Original article

The Role of Salivary Gland Scintigraphy in the Evaluation of Salivary Gland Dysfunction in Uncontrolled Type II Diabetic Patients

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Abstract

The aim of the present study was to evaluate the salivary gland dysfunction in patients with uncontrolled type II diabetes using salivary gland scintigraphy and then to compare these ratios with quantitative whole salivary secretion rates. Using a gamma camera (siemens-diacam) equipped with a low energy all-purpose collimator, 32 uncontrolled type II diabetic patients and 30 normal healthy patients were studied by injecting a radio isotope (technetium 99m pertechnetate) about 5 mCi was injected intravenously in to anticubital vein and the activity was measured for the 1st, 20th and 40th min. At 20 min after injection, vitamin C chewable tablet was given to stimulate the secretion and continued until the end of the study period (40 min). Before scintigraphy, salivary sampling was carried out in both diabetic and normal individuals in a quiet room, saliva was allowed to accumulate and was expectorated into the collecting vessel approximately once a minute for 15 min and the volume was recorded as Unstimulated salivary flow rate and after 5 min break vitamin C chewable tablet was given to stimulate the secretion and the patient was asked to expectorate the saliva in the collecting vessel for 5 min. The expectorated volume was recorded as stimulated salivary flow rate. The mean of the measurements of scintigraphic ratio and salivary secretion rates were compared using the paired Student's *t*-test. The scintigraphic mean uptake and excretory ratio (ER) and the salivary flow rates were correlated. The result shows that there was a significant correlation between salivary flow rate and scintigraphic uptake and ER. However, statistically significant result could not be derived as it may be due to smaller sample size and marginal difference in the scintigraphic values between the groups. Salivary gland scintigraphy plays a significant role in the evaluation of salivary gland dysfunction. However, its role as an independent investigative procedure in the evaluation of salivary gland dysfunction requires a study with a larger sample size, may yield a statistical significant result and it can also act as an adjunct along with salivary flow rate procedure.

Keywords: Salivary dysfunction, scintigraphy, technetium-99m pertechnetate, uncontrolled type II diabetes

Introduction

There are various body fluids, which are essential for proper function of our body of which saliva is the most valuable fluid that can aid in diagnosis of various diseases, e.g.: Human immunodeficiency virus, hepatitis and renal disease. Hence this valuable oral fluid is critical to the preservation and maintenance of oral health, yet it receives little attention until the quantity is diminished.[1]

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In salivary gland dysfunction it can present as either hypersalivation or hyposalivation. Hyposalivation can occur in localized disease, systemic disease, radiation therapy and salivary duct stones.[2] There is great variability in salivary flow rates, the accepted range of normal flow for unstimulated saliva is anything above 0.1 ml/min. For stimulated saliva, the minimum volume for the accepted norm increases to 0.2 ml/min. Any unstimulated flow rate below 0.1 ml/min is considered hypo function and stimulated anything below 0.5 ml/min is considered abnormal.[1,3] Various factors affecting salivary secretion include diabetes mellitus, Parkinson's disease, cystic fibrosis and sarcoidosis of which diabetes

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is the most commonly reported disease in daily dental practice.

Diabetes is characterized by increased levels of glucose in the blood and abnormalities in the metabolism of lipid, protein induced by diminished levels or total absence of insulin. The incidence of diabetes has increased as people move away from their traditional life-style and patients with diabetes have various oral manifestations such as gingivitis, periodontitis, candidiasis, burning mouth syndrome, delayed wound healing and those who have poor glycemic control are more likely to complain of xerostomia and may have decreased salivary flow up to 82.5%.[4] The cause of salivary dysfunction may be related to polyuria or to alterations in the basement membrane of salivary glands, an investigation revealed parotid gland basement membrane abnormalities in all diabetic subjects as indicated by the binding of immunoglobulin G, albumin and polyvalent immunoglobulin's to ductal and acinar basement membranes'. So variation in parotid diabetic basement membranes evidenced that membranopathy in this is systemic in nature.[5,6]

There are various methods of measuring the volume and weight of saliva, which are divided in to those that measure secretions from specific glands and those that measure whole or pooled saliva. These methods can be performed under conditions of unstimulated (resting) or stimulated flow. Assessment of whole pooled saliva may be an accurate indicator of overall salivary gland function.[7] There are various imaging techniques used for salivary gland, e.g.: Sialograms, computed tomography, magnetic resonance imaging and ultrasound of which scintigraphy is the only method available that can provide qualitative and quantitative functional assessment of the major salivary glands.[8]

Scintigraphy has been widely used for bone, thyroid, tumors and inflammatory conditions, now recently it is being used for detecting salivary gland hypofunction. Scintigraphy is particularly a valuable tool because it produces dynamic, objective and quantitative measurement of the major salivary gland function and allows for differentiation of abnormalities in saliva production as uptake ratios (UR) and secretion as excretory ratios (ER).[9]

The specific objective were: To evaluate the changes in salivary gland function in patients with uncontrolled type II diabetes using salivary gland scintigraphy.

Materials and Methods

Patient selection criteria

Patients were randomly selected in the Department of oral medicine and the study comprised of 32 uncontrolled type II diabetic patients (22 females and 12 males) and 30 normal healthy individuals (16 females and 14 males) included in the study with age and sex matched. Age group ranges from 40 to 60 years. Patients having any other systemic or nervous illness or taking any medications or having suffered in the past with any type of illness or treatment that could have an effect on the normal functioning of the salivary gland were excluded from the study. Moreover, the study was carried out with patients consent.

Diabetic diagnostic protocol

The American Diabetes Association Expert Committee in 1997 and 1998 revised the diagnostic criteria for diabetes.[10]

A lower cut-off level for fasting plasma glucose (126 mg/dl) and to diagnose diabetes.

Blood glucose test values as related to control of diabetes.[11]

Normal, well-controlled – fasting plasma glucose <126 mg/dl, postprandial <160 mg/dl, hemoglobin (HbA1c)-<6%.

Moderate control-fasting plasma glucose <160/dl, postprandial - <160-200 mg/dl, HbA1c-6-7%.

Uncontrolled – fasting plasma glucose >160 mg/dl, postprandial - >200 mg/dl, HbA1c - >8%.

Saliva sampling

The patients were instructed not to eat, drink or put anything in their mouth or brush their teeth for at least 90 min before the examination. The saliva was collected in a quiet examination room between 7.30 a.m and 9.30 a.m. Unstimulated whole saliva was collected for 15 min. The patients were told to sit still, bow their head and try not to move. Immediately before the test, they were instructed to swallow any saliva, present in their mouth. Saliva was allowed to accumulate and was expectorated in to the collecting vessel approximately once a minute. The volume was recorded and the unstimulated whole salivary secretion rate (USSR) was expressed as ml/min. after 5 min break, stimulated whole saliva was collected for 5 min. The patients were asked to chew vitamin C chewable tablets without swallowing and then expectorate the stimulated saliva in to collecting vessel [Figure 1]. The expectorated volume was recorded and stimulated whole salivary secretion rate (SSSR) expressed as ml/min. USSR and SSSR below or equal to 0.1 ml/min and 0.5 ml/min respectively was considered abnormal. Salivary secretion rates were expressed as mean and standard deviation.[12]

Scintigraphy

After salivary sampling, the salivary gland scintigraphy was performed in the department of nuclear medicine with a gamma camera (siemens-diacam) equipped with a low energy all-purpose collimator. The patients were placed in the supine position with the gamma camera close above the face to record activity in the major salivary glands and the surrounding tissues [Figure 2] technetium-99m pertechnetate [Figure 3] about 5 mCi (135MBq) was injected intravenously in to antecubital vein. The activity was measured for the 1st, 20th and 40th min. At 20 min after the injection; vitamin C chewable tablet was given to stimulate the secretion and continued until the end of the study period (40 min). The data were replayed and the regions of interest were selected over four salivary glands to obtain the uptake and ER of the salivary glands[12,13] [Figure 4].

Statistical analysis

A standard statistical software package (SPSS version 12.0, Chicago, IL) was used for the data analysis. The data corresponded to mean ± standard deviation was calculated for both salivary flow rates and mean URs, between diabetic and control group. The measurements were statistically compared (salivary uptake and ER (%) with salivary flow rate using the paired Student's *t*-test ($P < 0.05$).

Figure 1: Armamentarium used for collection of saliva and scintigraphic procedure

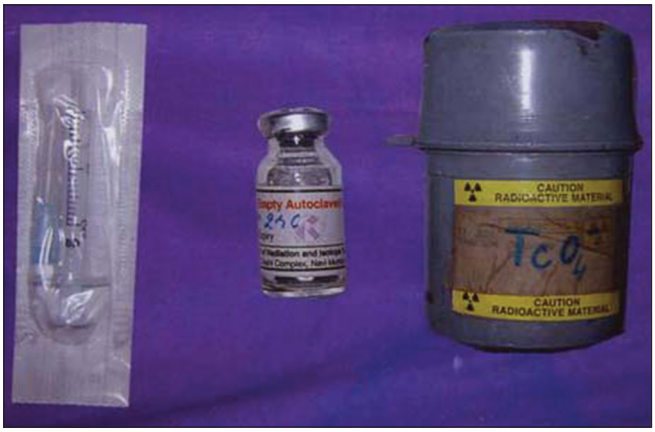


Figure 3: Technetium-99m pertechnetate-radioactive material

Results

The result of the current study, which was carried out in diabetic and control patients, shows the flow rate analysis between the groups under unstimulated and stimulated conditions. The result infers a significant reduction in the salivary flow rate in diabetic patients, when compared with the control group in both categories of unstimulated and stimulated and the *P* value was significant (<0.0001) [Table 1] [Graph 1].

The scintigraphic total uptake and ER in diabetic and control groups were compared, the values in these two categories showed a decrease in both uptake and ER in diabetic patients, when compared with control patients. However, when it was subjected to statistical analysis, it was found to be not significant, this could be due to lack of larger sample size and marginal difference between diabetic and control groups [Table 2a and b] [Graph 2].

The scintigraphic mean uptake and ER and the salivary flow rates were correlated. The result shows that there

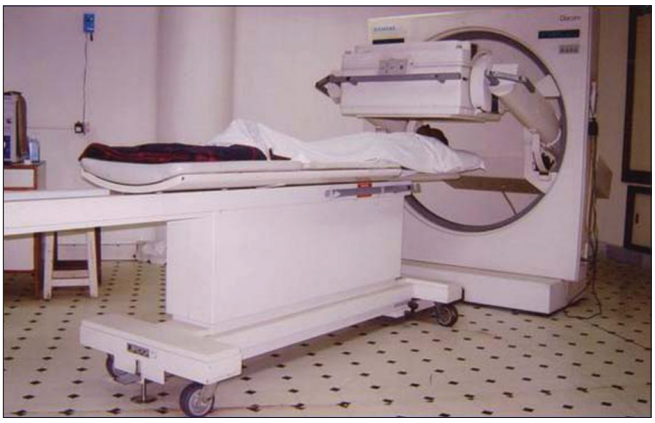


Figure 2: Gamma camera (siemens-diacam) with low energy all-purpose collimeter

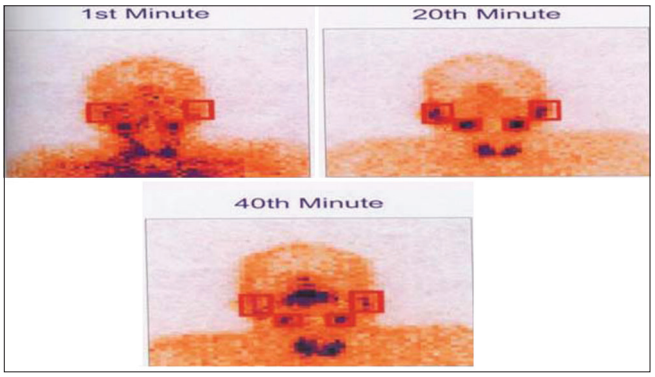


Figure 4: Scintigraphy in diabetic patients at 1st, 20 and 40th min

Table 1: Salivary flow rate analysis in diabetic and control patients with unstimulated and stimulated salivary flow measured in (ml/min)

Salivary flow rate			
Diabetic patients		Control patients	
Unstimulated	Stimulated	Unstimulated	Stimulated
For 15 min 1.0 ml	For 5 min 3.0 ml	For 15 min 4.1 ml	For 5 min 9.2 ml
For 15 min 1.3 ml	For 5 min 3.0 ml	For 15 min 3.7 ml	For 5 min 8.7 ml
For 15 min 1.1 ml	For 5 min 2.7 ml	For 15 min 3.6 ml	For 5 min 9.0 ml
For 15 min 1.2 ml	For 5 min 2.9 ml	For 15 min 3.6 ml	For 5 min 8.6 ml
For 15 min 1.0 ml	For 5 min 2.5 ml	For 15 min 3.5 ml	For 5 min 8.7 ml
For 15 min 1.2 ml	For 5 min 3.0 ml	For 15 min 3.4 ml	For 5 min 8.2 ml
For 15 min 1.0 ml	For 5 min 2.7 ml	For 15 min 3.5 ml	For 5 min 8.5 ml
For 15 min 1.4 ml	For 5 min 3.1 ml	For 15 min 3.2 ml	For 5 min 8.7 ml
For 15 min 1.2 ml	For 5 min 3.1 ml	For 15 min 4.0 ml	For 5 min 8.7 ml
For 15 min 1.0 ml	For 5 min 2.9 ml	For 15 min 3.5 ml	For 5 min 8.0 ml
For 15 min 1.0 ml	For 5 min 2.2 ml	For 15 min 3.2 ml	For 5 min 9.1 ml
For 15 min 1.0 ml	For 5 min 2.5 ml	For 15 min 3.2 ml	For 5 min 8.9 ml
For 15 min 1.4 ml	For 5 min 2.9 ml	For 15 min 4.0 ml	For 5 min 9.4 ml
For 15 min 1.0 ml	For 5 min 3.0 ml	For 15 min 3.2 ml	For 5 min 8.0 ml
For 15 min 1.4 ml	For 5 min 3.1 ml	For 15 min 3.2 ml	For 5 min 9.2 ml
For 15 min 1.5 ml	For 5 min 3.2 ml	For 15 min 3.5 ml	For 5 min 8.2 ml
For 15 min 1.0 ml	For 5 min 3.0 ml	For 15 min 3.5 ml	For 5 min 9.0 ml
For 15 min 1.2 ml	For 5 min 3.3 ml	For 15 min 3.6 ml	For 5 min 8.6 ml
For 15 min 1.2 ml	For 5 min 3.0 ml	For 15 min 3.2 ml	For 5 min 9.1 ml
For 15 min 1.2 ml	For 5 min 3.2 ml	For 15 min 3.6 ml	For 5 min 8.6 ml
For 15 min 1.4 ml	For 5 min 2.9 ml	For 15 min 4.1 ml	For 5 min 8.7 ml
For 15 min 1.2 ml	For 5 min 3.0 ml	For 15 min 3.5 ml	For 5 min 8.5 ml
For 15 min 1.6 ml	For 5 min 3.2 ml	For 15 min 3.5 ml	For 5 min 8.5 ml
For 15 min 1.2 ml	For 5 min 3.1 ml	For 15 min 3.2 ml	For 5 min 8.7 ml
For 15 min 1.5 ml	For 5 min 3.5 ml	For 15 min 4.0 ml	For 5 min 9.1 ml
For 15 min 1.5 ml	For 5 min 3.2 ml	For 15 min 3.4 ml	For 5 min 8.1 ml
For 15 min 1.3 ml	For 5 min 3.1 ml	For 15 min 3.7 ml	For 5 min 9.2 ml
For 15 min 1.5 ml	For 5 min 3.0 ml	For 15 min 3.5 ml	For 5 min 8.2 ml
For 15 min 1.2 ml	For 5 min 3.0 ml	For 15 min 4.1 ml	For 5 min 8.7 ml
For 15 min 1.2 ml	For 5 min 3.0 ml	For 15 min 4.0 ml	For 5 min 9.0 ml
For 15 min 1.5 ml	For 5 min 3.2 ml		
For 15 min 1.2 ml	For 5 min 2.9 ml		

Flow rate	Mean±SD		*P* value
Unstimulated	0.083±0.012	0.240±0.020	<0.001
Stimulated	0.602±0.052	1.742±0.078	<0.0001

Inference: The result of salivary flow rate analysis in both diabetic and control patients, shows a significant change in the salivary flow rates of both unstimulated and stimulated salivary flow between diabetic and control patients. Thus the result infers that, there is decreased salivary flow in diabetic patients when compared with control patients. And the *P* value was significant (<0.001). SD: Standard deviation

is a significant correlation between salivary flow rates and scintigraphic UR and ER, however statistically significant result could not be derived as it may be due to smaller sample size of 32 numbers and marginal difference in the scintigraphic values between the groups [Table 3a and b].

Discussion

The current study was carried out to detect whether diabetic patients have salivary gland dysfunction using salivary gland scintigraphy. And a correlation was made between the scintigraphic ratio and salivary flow rates. Various studies have reported that in India the incidence of diabetes is increasing at an alarming rate. Various literature studies have reported that diabetic patients have diminished salivary dysfunction[14-18] of which the xerostomia is seen in uncontrolled diabetic patients up to 82.5%.[4] the cause of salivary dysfunction may be related to polyuria or alteration in the basement membrane of the salivary glands. A lot of literature studies have reported the parotid gland basement membrane abnormalities in all diabetic patients.[4-6]

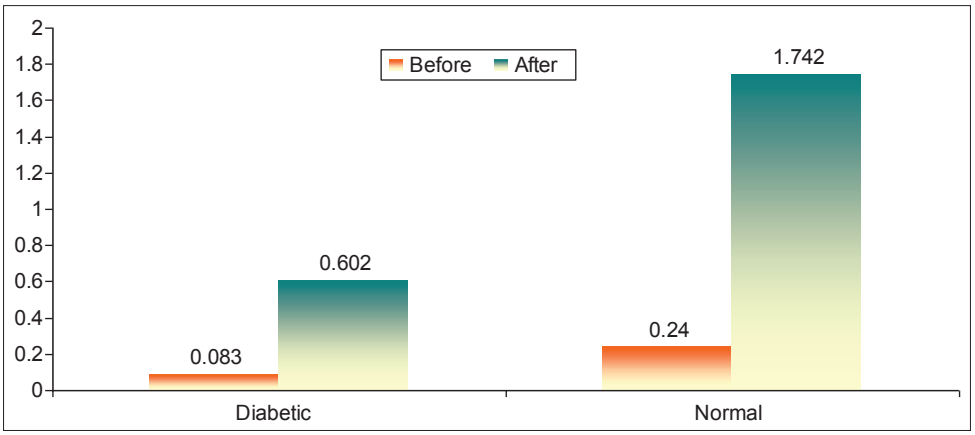
Previous studies have included diabetic patients with age group of 50-60 years[4] and another study have evaluated in diabetic patients with age of 50-90 years.[19,20] The present study was performed in sixty two patients (32 diabetic and 30 control) with age range between 40 and 60 years, which was same age range employed by various studies in evaluating the salivary dysfunction.[4,13] Studies have included more number of females when compared with males, owing to the above studies more number of females was included in the study and both diabetic and normal patients were excluded if they had any other systemic illness or were on any medication that could affect the salivary gland function.[4]

There are various methods of measuring the volume and weight of saliva and they are divided in to those that measure secretions from specific glands and those that measure whole or pooled saliva. These methods can be performed under conditions of unstimulated (resting) and stimulated flow.

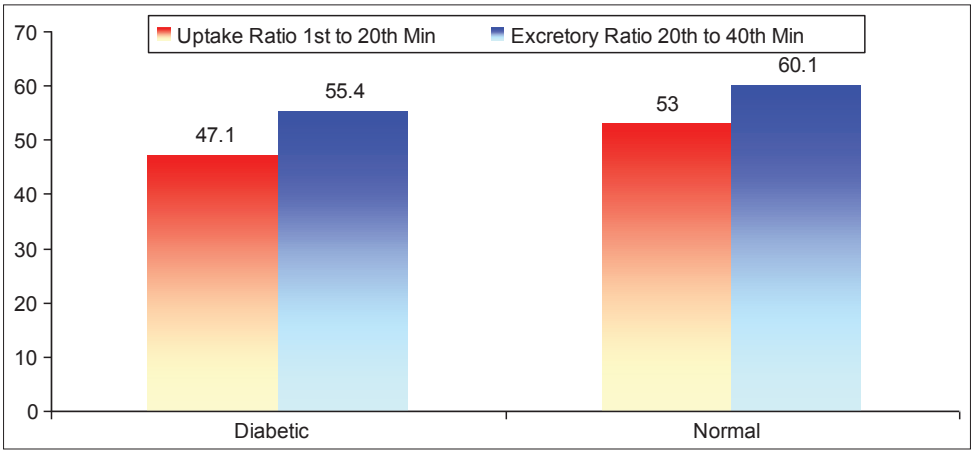
Previous studies have assessed that whole pooled saliva may be a more accurate indicator of overall salivary gland dysfunction, the draining and spitting methods being the simplest and more reproducible.[7,15,19,20] The whole salivary measurement are easier to perform, requiring only simple collection with weighing device,[7] the similar method was used as reported in the earlier studies.

For collection of saliva, various collecting vessels were used, e.g.: Centrifuge tubes, graduated tube fitted with glass funnel. Similar graduated tube fitted with glass funnel was used. Initially, unstimulated whole saliva was collected for 15 min and the stimulated saliva was collected for 5 min in individual containers. The collected saliva was measured in milliliters per minute.[19,20]

A lot of studies in the past have been carried out in diabetic patients to detect salivary dysfunction, but only few studies in the past have used scintigraphy for assessing the salivary dysfunction in diabetic patients.[13] The imaging techniques used for visualizing salivary gland include sialography, computed tomography, magnetic resonance imaging, ultrasound and scintigraphy.



Graph 1: A comparison of salivary flow rate analysis in diabetic and control patients with unstimulated and stimulated salivary flow measured in ml/min. Decrease in the salivary flow rate in the diabetic group compared to control group in unstimulated and stimulated conditions respectively



Graph 2: Comparison of mean uptake ratios between diabetic and control group. A decrease in the mean uptake and excretory ratio's in diabetic group, when compared with control group

Scintigraphy is the widely used method that can provide functional assessment of salivary glands.[8]

A number of studies in the past have used scintigraphy to detect the glandular dysfunction in diabetic patients, chronic renal failure; parenchymal damage after treatment with radio iodine and in patients with xerostomia due to aging and medication.[12,13,21-24] Hence scintigraphy was chosen as a choice in the present study.

A number of studies have used technetium99m pertechnetate for imaging of salivary dysfunction.[13,21,22] Technetium 99m pertechnetate with its monochromatic energy of 140 keV is physically the ideal isotope for imaging. Due to their short half-life these isotopes can be used in very large amounts of order of millicuries, without causing radiation hazards to patients. This paves for excellent images with sharp contrast.[25] Technetium 99m pertechnetate was injected in millicuries and about 5 mCi (135MBq) was injected in to anticubital vein and the activity was recorded using gamma camera equipped with a low energy all-purpose collimator for data analysis.[12]

This study was conducted to evaluate the role of scintigraphy in the detection of salivary gland dysfunction in uncontrolled type II diabetic patients. The study comprised of 32 uncontrolled type II diabetic patients and 30 normal individuals as controls, they were age and sex matched. Salivary flow rates, both unstimulated and stimulated were measured and compared between groups. It showed a marked decrease in the salivary flow rates in diabetic patients and it was found to be statistically significant.

The salivary gland scintigraphy with isotope technetium-99m pertechnetate was carried out in both the groups, the UR (unstimulated) and ER (stimulated) were recorded mean scintigraphic values of all four major salivary glands, when compared between diabetic and controls showed a marginal decrease in both UR (unstimulated) and ER (stimulated) in

Table 2a: Total uptake and excretory ratio of the major salivary glands in diabetic and control patients between 1st-20th and 20-40th min

Uptake and excretory ratio in percentage			
Diabetic (min)		Control (min)	
1-20th	20-40th	1-20th	20-40th
53.3	47.0	38.1	51.9
80.1	51.2	43.4	60.4
61.2	50.3	55.9	60.1
56.9	53.6	43.2	64.8
13.0	52.1	48.4	64.7
52.9	52.3	65.6	70.3
48.9	45.5	42.8	66.8
48.8	43.3	42.2	67.6
47.7	45.1	68.1	73.1
39.5	35.0	48.0	70.7
27.6	21.0	40.0	69.0
45.2	92.8	51.7	78.0
42.6	48.0	47.9	67.5
60.2	63.2	44.1	64.0
41.6	72.5	48.7	58.4
36.1	47.5	38.8	41.6
30.9	50.7	52.5	58.6
52.5	57.8	42.8	58.6
40.1	60.1	56.6	60.8
40.4	47.9	49.1	56.5
42.7	64.8	52.1	75.7
31.6	46.4	67.3	53.1
43.1	62.6	52.1	48.1
44.5	68.7	62.1	50.1
63.5	73.5	84.0	63.5
46.0	50.6	58.4	56.2
45.8	76.2	91.9	72.9
47.2	49.0	51.7	35.9
34.8	55.2	50.5	40.1
49.7	66.2	52.5	45.4
46.1	70.3		
50.3	51.9		

Table 2b: Comparison of mean uptake and excretory ratios between diabetic and control patients

Variable min (%)	Mean±SD		*P* value
	Diabetic	Control	
Uptake ratio 1st-20th	47.1±10.5	53.0±12.5	0.07
Excretory ratio 20-40th	55.4±13.5	60.1±10.8	0.07

*Mann-Whitney U-test was used to calculate the *P* value. There is decrease in the uptake ratio of 1st-20th and excretory ratio of 20-40th min in the major salivary glands of diabetic patients as compared to control patients. But however there was no statistically significant difference between the diabetic and control. *P*<0.05 was considered to be significant. SD: Standard deviation

diabetic patients which leads to conclusion that there is a decrease in salivary gland function in diabetic patients. However, statistical significant result could not be derived. This result was comparable with Kao *et al*. were all the four major salivary glands in type II diabetic patients had significantly lower uptake and ER.[13]

Table 3a: Correlation between uptake and excretory ratio (%) with salivary flow rate in diabetic patients

Variable (%)	Unstimulated		Stimulated	
	*r**	*P* value	*r*	*P* value
Uptake ratio 1st-20th min	0.096	0.60	-	-
Excretory ratio 20-40th min	-	-	0.097	0.60

*Spearman's rank correlation co-efficient. There is significant correlation between the uptake ratio of 1st-20th and excretory ratio of 20th-40th min with salivary flow rates (unstimulated and stimulated) of diabetic patients. But however there was no statistically significant change and the *P*<0.05 was considered to be significant

Table 3b: Correlation between uptake and excretory ratio (%) with salivary flow rate in control patients

Variable (%)	Unstimulated		Stimulated	
	*r**	*P* value	*r*	*P* value
Uptake ratio 1st-20th min	0.214	0.26	-	-
Excretory ratio 20-40th min	-	-	0.343	0.06

*Spearman's rank correlation co-efficient. There is significant correlation between the uptake ratio of 1st-20th and excretory ratio of 20-40th min with salivary flow rates (unstimulated and stimulated) of control patients. But however there was no statistically significant change and the *P*<0.05 was considered to be significant

The comparison of flow rate and scintigraphic analysis also showed a correlation between the individual values within the groups. The result of the present study leads to conclusion that salivary gland scintigraphy play a vital role in the evaluation of salivary gland dysfunction. However, its role as an independent investigative procedure in the evaluation of salivary gland dysfunction, requires a study with a larger sample size, may yield a statistical significant result and it can also act as an adjunct along with salivary flow rate procedure.

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