

The Correlation among the Incidences of Sialolithiasis, Urolithiasis, and Cholelithiasis in Samples from the Iraqi Populations

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Abstract

Background: There are three types of “stone diseases”: “sialolithiasis (SL), urolithiasis (UL) and cholelithiasis (CL),” which share comorbidities. The risk parameters are present in both spouse and familial profiles. **Objective:** The study aims to establish a correlation between the types of stone diseases and their familial history. **Materials and Methods:** The Marjan Teaching Hospital and Al-Hilla Teaching Hospital recorded familial relationships from various registration areas in all hospitals in Babylon province; they also obtained information on stone diseases from all patient records. Babylon-Iraq. The participants (243) had no signs and symptoms of any systemic diseases, and the enrolled participants were assessed for all involved samples without a history of the identified stone disease. Informed consent was obtained from all outpatients or participants. **Results:** The results of this current study revealed that the incidence of stone diseases was higher in females than in males, with a significant difference ($P > 0.001$). The age intervals ranged from 18 to 24 years, followed by 33–55 years, and finally 25–32 years. In terms of the incidence of SL, females with family histories exhibited a higher prevalence than males. **Conclusion:** In terms of the familial incidence of stone pathology, both SL and UL are more common than CL. This study proposed that familial clustering is unique to each stone disease and further indicated that the underlying disease mechanisms are distinct.

Keywords: Cholelithiasis, heritability, sialolithiasis, urolithiasis

INTRODUCTION

“Sialolithiasis (SL), also known as salivary stone, is a condition of salivary calculus, sialolith, or salivary stone that forms within the salivary glands and their ductal system.”^[1,2] The submandibular gland “Warton’s duct” is the most common location associated with the incidence of SL, due to the composition of saliva (calcium and phosphate) and the tortuous path of the submandibular salivary gland duct, whereas other major salivary glands, such as parotid and sublingual glands, are less frequently affected.^[3]

Risk factors involve inflammation, infectious status, diabetes, and finally Sjögren syndrome.^[3] There may be no genetic predisposition or familial risk of SL.^[4] The urinary tract stone disease, or urolithiasis (UL), covers stones inside the kidney (nephrolithiasis), while bladder or ureter

stones is a pathology commonly present in between 1% and 15% of the population globally, and the prevalence of this disease is increasing.^[5]

Cholelithiasis (CL) is a common disease among these three pathological statuses. Approximately 10 to 20% of people in Western countries develop CL,^[6] a phenomenon that is becoming more widespread due to the increasing prevalence of risk factors such as physical inactivity and obesity^[7] and other risk factors for stone conditions such as high age, female sex, family history, certain ethnic background, pregnancy, and genetic profile.^[8]

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According to X-ray microanalysis, stones in SL and UL share an elemental composition, and calcium salts are the main inorganic chemical constituents.^[9] In contrast, gallstones are made of organic compounds, with the most common ones being cholesterol stones and the rarer ones being bilirubin stones.^[10] Several epidemiological studies have observed comorbidities between these stone diseases.^[11]

The organic compounds are the main constituents of gallstones, the cholesterol stones are commonly present, and the rarer ones are bilirubin-type stones.^[12] These pathological diseases, including “stone disease,” share familial risk factors.^[13]

MATERIALS AND METHODS

The cross-sectional study was conducted; familial associations were recorded from multiple areas of registration in all hospitals in Babylon Province; data on stone diseases were obtained from all patient records documented in the Babylon Health Directorate/Ministry of Health in Iraq (2020–2023); Marjan Teaching Hospital, Al-Hilla Teaching Hospital by questionnaires. This questionnaire is filled out by direct questions and direct interviewing (open question); These participants (243) had no signs or symptoms of any systemic diseases, and the expected numbers of patients were calculated for all enrolled individuals without a history of the well-established stone disease. Informed consent was obtained from all participants.

The Regional Ethical Review Board at Hilla University College University has approved this current study.

The study adhered to the ethical principles outlined in the Declaration of Helsinki. A local ethics committee reviewed and approved the study protocol, subject information, and ethical approval form based on document number 10229, dated 12-3-2022, to obtain this approval.

Statistical analysis

“The data was analyzed by the application of Microsoft Excel and Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 23. The analysis arranges the outcomes into scale variables (means and standard deviation) and categorical variables. A *P* value of 0.5 or less is regarded as significant..”

RESULTS

As shown in Table 1, the study found that three types of stones – SL, UL, and CL – occurred more often in women than in men. This difference was statistically significant (0.001). We obtained these results from all enrolled patients through direct interviews using open-ended questions.

The age intervals ranged from 18 to 24 years; the most common age for stone incidence was 18–24 years, followed

by 33–55 and 25–32 years, with significant differences as shown in Table 2.

Forty-four (18.11%) of them have SL, as explained in Table 3.

Females with a family history had a higher incidence of SL than males in 32 (72.73%) out of 44 patients, but there were no significant differences (*P*-value = 0.736), as shown in Table 4.

CL was found in 51 (20.99%) out of 243 participants, as explained in Table 5.

Table 1: Sample distribution according to gender in all groups

Gender	No. of samples	%	χ^2	<i>P</i> value
Male	95	39.10	11.560	0.001**
Female	148	60.91		
Total	243	100		

** refer to significant difference at $P \leq 0.01$

Table 2: Sample distribution according to the age of the participant

Age (years)	No. of samples	%	χ^2	<i>P</i> value
18–24	143	58.85	86.617	$\leq 0.0001^{**}$
25–32	25	10.29		
35–55	75	30.86		
Total	243	100		

Table 3: Sample distribution according to the presence of sialolithiasis

Presence of stones	No. of samples	%	χ^2	<i>P</i> value
Yes	44	18.11	98.868	$\leq 0.0001^{**}$
No	199	81.89		
Total	243	100		

Table 4: Association between gender and family history for sialolithiasis

Family history	Yes	No	Total	χ^2	P value
		No. (%)			
Gender					
Male	4 (30.77)	8 (25.81)	12 (27.27)	0.114	0.736
Female	9 (69.23)	23 (74.19)	32 (72.73)		
Total	13 (100)	31 (100)	44		

Table 5: Sample distribution according to the presence of sialolithiasis

	No. of samples	%	χ^2	<i>P</i> -value
Yes	51	20.99	81.815	$\leq 0.0001^{**}$
No	192	79.01		
Total	243	100		

Significant differences were found between females and males, with an increased level of family history but higher incidence in males than in females, as shown in Table 6.

Ninety-four patients (38.68%) have UL, as shown in Table 7.

No significant differences were found between females and males, but males had increased prevalence of family history compared to females; as shown in Table 8.

The incidence and family history of SL and UL are more prevalent than other types of stones, as shown in Table 9.

DISCUSSION

The risks in the familial profile between stone pathoses were also modest, and there were no significant differences

between SL and UL, considering which cause, considering stone composition is similar.^[12]

“Although explaining such small familial risks between stone diseases is speculative, they nevertheless provide another argument against shared disease mechanisms underlying the reported comorbidities.”^[14]

The risk estimation and different medical examinations may be associated with the surveillance bias as chronic comorbidity involvement. These chronic comorbidities may be caused by shared susceptibility or risk factors and can be noted in a family setting.^[14] “The similar mechanisms of stone formation reported in the chemical similarities between SL and UL; these results were consistent with the results of Portincasa *et al.* 2023.”^[15]

Several types of genes predisposing to CL have been recorded, and these involve variants encoding lipid receptors, apolipoproteins, and proteins; they are also involved in the metabolism of cholesterol.^[16]

Another negative issue pertaining to motivation in the current study was the lack of literature on familial SL and the rare findings of literature on other stone diseases.^[17] The common strengths of this study were its wide-ranging scope, which included both medical diagnostics of stone diseases and comprehensive family profiles obtained from multiple generations.^[18]

Well-documented risk factors, such as physical inactivity and obesity, could demonstrate this truth. These stone diseases may share both inflammation and diabetes as risk factors. “Further evidence on unique familial clustering of each stone disease shows risks with family histories of a single stone disease, which for UL and CL were higher than those with family histories of multiple stone diseases.”^[19]

“Although both cholelithiasis and sialolithiasis are types of stones, their aetiologies are different. Gallstones are crystalline deposits in the gallbladder, most of which are categorised as cholesterol (37%–86%), pigment (2%–27%), calcium (1%–17%), or mixed (4%–16%).^[20] Imbalances between pro-nucleating factors and anti-nucleating factors in the bile result in cholelithiasis.²⁰ Excessive bile cholesterol, low bile salt levels, decreased gallbladder motility, and phosphatidylcholine can cause gallstones.^[17] Aging, female sex, ethnicity, estrogen treatment, obesity, Western diet, low physical activity, liver cirrhosis, diabetes mellitus, and dyslipidemia are known risk factors for cholelithiasis.¹⁸ Alcohol and smoking are controversial as risk factors for cholelithiasis.¹⁸ Sialolithiasis is defined as calcified concretions in the salivary glands.

Most sialolithiasis stones contain calcium phosphates (hydroxyapatite or carbonate apatite), although

Table 6: Association between gender and family history of cholelithiasis

Family history	Yes	No	Total	χ^2	P value
	No. (%)				
Gender					
Male	6 (42.86)	32 (86.49)	38 (74.51)	10.180	0.001**
Female	8 (57.14)	5 (13.51)	13 (25.49)		
Total	14 (100)	37 (100)	51 (100)		

Table 7: Sample distribution according to the presence of urolithiasis

	No. of samples	%	χ^2	P-value
Yes	94	38.68	12.449	$\leq 0.0001^{**}$
No	149	61.32		
Total	243	100		

Table 8: Association between gender and family history of urolithiasis

Family history	Yes	No	Total	χ^2	P value
	No. (%)				
Gender					
Male	28 (71.79)	40 (72.73)	68 (72.34)	0.010	0.086
Female	11 (28.21)	15 (27.27)	26 (27.66)		
Total	39 (100)	55 (100)	94 (100)		

Table 9: Association of stones location and family history

Family history	Yes	No	Total
	No. (%)		
Position of stones			
Sialolithiasis + urolithiasis+ cholelithiasis.	4 (11.43)	49 (29.70)	53 (26.5)
Sialolithiasis + urolithiasis	18 (51.43)	61 (36.70)	79 (39.5)
Urolithiasis + cholelithiasis	2 (5.71)	19 (11.52)	21 (10.5)
Sialolithiasis + cholelithiasis	11 (31.43)	36 (21.82)	47 (23.5)
Total	35	165	200

some stones have organic components.^[21] Secreted microcalculi from the salivary gland, food debris, and decreased saliva flow can cause sialolithiasis.²¹ Patients with sialolithiasis have shown reduced concentrations of the crystallisation inhibitors phytate, magnesium, and citrate.¹⁹ Smoking is suggested as a risk factor for sialolithiasis because it decreases salivary amylase levels, leads to inflammation, and decreases the antimicrobial potency of saliva.^[22] Therefore, we propose that these conditions are not similar, even though the calcium composition of the stones and the relevance of smoking history might suggest the possibility of a common pathophysiology.”^[22]

The limitations were the lack of records in primary healthcare.^[22] Also, many types of gene profiles contributing to the susceptible cause of UL are known, and these associated genes encode rare metabolic factors, including disturbances in the balance of both calcium and oxalate.^[23]

“Most sialolithiasis contains calcium phosphates (hydroxyapatite or carbonate apatite), although some stones have organic components.”^[24] “Secreted microcalculi from the salivary gland, food debris, and decreased saliva flow can cause sialolithiasis.”^[25] “Reduced concentrations of the crystallisation inhibitors phytate,” “magnesium and citrate have been observed in patients with sialolithiasis.”^[9]

Finally, to the best of our knowledge, there is no relation between CL and SL.

CONCLUSION

In the familial incidence of stone pathology, both SL and UL are more common than CL. This study showed that familial clustering is unique to each stone disease and further indicated that the underlying disease mechanisms are distinct.

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Conflicts of interest

There are no conflicts of interest.

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