



## Sialolithiasis– The unturned stone: Series of three case reports with review of literature

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### Abstract

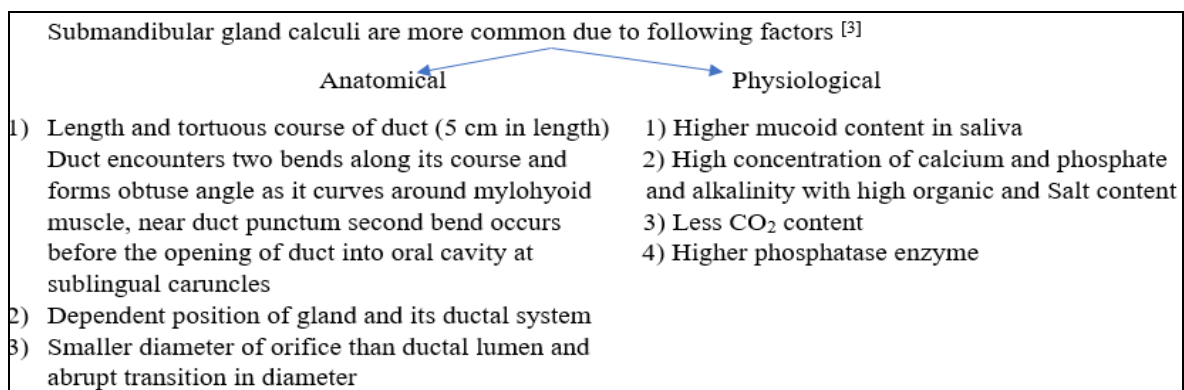
Salivary glands which produce saliva, exhibit variety of diseases ranging from infection, painful obstructions, benign and malignant tumors. Sialolithiasis is one of the most common disorder of the salivary gland which is characterized by typical history of pain and /or swelling during meals and may compromise gland function. In present times, various imaging modalities are available in a Clinicians armamentarium for easy diagnostics, each having its own advantages and demerits. For small and accessible stones conservative therapies like milking of ducts with palliative therapies produce satisfactory result whereas large and inaccessible stones require surgical management which include procedures that are expensive, time consuming and complicated and may lead to loss of gland function with troublesome sequelae such as xerostomia. In this paper we present 3 cases of sialolithiasis in submandibular gland along with brief review on existing literature.

**Keywords:** salivary gland calculi, bacteria, calcium, phosphates, lithotripsy

### Introduction

Saliva, a complex fluid produced by 3 major salivary glands *viz.* parotid mainly made of serous cells producing watery, enzyme rich saliva, Submandibular consists of both serous as well as mucous cells, sublingual primarily of mucous type which secrete more viscous fluid with lots of salivary glycoproteins called as mucins and hundreds of minor salivary glands located in buccal mucosa, palate and tongue. [1] Variety of infections, developmental anomalies, painful obstructions and benign and malignant tumors can occur in salivary glands among which obstructive sialadenitis, the most frequently encountered salivary gland disease with stones in the excretory duct accounting for most frequent cause of obstruction.

Sialolithiasis is a condition characterized by formation of calcified mass/calculi within a salivary gland/ducts accounting for 1.2% of major salivary gland swellings. Sialolith most frequently develops in submandibular gland (80-90%), followed by parotid gland (5-15%) and sublingual gland (2-5%) and rarely in minor salivary glands. Anatomically submandibular gland is located in the submandibular triangle whose anterior and posterior sides are formed by digastric muscle whereas mandible forms the inferior side. The draining channel, the Wharton's duct exists on the medial side of the gland. [2]



Sialolithiasis is more commonly observed in males and mainly affects people between the ages of 30 and 60 commonly afflicted with cyclic gland enlargement and pain related to eating. [4] Though no definitive etiology for sialolithiasis has been suggested, various genetic and environmental causative factors along with various risk factors like high urine calcium levels, Diabetes mellitus, Hyperparathyroidism, Gout, Hypertension, certain food habits and medications, obesity, Poor fluid intake and

family history are deemed responsible for stone formation.[5] Literature is insufficient on possible genetic predisposition for sialolithiasis.[6] Factors responsible for formation of sialolith can be categorized into two main categories

- Compositional (such as increased calcium content or altered enzyme function).
- Anatomical like duct stenosis or inflammation which affect saliva generation or flow.

### Various theories have been proposed to explain process of sialolith formation like <sup>[7]</sup>

- Formation of organic framework because of coalescence of organic molecules within saliva into a gel around which deposition of calcium crystals occur.
- Formation of sialo-microliths serving as a nidus for calculi formation.
- Precipitation of calcium phosphate due to alkalinity of saliva and increase in salivary pH.
- Accumulation of saliva due to obstructive atrophy, inflammation and compression of surrounding parenchyma creating an environment for deposition of calcium on phospholipid membrane.
- Retrograde migration of debris, bacteria or substances from oral cavity into ducts.

Chemical composition mainly comprises of microcrystalline apatite ( $\text{Ca}_5[\text{PO}_4]_3\text{OH}$ ) or whitlockite with apatite being most frequent component and whitlockite is found in core. Formation of either component depend on concentration of calcium and phosphate with high concentration favoring formation of whitlockite and low concentration favoring apatite deposition. Other crystalline forms like waddelite and brushite are present at the periphery of sialolith in small amount <sup>[8, 9]</sup> Harrison and Epivatianos described sialo-microliths which were considered as nidus around which further calcification occur. Harrison proposed a possible pathophysiology where secretory inactivity acts as an initiating factor which leads to accumulation of sialo-microliths, inflammation, obstructive atrophy and compression of surrounding parenchyma which leads to stagnation of saliva and creates an environment for calcium deposition on phospholipid membrane resulting in formation of sialolith.<sup>[10, 11]</sup> Others suggested that increased salivary pH and alkalinity of saliva results in precipitation of calcium phosphate, yet some others proposed that the retrograde migration of debris, substance or bacteria from oral cavity into salivary ducts serve as a nidus for stone formation <sup>[9]</sup>

Sialolith formation mostly tends to be unilateral which argues against a systemic mechanism and suggests that there may be more local factors at play.<sup>[9]</sup> Very less information is available on etiology and pathogenesis of sialolithiasis and its contributing systemic predisposing factor like urolithiasis <sup>[12]</sup>. Gall stones consists of calcium Bilirubinate, Palmitate,

Carbonate and Phosphate. Cholesterol is its main component along with biliary pigments and calcium salt. This suggests role of Calcium salts in gallstone formation, hence possibility suggested that pathogenesis for cholelithiasis and sialolithiasis share certain similarities but results vary among studies <sup>[12]</sup> Urolithiasis which means stones in the kidney (nephrolithiasis), ureter or bladder affects between 1- 15 % of population globally. Though exact cause remains unclear significant increase for nephrolithiasis and cholelithiasis was found in sialolithiasis patient compared to controls in case control studies from Taiwan <sup>[13]</sup>. Because 80% stones are composed of Calcium substrate abnormalities in Calcium metabolism is also a risk factor for nephrolithiasis <sup>[12]</sup>. Results of association between sialolithiasis and nephrolithiasis varied among different studies. <sup>[14, 17]</sup> An association between primary hyperparathyroidism and stone formation is a classic part of bones, stone, abdominal moans and psychic groans, although it is rarely seen today <sup>[7]</sup>.

### We have compiled few cases, which were seen in our Institute

**Case 1:** A 30-year-old male patient reported with recurrent episodes of pain during meals since last 2-3 years with last episode 1-2 months back and persistent pain since then, a swelling in right submandibular region and pain during meals. (Figure1A) Extraoral examination revealed mild swelling over right submandibular region with single tender submandibular lymph node palpable, bimanual examination revealed firm and tender submandibular gland. Intraoral examination revealed hard stone like structure in the floor of mouth on right side. (Figure1B) Mandibular occlusal radiograph revealed a single ovoid radiopacity extending from distal aspect of 45 tooth till mesial aspect of 46 tooth (figure 1C) On the basis of clinical and radiological findings, we diagnosed the case as a right submandibular Duct sialolithiasis. All preoperative investigations were normal. Under antibiotic coverage and local anesthesia intraoral incision was made in floor of mouth. Duct was opened and sialolith was removed in a single piece. Patient's postoperative course was uneventful, sutures were placed to close the area.

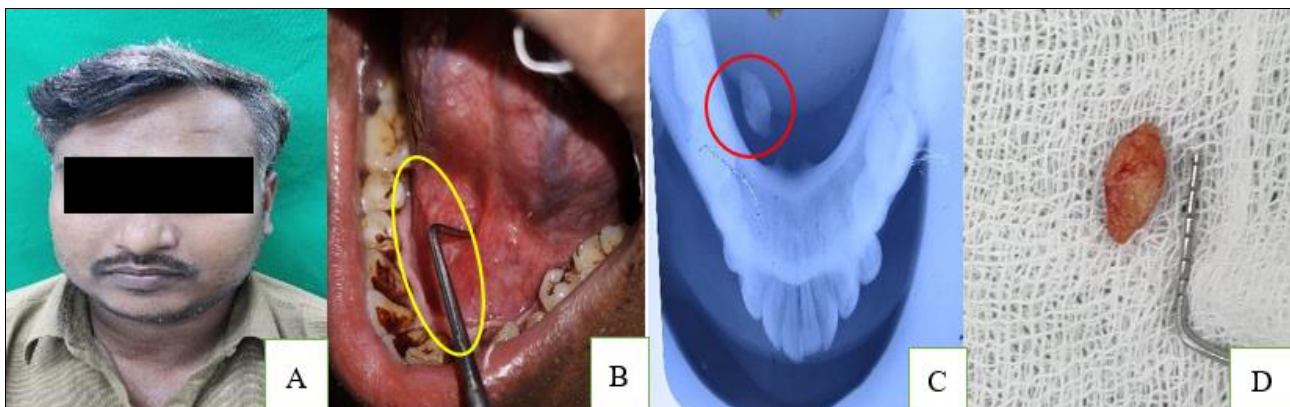


Figure 1A) Patients Picture, 1B) Swelling in floor of mouth on right side 1C) Mandibular occlusal radiograph showing sialolith in right submandibular region. 1D) Sialolith after removal.

**Case 2:** A 65-year-old male patient visited for replacement of missing teeth. On digital panoramic radiographic examination, a well-defined radiopaque structure was noted in the body of mandible as an incidental finding extending from lower right canine till first molar region suggestive of calcification most likely to be a sialolith. (Figure 2A) On intraoral examination a non-tender swelling was noted in floor of mouth on right side. (Figure 2B) Bimanual palpation revealed stony hard structure in the same region.

Mandibular occlusal cross-sectional radiograph showed well defined irregular radiopaque structure located lingual to the lingual cortex on right side extending antero-posteriorly from distal surface of lower right first premolar till distal to second molar. (Figure 2C) The posterior extent of the radiopacity is not visible completely in radiograph. Removal of the sialolith was advised but since it was asymptomatic patient denied further treatment

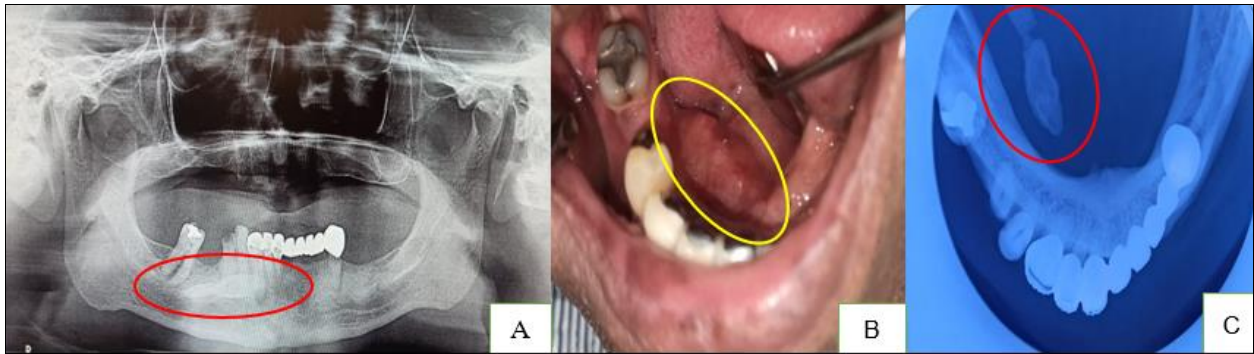


Figure 2A) Digital panoramic radiograph showing well defined radiopaque structure in the body of mandible, 2B) Swelling in floor of mouth on right side, 2C) Mandibular occlusal radiograph showing sialolith in right submandibular region.

**Case 3:** A 27-year-old female patient reported to our institute with C/O pain in lower left side of face and swelling in the same region while having food in the last 6 days which subside half an hour later. she also experienced sour sweet discharge in mouth at this time. I/O examination revealed inflamed, enlarged and erythematous duct on left

side of lingual frenum. MRI submandibular sialography (Figure 3) showed two calculi measuring 2.1 × 1.5 mm in left submandibular duct at its opening and 2.6 × 2 mm in left submandibular duct at the level of 1<sup>st</sup> mandibular molar tooth causing upstream dilatation of left Wharton’s duct of maximum diameter 3.1 mm.

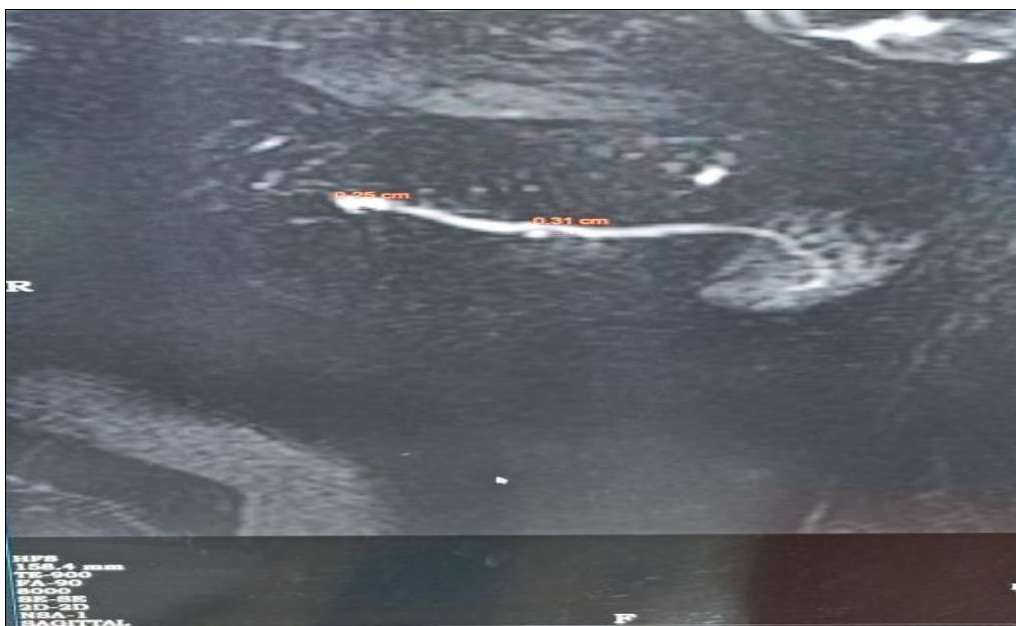


Fig 3: MRI submandibular sialography

A small 2.8 × 3.2 mm sized T<sub>2</sub> hyperintense cyst is seen adjacent to calculus at the level of 1<sup>st</sup> mandibular molar tooth. Left submandibular and sublingual gland appear T<sub>2</sub>/STIR hyperintense and mildly bulky in size. No significant focal lesion. The overall findings gave the impression of left submandibular sialadenitis due to sialolithiasis

**Imaging Alternatives**

Variety of imaging modalities aid in detection of salivary stones, each has its own advantages and disadvantages with regard to the cost, ionizing radiation and capacity to visualize duct system. Following table gives brief overview of these imaging modalities. [18, 24]

**Table 1**

<b>Imaging Modality</b>	<b>Advantage</b>	<b>Shortcoming/Limitation</b>
1) Plain Film Periapical radiograph Occlusal Radiograph Panoramic Radiograph	Cost effective Easily available Less radiation exposure Used for initial assessment of sialolith Sometimes calculus appears at the lower end of radiograph in shallow floor of mouth because film embraces the duct	Poorly calcified and small stones are difficult to visualize If patient is unable to tolerate the film posteriorly in mouth calculi in the posterior portion of duct are not visualized
2) Cone beam computed tomography	In patients with signs and symptoms of sialolithiasis very commonly used as first line imaging or second line after plain film Useful in detection of sialolith as well as provide accurate information on stone size and position. Cost effective	More radiation exposure as compared to plain film
3) Computed Tomography	Conventional CT demonstrates highest accuracy in visualization of salivary calculi among all the available imaging modalities When it is easily available it is often the method of choice for imaging. Detects very small and semi calcified calculi as well	High radiation exposure High cost Detects calcifications with high sensitivity but poorly visualize salivary ducts and lesions within them
4) Ultrasonography Sialoliths characteristically produce hyperechoic areas with distal signal loss (posterior acoustic shadowing)	Non-invasive Cost effective First line imaging in emergency and urgent care intraoral transducer helps in rapid visualization of course of main duct and body of major salivary glands	Hyperechogenic air bubbles mixed with saliva and simulating stones may be misleading Less precise in differentiating cluster of stones from single large stone
5) Sialography Visualizes the ducts and the parenchyma of the salivary gland after contrast administration into the main salivary duct	Helps to distinguish between mucous plugs, salivary stones and ductal strictures Though very old it is the best diagnostic tool in imaging subtle anatomy of salivary gland duct system. Determine no and location of salivary stones, including those smaller than 2mm in diameter. Visualizes non-opaque calculi in salivary ducts. Allows for high certainty discrimination of stone location, in the salivary duct/ in parenchyma which is a crucial for choice of right therapeutic method.	Patients' exposure to ionizing radiation and iodine contrast media. Pain during contrast medium insertion into salivary ducts Possibility of calculi dislocation towards inside of gland Movements artifacts Quality of results depend on examiners experience
Conventional sialography – uses panoramic, Occlusal and periapical radiograph	First line of approach when there is strong clinical suspicion of sialolithiasis	
b) Digital Subtraction Sialography	Recognized diagnostic method in suspicion of salivary gland calculi, Sialadenitis, Fistulas as well as stenosis.	Patients may feel moderate tenderness and slight edema of salivary glands for next 24 hours
c) CBCT sialography	Useful where plain film sialography has been inadequate, such as in more complex cases of salivary duct obstruction non-invasive superior to conventional sialography with respect to imaging salivary gland parenchyma and sialoliths	
d) MR Sialography	Does not require ductal cannulation and contrast medium, hence can be used in patients with iodine and contrast media allergies. No ionizing radiation Can be used in patients with acute sialadenitis	Although the MRI examination allowed for a precise evaluation of salivary calculi and salivary duct stenoses, the normal image did not exclude the presence of small calculi, of 2–3 mm in size, not leading to salivary duct dilatation.
e) CT Sialography	Allows simultaneous visualization of both salivary ducts and glandular tissue	Higher radiation dose as compared to conventional sialography Cannot visualize secondary and tertiary branches
f) Contrast sialography	visualizing parotid and submandibular glands ductal system and differentiating calcified phlebolith from sialolith	

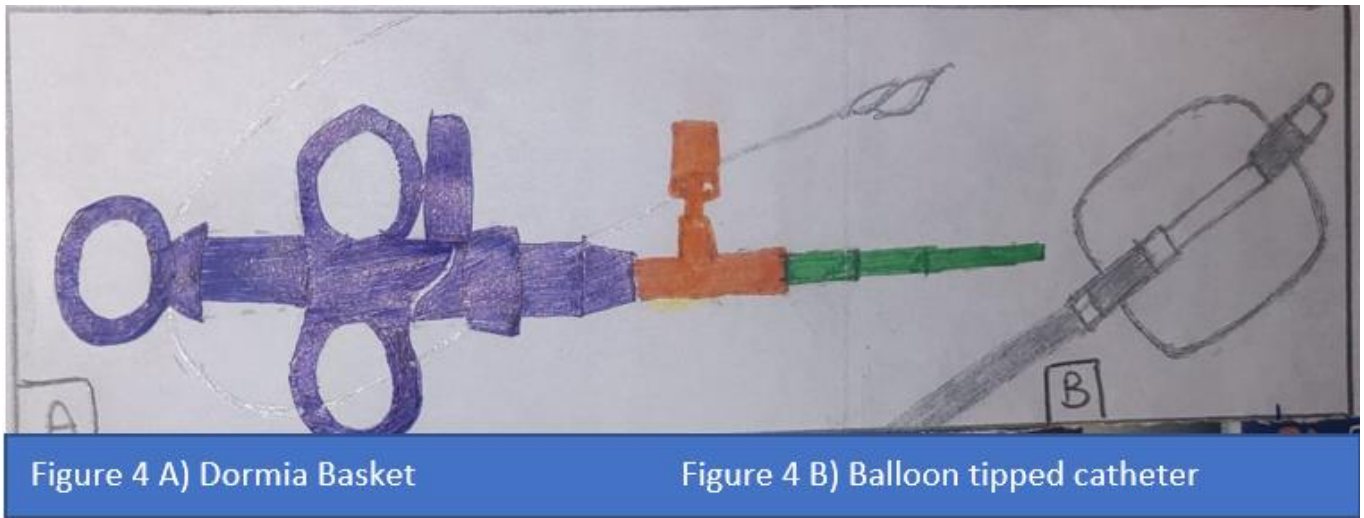
Sialendoscopy- This is the technique which helps in detecting the stone as well as assessing the condition of ducts and determining shape, size and mobility of the stone [25]

Indication- Mobile stone less than 5 mm in diameter  
As a supplementary method to ductotomy  
If sialoliths are immobile, less than 4-8 mm in diameter and situated in the main duct.

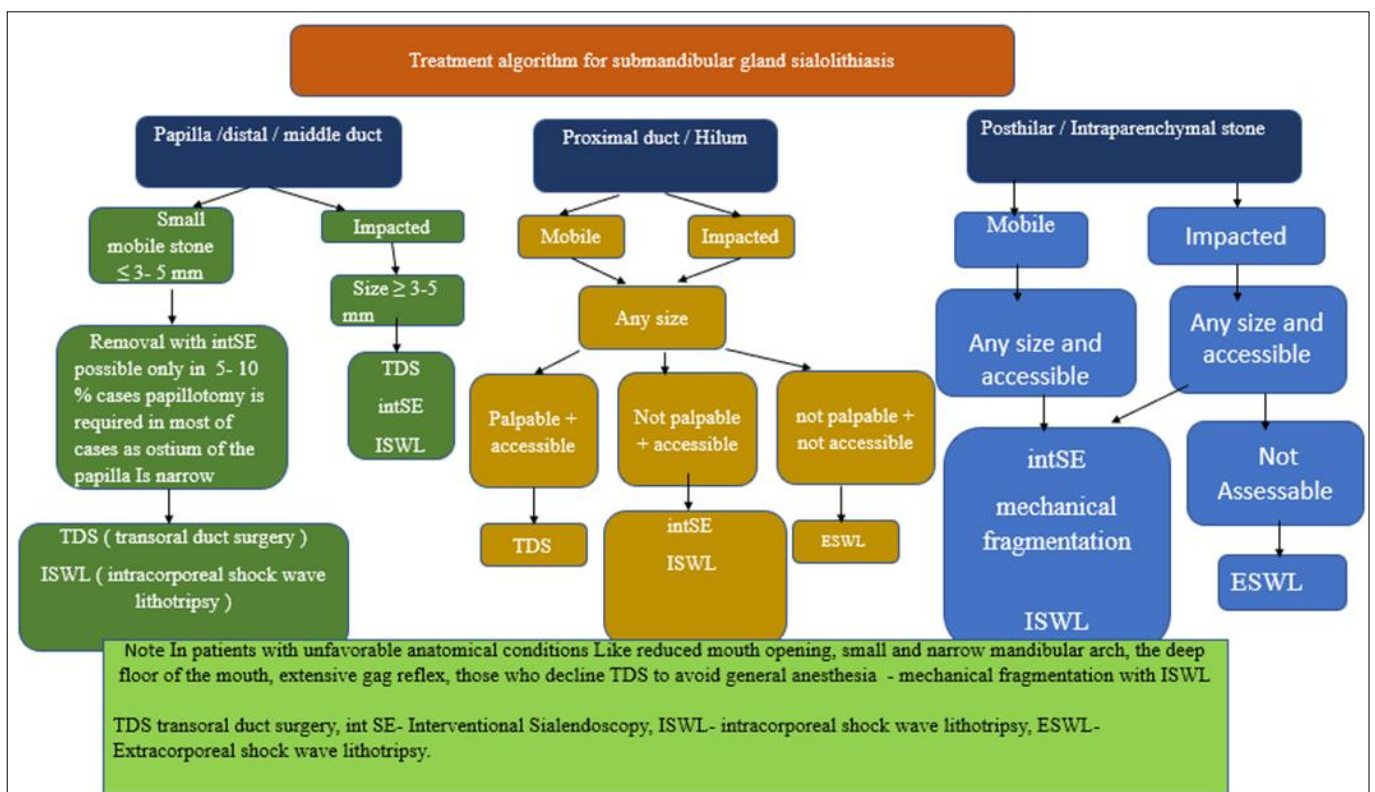
Contraindication – When stones are located behind areas of bending in distal parts

Procedure –

- 1) Using dormia basket for removal of calculi (figure 4A)
- 2) Use of balloons to dilate the stenosed duct and stenosis correction (figure4B)
- 3) Placement of 2-3 cm long stent in duct for about 7-10 day [25]



**Treatment modalities**



**Fig 5**

Varied treatment options for sialolithiasis have been tried since 1990. Gland resection rates has been reduced to less than 10 % or even less than 5 % between 1990- and first-decade of 2000 due to introduction of new minimally invasive techniques such as Extracorporeal shock wave lithotripsy (ESWL), Interventional Sialendoscopy (intSE). Size, location, mobility and shape of stones are prognostic

factors affecting the treatment Initially conservative measures like use of sialagogues, gland massage during or after gland stimulation, instrumental dilatation of papilla is indicated. Very small stones may be washed out. The figures 5 and 6 show general algorithm's for treatment of submandibular and parotid glands respectively [26]

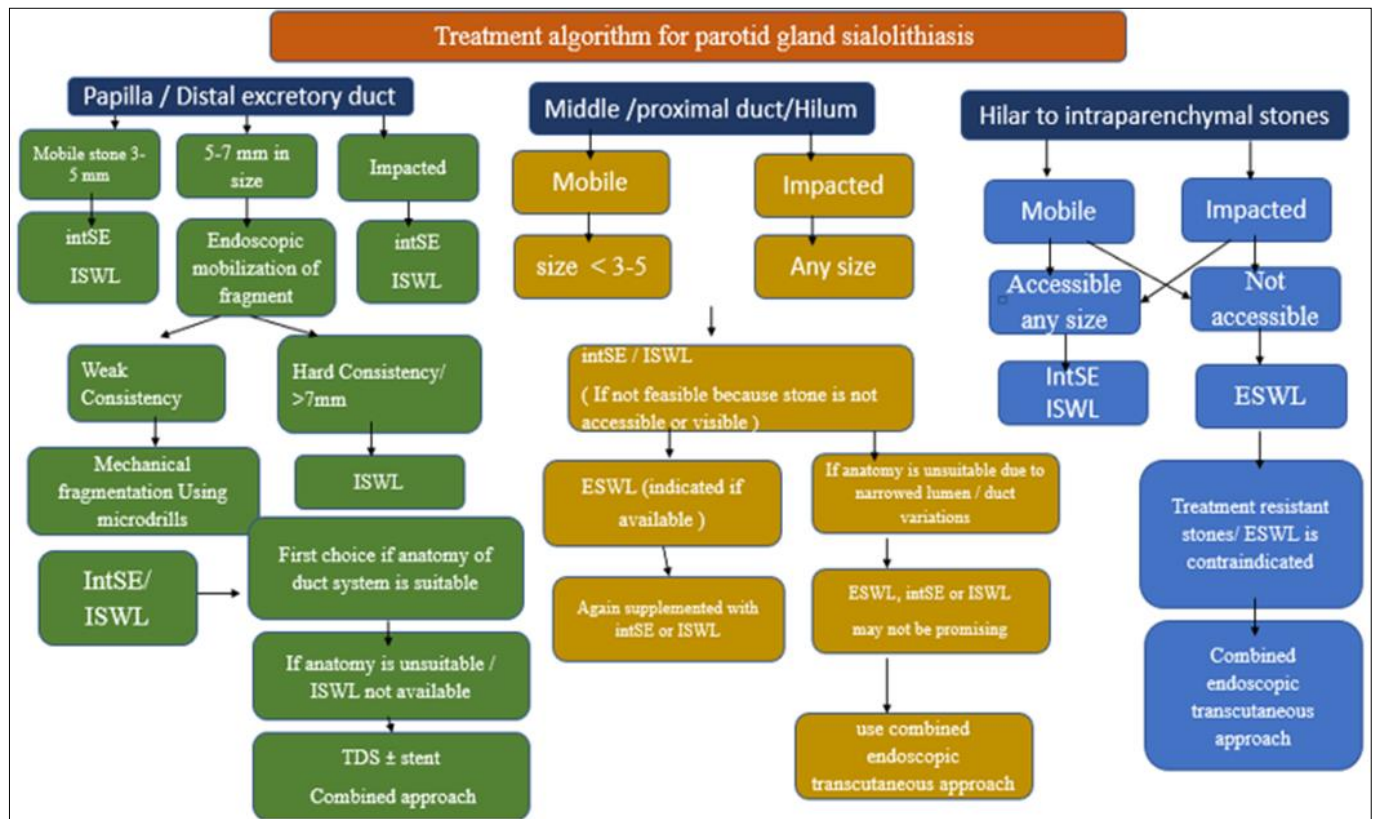


Fig 6

**Discussion**

Blockage / interferences due to stones / calculi mandates removal of them for which various imaging options are available, further the treatment modalities are based on location and degree of calcification as mentioned earlier in our article. Despite the relative frequency of sialolithiasis, the etiology of salivary stone formation still remains elusive. The first sialolith was described over 150 years ago, since then many theories have been proposed to explain the process of sialolith formation but the true mechanism is still unknown [9]. Wekeley in 1929 cultured bacteria from the core of salivary calculi but speculated that the actual cause of calculi was the precipitation of calcium salts while others theorized that inflammation in salivary gland resulted in changes in the secretion and precipitation of saliva components which ultimately lead to salivary stone formation [27]. Later it was theorized that organic molecules coalesce into a gel and leads to formation of organic framework around which Ca crystals deposit forming sialolith. Schroder *et al* suggested that altered ionic concentration of calcium, phosphorus and other ions contribute to sialolithiasis. They demonstrated high salivary conc of Calcium, potassium, chloride and phosphorus in patients with sialolithiasis [28]. Organic and Inorganic substances are present in varying ratios in sialolithiasis with organic substances like glycoprotein, mucopolysaccharides, cellular debris and inorganic substances being Ca carbonates and Ca phosphate. Calcium, phosphate and magnesium ion constitute about 20 – 25 % of mass while other minerals like iron, copper and manganese comprise the rest.[9]

Autophagosomes degenerate the stored secretory granules and organelles such as mitochondria, which are rich in Ca and P resulting in accumulation of these elements and crystallization on degenerating membranous debris in autophagosomes. Thus, to summarize the formation of

sialolith proceeds in two phases neurohumoral induction phase in which homeostasis is disturbed leading to salt precipitation which are bounded by certain mucopolysaccharides and hence the crystallized nidus of salivary calculus is formed. second phase which is purely physicochemical process in which organic and inorganic materials of saliva envelop the nucleus.[29]

Nowadays various habits like tobacco, alcohol consumption is common among youths. Tobacco and smoking adversely affects the cytotoxic activity of saliva, causes reduction in antimicrobial potential of saliva, reduces salivary amylase, which leads to multiplication of microbes within the ductal system providing substrate for salivary stone formation. Inflammation in oral cavity can be transmitted into duct and causes ductal swelling and narrowing which in turn induce salivary stasis and cause precipitation of stone. Though there is no definitive evidence found among studies between sialolith and alcohol consumption it can be considered as risk factor since there is dose dependent association between alcohol consumption and inflammation.[30]

**Conclusion**

For patients presenting with submandibular or facial pain particularly at mealtime sialolith should always be considered as a probable diagnosis. A careful history and correct imaging alternative are required for precise diagnosis and treatment planning. Occlusal radiographs are still useful in diagnosing sialoliths though advanced methods are available. Small stones can be treated conservatively but for larger stones surgical intervention is essential. In spite of the long-standing history of attempts at understanding etiology and pathogenesis it still remains a mystery.

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