Qualitative and Quantitative Salivary Changes and Subjective Oral Dryness among Patients with Thyroid Dysfunction

Abstract
Context: There is a paucity of literature regarding the effects of thyroid disorders on the oral cavity by influencing the salivary gland function. Aims: This study aims to understand the qualitative and quantitative changes that thyroid disorder can cause in the salivary function. Settings and Design: After obtaining ethical clearance, 46 consecutive newly diagnosed thyroid dysfunction patients were enrolled in this cross-sectional study, along with 45 age-and sex-matched controls. Subjects and Methods: Unstimulated and stimulated salivary flow rates, pH, and buffering capacity of the whole saliva were studied in addition to subjective oral dryness in the study participants. Statistical Analysis Used: The independent t-test was employed to compare the means between the two groups and Pearson’s Chi-square test was used to assess the goodness of fit. Results: The findings showed that females are more affected with thyroid disorders and that hypothyroidism is more commonly reported than hyperthyroidism. A significant reduction in the salivary flow rates and buffering capacity was observed among the affected group compared to the controls, whereas the salivary pH did not show significant differences between genders and also between the case and control groups. A feeling of subjective oral dryness was perceived by many affected patients. Conclusions: The study was able to establish an association between thyroid dysfunction and salivary gland function. We hope that this study leads to more high-impact research in this field as salivary diagnostics is gaining more popularity with every passing day.

Keywords: Buffering capacity, flow rates, hyperthyroidism, hypothyroidism, saliva, salivary pH

Introduction
Saliva is of emerging importance in the medical and dental worlds. It plays a crucial role in maintaining the health of the oral cavity by executing multiple host defense functions such as homeostatic processes, lubrication, antimicrobial activity, and control of demineralization/remineralization of teeth.[1] Subjective and objective functional losses have been reported by various studies that occur in people lacking the ability to produce adequate volumes of saliva. These functional losses include xerostomia, dysphagia, and an increased susceptibility for opportunistic infections.[2] Unstimulated saliva is an indicator of the basal production and confers most protection. It predominantly comprises of minor and submandibular glands’ output.[3] The factors affecting unstimulated salivary flow rate (USFR) are degree of hydration, body position, exposure to light, previous stimulation, circadian rhythms, circannual rhythms, and drugs.[4] Stimulated saliva offers protection during mastication and assists in deglutition. It is predominantly comprised of parotid gland output.[3,5] The factors affecting the stimulated salivary flow rate (SSFR) are nature of stimulus, vomiting, smoking, gland size, gag reflex, olfaction, unilateral stimulation, and food intake.[6] Any alteration in the quality and quantity of saliva will lead to disturbances in the protective functions of the saliva.[7]

Relationship of salivary gland function with various systemic disorders has been established. Certain systemic factors such as chronic renal failure, drug abuse, menopausal and hormonal effects, as well as side effects from medications affect the composition, quantity, and quality of saliva, directly or indirectly.[8,9] Other factors causing salivary gland hypofunction are oral disorders, chemotherapy, head-and-neck radiotherapy, psychogenic factors, and decreased mastication.[10-13] Salivary flow dysfunction is a common problem and is

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Meghal Mehul Naik, Vaishnavee Vassandacoumara
Department of Oral Medicine and Radiology, K. M. Shah Dental College and Hospital, Samandeep Vidyapeeth, Vadodara, Gujarat, India
frequently undiagnosed because the patient’s symptoms of oral dryness are a perceived feeling. Symptoms can be subjective as it is common for patients to be unaware of diminished salivary production until the resting flow rate is less than half of normal.[8]

Hypothyroidism and hyperthyroidism are common thyroid dysfunctions that affect multiorgan systems in the human body. Thyroid diseases are, arguably, among the most common endocrine disorders worldwide. India too is no exception. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases.[14] Even so, there is limited literature and research on the effects of thyroid gland and its disorders on the salivary glands. There are few studies on human subjects which have used salivary scintigraphy to study the association of salivary disturbances with thyroid dysfunction.[15-18] Salivary scintigraphy, however, does not give a true picture of salivary gland functioning. Only two studies have been published on thyroid dysfunction and salivary flow rate disturbances.[9,19] Therefore, this study was aimed at throwing some light on the association between them which still needs in-depth exploration. We started with the null hypothesis that there are no qualitative and/or quantitative salivary changes in thyroid dysfunction patients.

Subjects and Methods

Ethical approval: All procedures performed in this study involving human participants were in accordance with the ethical standards of the Institutional Ethics Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The nature and purpose of the study was briefly explained to each participating patient/subject in the vernacular language and through a participant information sheet and their written informed consent was obtained.

The sample size for this cross-sectional study had been estimated to be 91 using the following statistical formula:

\[ n = \frac{m(1 + (m - 1/N))}{z^2 \cdot \text{ME}^2}; \text{ME} = 0.05 \]

The study was conducted in the constituent medical college and hospital of our university. Forty-six thyroid dysfunction patients were enrolled in this study as cases along with 45 age-and sex-matched controls from the outpatient department (OPD) clinics of general medicine during the study of 2 months (August and September 2015). Pregnant women and patients with a history of tobacco use and significant variations from normal body mass index were not included in the study. Participants taking medication that have an effect on salivary secretion or those undergoing therapeutic head-and-neck irradiation and participants with a history suggestive of systemic diseases such as hypertension, rheumatoid arthritis, and diabetes mellitus were excluded from the study for cases as well as controls.

Newly diagnosed patients with hypo/hyperthyroidism, aged 18–45 years, and who were satisfying the selection criteria were included as cases in the study. The diagnosis of hypothyroidism was based on increased serum thyroid-stimulating hormone (TSH) >5 mIU/L and low serum free tetraiodothyroxine (FT4) <0.61 ng/dL. Hyperthyroidism was diagnosed based on decreased serum TSH <0.3 mIU/L and high serum FT4 >2 ng/dL. Patient data were collected using a specifically designed form to record basic demographic data, complete history, thyroid profile, and salivary profile. Follow-up thyroid disorder patients were also excluded from the study to prevent wide variations in the duration of illness in patients and any influence of treatment.

The patients presenting with nonthyroid complaints at the general medicine OPD were selected as controls after they had been examined by a specialist physician. Any patient presenting with minor thyroid symptoms or belonging to high-risk groups for subclinical hypothyroidism would be subjected to routine thyroid profiling and would be followed up to eliminate any chance of them being selected as a control.

Salivary analysis

Patients were instructed not to eat, drink, smoke, chew, or perform oral hygiene for 60 min before saliva collection. Saliva was collected at the same time of the day (between 9 and 11 am) for each patient to eliminate bias due to diurnal variation.[20]

Salivary flow rates

Unstimulated saliva was collected first by making the patient sit quietly, with the head bent down and mouth open to allow the saliva to drip from the lower lip into a sterile container (the draining method). It was followed by collection of stimulated whole saliva using unflavored paraffin wax according to standardized collection procedure described by Tenovuo and Lagerlöf.[21] Both the salivary flow rates were recorded. Tenovuo and Lagerlöf in 1994 categorized normal USFR as 0.25–0.35 ml/min, low USFR as 0.1–0.25 ml/min, and hyposalivation as <0.1 ml/min.[21] The SSFR values of the participants were categorized using Ericsson and Hardwick criteria. Participants with SSFR of 0.7–1 ml/min were classified as having low SSFR and <0.7 ml/min as having hyposalivation.[22]

Estimation of pH and buffering capacity

The stimulated whole saliva was then analyzed for its pH and buffering capacity. A handheld digital manual pH meter (Hanna) was used to measure the pH of saliva and Ericsson method (1959) was used to measure the buffering capacity of saliva wherein 1 ml of saliva was added to 3 ml
of 5 mmol/l HCl. The mixture was vigorously shaken and then centrifuged for 1 min and allowed to stand for 10 min when the final pH was measured using manual pH meter.[9]

**Oral dryness**

Symptoms of subjective oral dryness were recorded using a short questionnaire adopted from the study conducted by Farsi in 2007. The responses of the participants were assessed according to the criteria of Farsi, wherein the people who answered at least one question in affirmative were considered as positive for subjective complaints of oral dryness.[23]

**Results**

The study observations were entered in Microsoft Excel spreadsheet 2007, and appropriate statistical analysis was done using STATA 13 (StataCorp. 2013. Stata Statistical Software: Release 13, College Station, TX: StataCorp LP). The level of statistical significance was set at $P < 0.05$. Mean and proportions were calculated. The results of the statistical analysis were tabulated for interpretation.

In the study, out of the 46 newly diagnosed cases of thyroid dysfunction, 67.4% ($n = 31$) were females and 32.6% ($n = 15$) were males. Out of the 45 age- and sex-matched controls, 68.9% ($n = 31$) were females and 31.1% ($n = 14$) were males.

Among the cases, hypothyroidism was more commonly reported as compared to hyperthyroidism. About 67.39% ($n = 31$) of cases were hypothyroid and 32.61% ($n = 15$) were hyperthyroid.

The independent $t$-test was employed to compare the means between the two groups and Pearson’s Chi-square test was used to assess the goodness of fit.

The mean USFR in the case group was found to be 0.288 ± 0.145 mL/min, which was statistically significantly lower ($P < 0.001$) as compared to the control group with mean USFR of 0.465 ± 0.169 mL/min. On applying the Tenovuo and Lagerlöf criteria,[21] 41.3% ($n = 19$) of cases had low USFR (0.1–0.25 mL/min) and 6.52% ($n = 3$) cases had hyposalivation (<0.1 mL/min). In the control group, 13.33% ($n = 6$) had low USFR and there were no participants with hyposalivation.

The mean SSFR in the case group was found to be 1.460 ± 0.554 mL/min, which was statistically significantly lower ($P < 0.001$) as compared to the control group with mean SSFR of 1.861 ± 0.261 mL/min. On applying the Ericsson and Hardwick criteria,[22] 17.39% ($n = 8$) of cases had low SSFR (<1 mL/min) and 8.9% ($n = 4$) cases had hyposalivation (<0.7 mL/min). In the control group, there were no participants with hyposalivation or low SSFR.

The mean salivary pH of cases was 6.954 ± 0.3722 and the mean salivary pH of the controls was 6.869 ± 0.3747, which was not statistically significantly different ($P = 0.278$). The mean buffering capacity of the cases at 5.1848 ± 1.1505 was statistically significantly lower ($P < 0.001$) than the mean buffering capacity of the controls at 6.0067 ± 0.4797 [Table 1 and Figure 1].

We found it ideal not to compare the hypothyroid patients versus the hyperthyroid patients due to the unequal sizes of both groups as it is likely to introduce error in the study results.

**Analysis of the questionnaire**

The responses of the participants to the individual questions were tabulated. Among cases, 47.8% ($n = 22$) people said that their mouth feels dry while 6.7% ($n = 3$) in the control group reported dryness in the mouth. This difference was statistically significant between the groups ($P < 0.001$).

Among cases, 30.4% ($n = 14$) people said that they had to sip liquids to aid in swallowing dry food while 8.9% ($n = 4$) controls felt the need to sip liquids to aid in swallowing dry food. This difference was also statistically significant between the groups ($P = 0.016$).

About 21.7% ($n = 10$) of people in the case group felt dryness in the mouth while eating a meal, while among the controls, 6.7% ($n = 3$) of people find the mouth dry

![Table 1: Salivary parameters of cases and controls](image-url)

| Group | n  | Mean±SD | P     |
|-------|----|---------|-------|
| USFR (mL/min) | Case | 46 | 0.288 | 0.145 | <0.001 |
|        | Control | 45 | 0.465 | 0.169 |       |
| SSFR (mL/min) | Case | 46 | 1.460 | 0.554 | <0.001 |
|        | Control | 45 | 1.861 | 0.261 |       |
| pH     | Case | 46 | 6.954 | 0.3722 | 0.278 |
|        | Control | 45 | 6.869 | 0.3747 |       |
| Buffering capacity (pH) | Case | 46 | 5.1848 | 1.1505 | <0.001 |
|        | Control | 45 | 6.0067 | 0.4797 |       |

USFR=Unstimulated salivary flow rate, SSFR=Stimulated salivary flow rate, SD=Standard deviation

![Figure 1: Salivary parameters of cases and controls](image-url)
when eating a meal. This difference was not statistically significant between the groups ($P = 0.069$).

Nearly, 39.1% ($n = 18$) of cases felt that the saliva in their mouth seemed to be too little while only 8.9% ($n = 4$) among the controls felt the same. This difference was statistically significant between the groups ($P = 0.001$).

Among the cases, 8.7% ($n = 4$) people replied in affirmative to all four questions whereas there were no people in the control group who replied in affirmative to all the four questions. The difference was statistically not significant ($P = 0.117$). About 30.4% ($n = 14$) of cases and 80% ($n = 36$) of controls replied negatively to all the four questions. This difference between the groups was statistically significant ($P < 0.001$) [Table 2].

The responses were also studied between the hyperthyroid and hypothyroid patients and tabulated. The differences were not statistically significant between these patients for any of the four questions [Table 3].

About 69.6% ($n = 32$) of people among the case group and 20.0% ($n = 9$) of people in the control group qualified as positive (responded at least one question in affirmative) for subjective complaints of oral dryness.

**Discussion**

The relationship of salivary function with various systemic illnesses has been quoted by numerous authors. There is a well-established association of salivary function with common illnesses such as diabetes, oral submucous fibrosis, and asthma.\[24-26\] Thyroid disorders are one of the most common endocrine disorders globally as well as nationally,\[14\] but still there is a dire shortage of quality evidence that can establish its relationship with salivary function. Earlier studies in human subjects either assessed only hypothyroid participants\[9,29\] or used scintigraphy\[15-18\] or parotid gland flow rates.\[9\] Muralidharan \textit{et al.}, 2013, assessed only stimulated whole mouth saliva flow rate in thyroid disorder patients.\[9\] Warfvinge \textit{et al.} in 1992 attempted to establish a correlation using unstimulated whole sialometry and parotid scintigraphy only in hypothyroid patients.\[15\] In our study, we have estimated unstimulated and SSFRs in hyperthyroid and hypothyroid patients.

The observations of our study suggest that thyroid dysfunction is more commonly seen in females rather than males and that hypothyroidism was the most commonly encountered thyroid dysfunction. These findings are in accordance with the current literature.\[27,28\]

The unstimulated flow rate is important because it represents the protection conferred against caries in resting state.\[1,3\] The mean USFR in the case group ($0.288 \pm 0.145$) was within the normal range cited in literature whereas that of the control group ($0.465 \pm 0.169$) was slightly higher than normal.\[29\] Even the slightest movements of the tongue or cheeks made by patients during the collection of saliva hamper the true unstimulated saliva, thereby suggesting caution when we interpret the USFR results. However, this was applicable to both the cases and the controls and hence supports the significance of this difference.

The mean SSFR in the case group ($1.460 \pm 0.554$ mL/min) and in the control group ($1.861 \pm 0.261$ mL/min) was within the established normal limits for normal population.\[30\] These proportions are somewhat lower in our case group as compared to Muralidharan \textit{et al.}’s study.\[9\] This may be attributed to the smaller sample size in our study.

The observations also suggested that males had a higher USFR and SSFR compared to females. The possible explanation for this may be the smaller gland size in females and the greater basal metabolic rate and body mass in males.\[9,29\] Some menopausal women may suffer xerostomia which then improves as age advances.\[30\]

The mean pH values of both the cases and controls were in the normal range.\[31,32\] Gender differences were also not significant. This is in concordance with the study done by Muralidharan \textit{et al.}\[9\]

The mean buffering capacity among the cases ($5.1848 \pm 1.1505$) was lower than in the controls ($6.0067 \pm 0.479$). The low buffering capacity of saliva is associated with a reduced salivary flow and particularly increased risk for caries.\[33\] There was no significant correlation of buffering capacity with gender observed. This is in concordance with the study done by Muralidharan \textit{et al.}\[9\]

Table 2: Assessment of questionnaire responses between cases and controls

| Questions | Cases | Controls | $P$ |
|-----------|-------|----------|-----|
|           | Yes (%) | No (%) | Yes (%) | No (%) |
| 1         | 22 (47.8) | 24 (52.2) | 3 (6.7) | 42 (93.3) |
| 2         | 14 (30.4) | 32 (69.6) | 4 (8.9) | 41 (91.1) |
| 3         | 10 (21.7) | 36 (78.3) | 3 (6.7) | 42 (93.3) |
| 4         | 18 (39.1) | 28 (60.9) | 4 (8.9) | 41 (91.1) |

Table 3: Assessment of questionnaire responses between hyperthyroid and hypothyroid patients

| Questions | Hyperthyroid | Hypothyroid | $P$ |
|-----------|--------------|-------------|-----|
|           | Yes (%) | No (%) | Yes (%) | No (%) |
| 1         | 5 (33.3) | 10 (66.7) | 17 (54.8) | 14 (45.2) |
| 2         | 3 (20.0) | 12 (80.0) | 11 (35.5) | 20 (64.5) |
| 3         | 3 (20.0) | 12 (80.0) | 7 (22.6) | 24 (77.4) |
| 4         | 5 (33.3) | 10 (66.7) | 13 (41.9) | 18 (58.1) |

Our study excluded subjects taking medication that have an effect on salivary secretion, subjects undergoing therapeutic head-and-neck irradiation, and subjects with a history suggestive of systemic diseases such as hypertension, rheumatoid arthritis, and diabetes mellitus as these factors...
have an effect on the salivary gland function and could affect the results.[23,34-36]

The limitations of our study include the possibility of subjects with subclinical thyroid dysfunction getting excluded from salivary assessment as cases as well as their inclusion in the control group. We have not assessed the thyroid status of the control group which may have detected few, if any; borderline thyroid dysfunction patients. The American College of Physicians suggests that screening to detect thyroid dysfunction may be indicated in high-risk groups such as women older than 50 years.[37] In our study, we have excluded subjects from high-risk groups. Moreover, there is a possibility of the presence of an underlying undiagnosed systemic condition in cases as well as control group which may have influenced the salivary parameters. As the study was conducted in a hospital setting in contrast to a population study, subjects enrolled as cases most likely represent patients with pronounced symptoms.

The questionnaire adopted from the study conducted by Farsi in 2007[23] was used to determine the perception of subjective oral dryness among the participants. To the best of our knowledge, such an assessment in thyroid dysfunction patients has not been published in literature. One of the questions gave the patient’s perception of resting saliva whereas the other three focused on the stimulated saliva. The results suggest that the experience of oral dryness was more among the thyroid disorder patients than the healthy controls.

The subjective assessment becomes increasingly important in assessing the changes in quality of saliva in addition to objective measures of salivary hypofunction in these patients. It also assesses their motivation to seek treatment. However, as the perception of the patients is variable and is not definitively proportional to the biological disease indicators, this should be used with caution.

Chronic hyposalivation may result in oral manifestations such as oral dryness, burning sensation, dental caries, oral mucositis, halitosis, and dysphagia. All of these sequelae affect the patient’s quality of life.[38]

**Conclusions**

The current study indicates an underlying association of thyroid dysfunction and salivary gland function in thyroid dysfunction patients. The study showed a statistically significant decrease in salivary parameters such as buffering capacity and flow rates. Hence, a patient with thyroid dysfunction should be subjected to regular dental checkups and proper preventive methods should be employed to assure good oral health and hygiene status to the patient. Conversely, when the well-established causes of salivary gland dysfunction fail to explain a patient’s chronic state of hyposalivation, a thyroid function assessment should be considered by the dental practitioner. Furthermore, prospective follow-up studies till euthyroid and with larger sample sizes need to be conducted to give a more established evidence for the association between thyroid dysfunction and salivary gland function. Future researches may compare the TSH and FT4 levels between the cases and controls to study the differences. Studies may explore the association between the thyroid and salivary parameters in the study groups to understand the pathophysiology of the disease processes.

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**Conflicts of interest**

There are no conflicts of interest.

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