Voice Evaluation in Patients with Hyperthyroidism

Original Article

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ABSTRACT

Background: Several studies reported voice changes in patients with thyroid disorders.
Objective: The objective of this study was to examine the voice characteristics of a group of patients with hyperthyroidism.
Patients and Methods: Twenty-one patients with clinical hyperthyroidism and Twenty-one healthy volunteers in the age range 24-55 years were subjected to voice assessment using both subjective (auditory perceptual assessment) and objective tools (acoustic and aerodynamic analyses).
Results: Despite the absence of perceptual voice changes in our patients with hyperthyroidism, subtle changes in the acoustic and aerodynamic parameters could be detected with a trend towards laryngeal dysfunction. Maximum phonation time and Harmonic/Noise ratio were significantly lower, and shimmer was significantly higher in hyperthyroid patients when compared to the reference group. Pitch and jitter were also higher in hyperthyroid patients, but the difference was not statistically significant.
Conclusion: These findings provide evidence that elevated levels of thyroid hormones potentially affect the phonatory function of the vocal folds.

Key Words: Acoustic; aerodynamic, hyperthyroidism; voice.

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INTRODUCTION

Voice production by the human larynx is a highly specialized and organized function that depends on multiple systems, including a properly functioning nervous system, a healthy respiratory system, and a physiologically active upper airway tract[1]. Vocal quality is greatly affected by hormones. Even though plenty of hormones are produced in the body, sex hormones and thyroid hormones directly affect the voice[2].

The thyroid gland secretes thyroxine (T4) and triiodothyronine (T3) hormones that are important for synthetizing proteins and controlling basal metabolism[3]. Evidence has shown that thyroid hormone receptors are found in the laryngeal tissue, and this suggests that thyroid hormones are vital for laryngeal development, physiology, and function[4].

Hyperthyroidism results in multi-system affection. It usually causes fatigue, palpitations, tremors, sleep disturbance, anxiety, weight loss, heat intolerance, perspiration, and polydipsia[5]. Excess thyroid hormone results in voice changes such as mild vocal instabilities, including "shaky" voice, breathy quality, and decreased loudness[6]. The symptoms of hy¬pothyroidism are more subtle than those of hyperthyroidism, and voice changes are one of the well-known symptoms of hypothyroidism[7]. Studies have shown that voice changes are present in 27% of patients with hyperthyroidism and 2%-98% of patients with hypothyroidism[8].

The majority of studies on voice changes in thyroid patients have focused on the impact of hypothyroidism on vocal function or voice changes post-thyroidectomy. However, few studies investigated the effect of hyperthyroidism on voice. This study aimed to examine the voice characteristics of a group of patients with hyperthyroidism, which would allow for early detection and a better understanding of voice changes in these patients.

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PATIENTS AND METHODS:

Study Design:

Observational comparative cross-sectional study from consecutive patients with clinical hyperthyroidism who were referred to the outpatient clinic of Phoniatrics from the endocrinology unit (internal medicine department).

Subjects:

This study was conducted on 42 patients in the age range 24-55 years, who were divided into two groups. The first group (the patient group) consisted of 21 patients with hyperthyroidism with a mean age of 39 (± 12) years. The reference group consisted of 21 healthy volunteers (with perceptually normal voice quality without thyroid disorder) with a mean age of 34.6 (± 6.6) years. The patient selection criteria were medical diagnosis of symptomatic hyperthyroidism, no history of previous surgical intervention in the neck or larynx, absence of other known causes of voice changes (such as vocal fold lesions, vocal fold paralysis, and current respiratory tract infection), patients did not receive previous voice therapy, and they were not smokers or ex-smokers. The patient group was further divided into two subgroups. The first subgroup comprised 11 patients with clinical hyperthyroidism under medical antithyroid treatment for no less than one month, in the form of carbimazole and beta-blocker. The second subgroup comprised 10 newly discovered patients with clinical hyperthyroidism but not started medical antithyroid treatment. The study was approved by the Institutional Research Board of Mansoura faculty of medicine. All participants signed a consent form.

Methods:

Hyperthyroidism diagnosis was made at the endocrinology unit, Internal Medicine department, and determination of hormones in serum (thyroid-stimulating hormone [TSH], triiodothyronine, thyroxine). The blood samples (3-5ml) were collected from each patient, centrifuged at 3000-5000 revolutions per minute where enzyme-linked immunosorbent assay (ELISA) by HUMAN diagnostics worldwide kits have been adopted as thyroid hormone assay method[9].

All participants were subjected to voice evaluation in the outpatient clinic of Phoniatrics at Mansoura University Hospital, using the following assessment protocol:

Subjective voice evaluation

Auditory perceptual assessments of voice (APA) were carried out using a modified GRBAS (Grade, Roughness, Breathiness, Aesthenia, Strain) scale[10] with four grades from 0 (normal) to 3 (severe dysphonia). A dynamic microphone and a laptop were used to record APA. Perceptual analysis was conducted by two phoniatricians experienced in the assessment of voice disorders.

Objective voice evaluation

Acoustic analysis was conducted in a quiet room with a dynamic microphone 3-cm from the subject's mouth. The subject was instructed to produce a prolonged /a/ sound recorded via a laptop. The middle portion of each vowel production was analyzed using PRAAT 64-bit edition[11] to determine the fundamental frequency (Hz), jitter (%), shimmer (%), and harmonic to noise (H/N) ratio (dB).

For aerodynamic analysis, maximum phonation time (MPT) was calculated using a stopwatch during the production of sustained /a/ sound at comfortable loudness and pitch after taking a deep breath.

Laryngoscopic examination of the patient group was performed with a 70° rigid endoscope. The laryngoscopic finding was bilateral normal vocal folds mobility and no pathological laryngeal lesions. Patients with abnormal laryngeal findings were excluded from the study.

Statistical Analysis:

Data entry and analysis were done by the statistical package of social sciences "SPSS" version 23. Qualitative variables were summarized in number & percent. Chi-square test was used to compare qualitative variables in different groups. Quantitative variables were described as mean & standard deviation for normally distributed data. The median, minimum, and maximum were used to describe non-normally distributed data. The Shapiro–Wilk test was employed to determine whether the data had a normal distribution. An independent t-test was used to compare two different means and a one-way ANOVA to compare three different means. For non-normally-distributed data, the Mann-Whitney test was used to compare variables in two different groups and the Kruskal Wallis test in three different groups. Statistical significance is defined as a level of significance less than 0.05.

RESULTS:

Demographic and basic data:

The patient group consisted of 21 patients with hyperthyroidism with a mean age of 39 (± 12) years. Three patients were males (14.3%), and eighteen patients were females (85.7%). The reference group consisted of 21 healthy volunteers with a mean age of 34.6 (± 6.6) years, including two males (9.5%) and 19 females (90.5%). Both groups were matched for age and gender. None of the subjects was a professional voice user (Table 1).

Table 1: Demographic characteristics of the studied groups:

	Patients group n=21	Reference group n=21	*P-value*
Age			
Mean (SD)	39.0 (12.01)	34.6 (6.6)	0.1
Gender Number (%)			
Male	3 (14.3)	2 (9.5)	1.00
Female	18 (85.7)	19 (90.5)	
Residence Number (%)			
Urban	7 (33.3)	12 (57.1)	0.3
Rural	14 (66.7)	9 (42.9)	

The most frequent manifestation of hyperthyroidism in the patient group was shortness of breath (62%), followed by fatigue and loss of weight (28.6% each). The disease duration ranged from 1 month to 9 years (median 12 months) (Table 2).

Table 2: Baseline symptoms among hyperthyroid patients

Variable	Studied Patients (n=21) Number (%)
#Clinical symptoms	
Shortness of breath	13 (62%)
Fatigue	6 (28.6%)
Loss of weight	6 (28.6%)
Exophthalmos	4 (19%)
Nervousness	2 (9.5%)
Disease duration in months	
Median	12.0
Min-max	(1.0-108.0)

 # Total number is not absolute

It was found that the median of T3, T4, and TSH levels in the hyperthyroid subgroup that did not receive medical treatment was 1.01 (0.4-1.4), 3.4 (1.4-34.0), 0.01 (0.005-0.05) ng/dl, respectively.

3.2. Subjective voice evaluation:

No dysphonia was detected in any of the patients enrolled in the study.

3.3. Objective voice evaluation:

Maximum Phonation Time and H/N ratio were reduced in hyperthyroid patients compared to the reference group with a statistically significant difference ($p<0.05$). Shimmer was significantly higher in hyperthyroid patients than in the reference group ($p<0.05$) (Figures 1 and 2). Pitch and jitter were also higher in hyperthyroid patients, but the difference was not statistically significant ($p>0.05$) (Table 3).

Table 3: Comparison of aerodynamic and acoustic measures among studied groups:

	Patients group n=21	Reference group n=21	*P-value*
MPT			
Mean (SD)	10.8 (4.1)	13.8 (4.2)	0.02*
Median	10.0	14.0	
#Pitch			
Median	226.1	218.4	0.1
(min-max)	(90.1-269.5)	(87.5-264.7)	
Jitter			
Mean (SD)	0.37 (0.1)	0.33 (0.1	0.4
Median	0.31	0.32	

#Shimmer			
Median	2.37	1.65	0.002*
(min-max)	(1.2-10.7)	(0.87-5.06)	
H/ N ratio			
Mean (SD)	22.9 (4.2)	26.3 (3.1)	0.006*
Median	23.4	26.3	

MPT: maximum phonation time, SD: standard deviation, H/N: Harmonic /Noise Independent t-test, #Mann -Whitney test

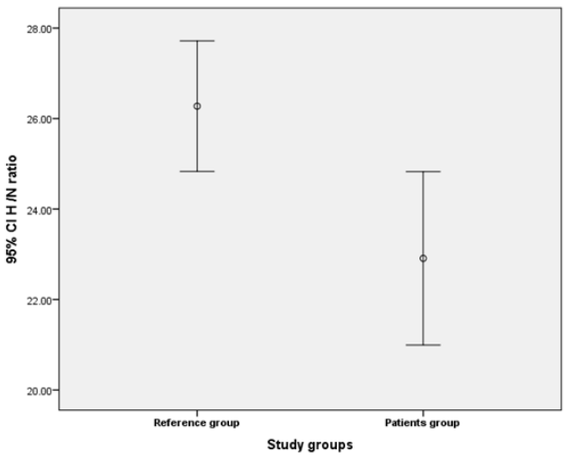

Fig. 1: Error bar chart for comparison of average harmonic noise (H/N) ratio among studied groups

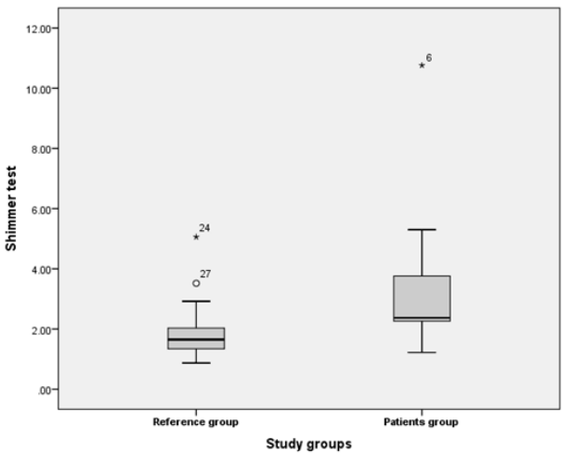

Fig. 2: Box-plot graph for comparison of shimmer among studied groups

When comparing the reference group with the two patient subgroups, none of the parameters showed a significant difference between patients receiving and patients not receiving medical antithyroid treatment. However, the shimmer, jitter, and H/N ratio values were better in the subgroup receiving antithyroid therapy. On the other hand, both patient subgroups showed lower H/N ratio and higher shimmer values than the reference group with statistically significant differences ($p<0.05$) (Table 4).

Table 4: Comparison of aerodynamic and acoustic measures among

	Patients receiving treatment (n=11)	Patients not under treatment (n=10)	Reference group (n=21)	*P-value*
MPT				
Mean (SD)	10.7 (4.02)	10.9 (4.4)	13.8 (4.2)	0.08
Median	10.0	11.0	14.0	
#Pitch				
Median	221.1	226.9	218.4	0.3
(min-max)	(140.0-269.5)	(90.1-262.7)	(87.5-264.7)	
Jitter				
Mean (SD)	0.31 (0.1)	0.43 (0.2)	0.33 (0.1)	0.2
Median	0.28	0.37	0.32	
#Shimmer				
Median	2.37 C	2.38 C	1.65	0.009*
(min-max)	(1.22-4.9)	(1.28-10.7)	(0.87-5.06)	
H/N ratio				
Mean (SD)	23.4 (3.2)C	22.4 (5.1)C	26.3 (3.1)	0.02*
Median	24.3	22.9	26.2	

MPT: maximum phonation time, SD: standard deviation, H/N: Harmonic /Noise
One way ANOVA, # Kruskall Wallis test

studied groups as regards treatment of hyperthyroidism:

DISCUSSION

Thyroid hormones are essential for the growth and development of many vital organs. The thyroid hormones affect humans' voices highly; this is interpreted by the presence of receptor alpha (TR-alpha) in the lamina propria, the glandular structures, and the thyroid cartilage, whereas TR-beta was existent only in the lamina propria[4]. This indicates the importance of thyroid hormones in voice production and laryngeal development.

Hyperthyroidism results in multi-system affection, which includes the larynx. Our study aimed at studying subjective and objective voice characteristics of patients with hyperthyroidism. Twenty-one patients with clinical hyperthyroidism and twenty-one healthy volunteers were subjected to voice assessment using subjective and objective means.

The female predominance in the patient group in our study was in agreement with previous studies by Bone *et al*.[12] and Costa and Pernambuco[13], as thyroid diseases are hormonal dependent and common in females with a 4:1 female to male ratio.

The objective voice assessment, particularly the acoustic analysis, has received considerable attention because of its low cost, easy applicability, and quantitative output[14]. According to de Felippe *et al*.[15], "the differences in the programming of the various acoustic analysis systems, as well as the use of recording criteria and computers, microphones, and other devices make each one of these systems a single one, thus, precluding a single normalization. Therefore, users should base themselves on their own normalization".

Jitter and shimmer are both parameters of acoustic analysis. They refer to frequency and amplitude variation, respectively, from cycle-to-cycle of sound waves[10]. Decreasing jitter and shimmer denotes better periodicity and symmetry in glottic wave vibration, which is reflected as a better subjective impression of voice.

The present results showed that the value of shimmer in the hyperthyroid group was significantly higher than that of the reference group. Similarly, jitter was higher in the hyperthyroid group, but the difference did not reach statistical significance. This might indicate that increasing the level of thyroid hormones has a potential effect on the vocal folds' frequency and amplitude of vibration.

H/N ratio is defined as the ratio between periodic and aperiodic components of a sound wave[16]. The periodic component arises from vocal fold vibration, whereas the aperiodic part follows from the glottal noise. Therefore high H/N ratio is associated with sonorant and harmonic voice.

Our results revealed that hyperthyroid cases had a lower H/N ratio than the reference group, with a statistically significant difference. This denotes that the voice of hyperthyroid cases is more liable to asthenia and dysphonia. As suggested by Kovacic[17], the general weakness and fatigue caused by hyperthyroidism reflect on laryngeal and respiratory musculature causing asthenic voice quality.

The non-significant difference between our patients and the reference group as regards fundamental frequency was contradictory to the result of Kovacic[17], who reported that female subjects diagnosed with hyperthyroidism demonstrated low fundamental frequency. The latter author stated that "deep voice is the most remarkable and should be added to clinical features of hyperthyroidism".

Maximum phonation time (MPT) is one of the aerodynamic measures considered a good functional indicator of glottal competence[18]. It usually ranges from 15-20 seconds for adults[19]. Our results showed a decrease in the mean value of MPT of hyperthyroid cases compared to the reference group with a statistically significant difference. This could be explained by respiratory muscle weakness with reduced subglottic pressure in patients with hyperthyroidism, as suggested by Junuzović-Žunić *et al*.[20].

Although the results of acoustic and aerodynamic assessments were not in favor of the hyperthyroid cases, none of them had dysphonia. This is attributed to the fact that the shimmer, jitter, H/N ratio, and MPT values did not reach the threshold of pathological voice. Nevertheless, these results make hyperthyroid patients more vulnerable to dysphonia than their euthyroid peers. Moreover, this denotes that increasing the levels of T3 and T4 may cause subclinical affection of phonatory functions of the larynx. Indeed, alteration of voice quality in patients with hyperthyroidism was reported in studies such as Youssef *et al*.[21]. Pfaff *et al*.[22] mentioned that voice problems are common presenting complaints in patients with thyroid disorders.

Even when treated preoperatively, hyperthyroidism is frequently associated with poor voice outcomes[22]. Muscle weakness, dehydration, tremors, as well as physiologic changes in laryngeal structure could contribute to voice changes in hyperthyroid patients[23]. As stated by Altman *et al*.[4], thyroid hormone receptors may play a role in the histologic and physiologic alterations in a voice that occur in thyroid dysfunction.

The present study results are in line with the results of the Kovacic[17] study, which indicated that acoustic voice characteristics and laryngeal efficiency in patients with hyperthyroidism fall outside normal ranges. However, contrary to the present results, Birkent *et al*.[24] assumed that the acoustic parameters could not detect subtle vocal fold changes. It is unlikely to identify any change without a significant vibra¬tory or epithelial disease.

The present study revealed a non-significant difference between both patient subgroups when comparing the acoustic and aerodynamic results. However, the shimmer, jitter, and H/N ratio values were better in the subgroup receiving antithyroid therapy. The non-significant difference might be attributed to insufficient treatment duration. As stated by Hari Kumar *et al*.[1], voice changes caused by the thyroid gland disorders may disappear completely within 3-6 months after achieving euthyroidism.

Regardless of the limitation by the small sample size, this study indicates that the effect of hyperthyroidism on vocal function measures is an area of further research.

CONCLUSION

Despite the absence of perceptual voice changes in our patients with hyperthyroidism, subtle changes in the acoustic and aerodynamic parameters could be detected with a trend towards laryngeal dysfunction. This provides evidence that elevated levels of thyroid hormones potentially affect the phonatory function of the vocal folds. However, further studies need to be conducted with larger samples and with various objective voice measurements applied to better understand the laryngeal status in hyperthyroid patients.

CONFLICT OF INTEREST

There are no conflicts of interest.

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