RELATIONSHIP BETWEEN TYPE 2 DIABETIC MELLITUS AND VOCAL PARAMETERS IN ADULT NIGERIANS

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ABSTRACT

Voice is a reflection of the entire being, and as such, it is often affected by systemic disturbances in the body, one of them being diabetes.

Objectives: *We aimed to study the prevalence of phonatory symptoms in patients diagnosed with Type II diabetes and correlations, if any, between these symptoms, vocal acoustic parameters and findings from laryngeal examinations.*

Methodology: *The study was a case-controlled study involving adult diabetic patients with an equal number of healthy age and sex-matched control subjects. We administered a semi-structured questionnaire to the participants for relevant data collection and conducted voice acoustic and perceptual voice analyses on all study participants.*

Results: *There were 130 study participants with an equal number of diabetic and control subjects. Vocal strain and tiring were significantly higher in the diabetic group with associated increased and significant odds ratios. These findings were supported by the Grade, Strain, and Asthenia components of the GBRAS findings.*
Except for the Fundamental Frequency (F_0), the groups' acoustic parameters significantly differed. There were increased odds ratios for vocal straining and tiring in subjects with established diabetes mellitus. Subjects with established diabetes perturbation measures also showed significant differences with respect to the duration. We also found Significant correlations between the Sensory Test Score, glycosylated hemoglobin, Harmonic-to-Noise ratio, and Shimmer.

Conclusions: ***Vocal straining and tiring were commoners in the diabetic subjects. We inferred that neuropathy plays a significant, but not exclusive role in the mechanism of these symptoms.***

Keywords: *Voice disorders, Diabetes mellitus, neuropathy; dysphonia*

INTRODUCTION

Voice production is a complex function that is related to a properly functioning neurological, respiratory, and aerodigestive system. This relationship exists because of the complex coordination between the various muscles involved in voice production, coupled with the additional need to temporarily cease the vital functions of the upper aerodigestive tract, such as breathing and deglutition during voice production.[1] Consequently, the development of voice Disorders (VD) could result from abnormalities in any part of this integrated mechanism.

Identifying voice disorder in a subject includes a simple concept as when an individual expresses concern about having an abnormal voice that does not meet daily needs despite others not perceiving the subject's voice as deviant.[2] However, tools can be used to qualify and quantify the degree of the disorder in a reproducible manner. An example is the perceptual analysis (PA) which is based on the grading using the GRBAS scale that involves scoring the dysphonia grade, roughness, breathiness, asthenia, and strain.[3] The voice acoustic analysis (VAA) also allows objective evaluation of recorded vocal data by extracting the acoustic parameters (AP) from vocal samples to help understand the pathophysiology of abnormal voice production and the evolution of changes accompanying varying clinical conditions.[4, 5]

The basic parameters from VAA are Fundamental Frequency (F_0), Jitter, Shimmer, and Harmonics-to-Noise ratio (HNR). This type of analysis requires a voice laboratory setup that uses proprietary or open-source computer software. We used PRAAT®, an open-source software, in our study due to its availability and support from clinicians and scientists worldwide.[5] Other assessments of the voice also include visualization of the vocal process through laryngoscopy and videostroboscopy.

Diabetes mellitus (DM) is an aetiologically multifactorial metabolic disorder characterized by chronic hyperglycemia. A common variant, known as type II diabetes mellitus (T2DM), affects individuals of all ages[6, 7 8]. It is characterized by hyperglycemia in the context of insulin resistance or relative lack of insulin. The complications related to this disease are multisystemic[9], and some may perhaps have a bearing on the vocal process.

Such complications include neuropathy, which, apart from being a common accompaniment of long-standing diabetes[10], may impact voice production through the affectation of the muscles directly involved in the vocal sound production and the other accessory muscles indirectly involved in the eventual vocal output. A typical tool for assessing peripheral neuropathy is the Modified Toronto Clinical Scoring System developed by Bril et al.[11]

Also found to be prevalent in long-standing diabetics is xerostomia. The xerostomia found in this situation is linked to the development of autonomic neuropathy.[12, 13] Whether voice disorders could result due to xerostomia as a consequence of the possible reduction in laryngeal lubrication needed to be explored.

There are previous works that examined voice characteristics and phonatory changes among patients with diabetes, and we propose to add to this corpus of knowledge using T2DM patients in our setting.[14 15]

We set out to determine whether phonatory symptoms are more prevalent in type II diabetic patients due to possible laryngeal examination findings. We also intended to demonstrate the possible mechanism of these symptoms and potential correlates that could be inferred from our study.

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MATERIAL AND METHODS

After obtaining Institutional Review Board approval for the conduct of this research, we recruited type II diabetic (T2DM) patients aged 18-65 years clinically diagnosed for at least one year with glycosylated hemoglobin level (HbA1c) >6.5% and fasting blood sugar (FBS) greater than 126mg/dl. We also recruited sex-matched non-diabetic control subjects who had no significant smoking histories, were not in occupations that require professional use of voice and did not have upper respiratory tract infections in the last three weeks before recruitment. Subjects who had previous laryngeal procedures were excluded from the study.

We obtained informed consent from the participants, after which we administered proforma to collect the study participants' biodata and phonatory symptoms. For the diabetic group, additional questions included medications, disease duration, and glycemic control (using the most recent HbA1c obtained from the subjects' chart). We then carried out general physical and ENT examinations. As a part of the examination, we evaluated the diabetic subjects for neuropathy using the Modified Toronto Clinical Scoring System. [11]

The vocal samples acquisition was performed at the ENT departmental audiology room with ambient noise less than 45db using the PRAAT® software set at a sampling frequency of 44100Hz.[16] While seated with a head-mounted low impedance microphone placed 10 cm away from their mouth at 45°-50° off the mouth, each participant is asked to repeat a prepared sentence at a comfortable pitch and loudness, which was recorded. Each participant was also asked to sustain vowel /a/ at a comfortable pitch and loudness for at least 4 seconds for acquisition.

From the recorded sample, a consistent segment of about 3 seconds (Figure 1) was selected from the spectrograph, and the vocal acoustic parameters were extracted (Figure 1). The recordings of each subject, namely the sustained /a/ and sentence reading, were also evaluated blindly by one of the co-authors and the speech therapist on the GRBAS scale. These scores were later compared for inter-rater agreement using the Fleiss Kappa (κ) test.

The laryngoscopic examination was also carried out in the ENT endoscopic room on each participant using a flexible laryngoscope, and the findings were recorded. The mean values of quantitative parameters were computed, and comparisons were made between the means of the groups using the Mann–Whitney U test. Comparisons were also made within the T2DM group based on disease duration, glycemic control adequacy, neuropathy, and xerostomia. Pearson's Chi-square test was applied for categorical variables comparisons. All analyses were conducted using the IBM SPSS version 22. A p-value of less than 0.05 was considered statistically significant.

RESULTS

We recruited 130 participants (65 diabetic and 65 non-diabetic) for this study. The mean ages for the diabetic and non-diabetic groups were 56.8 ± 8.57 and 56.4 ± 10.35 years (p = 0.08) respectively. There were 28 (43.1%) male subjects in the T2DM group and 34 (52.3%) in the control group (p=0.29). Table 1 shows details of the two groups and the information related to the T2DM group only. Table 2 shows the distribution of the phonatory symptoms and other findings on laryngoscopy. We found increased and significant odds of vocal straining and tiring in the diabetic group.Table 3 shows the distribution of perceptual parameters, and shows acoustic parameter comparisons between groups and gender. The details of the relationship between the features of established or severe T2DM and phonatory symptoms are shown in Table 4. From the table, neuropathy shows a consistent significance and increased odds ratio in relation to vocal straining and tiring.

Table 4, Figure 3, and Figure 4 show the relationship between features of established DM and perturbation measures. The main finding is that the perturbation measures were not significantly different in T2DM subjects who complained of xerostomia. There is a strong and significant negative correlation between the Sensory Test Score (STS), HbA1c, and HNR and a positive correlation between STS and Shimmer (Figure 5)

DISCUSSION

We found in our study that subjects with T2DM present significantly with more vocal symptoms, particularly vocal straining and tiring. An increase in vocal symptoms in the diabetic patient is already demonstrated in the literature.[17] We also found significantly worse perceptual parameters (PP) in the T2DM group, except for the asthenia and breathiness subcomponents. This finding shows that there are humanly perceptible changes or worsening of the voice that a third party can detect in diabetic patients and thus further consolidates the utility of the GBRAS system in voice assessment. The relevant literature we found comparing the GBRAS grades between similar groups did not show a significant difference between diabetics and normal subjects. [14]

The acoustic parameter (AP) is more objective in voice assessment as the measurements are not impaired by the observer's subjectivity seen in perceptual parameter assessment.[18] Our study found that the acoustic parameters (AP) except the fundamental frequency (F_0) showed a highly significant difference between the diabetic and the control group. Based on this finding, we could say that the ability to maintain constant pitch and loudness in a person with diabetes is impaired, in addition to their voice being less sonorous. Thus, it is safe to assert that voice disorder is more prevalent in T2DM.

The phonatory symptoms, abnormal PP, and AP demonstrated more in the diabetic group could be related to the neuropathic effect of DM at the levels of the local innervation of the larynx and the neural supply to the accessory muscles necessary for adequate voice production.[10] This theory is corroborated by our finding of significantly increased odds of phonatory symptoms of vocal straining and vocal tiring in the subjects classified as having neuropathy. (Table 5) The other relevant finding in this respect is the increase in the odds of vocal tiring with respect to the long duration of DM.

In this study, we assessed neuropathy using the STS. The role of STS in assessing neuropathy in DM is well established, and the limitations are also documented. [11] In clinical settings where time is of the essence, we tried to see if the perturbation measure could be a quicker and more quantitative means of assessing the neurological deficit associated with T2DM considering the more cumbersome procedure of carrying out STS. The demonstrated correlations, i.e., the negative correlation of HNR to the STS, could be used clinically in monitoring the degree and progression of neuropathy in T2DM patients in clinical settings.

Myopathy is also a known complication of diabetes mellitus and is usually associated with poorly controlled long-standing disease. Pathologically, it is a spectrum of diseases that presents with muscular changes, including inflammation, ischemia, hemorrhage, infarction, necrosis, and atrophy. A provisional diagnosis of myopathy may be inferred clinically, but radiological and electromyographic findings usually support the diagnosis.[19] Distinguishing between different types may require a biopsy since there are no direct markers that are presently known that can give this information.[19, 20] The inaccessible nature of laryngeal muscles to carry out such a biopsy precludes this option in our study. However, we could infer that myopathy in more accessible peripheral muscles may be a pointer to myopathy involving laryngeal musculature. The apparent limitation of this assertion is that muscle groups are affected differently in myopathy secondary to T2DM, and the level of susceptibility of vocal muscles is a subject for future reference.[19] We did not assess for myopathy in this study either through radiology, biochemical test, or assessment of other accessible muscle groups. However, we found significant and increased odds of asymmetry and abnormal movement affectation of the supra-laryngeal structures, particularly the aryepiglottic folds

in the T2DM group, an association that has been linked to the existence of laryngeal myopathy in people with diabetes. [14]

Although xerostomia was found only in the T2DM group (and in significant proportion), we could not make conclusive inferences until we examined this factor in the diabetic group alone to indicate established or poorly managed DM. Our analysis showed that xerostomia is not present more significantly in subjects with vocal symptoms, nor does it affect the perturbation measures, as shown in Figure 2, when examined as a factor of established or severe DM. Thus, one can surmise that the presence of xerostomia as a factor had little effect on the voice disorder in our study. Perhaps laryngeal lubrication is not dependent on the lubrication from salivary glands draining into the oral cavity.

Structural abnormalities affecting the vocal process may also present in people with diabetes, thus causing voice disorders. Such abnormalities include edema, laryngopharyngeal reflux, and other gross laryngeal lesions not necessarily as a direct consequence of T2DM. Our Laryngoscopic examination of the larynx did not show significantly more abnormal findings except the asymmetry and abnormal movement of the aryepiglottic fold, which we earlier implied may be due to myopathy.

Through this study, we have shown that the prevalence of voice disorder is higher in patients with T2DM, and these parameters are related to features of established DM. Our study also showed that the voice disorder may be related more to the neuropathy seen in this group of patients. We also found that the HNR could be used as a surrogate for quantifying the degree and progression of neuropathy in T2DM.

However, we found a limitation in attributing vocal derangement to one mechanism or proving a direct causal relationship. We recommend more detailed studies involving more health parameters related to DM and longitudinal designs. In addition, electromyography, videostroboscopy, and tissue sampling will give more evidence of causal relationships and establish a more conclusive pathophysiological pathway.

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Table 1. Demographic characteristics and other details of subjects

	Patient (n = 65)	**Control (n = 65)**	**p**
Age in years (Mean± SD)	56.8 ± 8.57	56.4 ± 10.35	<0.08
Gender			
Male	28(43.1%)	34(52.3%)	0.29
Female	37(56.9%)	31(47.7%)	
Reflux	11(17%)	6(9.2%)	0.193
Xerostomia	16(24.6)	0	<0.0001
Neuropathy			
Absence	49(75.4)	65(100)	
Mild	9(13.8)	0	NA
Moderate	7(10.8)	0	
Severe	0	0	
Duration of disease			
< 5 years	33(50.7%)		
5 – 10 years	23(35.4%)	NA	NA
> 10 years	9(13.8%)		
Glycemic control			
Good	40(61.5%)		
Average	12(18.5%)	NA	NA
Poor	13(20%)		
Medication			
Single Oral Drug Oral Drug	21(32.3%)		
More than one Oral Drug	41(63.1%)	NA	NA
Combined Oral Drug + Insulin	3(4.7%)		

Table 2: Phonatory Symptoms and Laryngoscopic Findings in Diabetic Group and Control Group

	Diabetics	Controls		
	n (%)	**n (%)**	p	OR$^{\alpha}$ (95%CI) p
Phonatory Symptoms				
Voice Straining	25(38.5)	3(4.6)	< .001	12.9(3.7-45.7) <.001
Vocal Tiring	22(33.8)	9(13.8)	0.01	3.2(1.3-7.6)0.013
Hoarseness	18(27.7)	10(15.4)	0.088	2.1(0.9-5.0) 0.134
Laryngoscopy Findings				
Base of Tongue				
Enlarged Papillae	4(6.2)	0(0.0)	0.04	9.6(0.5-∞) 0.119
Abnormal Vallecula	3(4.6)	0(0.0)	0.08	7.3(0.4-∞) 0.24
Abnormally Shaped Epiglottis	2(3.1)	0(0.0)	0.15	5.2(0.2-∞) 0.50
Aryepiglottic Fold				
Edema	3(4.6)	0(0.0)	0.08	7.3(0.4-∞) 0.24
Asymmetry	14(21.5)	0(0.0)	<.001	36.9(2.1-∞) <0.001
Abnormal Movement	10(15.4)	0(0.0)	<.001	24.8(1.4-∞) 0.001
False Cord				
Masses	0(0.0)	0(0.0)	NA	NA
Inflamed	3(4.6)	1(1.5)	0.61	0.3(0.03-3.1)
Edematous	4(6.2)	1(1.5)	0.36	0.2(0.03-2.2)
True Vocal Cords				
Edematous	2(3.1)	2(3.1)	1.0	NA
Inflamed	2(3.1)	2(3.1)	1.0	NA
Vocal Polyps	2(3.1)	0(0.0)	0.15	5.2(0.2-∞) 0.50
Vocal Nodule	0(0.0)	2(3.1)	0.15	5.2(0.2-∞) 0.50
Abnormal Mobility	0(0.0)	0(0.0)	NA	NA

α: Odds Ratio (Fisher Exact)

Table 3: Distribution of Severity of Perceptual Parameters of Type Diabetic and Controls

	Diabetic n (%)	Control n (%)	p value
Grade			
Normal	44(67.7)	56(86.2)	
Mild	20(30.8)	9(13.8)	0.037*
Moderate	1(1.5)	0	
Roughness			
Normal	42(64.6)	61(93.8)	
Mild	23(35.4)	4(6.2)	0.000*
Moderate	0	0	
Breathiness			
Normal	56(86.2)	59(90.8)	
Mild	9(13.8)	6(9.2)	0.292
Moderate	0	0	
Asthenia			
Normal	59(90.8)	64(98.5)	
Mild	6(9.2)	1(1.5)	0.063
Moderate	0	0	
Strain			
Normal	41(63.1)	50(76.9)	
Mild	24(36.9)	15(23.1)	0.027*
Moderate	0	0	

Table 4. Phonatory Symptoms and Relationship with Features of Established or Severe Diabetic Mellitus

	Greater than 10 years		**Poor Glycemic Control**		**Neuropathy**		**Xerostomia**	
	N=65		**N=65**		**N=65**		**N=65**	
	n (%)	**OR (95%CI)**	**n (%)**	**OR (95%CI)**	**n (%)**	**OR (95%CI)**	**n (%)**	**OR (95%CI)**
	p	**p**	**p**	**p**	**p**	**p**	**p**	**p**
Voice Straining	**6(9.2)**	**3.9**	**13(20)**	**2.5**	**11(16.9)**	**5.5**	**9(13.8)**	**2.7**
	0.06	(0.9-7.3)	0.07	(1.0-8.0)	0.01	(1.6-8.7)	0.09	(0.8-8.4)
		0.08		0.07		0.01		
Vocal Tiring	**6(9.2)**	**5**	**12(18.5)**	**2.8**	**11(16.9)**	**7.6**	**7(10.8)**	**1.8**
	0.03	(1.1-2.5)	0.13	(0.8-10. 0)	0.01	(2.2-6.6)	0.34	(0.6-5.6)
		0.05		0.11		0.01		0.37
Hoarseness	**1(1.5)**	**0.29**	**10(15.4)**	**2.6**	**7 (10.8)**	**2.7**	**7(10.8)**	**2.7**
	0.09	(0.0-2.5)	0.21	(0.5-6.8)	0.1	(0.8-8.9)	0.1	(0.8-8.9)
		0.43		0.49		0.12		0.12

Illustrations

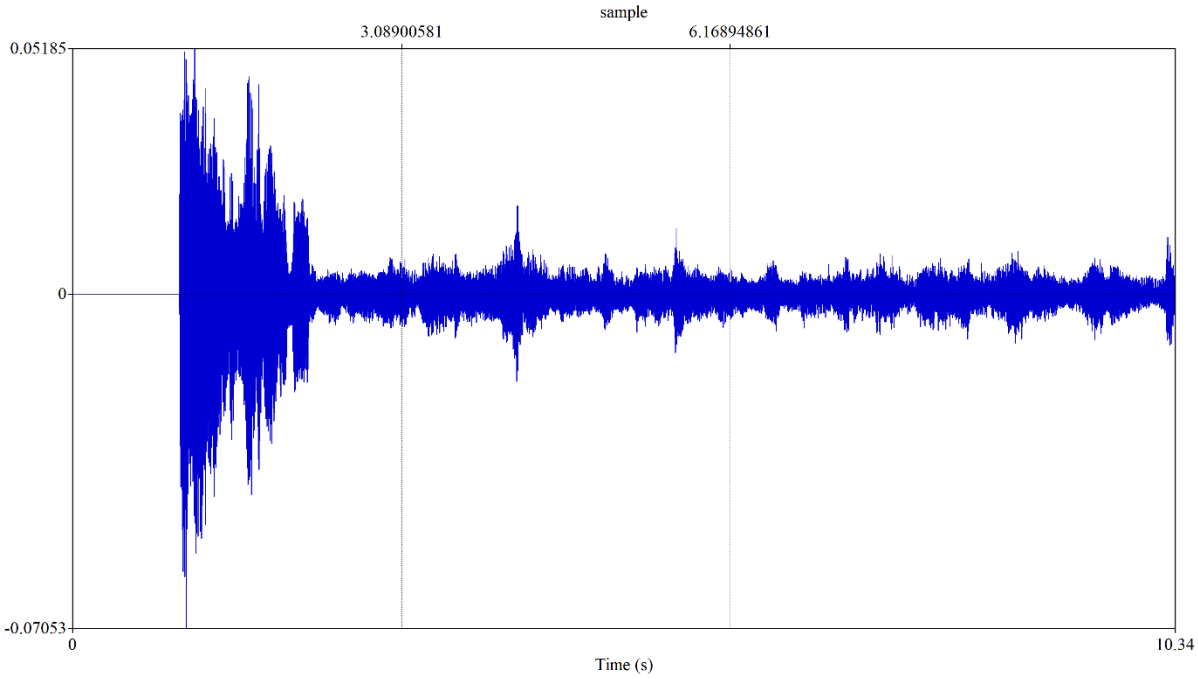

Figure 1. Sample spectrograph of one of the subjects showing a selection of consistent segments from 3.1 seconds to 6.2 seconds.

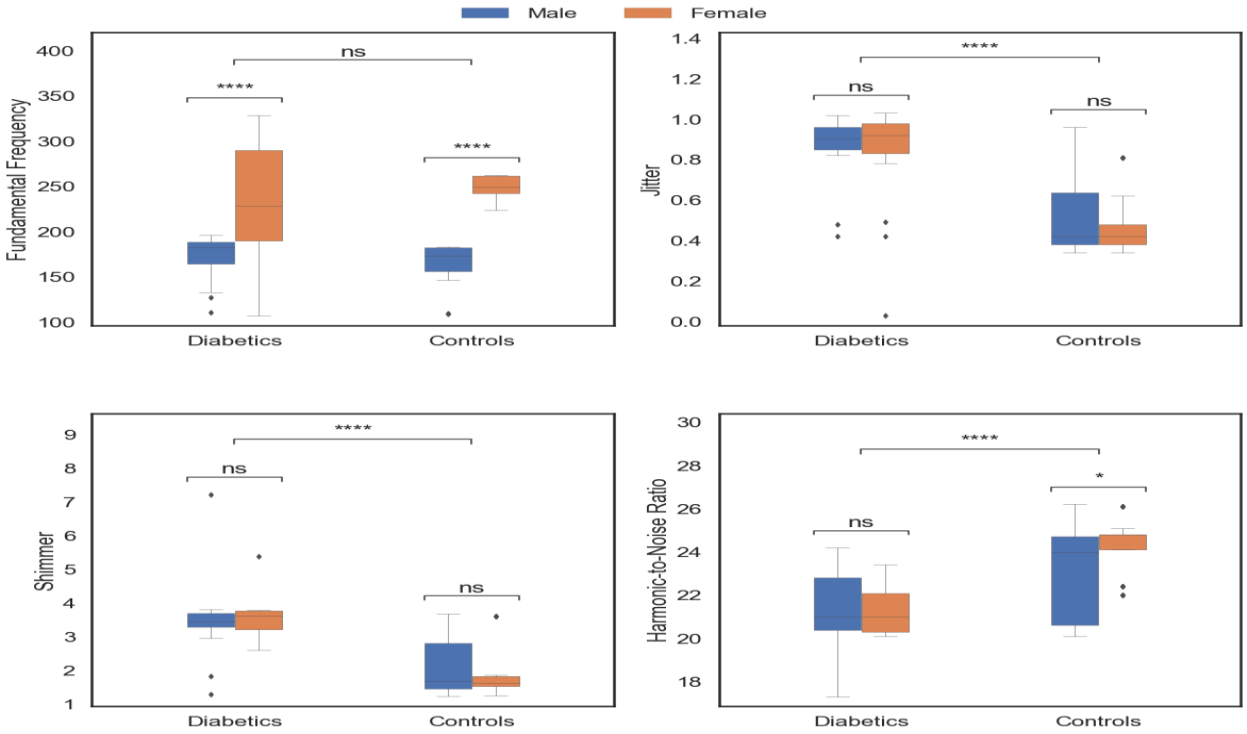

Figure 2. Comparison of acoustic parameters (AP) between the T2DM group and control subjects (*: p<0.05, **: p < 0.01, ***: p < 0.001, ****: p < 0.0001)

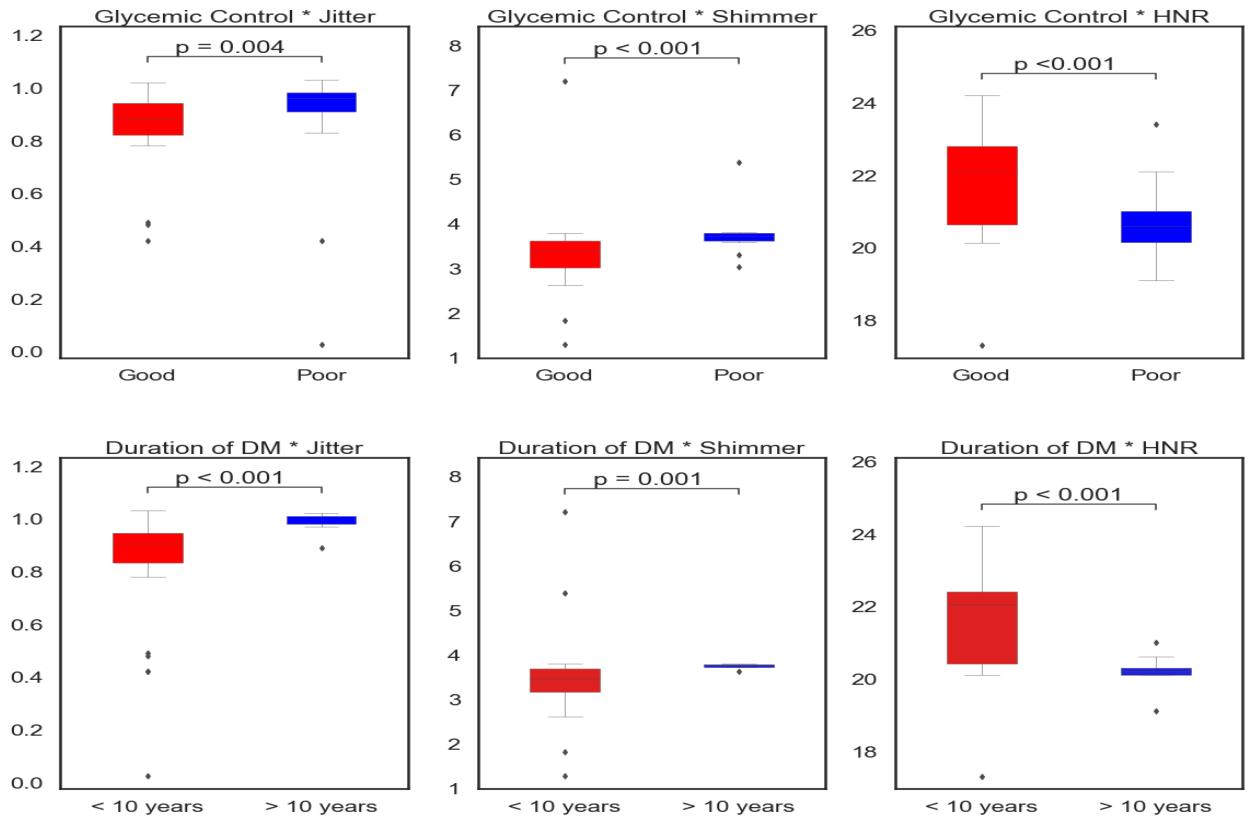

Figure 3. Relationship between acoustic parameters and features of established DM (Glycemic control and Duration of Diabetes)

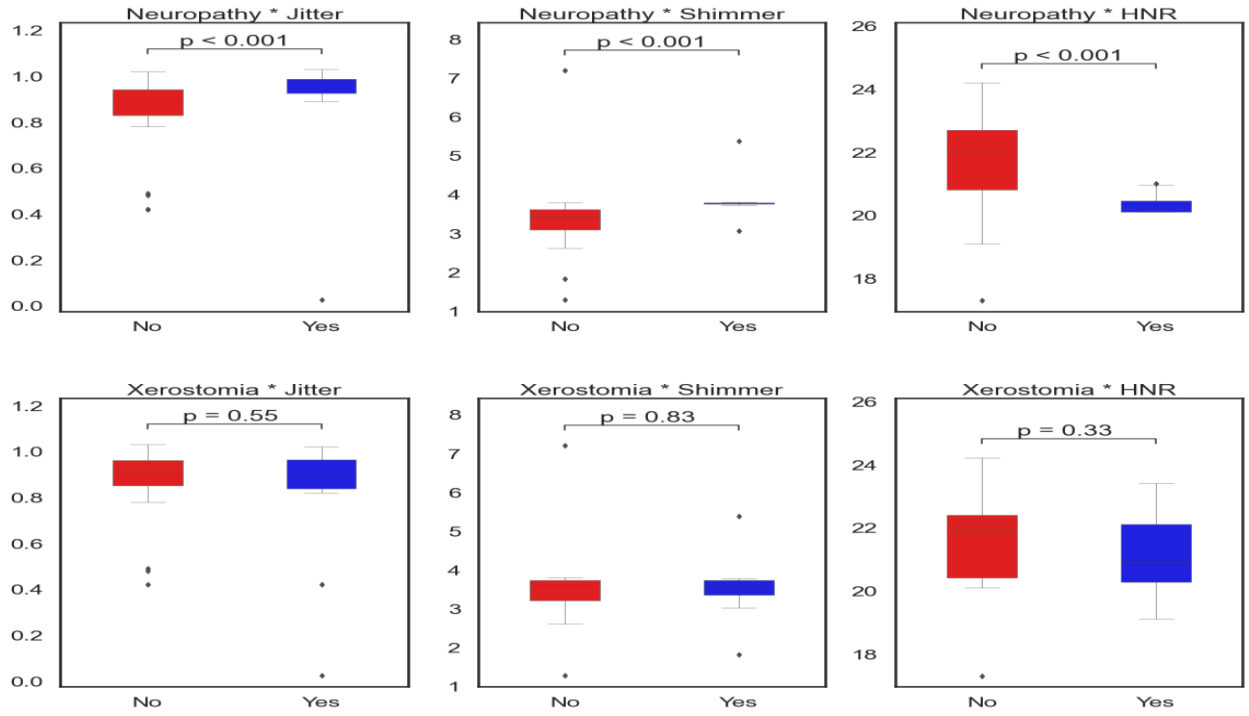

Figure 4. Relationship between acoustic parameters and features of established DM (Neuropathy and Xerostomia)

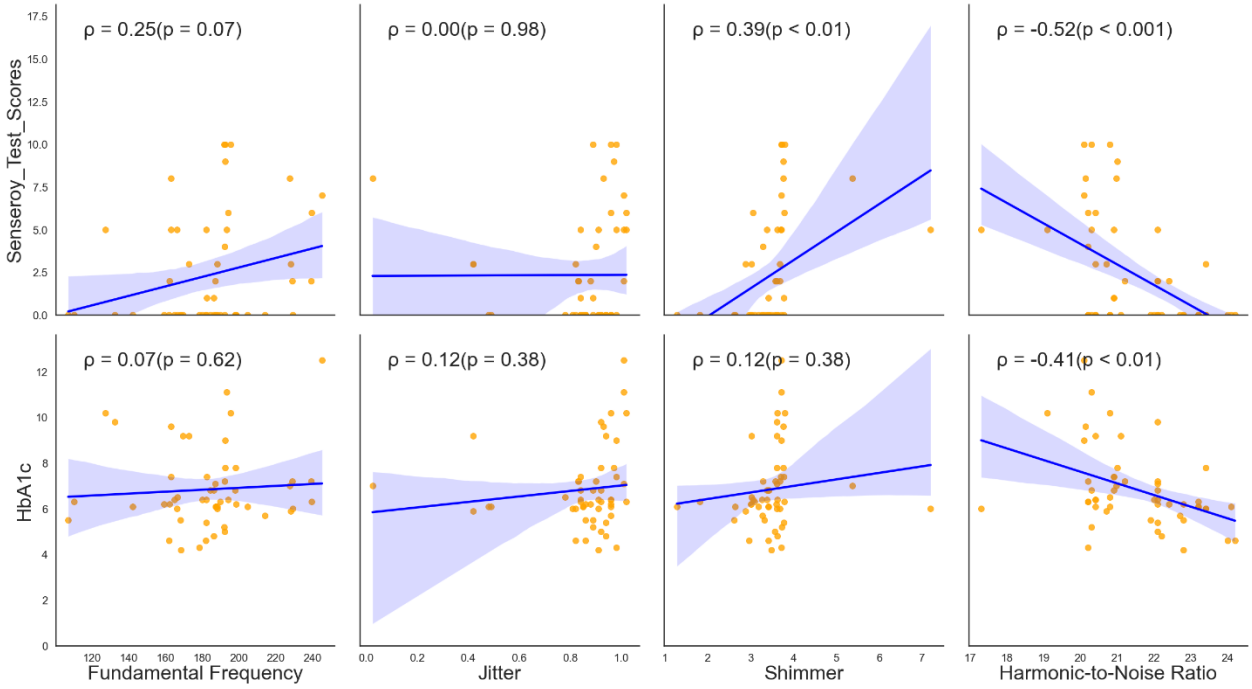

Figure 5. Correlation between sensory test score, HbA1c and acoustic parameters and HbA1c