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RESEARCH ARTICLE

Assessment of altered voice physiology in hypothyroidism

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ABSTRACT

Background: Hypothyroidism is a common endocrine disorder in our country with a prevalence of 11%, voice is multidimensional and its production involves a complex arrangement between various organs such as oral and nasal cavity, pharynx, larynx, respiratory muscles, and entire respiratory tract, all of which function in a synchronized way on receiving central command from the brain. Reduced thyroid levels lead to altered voice production and voice quality. Hoarseness of voice that is observed in hypothyroidism is usually overshadowed by a plethora of other complaints. **Aims and Objectives:** The aim of the study was to profile and document the various voice changes in subjects with hypothyroidism using a comprehensive voice protocol. **Materials and Methods:** This cross-sectional study included 50 subjects with hypothyroidism (cases) with age- and sex-matched 50 euthyroid controls. Voice analysis was done on all subjects with hypothyroid on the day of diagnosis after obtaining the institutional ethical clearance. Both the groups underwent aerodynamic measurements, i.e., maximum phonation time (MPT), s/z ratio, acoustic analysis of voice, namely phonation profile, speaking profile, jitter, shimmer, fundamental frequency, and dysphonia severity index (DSI). Perceptual evaluation of voice was done using a grade, roughness, breathiness, asthenia, and strain (GRBAS) scale. Voice disorder outcome profile was used to document the effect of voice problem in day-to-day activities. **Results:** Change in voice and fatigue were the major complaint among the hypothyroid cases. MPT and s/z ratio were prolonged in hypothyroid cases when compared to controls. Objective voice analysis revealed a significant change in frequency range, shimmer, and DSI among the cases when compared to controls ($P < 0.05$). Parameters in GRBAS scale were deviant in hypothyroid cases when compared to controls and were statistically significant ($P < 0.05$). **Conclusion:** The alterations in various parameters of voice observed in hypothyroid patients when compared to euthyroid will help us in better understanding of the pathophysiological changes occurring in hypothyroidism pertaining to voice production.

KEY WORDS: Aerodynamic Evaluation; Acoustic Voice Analysis; Dysphonia Severity Index; Hypothyroidism; Perceptual Evaluation of Voice; Voice disorders

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INTRODUCTION

Voice is a complex physiological function and the most sophisticated version of it is seen among the humans. The more precise definition of voice is the acoustic output from the vocal tract that is characterized by their dependence on vocal fold vibratory patterns and the interaction of subglottal

pressure, tissue elasticity, and constriction within the airflow caused by the vocal folds. Sustained phonation is possible as long as pressure, flow and vocal fold approximation are maintained.[1,2] This coordination of phonatory and articulatory behavior represents arguably the most advanced sensorimotor system found in the human body. This complex physiological phenomenon can be altered by various causes such as inflammatory, structural, neoplastic, endocrine, and neuromuscular abnormalities.

Thyroid has many physiological effects and is vital for the normal growth, development, and the maintenance of basal metabolic rate. Larynx is an end-organ target for thyroid hormone and the impact of thyroid hormone on the developing larynx was proven in a frog model.[3] The presence of thyroid receptors in both male and female larynx of human cadavers has been demonstrated.[4] Change in voice quality is a commonly noted symptom in individuals with thyroid dysfunction. Deposition of proteoglycans in laryngeal and respiratory muscles, the presence of mucopolysaccharides and fluid accumulation in vocal folds, paresis of the vocal cord due to an enlarged thyroid gland, and edema of the vagal nerve are among the various causes for voice abnormalities seen in a hypothyroid patient.[5] The hoarseness is gradual in onset and progressive in nature, and the voice is of low pitch and has a roughness/raspy quality with a decreased range and vocal fatigue. Profiling and documenting these voice changes are essential for understanding the physiological basis and for further management. The objective of this study was to profile and analyze the voice changes in subjects with hypothyroid using a comprehensive voice analysis protocol.

MATERIALS AND METHODS

This was a cross-sectional observational study conducted among 50 subjects diagnosed with hypothyroidism visiting endocrinology Outpatient Department at a tertiary care hospital Sri Ramachandra University. Fifty sex- and age-matched controls were included in the study (sex ratio of F: M being 6:1). The Institutional Ethical Committee clearance was obtained for the study (REF: CSF/10/APR/09/14). All subjects (cases and controls) signed the consent form before the commencement of the study. Hypothyroidism was diagnosed based on serum thyroid-stimulating hormone (TSH) >10 mIU/L and low free T_4 (FT_4), and subjects were included based on the following criteria:

Inclusion Criteria for Hypothyroid Cases

a. Newly diagnosed hypothyroid cases in the age group (20–50 years).

Inclusion criteria for controls

a. Vocally healthy subject with perceptually normal voice quality without thyroid disorder.

Exclusion Criteria for Hypothyroid Cases and Controls

a. H/o allergic rhinitis, asthmatics, oral, laryngeal and pharyngeal malignancy, systemic illness, and acute respiratory illness during the procedure
b. H/o smokers.

Data Collection

A detailed history using a questionnaire and a complete physical examination was carried out on all the hypothyroid cases and controls. The new Zulewski score was used to assess the signs and symptoms in hypothyroid cases. Blood samples were collected for testing TSH and FT_4 (using ultrasensitive sandwich chemiluminescent immunoassay) in subject with hypothyroid and TSH in controls.

Voice Protocol

a. Perceptual assessment: Two experienced speech-language pathologists blindly rated voice sample on the grade, roughness, breathiness, asthenia, and strain (GRBAS) scale in spontaneous speech/reading/counting numbers. Voice profile pitch, loudness, voice quality, pitch breaks, and voice breaks in phonated voice were also assessed. GRBAS was rated on a four-pointing rating scale, i.e., 0 – normal, 1 – mild deviation, 2 – moderate deviation, and 3 – severe deviation
b. Aerodynamic measures: Maximum phonation time (MPT) and s/z ratio are the two simplest aerodynamic parameters used widely. MPT was noted as the maximum time an individual can sustain phonation after deep inspiration. They were asked to phonate the vowels/a/,/i/, and/u/and sustain/s/ and/z/as long as possible and its ratio was calculated
c. Acoustic analysis: Acoustic analysis was done using the lingWaves software. The following acoustic measures such as frequency (F_O) and intensity-related parameters, (I) jitter, shimmer, and dysphonia severity index (DSI) were analyzed. DSI was calculated using the following formula:

$$DSI = 0.13 \times MPT + 0.0053 \times F_O - High - 0.26 \times I - Low - 1.18 \times jitter\ (\%) + 12.4$$

A perceptually normal voice gives a maximum value of +5, whereas lesser values (to a minimum of −5) represent worsening degrees of dysphonia.

a. Self-evaluation of voice: Voice disorder outcome profile (V-DOP) developed by Mahalingam *et al.* in local language Tamil was used in assessing an individual's perception of his or her voice under physical, emotional, and functional domains.

Statistical Analysis

Data were analyzed using SPSS for Windows (version 17) software package. Differences between mean values for quantitative variables were evaluated using Student's *t*-test, Chi-square. Mann–Whitney U-test was used for analysis of nominal and ordinal variables. The correlation between variables was examined by Pearson's correlation of coefficient.

RESULTS

The mean age was 32.66 and 30.94 in the range of 20–50 years for cases and controls, respectively. The mean TSH among cases was 61.8 mIU/L while the mean TSH among controls was 2.1 mIU/L.

Voice-related Symptoms and Structural Abnormalities Seen among Hypothyroid Cases

The symptoms experienced by the hypothyroid cases were expressed using percentage analysis as shown in Table 1. About 32% of hypothyroid cases reported having a voice problem. The main complaints pertaining to voice in hypothyroid cases were change in voice including hoarseness (20%), vocal fatigue (10%), and slurring (2%). The average duration of the symptoms experienced by the hypothyroid cases was between 6 months and 1 year.

Perceptual Evaluation of Voice

Perceptual evaluation remains an important feature of voice assessment both in research and clinical practice. Results are reflected in Tables 2 and 3. Two experienced voice clinicians rated each blinded sample on the five parameters of the GRBAS scale and on pitch, loudness, voice quality, pitch break, and voice break. The voice sample was provided to the judges after randomizing the blinded samples. Since the perceptual judgment of voice involved two independent judges, an overall inter-rater reliability test was done and proven to be statistically significant overall perceptual qualities of voice revealed mild-to-severe deviance in grade, breathiness, and asthenia. Roughness and strain were perceived to have mild-to-moderate deviance. Deviation in the pitch was found in 24% of subjects. The severity of hoarseness which is quantified by the parameter G (relating to overall voice quality) and breathiness (parameter B) was the two most affected (72% ranging from mild to severe) voice parameters when compared to controls. There is a significant difference in the mean score of all the five perceptual parameters in the hypothyroid group when compared to controls. It is also noticeable that the mean score was above 1, indicating mild deviation from normal with respect to the overall grade of the voice (G) in the hypothyroid groups. Hoarseness as assessed by the voice pathologist was reported in 82% of hypothyroid cases and only in 6% of controls.

Table 1: Voice-related symptoms among hypothyroid cases

Voice complaints among hypothyroid cases	Expressed as percentage
Change in voice	20
Vocal fatigue	10
Slurring	2

Table 2: Distribution of the severity of perceptual evaluation parameters – GRBAS rating for cases and controls

Parameters of perceptual evaluation	Cases (%)	Control (%)	*P* value
Grade			
Normal	14 (28.0)	41 (82.0)	**0.001
Mild	19 (38.0)	8 (16.0)	
Moderate	13 (26.0)	1 (2.0)	
Severe	4 (8.0)	_	
Roughness			
Normal	28 (56.0)	47 (94.0)	**0.001
Mild	21 (42.0)	2 (4.0)	
Moderate	1 (2.0)	1 (2.0)	
Asthenia			
Normal	28 (56.0)	42 (84.0)	**0.003
Mild	15 (30.0)	8 (16.0)	
Moderate	7 (14.0)	_	
Breathiness			
Normal	14 (28.0)	36 (72.0)	**0.001
Mild	23 (46.0)	14 (28.0)	
Moderate	13 (26.0)	_	
Strain			
Normal	28 (56.0)	49 (98.0)	**0.001
Mild	15 (30.0)	1 (2.0)	
Moderate	7 (14.0)	_	

**Significant at $P<0.01$, GRBAS: Grade, roughness, breathiness, asthenia, and strain

Table 3: Comparison of perceptual evaluation parameters – GRABS classification

Parameters	Cases (Mean±SD)	Control (Mean±SD)	*P* value
Grade	1.14±0.9	0.2±0.45	<0.001
Roughness	0.46±0.5	0.08±0.3	<0.001
Asthenia	0.58±0.7	0.16±0.4	<0.001
Breathiness	0.98±0.7	0.28±0.5	<0.001
Strain	0.58±0.7	0.02±0.1	<0.001

GRBAS: Grade, roughness, breathiness, asthenia, and strain, SD: Standard deviation

Aerodynamic Assessment

Mean and standard deviation (SD) of MPT and s/z ratio are shown in Table 4. The simplest aerodynamic parameter of

voice is the MPT (in seconds). MPT in males and females was reduced (normal range for males being 25–35 s and for females between 15 and 25 s) and showed a statistically significant decrease ($P < 0.05$) when compared to controls in female hypothyroid cases. In this study, the mean ratio of s/z is 1.79 in hypothyroid female cases (normal ratio <1.40) and 1.29 in male hypothyroid cases.

Acoustic Analysis of Voice

Table 5 depicts the various parameters under acoustic analysis. Highest F_0 and the frequency range were significantly low ($P < 0.05$) among cases when compared to controls. SD of F_0 which reflects the deviation of F_0 from average was more in hypothyroid female cases (53.72–45.02%). Perturbation parameters such as jitter % and shimmer % along with intensity were measured in the study. Jitter and shimmer percentage were higher and statistically significant in hypothyroid cases when compared to controls ($P < 0.05$). Intensity-related parameters show that high I_O and the range of intensity were compromised in hypothyroid cases when compared to controls. The DSI revealed mild-to-severe deviation in male and female hypothyroid cases. There was a statistically significant decrease ($P < 0.05$) in DSI among hypothyroid when compared to euthyroid.

Subjective Self-perception

In this study, self-evaluation of voice in subjects with hypothyroid using V-DOP, the mean and SD for overall severity was 3.64 (2.80) in males and 2.73 (3.05) in female hypothyroid cases.

DISCUSSION

In the present study, a comprehensive voice analysis was conducted on 50 newly diagnosed hypothyroid cases and the results compared to 50 sex- and age-matched euthyroid. Subjective voice problems were noted in 32% of hypothyroid cases [Table 1]. Vocal fold edema (22%) was the most common structural abnormality seen [Table 6]. There was a mild-to-severe deviance in grade, breathiness, and asthenia components of perceptual evaluation of voice with a significant difference in the mean score of all the five parameters between the two groups [Tables 2 and 3]. MPT was reduced and s/z ratio increased among the hypothyroid subjects [Table 4]. Acoustic analysis of voice in Table 5 shows that jitter % and shimmer % were higher in hypothyroid cases and a statistically significant decrease in DSI was also observed.

Change in voice or hoarseness is one of the cardinal features of hypothyroidism.[6] Association of hypothyroidism with increased hyaluronic acid and accumulation of mucopolysaccharides leads to fluid retention and altered mass in the vocal folds which can present itself as hoarseness and vocal fatigue. Higher percentage of voice-related complaints has been reported by Gupta *et al.*, i.e., 40.9% with hoarseness

Table 4: Aerodynamic measurements in cases and controls

Aerodynamic measures	Males		*P* value	Females		*P* value
	Case	Control		Case	Control	
/a/(in seconds)	14.26 (3.72)	17.43 (4.46)	0.17	11.01 (3.43)	13.28 (3.31)	0.000**
/i/(in seconds)	15.29 (3.35)	19.29 (3.09)	0.03*	11.02 (3.74)	16.12 (3.55)	0.000**
/u/(in seconds)	13.57 (2.93)	17.71 (2.13)	0.01*	11.05 (3.77)	16.21 (3.66)	0.000**
s/z ratio	1.29 (0.46)	1.00 (0.11)	0.06	1.79 (1.10)	1.03 (0.17)	0.000**

*Significant at $P<0.05$, **Significant at $P<0.01$

Table 5: Mean and SD of acoustic voice parameters in patients with hypothyroidism and controls

Acoustic parameters	Males			Females		
	Case	Control	*P* value	Case	Control	*P* value
Fundamental frequency (Hz)	126.00 (17.21)	129.28 (45.58)	0.476	237.16 (45.02)	221.04 (53.72)	0.135
F_0 max. (Hz)	330.26 (70.62)	186.80 (44.03)	**0.001	352.39 (50.52)	292.87 (67.80)	**0.001
F_0 min. (Hz)	180.8 (46.03)	106.55 (10.24)	**0.001	196.83 (47.97)	185.80 (23.05)	0.178
F_0 range	188.85 (41.61)	80.05 (57.69)	**0.001	181.09 (50.52)	108.80 (50.01)	**0.001
Jitter (%)	0.08 (0.04)	0.25 (0.239)	0.08	0.11 (0.06)	0.22 (0.34)	0.40
Shimmer (%)	2.31 (0.60)	5.22 (1.89)	**0.002	2.06 (0.51)	5.52 (2.24)	**0.000
Intensity (high)	84.10 (6.22)	81.13 (4.71)	0.33	84.05 (5.15)	79.19 (4.93)	**0.000
Intensity (low)	56.36 (3.27)	55.71 (3.54)	0.73	56.12 (5.03)	57.74 (4.42)	0.116
Dynamic range	33.07 (5.89)	24.41 (7.16)	*0.03	32.53 (6.87)	24.23 (12.08)	**0.000
DSI	−1.72 (0.35)	0.68 (1.15)	*0.041	−2.15 (0.7)	0.00 (1.39)	**0.000

*Significant at $P<0.05$; **Significant at $P<0.01$, SD: Standard deviation

Table 6: Structural abnormalities of vocal cord

Structural abnormalities	Hypothyroid cases (expressed as percentage) (%)
Vocal fold edema	22
Left superior laryngeal nerve palsy	2

and 25.8% with vocal fatigue in their study.[7] In a similar study, Briknell *et al.* have reported patients suffering from mild hypothyroidism complained of voice weakness at the end of the day. Slurring of speech (2% in our study) can be attributed to dysarthria which is seen in hypothyroidism. The edematous swelling of laryngeal, hypopharyngeal structures with macroglossia is known to cause dysarthria in hypothyroidism.[8] Perceptual evaluation of voice using GRBAS scale helped us in subjectively assess the degree of hoarseness in hypothyroid cases when compared to controls. Although all the parameters of the GRBAS scale showed deviance, the parameter G which quantifies the overall voice quality was the most deviant one (36% ranging from mild to severe). The presence of increased levels of acid mucopolysaccharide in the vocal cord has been confirmed from biopsies taken from hypothyroid subjects.[9] This increase in mass changes the dynamics of the vocal fold function. Breathiness (B) which was the next most affected parameter is an auditory impression of air leak through an insufficiently closed glottis. Complete glottic closure is essential for normal sound production. The reasons for the incomplete glottic closure can be vocal paresis, vocal edema, increase in vocal mass thickness, muscle edema, and changed myoelectrical activity and all of which can be attributed to hypothyroidism. There is a significant difference in the mean straining score (S) among hypothyroid cases with 22% having mild-to-moderate straining compared to 1% in euthyroid controls. The reasons can be again paresis or paralysis of the nerve due to stretching or compression or edema, reduced vocal fold muscle activity. Netto *et al.* in their study of voice quality and vocal self-assessment after thyroidectomy have shown that 29.7% of the thyroid group had subjective voice change using GRBAS.[10] Six parameters of Consensus Auditory-Perceptual Evaluation of Voice were statistically significant among the experimental group of hypothyroid patients when compared to controls groups for the parameter of overall severity and roughness in a study by Lisa Allison.[11]

Increased vocal fold mass and slower rate of muscle contraction are also reported leading to in coordination in phonation and respiration as MPT also depends on the supportive respiratory component, especially the vital capacity. As one of the most common complaints among hypothyroid patients being vocal fatigue, the changes seen in MPT in our study are consistent, for MPT are known to be extremely sensitive to fatigue effects.[12] In this study, the mean ratio of s/z is 1.79 in hypothyroid female cases (normal ratio <1.40) and 1.29 in male hypothyroid cases. Eckel and Boone have shown that 95% of people who have difficulty in the movement of vocal folds have an s/z ratio of more than 1.40.[13]

The deposition of proteoglycans along the vocal cord, leading to excess mass, can hamper the higher vibratory rates which are reflected as reduced high $F_{0.}$ The same can be responsible for increasing the glottal resistance so that greater pressure is required to initiate and maintain vocal fold vibration, leading to increase in lowest intensity (low I_0). The highest and the lowest frequencies and the softest intensity are the most sensitive parameters for changes in voice quality. The deviance noticed in DSI is conceivable as the parameter such as highest F_0 is reduced, lowest Io is increased, and MPT is reduced. Changes in the perturbation measures such as jitter and shimmer can be explained due to the degree of irregularities in the vocal cord vibration most probably due to myxedematous infiltration of the vocal cords. This is consistent with Sataloff's observation that patients with hypothyroidism may present with abnormally low-pitched voices.[14] A negative correlation was seen between TSH value and DSI, implying that more the thyroid derangement, voice parameters tend to be significantly affected. The small sample size could be one of the reasons for it not being statistically significant though. Although 34% of hypothyroid patients had voice-related abnormalities, the low score in the subjective self-perception may be due to voice complaints getting submerged in the plethora of other symptoms of hypothyroidism. Another reason for the overall low severity was probably due to tolerance for negative outcome after a disability being noted higher in India.[15] Studies have shown that the perception of a disability with its effect on various aspect of an individual's life varies among people from different cultures.[16] Prakash *et al.* in a survey of 400 Indian professional voice users found that more than 50% of them do not seek consultation for their voice problem in immediate future.[17] These might be the various reasons for the lower score obtained in the overall severity in the voice-related quality of life questionnaire. Perception of lower pitch, roughness, decreased vocal range, and patient perceptions of vocal fatigue occur during hypothyroidism.[18] These findings are consistent with our study findings.

Limitations of the Study

The study is a cross-sectional study, the assessment of voice after treatment with thyroxine supplements could not be done. Being a pilot study, the sample size was small. Measuring vital capacity and calculating phonation airflow or PQ would have reduced the bias supporting respiratory mechanism compensating for vocal cord abnormalities.

CONCLUSION

Any of the speech subsystems such as respiration, phonation, resonance, and articulation can be affected by hypothyroidism.

The involvement of voice in a thyroid disorder is usually seen due to a locally infiltrating thyroid cancer, large compressive goiter, or following recurrent laryngeal nerve injury postoperatively.[19] However, in our study with only one case of the left superior laryngeal nerve palsy, no visible goiter (by inspection and palpation) the reason for various voice-related findings can be hypothesized to be due to the myxedematous infiltration of laryngeal tissues, nerve, or muscle, among newly diagnosed hypothyroid cases.

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