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# **REVIEW ARTICLE**

# What is the impact of previous cholelithiasis on sialolithiasis: A systematic review and meta-analysis



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# **KEYWORDS**

Salivary Gland Calculi; Salivary Duct Calculi; Sialolithiasis; Cholelithiasis: Choledocholithiasis: Gallstone

Abstract Introduction: A sialolith is a salivary stone usually presenting with swelling and pain in the affected salivary gland, most commonly the submandibular gland. There have been speculations about the association between this condition and other systemic diseases, especially those forming stones, such as nephrolithiasis and cholelithiasis. This systematic review and meta-analysis aimed to summarize the studies assessing the relationship between cholelithiasis and sialolithiasis.

Methods: PubMed/MEDLINE, Scopus, Web of Science, and Embase electronic databases were searched according to the keywords related to both disorders without any publication date or language restriction. Case-control and cohort studies evaluating the relationship between salivary and biliary stones were considered eligible. Quality assessment was performed following Newcastle-Ottawa Scale (NOS) for quality assessment of case-control studies. All meta and statistical analyses

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1013-9052 © 2023 THE AUTHORS. Published by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). were performed with Comprehensive Meta-Analysis software.

*Results:* Two studies fully complied with the defined eligibility criteria and were included, both of which were case-control studies using national-scale databases. In both surveys, the prevalence of previous gallstones in patients with sialolithiasis was compared to that of a control group. Though one of the studies found that there is no relationship between sialolithiasis and cholelithiasis, the meta-analysis revealed that previous cholelithiasis is significantly more prevalent among patients with sialolithiasis (P = 0.000), with an odds ratio of 2.04.

*Conclusion:* It seems that cholelithiasis is significantly associated with an increase in salivary stone formation. Therefore, a thorough salivary examination in all patients declaring current or past cholelithiasis is recommended. However, more studies, especially prospective cohorts, are needed to make firmer conclusions.

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## Contents

1.	Intro	oduction	45
2.	Mat	erials and methods	46
	2.1.	Protocol	46
	2.2.	Information sources and search strategy	46
	2.3.	Eligibility criteria	46
	2.4.	Study selection and data extraction	46
	2.5.	Assessment of bias	46
	2.6.	Meta-analysis	46
3.	Resi	ults	47
	3.1.	Search and study selection	47
	3.2.	Quality assessment	47
	3.3.	Characteristics of included studies	47
	3.4.	Qualitative analysis	48
4.	Disc	sussion	48
5.	Con	clusion	49
	Fundi	ng	49
	Ethica	ll statement	49
	CRed	iT authorship contribution statement	50
	Apper	ndix A. Supplementary material	50
	Refere	ences	50

## 1. Introduction

Salivary stones, also known as sialolithiasis, are pathologic calcified entities found in the parenchyma or ductal system of salivary glands, most commonly the submandibular gland and Wharton's duct (Williams, 1999). Typically, a sialolith consists of concentric layers of organic and inorganic material surrounding an amorphous, mineralized core that is softer than its outer sections (Harrison, 2009, Kraaij et al., 2014). The most frequent symptoms of this condition are saliva flow obstruction and subsequent swelling and pain in the affected gland (Zenk et al., 2012, Kraaij et al., 2014). The pain and swelling are often intensified during meals and can last several hours, interspersed with symptom-free periods (Levy et al., 1962).

Salivary stones are the second most common disease of the major salivary glands after mumps, accounting for almost one-third of all salivary gland disorders, with a reported incidence of one in 10,000 to one in 30,000 (El Deel et al., 1981, Huoh and Eisele, 2011). Also, the rate is higher among males than women, and the disease is primarily observed in patients

between the age of 30 and 60 (Grases et al., 2003, Smith et al., 1996).

Despite the fact that the pathophysiology of sialolithiasis is unclear, two main theories have been put forth. According to certain theories, intracellular microcalcifications discharged into the canal may serve as a nidus for further calcification (Epivatianos et al., 1987, Harrison et al., 1997). According to a second theory, germs, food particles, or other detritus from the oral cavity may enter the salivary ducts and serve as a focal point for the formation of calcification (Marchal et al., 2001).

Changes in the flow and composition of saliva might predispose to sialolith formation. Higher protein content, viscosity, and calcium concentration have been detected in patients with salivary stones (Grases et al., 2003, Harrison, 2009, Su et al., 2010). Moreover, the saliva of patients developing sialolith contains a lower level of crystalization inhibitors, including phytate, magnesium, and phosphate (Proctor et al., 2007, Su et al., 2010). Additionally, patients with systemic conditions that reduce saliva flow, such as diuretic use and smoking, are more likely to experience salivary stones (Huoh and Eisele, 2011, Nederfors et al., 2004); however, even though Sjögren's

syndrome causes a significant decrease in saliva flow, sialoliths are not more common in Sjögren's syndrome patients (Proctor et al., 2007).

Lithiasis or stone formation also occurs in other parts of the body, such as the urinary system (nephrolithiasis or urolithiasis) and biliary system (cholelithiasis). This condition has been on the rise globally, affecting approximately 5% of the population, with a higher incidence among males aged 30–50 (Nagy et al., 2017).

Cholelithiasis, commonly known as gallstone, affects virtually 10% to 20% of adults worldwide and is considered one of the most economically costly hepatobiliary diseases (Lammert et al., 2016). Additionally, it is a significant risk factor for the development of gallbladder cancer (Stinton and Shaffer, 2012). Gallstone development is impacted by a number of factors, including heredity, environmental influences, diabetes, and metabolic syndrome, with high cholesterol secretion being a major cause (Crawford et al., 2010). The prevalence of cholelithiasis increases with age, with 15% of men and 24% of women having gallstones by the age of 70. By the age of 90, these numbers increase to 24% and 35%, respectively (Attili et al., 1995, Sanson and O'Keefe, 1996). However, over 80% of individuals with cholelithiasis remain asymptomatic without any complications (Marschall and Einarsson, 2007, Shrikhande et al., 2010).

Although these conditions affect different body parts, some common factors contribute to their development; for instance, because salivary stones are mainly made up of calcium carbonate and calcium phosphates (Marchal and Dulguerov, 2003), some researchers have suggested that there might be a link between sialolithiasis and nephrolithiasis, as they may share a similar underlying pathology (Lustmann et al., 1990, Wu et al., 2016). Some associations between salivary stones and stones in other organs or disorders have been proposed in the literature. It has been reported that patients with sialolithiasis are more prone to developing nephrolithiasis (Harrison, 2009, Lustmann et al., 1990). Also, an association between sialolithiasis and osteoporosis, which has been shown to be linked with abnormal mineral concentrations in the blood, is reported (Hung et al., 2016, 2019). Gout disease seems to predispose the formation of salivary stones predominantly composed of uric acid (Williams, 1999). Some studies have suggested that sialolith development is related to gallstone (Hung et al., 2016, Kim et al., 2019).

This study aims to assess the association between sialolithiasis and cholelithiasis, given the high incidence of both situations and their potential shared risk factors. The objective of this study is to inform both healthcare providers and patients about the potential relationship between sialolithiasis and cholelithiasis and to emphasize the importance of considering cholelithiasis as a prognostic factor for sialolithiasis in order to prevent further health complications.

# 2. Materials and methods

# 2.1. Protocol

This review was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (Page et al., 2021).

#### 2.2. Information sources and search strategy

PubMed/MEDLINE, Scopus, EMBASE, and Web of Science online databases were electronically searched using the terms sialolithiasis, sialolith, salivary gland calculus or stone, salivary duct calculus or stone, and cholelithiasis, choledocholithiasis, gallstone, biliary tract calculus or stone in March 2023. No language or publication date or status restriction was exerted. Selected citations were imported into EndNote 20.5 (Clarivate).

# 2.3. Eligibility criteria

Original research articles were selected on the basis of our PECO question, which consists of the following criteria.

1. Participants: Both retrospective or prospective longitudinal studies investigating the general population were included.

2. Exposure: The study needed to regard cholelithiasis or gallstone as exposure. Studies considering other stones, including nephrolithiasis or urolithiasis, and other hepatobiliary diseases, such as jaundice or cirrhosis, were excluded.

3. Comparison: Since the prevalence of cholelithiasis can vary significantly between groups of different races, sex, age, and even socioeconomic status (Figueiredo et al., 2017, Nascimento et al., 2022, Sun et al., 2009), studies had to include a matched control group in order to compare the results.

4. Outcome: Studies reporting sialolithiasis or salivary stone in one or more major salivary gland(s) or its related salivary duct were included. Patients who had a history of sialolithiasis could be involved too. Although, the studies regarding other salivary diseases, such as sialadenitis, Sjogren's syndrome, or sialectasis, were excluded. Included studies needed to report the exact number of exposed and unexposed patients developing sialolithiasis. However, studies reporting risk ratio or odds ratio in which the number of affected and unaffected patients could be calculated were also included.

#### 2.4. Study selection and data extraction

Two authors (NF and RS) independently screened the imported citations according to the eligibility criteria. A third author (PH) settled conflicts. Finally, an expert author (HM) investigated all the included studies. Full texts of included studies were retrieved, and two authors (AA, AT) independently extracted the following data into predesigned tables:

- a) Number of cases and controls.
- b) Age and gender distribution of patients.
- c) Number of cases and controls developing gallstone.

## 2.5. Assessment of bias

Quality assessment was performed according to the Newcastle-Ottawa Scale for Quality Assessment of Case-Control Studies (Wells, 2011).

# 2.6. Meta-analysis

All statistical analyses, including meta-analysis, were performed with Comprehensive Meta-Analysis V4 (Biostat).



Fig. 1 PRISMA flowchart of the systematic review.

Cholelithiasis and sialolithiasis were defined as exposure and event, respectively (Borenstein, 2022).

# 3. Results

# 3.1. Search and study selection

Three hundred and eighty-seven citations were imported from the online database, 101 of which were duplicates and deleted. After screening the imported citations by title and abstract, 14 articles were considered for full-text appraisal. Only two studies ultimately met the eligibility criteria of this review mentioned in section 2.3 and were included. Fig. 1. depicts the PRISMA flow diagram of the current systematic review.

# 3.2. Quality assessment

According to Newcastle-Ottawa Quality Assessment Tool for Ccase-Controol Studies, the quality of both studies was evaluated based on object selection, comparability, and exposure. Table 2 illustrates a summary of the quality of included studies. Each star in front of a question describes an appropriate entry.

# 3.3. Characteristics of included studies

Both studies were retrospective case-control surveys, and they both used databases of patients' information. Kim et al. (2019) used The Korean National Health Insurance Service (NHIS) database, which includes records of the population of South Korea. On the other hand, Hung et al. (2016) chose cases and controls from the Taiwan National Health Insurance (NHI) database, with more than 23.72 million records. They both considered cholelithiasis as the exposure of their casecontrol study. In both studies, cases were patients with a history of sialolithiasis; however, those who had a sialolith before cholelithiasis were excluded. Controls were selected from the general population and matched with cases according to age, gender, urbanization level, and income. Characteristics of the included studies and their descriptives are summarized in Table 1. In the surveys of Hung et al. (2016) and Kim et al. (2019), 62% and 73.1% of cases with sialolithiasis were between 30 and 60 years old. Sialolithiasis was more common in men in the Taiwanian cases studied by Hung et al. (2016), although it was more frequently observed in women, as reported by Kim et al. (2019). Even though Kim et al. (2019) reported a significant relationship between sialolithiasis and cholelithiasis, Hung et al. (2016) could not find any association between the two entities.

 Table 1
 Characteristics of the included studies.

Authors,	Study type	Matched Controls (Ratio)	Sex distribution of cases	Participants				Results
year				Casee (Sialolithiasis)		Controls (No-Sialolithiasis)		
				Cholelithiasis	No- Cholelithiasis	Cholelithiasis	No- Cholelithiasis	
Hung et al., 2015	Case- Control	Yes, age and sex (1:5)	M: 51.7% F: 48.3	64	681	152	3573	A significant association between cholelithiasis and sialolithiasis was observed.
Kim et al., 2019	Case- Control	Yes, age, sex, income group, region of residence, and past medical history (1:4)	M: 46.9% F: 53.1%	8	753	27	3017	No significant association between cholelithiasis and sialolithiasis was found.

#### 3.4. Qualitative analysis

Meta-analysis revealed that prior cholelithiasis has a statistically significant correlation with the later development of salivary stones (P = 0.000). Moreover, the calculated odds ratio was 2.04 (1.53 – 2.70), which means people with cholelithiasis are at higher risk of developing sialolithiasis. Fig. 2. depicts the forest plot of this study with a confidence interval of 95%.

## 4. Discussion

Salivary gland or duct stones are the main cause of one-third of salivary gland diseases and are typically characterized by congestion in the salivary flow (Williams, 1999). Patients with sialolithiasis usually suffer from swelling of the affected gland, pain, and mal-tasted secretion, periodically (McGurk et al., 2005). The association between prior cholelithiasis and later sialolithiasis has been suggested in the literature (Hung et al., 2016). Since the incidence of cholelithiasis is approximately 1000 times that of sialolithiasis (Huoh and Eisele, 2011, Lammert et al., 2016), and the early diagnosis of sialolithiasis can minimize the morbidity after the treatment (Avishai et al., 2021), this possible relationship can be important for monitoring patients who have suffered from cholelithiasis for early diagnosis of sialolithiasis to lessen the burden of the treatment for them. Therefore, this study has been set to be conducted using a systematic search in the available literature to assess the strength of this association. The results of the present study showed that prior cholelithiasis has a very significant association with later sialolithiasis development in patients (P = 0.000), and patients with cholelithiasis are 2.04 times more likely to have sialolithiasis in the future compared to others.

Seventy to eighty percent of the chemical compound of submandibular salivary stones and 50% of that of parotid stones are made up of inorganic components (Ekberg and Isacsson, 1981). The inorganic matrix is mainly composed of Octacalciumphosphate (Ca<sub>8</sub>H<sub>2</sub>(PO<sub>4</sub>)<sub>6</sub>·5H<sub>2</sub>O), Whitlockite (Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>), Brushite (CaHPO<sub>4</sub>·2H<sub>2</sub>O), and Hydroxyapatite (Ca<sub>5</sub>(PO<sub>4</sub>)<sub>3</sub>-OH). (Burnstein et al., 1979), all of which contain calcium in their structures. Besides, it has been shown that high amounts of dietary calcium and hyperparathyroidism, which leads to high blood and saliva calcium levels, can be associated with the incidence of sialolithiasis (Stack Jr and Norman, 2008, Waseem and Forte, 2005, Weinberger et al., 1974). On the other hand, pigmented cholelithiasis prevalence is about 15% among all gallstones (Jones et al., 2017), which is remarkable, and calcium participates as calcium bilirubinate, calcium carbonate, calcium phosphate, and calcium palmitate in the structure of pigmented cholelithiasis and mixed stones (Weerakoon et al., 2015). Furthermore, the relationship between hyperparathyroidism and hypercalcemia and cholelithiasis was suggested before (Saito et al., 2021, Selle et al., 1972). These common points could be a rationale for the strong correlation between cholelithiasis and sialolithiasis.

Kim et al. (2019) evaluated the association between cholelithiasis and sialolith development. According to their findings, cholelithiasis was not more frequently observed in the sialolithiasis group (1.05% [8/761]) than in the control II group (0.88% [27/3044]), and there was no statistically significant difference between the two groups (Kim et al., 2019). Despite a large number of participants (approximately 1 million), only 761 patients were diagnosed with sialolithiasis. Also, the included subjects were limited to the ones who showed symptoms and visited a hospital seeking treatment, while not all cases of cholelithiasis and sialolithiasis were symptomatic. Therefore, their inclusion criteria underestimated the incidence and association between sialolithiasis and cholelithiasis.

In a case-control research, Wu et al. (2016) examined the potential connection between sialolithiasis and nephrolithiasis utilizing a population-based dataset. They reported a significant difference in the prevalence of prior nephrolithiasis between the patients diagnosed with sialolithiasis and patients who were not (10.25% vs. 2.28%) with an odds ratio of 4.74 and 3.41–6.58 confidence interval (Wu et al., 2016). The macro- and micro-structure of the hydroxyapatite salivary calculi in patients suffering from sialolithiasis are roughly the same as those in hydroxyapatite renal calculi. Thus, it is likely that they share a similar mechanism of formation. While the exact mechanism of sialolith formation remains a mystery, their study demonstrates that sialolithiasis is significantly associated with nephrolithiasis, proposing that the two could have certain predisposing factors in common.

 
 Table 2
 Newcastle-Ottawa quality assessment tool for casecontrol studies.

Criteria	Question	Hung et al.	Kim et al
<u></u>		et un	et un
Selection	Is the case definition adequate?		
(Maximum	Representativeness of the cases	*	*
	Selection of Controls	*	*
	Definition of Controls	*	*
<b>Comparability:</b>	Comparability of cases and	**	**
	controls on the basis of the design		
	or analysis		
Outcome	Ascertainment of exposure		
	Same method of ascertainment	*	*
	for cases and controls		
	Non-Response rate	*	*
Total	_	7	7
		Stars	Stars

In a case-control study, the risk of sialolithiasis in nephrolithiasis patients was evaluated by Choi et al. (2018). Using data from the same database of the Korean population that Kim et al. (2019) used to assess the relationship between sialolith and gallstone, 24,038 patients with nephrolithiasis were selected. The rates of sialolithiasis in the nephrolithiasis and the control groups were not significantly different (0.08% vs. 0.1%), and they reported no evidence of an increased risk of sialolithiasis associated with nephrolithiasis (Choi et al., 2018). Although this was the first study using a national public database to report a lack of association between the prevalence of nephrolithiasis and sialolithiasis, it was not a randomized clinical trial, and the subjects were all Koreans. The stone disease varies between different ethnic groups. While sialolithiasis has a high incidence and potential shared risk factors with cholelithiasis, a limited number of studies discuss the correlation between them. Therefore, there is insufficient data to comprehensively examine the role of cholelithiasis as a prognostic factor for sialolithiasis. Hence the two studies included in this article were done in the Thai and Korean populations; studies in the other ethnical populations should be done for more information in this field. Moreover, given the similarities in structure and risk factors of these calculuses, we highly recommend that more prospective studies be done on the relationship between sialolithiasis and cholelithiasis.

# 5. Conclusion

We found that cholelithiasis is significantly associated with an increase in salivary stone formation. Therefore, a thorough salivary examination in all patients declaring current or past cholelithiasis is recommended. However, there is a lack of evidence to make a firm conclusion, and further prospective studies should be conducted regarding this association.

#### Funding

None.

## Ethical statement

All components of this systematic review were done in an ethical manner. There is no evidence of any form of plagiarism. All the relevant papers and sources that were checked were properly cited. The Institutional Ethical Committee's clearance was not necessary for this study because it was a review.



Fig. 2 Forest plot of the included case-control studies with odd ratios (95% confidence interval (CI)) of cholelithiasis for patients with and without sialolithiasis. Horizontal lines and squares represent study-specific odds ratios, and the diamond represents the pooled odds ratio.

# **CRediT** authorship contribution statement

Hamed Mortazavi: Conceptualization, Supervision, Writing – review & editing. Ashkan Tizno: Writing – original draft, Writing – review & editing. Ali Azadi: Writing – original draft, Writing – review & editing. Rojin Samani: Writing – original draft, Writing – review & editing. Negin Firoozi: Writing – original draft, Writing – review & editing. Parham Hazrati: Conceptualization, Writing – original draft, Writing – review & editing.

# Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sdentj.2023.08.010.

#### References

- Attili, A.F., Carulli, N., Roda, E., Barbara, B., Capocaccia, L., Menotti, A., Okoliksanyi, L., Ricci, G., Capocaccia, R., Festi, D., et al, 1995. Epidemiology of gallstone disease in Italy: prevalence data of the Multicenter Italian Study on Cholelithiasis (M.I.COL.). Am. J. Epidemiol. 141, 158–165.
- Avishai, G., Rabinovich, I., Gilat, H., Chaushu, G., Chaushu, L., 2021. Surgical treatment of sialolithiasis leads to improvement in the complete blood count. Biol.-Basel 10, 414.
- Borenstein, M., 2022. Comprehensive meta-analysis software. Systemat. Rev. Health Res., 535–548
- Burnstein, L.S., Boskey, A.L., Tannenbaum, P.J., Posner, A.S., Mandel, I.D., 1979. The crystal chemistry of submandibular and parotid salivary gland stones. J. Oral Pathol. 8, 284–291.
- Choi, H.G., Bang, W., Park, B., Sim, S., Tae, K., Song, C.M., 2018. Lack of evidence that nephrolithiasis increases the risk of sialolithiasis: A longitudinal follow-up study using a national sample cohort. PLoS One 13, e0196659.
- Crawford, R.W., Rosales-Reyes, R., Ramírez-Aguilar Mde, L., Chapa-Azuela, O., Alpuche-Aranda, C., Gunn, J.S., 2010. Gallstones play a significant role in Salmonella spp. gallbladder colonization and carriage. PNAS 107, 4353–4358.
- Ekberg, O.I., Isacsson, G., 1981. Chemical analysis of the inorganic component of human salivary duct calculi. Arch. Oral Biol. 26, 951–953.
- El Deel, M., Holte, N., Gorlin, R.J., 1981. Submandibular salivary gland sialoliths perforated through the oral floor. Oral Surg. Oral Med. Oral Pathol. 51, 134–139.
- Epivatianos, A., Harrison, J.D., Dimitriou, T., 1987. Ultrastructural and histochemical observations on microcalculi in chronic submandibular sialadenitis. J. Oral Pathol. 16, 514–517.
- Figueiredo, J.C., Haiman, C., Porcel, J., Buxbaum, J., Stram, D., Tambe, N., Cozen, W., Wilkens, L., Le Marchand, L., Setiawan, V. W., 2017. Sex and ethnic/racial-specific risk factors for gallbladder disease. BMC Gastroenterol. 17, 153.
- Grases, F., Santiago, C., Simonet, B.M., Costa-Bauzá, A., 2003. Sialolithiasis: mechanism of calculi formation and etiologic factors. Clin. Chim. Acta 334, 131–136.
- Harrison, J.D., 2009. Causes, natural history, and incidence of salivary stones and obstructions. Otolaryngol. Clin. North Am. 42, 927– 947.
- Harrison, J.D., Epivatianos, A., Bhatia, S.N., 1997. Role of microliths in the aetiology of chronic submandibular sialadenitis: a clinicopathological investigation of 154 cases. Histopathology 31, 237– 251.

- Hung, S.H., Lin, H.C., Su, C.H., Chung, S.D., 2016. Association of sialolithiasis with cholelithiasis: A population-based study. Head Neck 38, 560–563.
- Hung, S.-H., Xirasagar, S., Cheng, Y.-F., Lin, H.-C., 2019. A casecontrol study of the association between sialolithiasis and osteoporosis. Clin. Otolaryngol. 44, 343–348.
- Huoh, K.C., Eisele, D.W., 2011. Etiologic factors in sialolithiasis. Otolaryngol. Head Neck Surg. 145, 935–939.
- Jones, M.W., Weir, C.B., Ghassemzadeh, S., 2017. Gallstones (Cholelithiasis). Treasure Island, Florida.
- Kim, S.Y., Kim, H.-J., Lim, H., Lim, M.S., Kim, M., Park, I.I.S., Choi, H.G., 2019. Association between cholelithiasis and sialolithiasis Two longitudinal follow-up studies. Medicine 98, e16153.
- Kraaij, S., Karagozoglu, K.H., Forouzanfar, T., Veerman, E.C., Brand, H.S., 2014. Salivary stones: symptoms, aetiology, biochemical composition and treatment. Br. Dent. J. 217, E23.
- Lammert, F., Gurusamy, K., Ko, C.W., Miquel, J.F., Méndez-Sánchez, N., Portincasa, P., van Erpecum, K.J., van Laarhoven, C. J., Wang, D.Q., 2016. Gallstones. Nat. Rev. Dis. Primers 2, 16024.
- Levy, D.M., ReMine, W.H., Devine, K.D., 1962. Salivary gland calculi: pain, swelling associated with eating. J. Am. Med. Assoc. 181, 1115–1119.
- Lustmann, J., Regev, E., Melamed, Y., 1990. Sialolithiasis: a survey on 245 patients and a review of the literature. Int. J. Oral Maxillofac. Surg. 19, 135–138.
- Marchal, F., Dulguerov, P., 2003. Sialolithiasis management: the state of the art. Arch. Otolaryngol.-Head Neck Surg. 129, 951–956.
- Marchal, F., Kurt, A.M., Dulguerov, P., Lehmann, W., 2001. Retrograde theory in sialolithiasis formation. Arch. Otolaryngol. Head Neck Surg. 127, 66–68.
- Marschall, H.U., Einarsson, C., 2007. Gallstone disease. J. Intern. Med. 261, 529–542.
- McGurk, M., Escudier, M.P., Brown, J.E., 2005. Modern management of salivary calculi. Br. J. Surg. 92, 107–112.
- Nagy, E.N., Tilinca, M.C., Iacob, A., Ormenisan, A., Fazakas, Z., Barbu, H.M., Kolcsar, M., Maier, A.C., Vida, A.O., Orsolya, M., 2017. Study on chemical composition of urinary and salivary gland stones in relationship with laboratory parameters and lifestyle habits of patients with lithiasis. Rev. Chim. 68, 680–682.
- Nascimento, J., Tomaz, S.C., Souza-Filho, B.M., Vieira, A.T.S., Andrade, A.B., Gusmão-Cunha, A., 2022. A population study on gender and ethnicity differences in gallbladder disease in Brazil. Arq. Bras. Cir. Dig. 35, e1652.
- Nederfors, T., Nauntofte, B., Twetman, S., 2004. Effects of furosemide and bendroflumethiazide on saliva flow rate and composition. Arch. Oral Biol. 49, 507–513.
- Page, M.J., Moher, D., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J.M., Hróbjartsson, A., Lalu, M.M., Li, T., Loder, E.W., Mayo-Wilson, E., McDonald, S., McGuinness, L.A., Stewart, L.A., Thomas, J., Tricco, A.C., Welch, V.A., Whiting, P., McKenzie, J.E., 2021. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ 372, n160.
- Proctor, G.B., Osailan, S.M., McGurk, M., Harrison, J., 2007. Sialolithiasis-pathophysiology, epidemiology and aetiology. Modern Manage. Preserv. Salivary Glands, 91–142.
- Saito, Y., Takami, H., Abdelhamid Ahmed, A.H., Nakao, A., Ho, K., Tokuda, T., Miyata, R., Randolph, G.W., Ando, N., 2021. Association of symptomatic gallstones and primary hyperparathyroidism: a propensity score-matched analysis. Br. J. Surg. 108, e336–e337.
- Sanson, T.G., O'Keefe, K.P., 1996. Evaluation of abdominal pain in the elderly. Emerg. Med. Clin. North Am. 14, 615–627.

- Selle, J.G., Altemeier, W.A., Fullen, W.D., Goldsmith, R.E., 1972. Cholelithiasis in hyperparathyroidism: a neglected manifestation. Arch. Surg. 105, 369–374.
- Shrikhande, S.V., Barreto, S.G., Singh, S., Udwadia, T.E., Agarwal, A.K., 2010. Cholelithiasis in gallbladder cancer: coincidence, cofactor, or cause! Eur. J. Surg. Oncol. 36, 514–519.
- Smith, B.C., Ellis, G.L., Slater, L.J., Foss, R.D., 1996. Sclerosing polycystic adenosis of major salivary glands: a clinicopathologic analysis of nine cases. Am. J. Surg. Pathol. 20, 161–170.
- Stack Jr, B.C., Norman, J.G., 2008. Sialolithiasis and primary hyperparathyroidism. ORL 70, 331–334.
- Stinton, L.M., Shaffer, E.A., 2012. Epidemiology of gallbladder disease: cholelithiasis and cancer. Gut Liver 6, 172–187.
- Su, Y.X., Zhang, K., Ke, Z.F., Zheng, G.S., Chu, M., Liao, G.Q., 2010. Increased calcium and decreased magnesium and citrate concentrations of submandibular/sublingual saliva in sialolithiasis. Arch. Oral Biol. 55, 15–20.
- Sun, H., Tang, H., Jiang, S., Zeng, L., Chen, E.Q., Zhou, T.Y., Wang, Y.J., 2009. Gender and metabolic differences of gallstone diseases. World J. Gastroenterol. 15, 1886–1891.
- Waseem, Z., Forte, V., 2005. An unusual case of bilateral submandibular sialolithiasis in a young female patient. Int. J. Pediatr. Otorhinolaryngol. 69, 691–694.

- Weerakoon, H., Navaratne, A., Ranasinghe, S., Sivakanesan, R., Galketiya, K.B., Rosairo, S., 2015. Chemical characterization of gallstones: an approach to explore the aetiopathogenesis of gallstone disease in Sri Lanka. PLoS One 10, e0121537.
- Weinberger, A., Sperling, O., De Vries, A., 1974. Calcium and inorganic phosphate in saliva of patients with primary hyperparathyroidism. Clin. Chim. Acta 50, 5–7.
- Wells, G. A., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M., Tugwell, P., 2011. The Newcastle Ottawa Scale (NOS) for Assessing the Quality of Non-Randomised Studies in Meta-Analyses. Retrieved May, 2023, from http://www.ohri.ca/programs/clinical\_epidemiology/oxford.asp.
- Williams, M.F., 1999. Sialolithiasis. Otolaryngol. Clin. North Am. 32, 819–834.
- Wu, C.-C., Hung, S.-H., Lin, H.-C., Lee, C.-Z., Lee, H.-C., Chung, S.-D., 2016. Sialolithiasis is associated with nephrolithiasis: a casecontrol study. Acta Otolaryngol. 136, 497–500.
- Zenk, J., Koch, M., Klintworth, N., König, B., Konz, K., Gillespie, M. B., Iro, H., 2012. Sialendoscopy in the diagnosis and treatment of sialolithiasis: a study on more than 1000 patients. Otolaryngol. Head Neck Surg. 147, 858–863.