EVALUATION OF THE REMINERALIZATION CAPACITY OF SALIVA (IMK) IN PATIENTS WITH SJÖGREN SYNDROME

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ABSTRACT

Sjögren's syndrome is an autoimmune disease that is associated with inflammatory changes, reduced salivary flow, and altered saliva composition. The effects of medications and injuries to the salivary ducts can contribute to the increased salivary viscosity with serious consequences for the teeth and soft tissues. The remineralization capacity of saliva is based on its ability to provide the necessary minerals, maintain a favorable pH balance, and support the natural mechanisms implied in the repair processes of the tooth structure. **The aim of this study** is to evaluate the impact of salivary pathology in Sjögren's Syndrome, and the correlations on certain cariogenic risk parameters. **Materials and method:** The study was conducted on 30 patients: Study group (15 patients) with primary Sjögren's Syndrome; Control group (15 patients) - without associated general pathology. The evaluation focused on the analysis of DMFT and the following salivary parameters: resting salivary flow (RSF), stimulated salivary flow (SSF), buffering capacity (BC), saliva viscosity (SV), and the index of salivary microcrystallization (IMK). The evaluated **results** demonstrate that the effects of Sjögren's syndrome on the selected indicators (DMFT, RFR, RFS, CT, SV, IMK) are significantly different compared to the control group, indicating the Sjögren syndrome's impact on the dental and salivary status of affected patients. **Conclusions:** There is a correlation between dental caries, saliva, and Sjögren's syndrome. Reduced saliva production in Sjögren's syndrome can lead to xerostomia-associated phenomena, disturb the balance between demineralization and remineralization processes, and may contribute to an increased risk of caries.

***Key words**: saliva, Sjögren's Syndrome, remineralization, index of salivary microcrystallization*

INTRODUCTION

Sjögren's syndrome is an autoimmune disease that can affect up to 3-5% of the adult population over 50-55 years old, where the body produces antibodies against its own cells or tissues [1-5].

Sjögren's Syndrome can occur alongside other autoimmune conditions such as rheumatoid arthritis, systemic lupus erythematosus, and primary biliary cholangitis [3].

There are two forms: primary Sjögren's syndrome - occurs alone, and secondary Sjögren's Syndrome - occurs together with another autoimmune condition (e.g., lupus) [6,7].

In addition to systemic changes (peripheral neuropathy, headache, anxiety, depression, thyroid dysfunction, renal failure, pulmonary conditions (bronchiolitis, interstitial lung disease), vasculitis, Raynaud's phenomenon) that occur in this syndrome, it often also involves damage to the salivary and lacrimal glands, causing reduced saliva production, difficult swallowing, and dry eyes (xerophthalmia) [5].

This condition can have also an unfavorable impact on dental health, as saliva plays an important role in protecting the teeth against dental caries [3-5].

Teeth require an adequate quantitative and qualitative level of saliva to neutralize the acid produced by mouth bacteria and to wash away food debris and bacterial plaque [8-11].

This can increase the risk of dental caries [12,13]. There are several mechanisms through which saliva plays an important role in preventing dental caries.

Firstly, saliva contains antibacterial substances that can inhibit the growth of

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bacteria in the oral cavity. Additionally, saliva helps to neutralize the acid produced by bacteria, maintaining a neutral or slightly alkaline pH environment, which is favorable for dental health [14-16].

In the case of Sjögren's syndrome, reduced saliva production can disrupt these protective mechanisms and contribute to the development of dental caries. The salivary glands are affected by the autoimmune processes of the disease, leading to a reduced level of saliva production [4,5,17-19].

Additionally, the composition of the saliva changes by enzymatic disturbances and imbalances in antibacterial components, making the saliva more viscous [18,20].

This can reduce its ability to neutralize the acid produced by bacteria and to prevent the formation of caries (Denisiv 2003; 2006). Normal saliva has a slightly alkaline pH, which helps to maintain the acid-base balance in the oral cavity [21-24].

In the case of Sjögren's syndrome, decreased salivary flow and changes in saliva composition can lead to an increase in acidity in the mouth. This acidic environment can erode dental enamel and contribute to demineralization and the formation of caries and non-cariogenic lesions, often encountered in Sjogren's syndrome [25-28].

The remineralization capacity of enamel may also be affected, thus increasing the vulnerability of teeth to the development of caries [10-15; 29].

with this condition are usually advised to maintain rigorous oral hygiene and to avoid foods and drinks with high sugar content, as these can increase the risk of caries in the absence of normal saliva production [30-31].

In the case of Sjögren's syndrome, it is important to consider supplementation with artificial saliva or products that stimulate salivation, such as sugar-free chewing gum or salivary stimulant tablets.

These can help maintain adequate mouth hydration and prevent dental caries. Some medications prescribed to patients with Sjögren's syndrome, such as immunosuppressive or diuretic drugs, can also affect saliva production and composition.

These medications can lead to a decrease in salivary flow and an increase in salivary viscosity [32,33-38]. In severe cases of Sjögren's syndrome, injuries to the salivary ducts can occur, leading to partial or complete obstruction of these ducts.

This can lead to the accumulation of saliva which becomes more viscous due to stasis and can contribute to an increase in salivary viscosity.

The remineralization capacity of saliva is based on its ability to provide the necessary minerals, to maintain a favorable pH balance, and to support the natural mechanisms of tooth structure repair [8-16]. This feature is important for patients with early non-cavitated dental caries characterised by significant decrease of calcium and phosphat ions levels [39].

Changes that occur in this pathology in the composition of saliva, including the reduced mineral content and altered pH levels, can compromise the remineralization process [15,16; 40-45].

This can make teeth more susceptible to the progression of dental caries. There is a hypothesis that all these changes caused by Sjögren's Syndrome, including inflammation and glandular destruction, decreased salivary flow, changes in saliva composition, the effects of medications, and injuries to the salivary ducts, can contribute to an increase in salivary viscosity in patients affected by this syndrome [34-38].

The lack of comprehensive and unanimous research on the remineralization capacity of saliva and its correlations with other salivary markers in Sjögren's syndrome requests this analysis.

AIM OF STUDY

The aim of this study is to assess the impact of salivary pathology in Sjögren's syndrome, and correlations with some cariogenic risk parameters.

MATERIALS AND METHOD

In conducting this study, we adhered to the current regulations approved by the Ethics and Research Committee of the Faculty of

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Dental Medicine at the University of Medicine and Pharmacy 'Gr.T.Popa' Iași, in accordance with the Research Act No. 206 of May 27, 2004, on good conduct in scientific research, technological development, and innovation, the guide to integrity in scientific research (published by the National Council for Ethics in Scientific Research, Technological Development, and Innovation on November 12, 2020), as well as current European legislation. The patients included in the study signed an informed consent form.

The study was conducted on 30 patients selected from those presenting for various dental treatments at the "M. Kogalniceanu" Clinical Dental Base of UMF Iași.

The patients, aged between 19-65 years, met the following inclusion criteria: patients with Sjögren's syndrome (study group) and patients with dental caries without general conditions, representing the control group.

Additional inclusion criteria were other associated systemic diseases (metabolic, degenerative, congenital, infectious, psychological, pregnancy, etc.).

The evaluation targeted the analysis of DMFT index and the following salivary parameters: resting salivary flow (RSF), stimulated salivary flow (SSF), saliva buffering capacity (BC), saliva viscosity (SV), and the index of salivary microcrystallization (IMK).

The determination of the resting salivary flow rate was conducted according to next protocol: the patient sits upright, head slightly forward, is asked to swallow the saliva they have, timing starts, then they are asked to expel the accumulated saliva every 2 minutes or more frequently into a graduated vessel (sialometer), and after 5 minutes the volume is measured [12-15].

the stimulated salivary flow rate, the patient, seating as in the previous test, was asked to chew a piece of paraffin for 30-60 seconds and then swallow the accumulated saliva.

Timing starts from this point, allowing the patient to chew for 5 minutes and expel saliva into a graduated container. The quantity of saliva accumulated is divided by time, and the result is expressed in ml/min. Normal values are presented in the table below (Table 1).

Table 1. Normal values for RSF and SSF.

	RSF - Unstimulated (resting) salivary flow (ml/min)	**SSF - Stimulated salivary flow (ml/min)**
Normal **Hyposalivation**	0.25 – 0.35 <0.1	1 – 3 <0.7

Saliva viscosity (SV) was determined using the simplified VK-4 viscometer method. Normal values, favorable viscosity = 1.0-4.0. Saliva with unfavorable viscosity = 6.0-9.0.

We recorded the saliva buffer capacity using the manufacturer's color chart as a reference (low, pH 4; medium, pH 5; high, pH 6). We did this by applying one drop of saliva to a Dentobuff test strip (Orion Diagnostica, Espoo, Finland) and reading the result after three minutes.

The index of salivary microcrystallization (IMK) was calculated using the Leus method, modified after Belischaia [14,15].

The results were classified into three types of microcrystallization: type I (high), type II (medium), type III (low) (Figure 1.), depending on the score received, with distribution as follows:

IMK = 0.6–1 indicates a high level of microcrystallization;

IMK = 0.4–0.6 indicates a medium level of microcrystallization;

IMK = 0–0.4 indicates a low level of microcrystallization.

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The statistical analysis of data was performed using SPSS v.17 software.

RESULTS AND DISCUSSIONS

The mean values of DMFT, RSF, SSF, BC, SV, IMK are exposed in Table 2 and Fig.2.

To statistically analyze the data presented in the table, we first calculated the average values for each group and variable, their distribution according to variables and study group, and then conducted a t-test to compare the two groups (Group I - Control versus Group II - Sjögren's syndrome) for each variable (DMFT, SRF, SSF, BC, SV, IMK). The average values for each variable in the two groups are presented in Table 2.

The diagram below (Figure 2) shows the average values of the variables for Group I (Control) and Group II (Sjögren's syndrome). It highlights the differences between the two groups for each of the variables DMFT, SRF, SSF, BC, SV, and IMK.

The significant differences observed in the statistical tests are also visually reflected in this diagram, underscoring the different impact of Sjögren's Syndrome on dental and salivary health when compared to the control group.

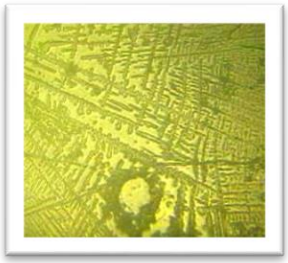
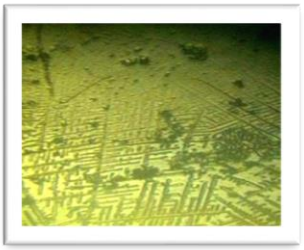
Control group (LM)			
	microcrystallization type I (High)	microcrystallization type II (Medium)	microcrystallization type III (Low)
Study group (LS)			
	microcrystallization type I (High)	microcrystallization tip II (Medium)	microcrystallization tip III (Low)

Figure 1. Micro-crystallization index

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Table 2. Values of DMFT, RSF, SSF, BC, SV, IMK for study group and control group

Groups	Nr	DMFT	RSF	SSF	BC	SV	IMK
Control group (M)	1.	4	0.38	2.1	5.4	2.20	0.6
	2.	6	0.37	2.2	5.3	2.19	0.7
	3.	4	0.31	2.6	5.4	2.22	0.6
	4.	5	0.39	2.2	5.5	1.18	1.0
	5.	6	0.36	2.5	5.4	3.21	0.9
	6.	8	0.49	1.9	4.9	2.11	0.8
	7.	5	0.40	1.7	5.2	2.08	1.0
	8.	9	0.35	2.2	5.4	2.12	0.7
	9.	5	0.37	2.7	5.1	3.09	0.8
	10.	9	0.38	3.0	5.5	2.10	1.0
	11.	5	0.36	2.6	5.5	2.28	0.6
	12.	6	0.39	2.4	5.4	1.27	1.0
	13.	7	0.40	2.5	4.9	2.29	0.9
	14.	5	0.35	1.8	5.2	3.30	0.8
	15.	4	0.34	1.7	4.9	1.29	1.0
Mean value		**5.87**	**0.38**	**2.27**	**5.27**	**2.20**	**0.83**
Sjögren 's syndrome group (S)	1.	12	0.20	0.9	3.3	5.20	0.2
	2.	14	0.21	1.1	3.9	6.19	0.2
	3.	24	0.17	0.8	4.1	6.22	0.1
	4.	21	0.21	1.2	3.8	7.18	0.4
	5.	16	0.16	0.9	3.8	3.21	0.5
	6.	17	0.19	0.9	3.7	8.11	0.2
	7.	18	0.19	1.1	3.6	4.12	0.3
	8.	22	0.18	0.6	4.6	6.09	0.1
	9.	21	0.21	1.3	4.8	5.10	0.7
	10.	17	0.22	0.7	4.5	5.28	0.6
	11.	11	0.23	1.4	4.4	1.27	0.7
	12.	13	0.20	1.3	3.5	7.29	0.7
	13.	14	0.19	0.9	3.8	8.30	0.4
	14.	11	0.22	0.8	3.3	6.29	0.5
	15.	9	0.17	0.7	3.2	6.28	0.3
Mean value		**16.00**	**0.20**	**0.97**	**3.89**	**5.74**	**0.39**

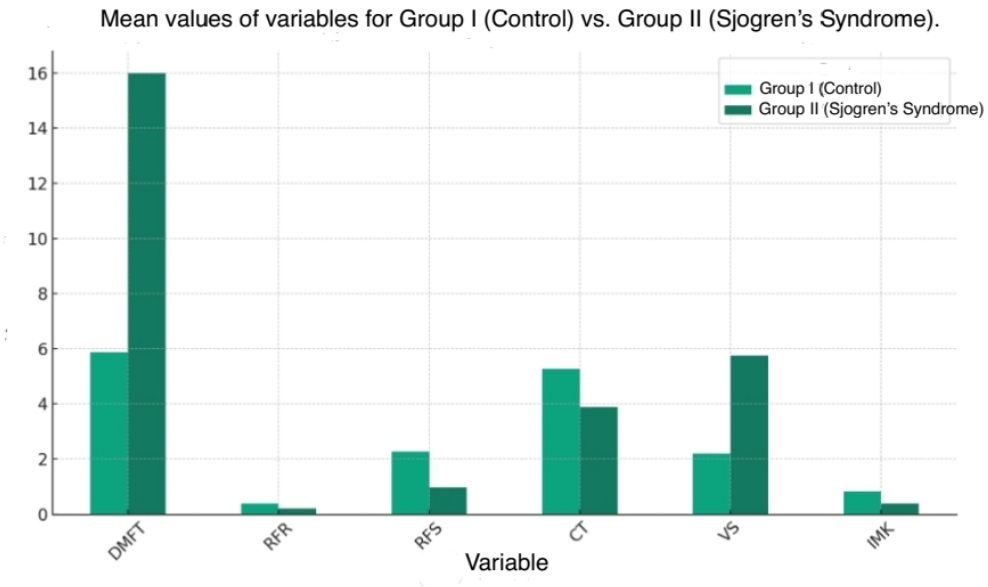

Figure 2. Mean values of variables for control group (I) and study group (II) (Sindrom Sjögren)

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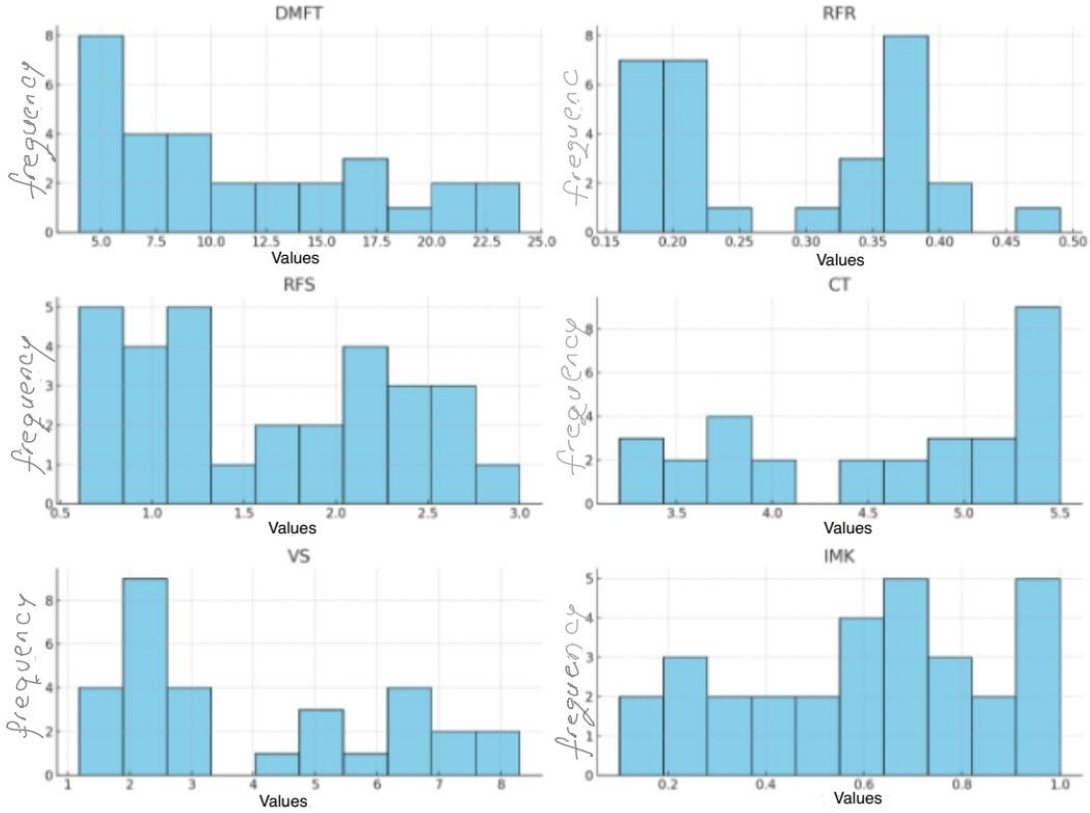

Figure 3. Distribution of values for DMFT, SRF, SSF, BC, SV, IMK

Table 3 . Results of test t for study group and control group

Variable	t_stat	p_value
DMFT	-8.11	< 0.00001
RFR	15.50	< 0.00001
RFS	10.95	< 0.00001
CT	9.79	< 0.00001
VS	-7.03	< 0.00001
IMK	6.28	< 0.00001

For all variables, the p_value is significantly lower than the standard significance level (0.05), indicating that there are statistically significant differences between the control group (I) and the Sjögren's syndrome group (II) for all analyzed variables (DMFT, RSF, SSF, BC, SV, IMK).

To correlate the variables in the table for each group (Group I - Control (M) and Group II - Sjögren's syndrome (S)), we will calculate the Pearson correlation coefficient for each pair of variables.

The correlations between variables for each group are represented in the tables (Table 4, 5) .

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Table 4. Values of Pearson correlation coefficient for control group (I)

Group I (Martor -M)

Variable	DMFT	RFR	RFS	CT	VS	IMK
DMFT	1	0.42	0.29	0.01	0.01	0.18
RFR	0.42	1	-0.21	-0.39	-0.16	0.27
RFS	0.29	-0.21	1	0.45	0.19	-0.13
CT	0.01	-0.39	0.45	1	-0.06	-0.22
VS	0.01	-0.16	0.19	-0.06	1	-0.36
IMK	0.18	0.27	-0.13	-0.22	-0.36	1

Table 5 . Values of Pearson correlation coefficient for study group (II) (Sjögren's syndrome- S)

Group II (Sjogren's Syndrome)

Variable	DMFT	RFR	RFS	CT	VS	IMK
DMFT	1	-0.24	-0.07	0.59	0.14	-0.29
RFR	-0.24	1	0.49	0.23	-0.17	0.53
RFS	-0.07	0.49	1	0.13	-0.30	0.58
CT	0.59	0.23	0.13	1	-0.30	0.23
VS	0.14	-0.17	-0.30	-0.30	1	-0.35
IMK	-0.29	0.53	0.58	0.23	-0.35	1

The correlation are exposed in figure 4 as diagrams for study group and control group.

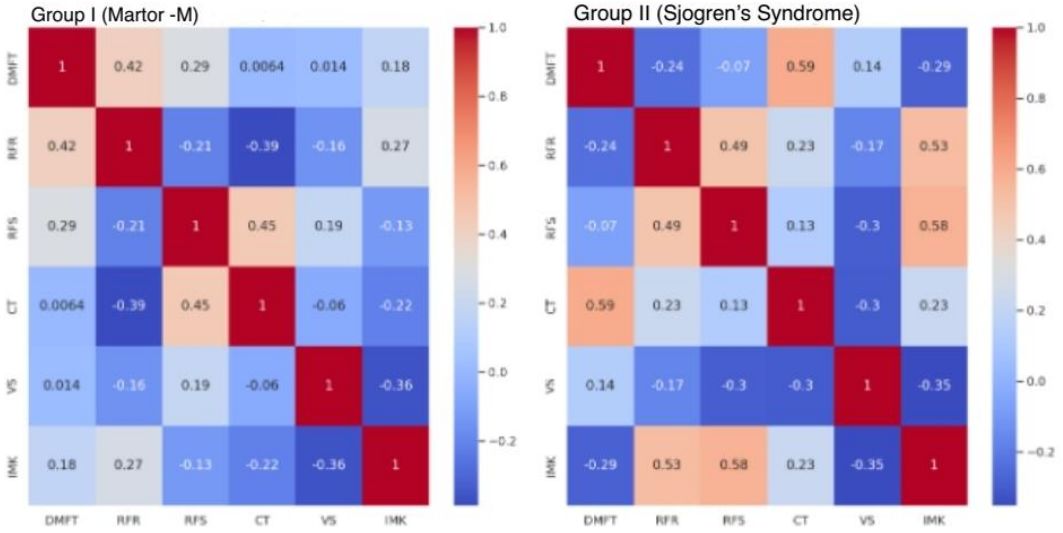

Figure 4. Correlations between variables for Group I (Control- M) and Group II (Sjögren's syndrome - S).

The diagram presented previously illustrates the correlations between variables for Group I (Control - M) and Group II (Sjögren's Syndrome - S) (Figure 4).

Each square represents the correlation coefficient between the respective variables, with the color scale indicating the intensity and direction of the correlation (red for positive

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correlation, blue for negative correlation).

These diagrams provide an immediate visualization of the relationships between variables, particularly highlighting those variables that are more strongly correlated within each group.

Following the analysis of the results, a positive correlation of all assessed parameters was noted.

These results suggest that the effects of Sjögren's syndrome on the selected indicators (DMFT, RFR, RFS, BC, IMK) are significantly different compared to the control group, indicating the impact of the syndrome on the dental and salivary condition of the affected patients.

Previous studies reveal numerous associations between Sjögren's Syndrome and oral pathology [47-50]. Although xerostomia and hyposalivation have been frequently reported in these patients, not many studies have examined other oral symptoms [1-5].

It is important to note that changes in salivary viscosity in Sjögren's syndrome can have significant consequences on dental health, including increased risk of dental caries and gingival conditions [50].

Patients with this syndrome must be aware of these changes and adopt appropriate preventive measures, such as regular oral hygiene and the use of moisturizing or salivation-stimulating products, under the guidance of a specialist.

In Sjögren's syndrome, changes in salivary viscosity can affect several factors and components of saliva, including the composition of saliva [10,11].

Normal saliva contains a variety of substances, including water, proteins, enzymes, minerals, and antibodies. Changes in salivary viscosity can influence the content of these components [14-16;40,41,45].

For example, an increase in salivary viscosity can cause an increase in the concentration of proteins or other substances

It is important for patients with Sjögren's syndrome to be aware of these changes and to adopt appropriate preventive measures, such as rigorous oral hygiene, use of

It is important for patients with such as salivary enzymes, which can alter their activity and disrupt the normal functions of saliva.

Increased salivary viscosity can also affect salivary flow, meaning that saliva flows slower and may be more difficult to expel from the mouth. This can contribute to the sensation of dryness in the mouth and create an environment conducive to the development of dental caries and other dental conditions.

Increased salivary viscosity in this syndrome can also affect the enamel remineralization capacity [13].

Dental remineralization is a process in which essential minerals, such as calcium and phosphate, are redeposited onto dental enamel, repairing and strengthening the demineralised areas [14-16, 41].

Saliva plays a crucial role in the remineralization process, as it provides the necessary minerals and creates a favorable environment for this process [14,41].

However, when saliva becomes more viscous in Sjögren's syndrome, its capacity to supply minerals and maintain an adequate remineralising environment is compromised.

Normal saliva has a slightly alkaline pH, which helps maintain a neutral or slightly alkaline oral environment, protecting the teeth against acids and demineralization. Changes in salivary viscosity can affect its buffering capacity [14,41,46].

More viscous saliva may have difficulty neutralizing the acidity in the mouth, thereby potentially favoring an increase in local acidity and the risk of dental caries.

All these factors affected in the relationship between salivary viscosity and its components can contribute to disorders and conditions of the oral cavity encountered in Sjögren's Syndrome, including dry mouth (xerostomia), increased risk of dental caries, gingival conditions, and difficulties in normal processes of chewing and speaking, including painful fungal infections.

Sjögren's syndrome to be aware of these changes and to adopt appropriate preventive measures, such as rigorous oral hygiene, use of salivation-stimulating products, avoidance of high-sugar foods and drinks, and regular check-

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ups for dental health monitoring.

CONCLUSIONS:

In conclusion, there is a correlation between dental caries, saliva, and Sjögren's Syndrome. A reduction in saliva production in Sjögren's Syndrome can lead to phenomena associated with xerostomia, disrupt the balance between demineralization and remineralization processes, and may contribute to an increased risk of caries. It is important for individuals with Sjögren's syndrome to pay special attention to oral hygiene and follow the dentist's recommendations regarding caries prevention and treatment

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