Internal Medicine: Open Access

Hafez et al., Intern Med 2018, 8:3
DOI: 10.4172/2165-8048.1000276

Research Article Open Access

Salivary Flow Rate as a Noninvasive Method for an Early Prediction of Pre Diabetes in Patients at Tanta University Hospitals

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Received date: May 11, 2018; **Accepted date:** May 21, 2018; **Published date:** May 25, 2018

Abstract

Purpose: Early diagnosis of pre-diabetes mellitus is essential for oral health and prevention of diabetes complications. It has been suggested that xerostomia may be an early indication of diabetes screening.

Materials and Methods: The present study was carried out on 90 subjects, 34 (37.8%) males and 56 (62.2%) females. The mean age was 36.37+7.9 years, ranged from (20-60) years old with no history of diabetes and suffering from xerostomia. To diagnose xerostomia, a questionnaire was applied to the patients to be answered by yes or no illustrating presence of xerostomia. The selected patients divided into three groups according to their complain of xerostomia, Group I: Control, Group II: Xerostomia and Group III: Hypo-salivation patients. Un-stimulated whole saliva flow rates (UWSFRs) and HbA1c values were determined. Statistical analysis of the collected data was carried out.

Results: UWSFRs is markedly decreased in groups II& III in comparison to its corresponding value in group I. There is statistically significant difference between the studied groups (F value was 98.242, P value<0.0001[*]).

Conclusion: a dental office could be a good location for (pre)diabetes screening in patients with xerostomia.

Keywords: Salivary flow rate; Pre-diabetes; HbA1c; Xerostomia

Introduction

Diabetes mellitus is a rising health problem and its prevalence is globally growing [1]. The prevalence of diabetes was estimated at 415 million adults worldwide in 2015 and this is expected to rise to 642 million by 2040 (International Diabetes Federation (IDF) 2015 World Congress). Egypt is the 9th country in 2011for numbers of people aged 20-79 years with diabetes (7.3) million, by 2030 will be expected to be the 8th with (12.4) million [2].

However, due to the absence of disease related symptoms, diabetes often goes unnoticed, and around one third of people with diabetes are not diagnosed. The early diagnosis and intervention of pre-diabetes avoid the common micro vascular and macro vascular complications. Thus, risk indicators for pre-diabetes screening are needed and suggested [1].

So, the awareness of normal salivary flow rate (SFR) is very important when treating dental patients. Early diagnosis and treatment of xerostomia and hypo-salivation will preserve the health of oral structures or tissues and lower the incidence of dental caries, fungal infections, and other oral diseases that might result from inadequate SFR. Though, it receives small attention until its quantity diminishes or its quality becomes changed [3].

The use of saliva as a substitute method of diagnosis or as a mean to screen the development of certain illnesses is a promising track. Its attractions for diagnosis are augmented by the commercial availability of a simply used test; the accessibility of saliva and the non-invasive method of obtaining the specimen are further benefits of using saliva as a diagnostic tool, and the positive correlation between several parameters in serum and saliva [4].

For years, dental health specialists have used saliva to help assess the hazard of caries. Now, saliva is being used as an investigational aid in the diagnosis of systemic diseases that affect the function of the salivary glands and the composition of the saliva, such as Sjögren's syndrome, alcoholic cirrhosis, cystic fibrosis, sarcoidosis, diabetes mellitus, diseases of the adrenal cortex, oral and breast cancer research [5].

Older and adults with poorly controlled diabetes have impaired salivary flow in comparison with subjects with better controlled diabetes and non-diabetic subjects, regarding age, sex, and duration of diabetes did not adversely affect salivary flow rates [6].

Salivary flow rates were impaired in subjects with diabetes mellitus (DM). Subjects with type 1 DM reported symptoms of dry mouth more frequently than control subjects did. In type 2 DM, un-stimulated and stimulated salivary flow rates were also significantly reduced [7].

Based on the above, the purpose of the present study was to determine HbA1c levels and confirm the presence of pre-diabetes in subjects suffering from dry mouth to help in early detection of pre-diabetes and prevention of diabetes complications.

Materials and Methods

The present study was conducted on 90 subjects selected from Internal Medicine Department out-patients clinic (endocrinology unit) Faculty of Medicine-Tanta University. Patients were 20-60 years of age with no history of diabetes and were being seen for routine check-ups suffering from xerostomia (Table 1). Written informed consent from patients was obtained. Patient having any of the following are not involved in the current study:

Patients suffering from xerostomia produced by specific causes such as:

- Local inflammation, focal infection and fibrosis of the major salivary glands.
- Autoimmune diseases e.g. Sjogren´s syndrome (primary and secondary) and Mikulicz´s disease.
- Malnutrition e.g. anorexia, dehydration.
- Alcoholism or smoking.
- Systemic diseases as patients with severe diabetic complications or hypertension or thyroid disease (hypo- and hyper-thyroidism) and late stage liver disease.

Questionnaire used for selection of subjects with xerostomia.	
1	Does your mouth feel dry when eating a meal?
2	Do you have difficulties swallowing any foods?
3	Do you need to sip liquids to aid in swallowing dry foods?
4	Does the amount of saliva in your mouth seem to be reduced most of the time?
5	Does your mouth feel dry at night or on awakening?
6	Does your mouth feel dry during the daytime?
7	Do you chew gum or use candy to relieve oral dryness?
8	Do you usually wake up thirsty at night?
9	Do you have problems in tasting food?
10	Does your tongue burn?
Response options	
Yes/No	

Table 1: Illustrating the protocol was applied to the patients suffering from low saliva flow rate, to be answered by yes or no [8,9].

- The use of hormonal replacement therapy (HRT) e.g. Estrogen or Estrogen/Progestin products.
- The use of medications known to affect salivary gland flow rate such as diuretics, anti-spasmodic, expectorants, decongestants, systemic bronchodilator…..etc.
- Patients under treatment for xerostomia.
- Past history of radiotherapy or chemotherapy as in cancer treatments.

Subjects who had at least one positive response entered the study group, and those without any positive responses, formed the control group. Once xerostomia were reported, patients were questioned about duration (onset) of xerostomia [10].

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The patients selected divided into three groups:

Group I: Control patients.

Group II: Xerostomia patients.

Group III: Hypo-salivation patients.

Clinical work

Materials

The salivary flow measurements for all patients were done according to Walsh [11] (Figure 1 and 2).

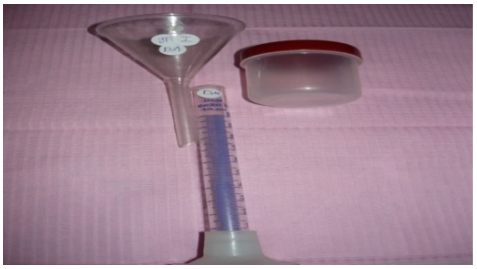

Figure 1: Tubes graduated in milliliters, a glass funnel and a plastic container used for saliva collection.

Figure 2: Showing sitting position in subjects.

In this study, the un-stimulated whole saliva was taken for the estimation of salivary flow rates (SFRs) as with stimulation there are alterations in SFRs because of difference in type and degree of stimulation. Determining un-stimulated whole salivary flow rates (UWSFRs) was done by the spitting or expectorating technique. The subjects were told to refrain from eating and drinking at least one hour prior to the examination time (between 9:00 am and noon) for all patients to minimize any circadian rhythm effects and so to avoid variation in salivary flow rates. Before taking a sample of saliva, subjects were allowed to rest for 30 to 60 minutes. The subjects were asked to sit in a quiet position with the head tilted forward (Figure 2),

they were asked to rinse their mouth with water in order to eliminate any possible detritus and to obtain a clean sample [12].

Each sample was obtained by having the patient expectorate or spit all saliva into a graduated test tube through a glass funnel every 1 minute, for 10 minutes. Once the sample had been obtained it was allowed to settle, placing the tube in a test tube rack, in order to achieve a better reading of the saliva volume. Then, volume of saliva was measured with milliliters (mL) and USFR was calculated by division volume on minutes (mL/min). USFR<0.1 mL/min are considered abnormally low and indicative of marked salivary hypo function, however, USFR ≥ 0.1 mL/min to 0.3 mL/min are considered xerostomia [13,14].

HbA1c values were obtained by the analysis of dry blood spots. HbA1c provides an integrated measure of average glycemia over the past 3 months [15] and has been endorsed by the International Expert Committee and the American Diabetes Association for the diagnosis of pre diabetes and diabetes [16]. The American Diabetes Association has defined normal as HbA1c<5.7 percent, pre diabetes as HbA1c 5.7-6.4 percent, and diabetes as HbA1c ≥ 6.5 percent [3]. We defined dysglycemia as pre diabetes or diabetes (HbA1c ≥ 5.7 percent).

Laboratory work

Blood collection and HbA1c analysis

HbA1c values were obtained by the analysis of dry blood spots by using Tri-stat Reagent Kits for use with the Tri-stat Analyzer, is a rapid in vitro diagnostic test for measurement of the percent of glycated hemoglobin (% HbA1c and mmol HbA1c/molHb) in human blood from finger stick or venous samples for clinical laboratory and point-of-care use.

Statistical analyses

Statistical analysis of the collected data was carried using GraphPadInStat software version 3.05. The following was done; Mean Standard error of mean (SEM), ANOVA and Tukey tests and linear correlation coefficient. P-value less than 0.05 were considered significant (Table 2).

Results and Discussion

Demographic data of the studied subjects		
Age/Y (Mean ± SD)	36.37 ± 7.9 (20-52)	
Sex (%)	Male	34 (37.8%)
	Female	56 (62.2%)

Table 2: Demographic data of the studied subjects.

The study included 34 (37.8%) males and 56 (62.2%) females. The mean age was 36.37+7.9 years. The range was (20-52) years old (Table 1) (Figure 1).

The study included 90 subjects, 21 subjects (23%) had normal salivary flow rate (group I). While 53 subjects (59%) showed xerostomia (group II), only16 subjects (18%) had hypo salivation (group III) (Table 3 and 4) (Figure 3 and 4).

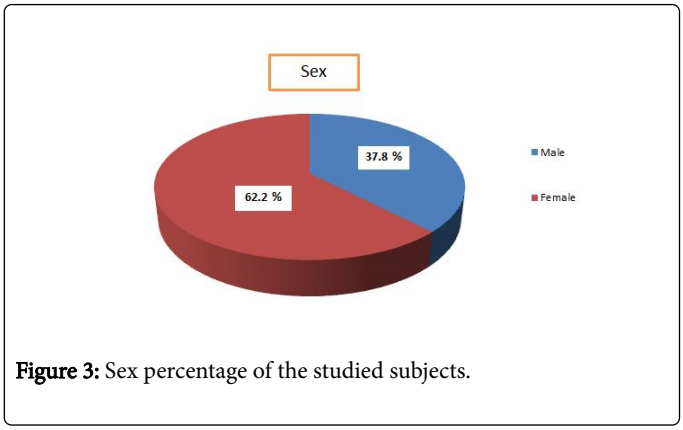

Figure 3: Sex percentage of the studied subjects.

Group I (normal)	Group II (Xerostomia)	Group III (Hyposalivation)
21 (23 %)	53 (59 %)	16 (18%)

Table 3: Classification of the studied subjects according to salivary flow rate.

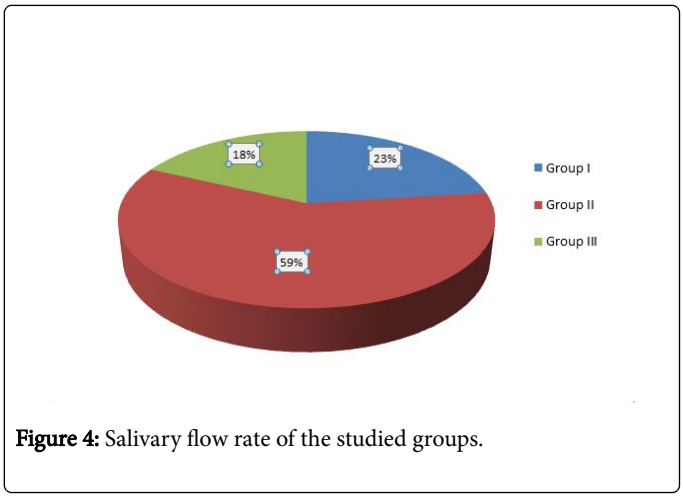

Figure 4: Salivary flow rate of the studied groups.

	Salivary flow rate (ml/min)		ANOVA	
	Range	Mean ± SD	F	P-value
Group I (normal)	0.4-3.0	1.371 ± 0.75	98.242	P<0.0001*
Group II (Xerostomia)	0.11-0.19	0.143 ± 0.025		
Group III (Hyposalivation)	0.01-0.09	0.045 ± 0.028		
Tukey's test				
	Group I		Group II	
Group II	P<0.001*		-	
Group III	P<0.001*		P>0.05	

*Significant P-value<0.05

Table 4: Statistical comparison between the studied groups as regard salivary flow rate (ml/min) using ANOVA test.

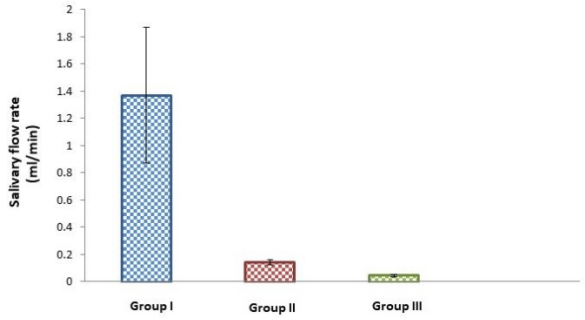

Figure 5: Statistical comparison between the studied groups as regard salivary flow rate (ml/min).

Table 4 and Figure 5 show a comparison of salivary flow rate (ml/min) among the studied groups.

Salivary flow rate is markedly decreased in group II and group III in comparison to its corresponding value in group I. There is statistically significant difference between the studied groups (F value was 98.242, P value<0.0001*) (Figure 6).

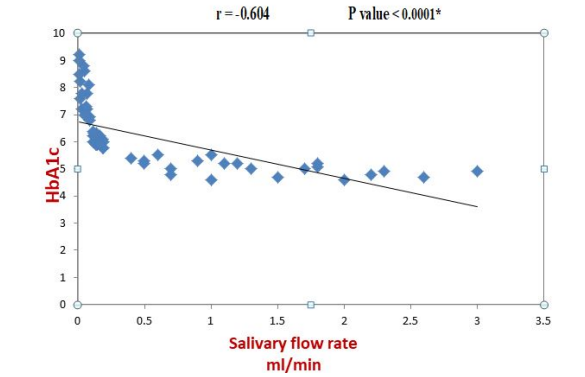

Figure 6: Negative correlation between salivary flow rate and HbA1c.

By using the multiple comparisons test (Tukey's test)

Salivary flow rate showed statistically significant difference in group III in comparison to its corresponding value in other groups in the experimental study. Its value in group II showed statistically significant difference when compared with its value in group I (Figure 7).

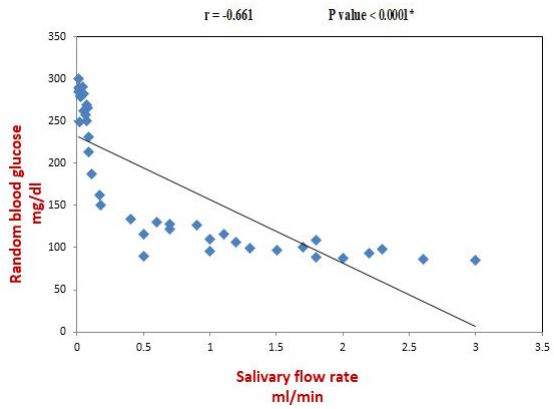

Figure 7: Negative correlation between salivary flow rate and random blood glucose.

In our study, salivary flow rate is markedly decreased in group II and III in comparison to its corresponding value in group I. There is statistically significant difference between the studied groups (F value was 98.242, P value<0.0001*).

In a study by Barasch et al. [17], they explored the utility of random plasma glucose levels for screening for pre diabetes or previously undiagnosed diabetes in community dental practices. Although this is consistent with our study, the difference was in use of the spitting or expectorating technique to calculate un-stimulated salivary flow rate (USFR) to detect xerostomia and explain the significant positive correlation with pre-diabetes and diabetes cases.

Other studies by Borrell et al. [18] and Lalla et al. [19] explored the importance of screening adult patients who presented for care at a dental clinic and had never been told they had pre diabetes or diabetes. The presence of ≥ 4 missing teeth or ≥ 26 percent of teeth with deep pockets (probing depth measurements and assessment of clinical attachment levels) correctly identified 73 percent of true cases. This explained the importance of periodontal disease and its sequelae as risk factors for dysglycemia. Accordingly, our cases age in this study was 20 to 60 years old not adult only as in study of Lalla et al., in addition to diagnosis of xerostomia or dry mouth of our study was done on larger sample size (n=90) so, criteria of xerostomia were clear by clinical examinations and group of questions illustrating presence of xerostomia which were explained in our method in this study.

The findings of the present study were different from studies of the northeastern United States (Kunzel et al. [20], Lamster et al. [21] and New Zealand (Forbes et al. [22] which has indicated that almost one-third of dentists are unwilling to screen for diabetes using finger-stick tests and fewer than 3 percent have ever done so. This might be attributable to invasive technique used (finger-stick tests) which is painful while our study was done depending on non-invasive technique (spitting technique) to calculate USFR to detect xerostomia and prove relationship between dry mouth (xerostomia) and pre-diabetes and diabetes cases.

On other hand, a study by Greenberg et al. [23] reported on attitudes toward, acceptance of, and perceived barriers to chair-side screening for medical conditions among practicing dentists. Seventy-seven percent thought it was very important for dentists to perform

chair-side screening for diabetes. Most (85 percent) were very willing to refer a patient for consultation with a physician. Only 55 percent were very willing to conduct chair-side screening them and only 29 percent were very willing to gather blood via finger stick. This was going inside with our study but our research did not depend only on screening for medical condition as, the spitting or expectorating technique was used in our method to calculate USFR and compare between xerostomia and others without xerostomia to clarify the relationship with dysglycemic cases.

Our data indicated that un-stimulated whole salivary flow rate (UWSFR) decreased in cases suffering from xerostomia (group II) and hypo-salivation (group III) compared to cases not suffering from xerstomia & hypo-salivation (group I) and using test HbA1c which provides an integrated measure of average glycemia over the past 3 months, we proved the relationship between dry mouth (xerostomia) and early predictor of pre-diabetes and diabetes cases in dental practices. This is in accordance with the findings of Genco et al. [24] recently reported a field trial of screening for pre diabetes and diabetes in dental practices. Participants had no history of diabetes and had not been tested for diabetes in the previous 12 months. Screening was performed with the American Diabetes Association Diabetes Risk Test and a point-of-care capillary hemoglobin A1C test. Nearly 41 percent of participants had dysglycemia defined by HbA1c ≥ 5.7 percent.

The last opinion by Strauss et al. [25] has suggested that measurement of gingival crevicular blood may be a more acceptable approach to diabetes screening in periodontal patients. Nevertheless, it is clear that although dental practitioners are receptive to performing preventive activities outside the traditional scope of dental practice, barriers remain to their widespread implementation. This is conflicting with ours in used technique and patient diagnosis. In our study, we used spitting technique to calculate USFR to detect xerostomia patients and explained the significant positive correlation with pre-diabetes and diabetes cases.

Conclusion

This study demonstrates the potential utility of chair-side screening and referral for definitive diagnostic testing and treatment. Early detection, prevention, and treatment may not only improve health and reduce medical costs, but enhance dentist's ability to prevent and treat xerostomia and its complications.

The dental office, with particular focus on patients with dry mouth, proved to be a suitable location for screening for pre (diabetes).

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