-value of 0.1127 suggests that there is insufficient evidence to reject the null hypothesis at the significance level of 0.05. In addition, the value of the Relative Risk (RR) is 1.338. This indicates that, in comparison to the control group, the occurrence occurring in the intervention group is roughly 1.338 times more likely.

The Standard Error (SE), which is 0.1836, is the next item on the list. This figure demonstrates the accuracy of our estimate. -0.0687 to 0.6512 is the 95% Confidence Interval (CI) for this estimate. This implies that the actual value is probably inside that range, and guess what? Our estimate of 0.2913 falls precisely inside the Figure 2 boundaries.

Since fluid consumption is closely linked to the incidence of nephrolithiasis, it is one of the most important components in dietary interventions intended to lower the risk of kidney stones. A major contributing reason to the rising incidence of nephrolithiasis is dietary and lifestyle choices. Notably, the development of nephrolithiasis is strongly correlated with modifiable factors such obesity, eating habits, and fluid intake. Thus, it is important to keep in mind that those who drink the most soft drinks may be at a surprisingly high risk of developing nephrolithiasis. This connection emphasises how crucial it is to encourage better food and lifestyle choices in order to reduce the risk of kidney stones and the related health issues.

DISCUSSION

Certain ingredients in carbonated drinks, especially phosphoric acid, are primarily responsible for the correlation between intake of these beverages and hypocalcaemia. A common ingredient in cola drinks, phosphoric acid adds to both the acidity and unique flavour of the drinks. The body may experience major physiological changes as a result of this acidity, especially in relation to calcium metabolism.

It has been demonstrated that phosphoric acid affects bone health and calcium absorption via a number of processes. First, a diet heavy in phosphorus can upset the body's delicate calcium-phosphorus balance. Reduced intestinal absorption of calcium can occur when phosphorus levels rise as a result of consuming too much phosphoric acid. This happens as a result of increased phosphorus levels stimulating the release of parathyroid hormone (PTH), which raises calcium excretion in the kidneys and decreases intestinal absorption. Accordingly, this imbalance may lead to hypocalcaemia and other disorders by lowering serum calcium levels (Healthline, 2023).

Additionally, research has shown that drinking cola might lower stomach pH after consumption, which may further hinder the digestive tract's ability to absorb and dissolve calcium (NCBI, 2016). High phosphorus levels from cola beverages can lead to a situation where calcium is not only poorly absorbed but also excreted in excess through urine. This combined effect increases the risk of hypocalcaemia, particularly in people who already have diseases like hypoparathyroidism that impair calcium metabolism.

These discoveries have important clinical consequences. People who often drink carbonated drinks may be more susceptible to hypocalcaemia and its associated problems, including osteoporosis and bone fractures, especially if they have diseases like hypoparathyroidism or chronic renal disease. According to the data, consuming too much phosphoric acid-rich beverages may eventually cause bone density to decrease, increasing the risk of fractures (Docimo et al., 2012; Mazariegos-Ramos et al., 1995).

Healthcare professionals must inform patients about the possible dangers of consuming large amounts of fizzy beverages. It is recommended that patients minimise their consumption of these drinks and instead concentrate on including items high in calcium in their diets, such as dairy products, leafy greens, and fortified meals. Additionally, keeping an eye on blood calcium levels in people that are at risk may help lessen the negative consequences of drinking carbonated beverages.

CONCLUSION

This research shows how drinking carbonated beverages can really affect the body, especially in causing low calcium levels, known as hypocalcemia. Our main goal was to gather solid, trustworthy data on how common this problem is along with the risks tied to consuming these kinds of drinks. To do this, we carried out a detailed systematic review and meta-analysis. The results provide evidence that points to a higher risk for hypocalcemia when people drink more carbonated beverages. These insights are very important. They can help prevent hypocalcemia and guide people toward better eating habits.

The results of the analysis showed a strong correlation between these drinks and the incidence of low calcium levels, with a combined relative risk (RR) of 1.34 and a 95% CI of 0.93 to 1.92, indicating that people who drink more carbonated drinks are more likely to develop hypocalcaemia. We found a moderate amount of variability when comparing the studies using the I^2 statistic.

This study highlights the significant health risks associated with excessive carbonated beverage consumption, particularly with regard to the body's calcium metabolism. Low calcium levels can result in a range of symptoms, from minor cramping in the muscles to severe problems with muscle function, which is a major public health concern.

Given the link found between these beverages and hypocalcemia, there is clearly a need for public health programs aimed at lowering consumption of carbonated drinks. Raising awareness about these risks and promoting healthier drink options may help reduce cases of hypocalcemia and its complications.

In conclusion, our findings support the link between drinking carbonated beverages and an increased risk of having low calcium levels. Future research should go deeper into how this association works, as well as examine the long-term health impacts of drinking these types of beverages on calcium balance in the body. Furthermore, conducting new studies with larger sample sizes and detailed assessments will allow us to investigate other relationships or perplexing elements that have been overlooked in previous research. This could lead to a better understanding of the complex link between carbonated beverage use and hypocalcaemia, influencing public health policy and nutritional guidance.

Overall, our findings stress how vital it is to pay attention to eating habits, especially when it comes to carbonated drinks – to help prevent low calcium levels & related health problems. Public health efforts should raise awareness regarding risks while encouraging healthier beverage choices for better calcium processing and overall well-being.

RECOMMENDATIONS

1. Monitor Calcium Levels: Regularly screen high-risk populations, especially frequent carbonated drink consumers, for calcium deficiency.
2. Track Beverage Consumption: Implement national surveys to assess carbonated beverage consumption patterns and identify at-risk groups.
3. Conduct Long-Term Studies: Launch longitudinal studies to explore the long-term effects of carbonated drinks on calcium balance.
4. Raise Public Awareness: Evaluate and improve public knowledge on the risks of carbonated drinks through awareness campaigns.
5. Promote Healthier Alternatives: Encourage the consumption of calcium-rich drinks like milk and fortified juices.
6. Taxation and Regulation: Consider taxes on sugary beverages and direct revenue toward public health initiatives promoting better choices.
7. Clear Labeling: Require warnings on carbonated beverages about the risks of calcium depletion.
8. School Programs: Educate students on the health risks of carbonated drinks and promote calcium-rich foods in schools.
9. Nutrition Guidelines: Update dietary guidelines to limit carbonated drink intake and promote calcium-rich diets.
10. Community Outreach: Implement community health education to reduce carbonated beverage consumption and encourage healthier habits.

These measures can help reduce hypocalcemia and promote better dietary choices.

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