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Salivary Stone Disease

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Abstract: The aim of this study was to identify existing gaps and outline future directions in research focused on predicting the development, progression, and outcomes of salivary stone disease (SSD). The analysis revealed that, to date, there is no well-founded experimental model of SSD, nor a scientifically validated system of prognostic tests suitable for hospital and outpatient use to assess the likelihood, course, and potential outcomes of the disease.

Keywords: salivary stone disease, Classification, Diagnosis.

Sialolithiasis (Salivary Stone Disease)

Sialolithiasis (SLD), or salivary stone disease, is one of the most common pathologies of the salivary glands (SG). According to both Russian and international studies, it accounts for about **50%** of all salivary gland disorders [10]. In certain regions, this figure reaches **52.3%** [5], **60.0%** [29], **61.1%** [10], **70.0%** [15], and even **80.0%** [23].

Despite the large number of studies devoted to the **diagnosis of SLD** [10, 11, 29] and the presence of well-known **clinical signs**, diagnostic errors remain common [12]. This often leads to **inadequate treatment strategies** and **suboptimal rehabilitation**, contributing to **chronic inflammation** and an increased risk of complications [17, 19].

Traditionally, management of SLD focuses mainly on **surgical removal of stones** and the **relief of acute inflammation**, while issues of **early diagnosis** and **prevention of stone recurrence** receive insufficient attention.

Diagnostic Challenges and the Role of Clinical Crystallography

A new and rapidly developing field known as **clinical crystallography** has emerged, offering diagnostic potential for diseases of various origins and localizations based on the **crystalline structure of biological fluids (BF)** [3, 16].

The structure of human biological fluids carries extensive information about the **state of organs, systems, and overall homeostasis** [26]. The development of a pathological process alters the crystalline pattern, changing both its **qualitative and quantitative characteristics** [7].

Among modern research priorities is the creation and application of **non-invasive diagnostic methods**. One such promising approach involves the analysis of **oral fluid (saliva)**, which can be collected easily, in sufficient quantities, and repeatedly without harming the patient [7, 16].

In this study, available domestic and international literature was reviewed, focusing on **experimental models**, **clinical diagnostic methods**, and **prognostic aspects** of SLD. The review also identified existing **gaps in knowledge** and outlined **future directions for research**. The analysis included **peer-reviewed journals** published over the last 15 years, as well as **key monographs and reference books** without a time limit. A **descriptive method** was used to analyze the collected materials.

Results and Discussion

The most frequent cause of complications in SLD is **diagnostic error**, primarily due to the absence of accessible and reproducible methods for predicting the **course and outcome** of the disease.

Sialoliths are **calcified masses** that form within the **ducts or parenchyma of the salivary glands**. According to current classifications, SLD progresses through **three clinicomorphological stages**:

1. **Initial stage**,
2. **Clinically expressed stage**,
3. **Late stage** [4, 9].

In the **initial stage**, clinical manifestations are minimal. **Salivary stasis** may lead to a slight enlargement of the affected gland, and patients may experience **mild discomfort** during eating or salivary stimulation [5]. However, many other salivary gland disorders present with similar symptoms, which complicates **early differential diagnosis** [6].

A comprehensive diagnostic work-up for SLD typically includes both **standard methods** (history taking, inspection, palpation) and **specialized imaging techniques** [20]. Common imaging modalities are **plain radiography**, **ultrasound**, **retrograde contrast sialography**, **scintigraphy**, **computed tomography (CT)**, and **magnetic resonance imaging (MRI)** [21, 28, 30].

However, experts note several limitations of radiological methods:

- They may not adequately reflect **disease dynamics**, especially during short observation periods.
- The **error rate** in imaging-based diagnosis ranges from **7% to 46%** [12, 25].
- About **15–40% of stones are radiolucent** and cannot be detected by standard imaging [6, 10].
- Non-mineralized sialoliths and stones **smaller than 2 mm** are often invisible.
- Soft-tissue pathology and ductal structure cannot be reliably assessed without contrast agents, which are frequently **highly allergenic** [14].

Thus, despite numerous studies on the **radiological diagnosis of salivary gland diseases**, the **diagnostic accuracy** and **informative value** of these methods remain **inconsistent** across the literature.

Etiological Considerations

The **etiology of sialolith formation** is still not fully understood. The **mechanism of stone formation** continues to be debated [10]. It is believed that the process is influenced by both **qualitative and quantitative changes in saliva**, as well as other contributing factors such as:

- **Trauma** to the salivary ducts or glands,
- **Salt deposition** on organic matter,
- **Alterations in the composition and properties of oral fluid**.

Pathogenesis and Theoretical Approaches to Sialolithiasis

The specialized literature also presents a theory suggesting that **retrograde infection** may play a role in the development of sialolithiasis. According to this concept, **food particles, chemical substances, or bacteria** may migrate into the salivary ducts, serving as **nuclei for further calcification**.

Among the general predisposing factors, researchers highlight **disturbances in mineral metabolism** and **hypo- or avitaminosis A** [8, 29]. It has been established that salivary stone disease often develops against the background of **systemic disorders** accompanied by **abnormalities in phosphorus–calcium metabolism** [18, 29]. As a result, **protein–carbohydrate and phosphorus–calcium complexes** may form within the salivary gland tissues and possibly in other organs, acting as **precursors of microliths**.

At sites where these microliths occur—especially in the presence of **individual anatomical features** or **local obstructive factors**—**retentive zones** are created, allowing **salt deposition and subsequent stone growth**. Support for the metabolic theory comes from the frequent observation that patients with sialolithiasis also develop **stones in the gallbladder or urinary tract** [13].

In this regard, **G.V. Martynov (2000)** introduced the concept of **"primary multiple biolithiasis"**, and **V.N. Matina et al. (1993)** noted that the mechanisms of **urinary, biliary, and salivary stone formation** share many similarities. Of particular relevance is the **proteolysis–ion theory** of nephrolithiasis proposed by **Yu.G. Ediny and V.S. Dzyurak (1999)**. This theory posits that stone formation requires two simultaneous conditions:

1. An **optimal pH** level for salt sedimentation, and
2. A **low level of proteolytic activity** in urine.

When proteolysis is insufficient, a **gel-like matrix** forms, which becomes the **nucleus for stone development**. It is possible that similar biochemical processes occur within the **salivary gland ducts**.

According to **A.B. Denisov et al. (1996)**, the formation of **mineral concretions in salivary glands** is a common phenomenon. In 80% of cases, the authors detected **microcalculi (about 25 μm)** within **acinar cells**, consisting of **calcium ions and fragments of cell membranes**. When salivary flow is impaired, these microstones may remain in the ducts and later cause **local obstruction**.
The relative rarity of stones in the **parotid glands** may be explained by the presence of **statherin**, a salivary protein that serves as a **potent inhibitor of calcium phosphate precipitation**.

Another hypothesis, the **reflex theory** of sialolith formation proposed by **M. Decaume, M. Bonneau, and I. Payen (2001)**, attributes the disease to **autonomic dysfunction of the salivary glands**, leading to **persistent ductal dilation**, **impaired salivary flow**, **secondary infection**, and ultimately, **stone formation**.

Other contributing factors include **dietary habits** and **the mineral composition of drinking water**, both of which influence the **electrolyte balance and pH of saliva**. Saliva is primarily composed of **micelles** that bind large amounts of water, calcium, and phosphate ions. The **stability and mineralizing potential** of these micelles depend on their structure. Deviations in pH from the physiological norm reduce micellar stability and promote precipitation.

Currently, most researchers agree that **sialolithiasis is multifactorial** in origin. The disease develops as a result of a **complex interaction of local and systemic factors**, though opinions differ as to which is the **primary initiating factor** responsible for the onset of stone formation. Unfortunately, there is still **no single unified theory** that fully explains the pathogenesis of sialolithiasis.

Research Gaps and Conclusions

A review of the available Russian and international literature revealed a **lack of studies** providing **objective, evidence-based data** supported by **systematic analysis** of **clinical and laboratory parameters** of oral fluid in patients with sialolithiasis. No publications were found that assess the **diagnostic accuracy** or **prognostic value** of these parameters.

Existing reports are largely **descriptive**, and only a few studies address **prognostic modeling** in salivary stone disease.

For example, **R.D. Yusupov and N.P. Batukhtina (2002)** attempted to identify correlations between **clinical and morphological manifestations** of submandibular gland sialolithiasis and **patient somatotype**. More recently, **J.O. Santos et al. (2018)** proposed using **three-dimensional reconstruction** of salivary gland calculi to evaluate their **volume and morphological relationship** with adjacent structures. According to the authors, **3D imaging** improves understanding of lesion morphology, facilitates **precise measurements**, and assists in selecting the **optimal surgical approach** [22].

However, information on the **experimental modeling** of sialolithiasis in major salivary glands remains extremely limited and fragmented. Previous experimental attempts were mainly aimed at addressing **surgical treatment techniques**, rather than exploring the **mechanisms of stone formation and progression**.

To date, there is **no adequate experimental model** that allows for a **comprehensive morphological and laboratory investigation** of the disease's pathogenesis. Such a model is necessary to identify **reliable diagnostic markers**, improve **prognostic assessment**, and develop **effective preventive strategies**.

In conclusion, current literature lacks:

- A **rational experimental model** for studying salivary stone disease;
- Objective data on the **diagnostic value** of **physico-biochemical and immunological parameters** of oral fluid;
- A **scientifically grounded system of prognostic tests** suitable for both **inpatient and outpatient practice** to predict the **development, course, and outcome** of sialolithiasis.

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