

## Voice and endocrinology

K. V. S. Hari Kumar, Anurag Garg<sup>1</sup>, N. S. Ajai Chandra<sup>1</sup>, S. P. Singh<sup>2</sup>, Rakesh Datta<sup>2</sup>

Departments of Endocrinology, <sup>1</sup>Anesthesiology and <sup>2</sup>ENT, Command Hospital, Chandimandir, Panchkula, Haryana, India

### ABSTRACT

Voice is one of the advanced features of natural evolution that differentiates human beings from other primates. The human voice is capable of conveying the thoughts into spoken words along with a subtle emotion to the tone. This extraordinary character of the voice in expressing multiple emotions is the gift of God to the human beings and helps in effective interpersonal communication. Voice generation involves close interaction between cerebral signals and the peripheral apparatus consisting of the larynx, vocal cords, and trachea. The human voice is susceptible to the hormonal changes throughout life right from the puberty until senescence. Thyroid, gonadal and growth hormones have tremendous impact on the structure and function of the vocal apparatus. The alteration of voice is observed even in physiological states such as puberty and menstruation. Astute clinical observers make out the changes in the voice and refer the patients for endocrine evaluation. In this review, we shall discuss the hormonal influence on the voice apparatus in normal and endocrine disorders.

**Key words:** Endocrinology, hormones, speech, voice

### INTRODUCTION

The human race has appreciated the importance of voice for many centuries that differentiates them from other living things on the planet. Voice is an important component that imparts self-confidence and socially acceptable behavior of an individual. The quality of the voice is an essential component of the self-assessment tool and reduces the social and physiological handicap of an individual.<sup>[1]</sup> Theory of evolution states that there is a bias regarding the vocalization. Higher degrees of vocalization are observed in females and in individuals with higher rank and social strata. Thus, voice helps in improving the self-esteem of an individual considerably. The pitch of the voice is considered as the main factor influencing the perception of the gender based on the voice. Volubility is defined as the amount of time spent in vocalizing or speaking and also the number of vocals or speech units per minute.<sup>[2]</sup>

**Corresponding Author:** Dr. K. V. S. Hari Kumar,  
Department of Endocrinology, Command Hospital, Chandimandir,  
Panchkula, Haryana, India.  
E-mail: hariendo@rediffmail.com

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The relation between voice and hormones was appreciated even in the medieval era. In ancient days, it was a common practice in Central Asia and European countries to castrate young male singers with exceptionally good voice. This prevented the cracking of their voice during puberty, giving them a long professional life. This practice was prevalent in 17<sup>th</sup> and 18<sup>th</sup> centuries and the popular castrated stars during that era include Baldassare Ferri (1610–1680) and Alessandro Moreschi (1858–1922).<sup>[3]</sup> Speech is one of the basic languages that exist in far higher proportion than the written languages. Vocalization helps in interspecies communication and humans utilize this for maximum efficiency. The current article aims to provide a brief overview of the role the endocrine system in voice alterations in health and disease.

### PHYSIOLOGY OF VOICE

The production of voice by the human being is a complex function which depends on multiple systems including a properly functioning neurological system, the respiratory

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system and an anatomically sound and physiologically active upper airway tract. Production of voice involves a complex coordination between various muscles and a temporary cessation of the vital functions of the upper aero-digestive tract like breathing and deglutition.<sup>[4]</sup> The larynx per se is a dynamic structure which can alter its shape and lumen by a system of articulated cartilages controlled by the Xth cranial nerve. Essentially, voice is produced by the vibration of a closed glottis during expiration. The air blast produced by the lungs induce a vibration in the glottis which produces voice which in turn gets articulated in the lubricated supra-laryngeal airway to form speech. This complex mechanism is important to understand as any change in any of these systems brought about by endocrine disorders would have an impact on the physiology of voice production. The characteristics of speech include the voice (audible sound waves), pitch (rate of vibration of the vocal folds), resonance (quality and depth in voice), intonation (variation of pitch without distinguishing of words), tone (pitch variation with distinguishing of words), intensity (pressure of sound), timbre (characteristic tone or quality), and articulation (production of vowels and consonant sounds).<sup>[5]</sup> The fundamental frequency (F0) corresponds to the number of vocal fold vibration cycles per second (Hz) and perceived as the pitch of the voice. The vocal cords in females are short and thin, leading to fast vibration, giving a higher pitch to their voice. There are changes in the F0 with age with the first change happening at puberty in males. Thereafter, with advancing age the pitch gets reduced in females and increases in males. The short vocal tract in the females gives the voice a higher resonance than male voice.<sup>[6]</sup>

## HORMONES AND VOICE

Voice is considered as an important secondary sexual characteristic which gives an independent imprint to the character and personality of an individual. The profound influence of sex hormones on the characteristics of voice is mediated by the hormonal receptors present within the vocal folds and apparatus.<sup>[7]</sup> Laryngeal structures are

exposed to the external environment constantly leading to alteration in the voice. There are certain sexual differences about the voice change observed during puberty.<sup>[8]</sup> Increased testosterone and dihydrotestosterone in males lead to increased bulk of laryngeal muscles and ligaments. This leads to drop in the higher octaves in the pitch of voice and frequent cracking. In the elderly males, the level of estrogens has a major influence on the voice rather than the prevailing androgens. A study done in an elderly population compared the voice characteristics in patients with and without hypogonadism. In patients with low estrogen levels, there is an increase in the mean fundamental frequency and a shift of the frequency ranges with alterations in the highest and lowest frequencies.<sup>[9]</sup>

In the females, the elevated estrogens and progestogens have minimal effect on the voice during puberty. The importance of hormonal influence on the female voice is appreciated during the cyclical changes of the menstrual cycle. The voice changes associated with the premenstrual syndrome are grouped under dystrophia premenstrualis.<sup>[10]</sup> The classical manifestation is the difficulty in singing high notes during the premenstrual period. There is laryngeal edema due to the high estrogenic state before the ovulation. However, the relative excess of androgens after menopause may lead to a slight drop in the pitch of the voice. Other voice changes observed after menopause include huskiness, vocal fatigue, and inability to reach high harmonics. These changes are appreciated more in professional singers and teachers who use the voice for living. Hormone replacement therapy has shown to reverse most of the observed voice changes in postmenopausal females.<sup>[11]</sup> The summary of the changes in voice during the normal aging process in females is given in Table 1.

## VOICE AND PITUITARY DISORDERS

The fundamental frequency is linked to the stature and the formant frequencies to multiple factors such as vocal tract, tongue, and facial bones. The excess and deficiency

**Table 1: Physiological changes of voice during female life cycle**

Phase of life	Hormonal change	Structural change	Voice change
Puberty	Increased estrogens Increased progestogens	Vocal cord growth	No significant change
Menstrual cycle			
Follicular phase	Increased estrogen	Laryngeal edema	Vocal fatigue
Ovulation	Increased estrogen	Thick vocal folds	Loss of higher harmonics
Ovulatory phase	Increased progesterone	Dry vocal folds	Premenstrual vocal syndrome
Menopause	Reduced estrogen Reduced progesterone Increased androgens	Reduced tonicity of laryngeal muscle Laryngeal muscles atrophy Ossification of laryngeal cartilage Vocal cords thicken Stiffening of vocal apparatus Reduced elasticity of the vocal cords	Decreased range Low intensity Vocal fatigue

of growth hormone (GH) have profound influences on the voice apparatus. GH excess results in the thickening of laryngeal cartilages and the vocal folds leading to a drop in voice frequency.<sup>[12]</sup> These patients are prone to the arytenoid cartilage dislocation leading to alteration of the voice. Patients with increased adrenocorticotropic hormone have voice changes akin to androgenization of the vocal apparatus. GH deficiency (GHD) results in the higher values of most formant frequencies due to the small sized oral and pharyngeal cavities. GHD results in nullifying the pubertal differences in the voice production and maintains a prepubertal acoustic quality of the voice. There is a negative association between the formant frequencies and the length of the maxilla and mandible in normal individuals. GHD results in reduced length of these bones leading to similar changes in the voice.<sup>[13]</sup> GHD also has shown to abolish the effects of aging on the fundamental frequency of the voice. Patients with GHD have reduced vocal perception, higher prevalence of laryngopharyngeal reflux, laryngeal constriction with a high pitch, and poor voice-related quality of life.<sup>[14,15]</sup>

## VOICE AND THYROID DISORDERS

Hoarseness of voice is a cardinal feature of the hypothyroidism along with the loss of range of voice. The hoarseness has a gradual onset and slow progression, thereby limiting the patient to notice the change of voice. These changes are due to the polysaccharide deposition and the fluid accumulation in the lamina propria of the vocal folds, paresis of the cords due to the thyroid gland enlargement, myxedema of the cricothyroid muscle and neural edema of the vagus nerve. Thyroid hormone receptors have been identified in the laryngeal tissue and the thyroid hormone plays an important role in the development of the larynx.<sup>[16]</sup> Thyroid hormone excess rarely leads to hoarseness of voice due to the stuttering movement of the vocal cords. The voice changes reverse completely within 3–6 months after achieving the euthyroidism.

Thyroid and parathyroid surgery has a risk of injuring the recurrent laryngeal nerve (RLN) leading to vocal cord paralysis and permanent dysphonia. Post-thyroidectomy distress is the term encompassing all the symptoms of voice and swallowing that affect the personal and professional life after undergoing thyroid surgery. The incidence of RLN injury after thyroid surgery varies between 1% and 13% based on the assessment methodology.<sup>[17]</sup> Transient RLN injury is seen in about 10% of patients, and permanent injury is seen in less number of individuals. The external branches of the superior laryngeal nerves (SLN) also remain in close proximity to the thyroid gland and are liable

to get damaged during the thyroidectomy. Voice assessment may be normal even in patients with RLN injury, and there may be voice disruption even with normal RLN and SLN.

The involvement of voice is seen mostly in patients with locally infiltrating thyroid carcinoma and large compressive goiter.<sup>[18]</sup> Routine preoperative screening using laryngoscopy in all patients before the thyroidectomy is a matter of debate and is determined by the institutional practice. Dysphonia is seen in the postoperative period, even in patients without RLN injury due to the laryngeal muscle edema, postintubation injury, injury to external laryngeal muscles and other reasons. Postoperative voice disorders that persist beyond 6 months after surgery are considered as permanent disorders, even without the presence of RLN injury. The symptoms do not differ between the males and females but are more noticeable in people with voice-based professions.<sup>[19]</sup>

## VOICE AND ADRENOGONADAL DISORDERS

Previous reports suggest that the untreated girls with Turner's syndrome have high pitched voices than healthy girls. This is due to the short stature homeobox haploinsufficiency leading to the smaller larynx, short stature, and partial androgen deficiency insufficiency. The use of oxandrolone along with the GH decreases the voice frequency and increases the depth of voice in a dose-dependent manner.<sup>[20]</sup> Congenital adrenal hyperplasia (CAH) is characterized by excess production of androgens despite medical management. The elevated androgens may lower the fundamental frequency in females by causing the laryngeal muscular hyperplasia. Women with CAH have felt the existence of a significant problem with the voice in their life and often speak with significantly lower mean fundamental frequency. The factors leading to voice problems in patients with CAH are late diagnosis, suboptimal therapy with glucocorticoids and high levels of androgens.<sup>[21,22]</sup>

Hyperandrogenism is a characteristic feature of the polycystic ovarian syndrome (PCOS). PCOS is seen in 10–15% of the adolescent females but the research pertaining to the voice changes in PCOS is scarce. Few authors have shown no impact of the hyperandrogenemia on the voice parameters, and others have shown that they have more vocal symptoms in comparison to the controls.<sup>[23]</sup> The conflicting results are explained by the prolonged hyperandrogenemia leading to structural changes in the larynx and also abnormal sensitivity of the laryngeal tissues to a normal level of androgens. Few reports suggest a threshold level of androgens (more than 200 ng/dl), for the appearance of voice changes in cases of androgen excess syndromes.<sup>[24]</sup>

Patients who have undergone female to male (FTM) gender reassignment and receiving high doses of androgens develop changes in the voice after 3–4 months of therapy. The transgender FTM patients develop the cracking in voice after a few months of the high dose androgens.<sup>[25]</sup> Pitch lowering abnormalities have been observed in about 10% of FTM population and correlates with the diminished androgen sensitivity in these individuals. The women receiving androgen therapy have been observed to notice the prevalence of vocal symptoms like lowering of the pitch of the voice and loss of control of singing tones. The male to female (MTF) transgender patients have more difficulties with reference to their voice. The prolonged exposure of the laryngeal apparatus to the high level of androgens results in failure to raise the F0 of the MTF patient's voice.<sup>[26]</sup> Laryngeal surgery was used by very few authors, and the results have generally been disappointing with the same.<sup>[27]</sup>

## VOICE AND DIABETES

Diabetes mellitus *per se* has no influence on the vocal apparatus. The effect is indirectly mediated through the hyperglycemia-induced alteration in the fluid and electrolyte balance. Xerostomia is a common accompaniment of long standing diabetes and autonomic neuropathy. This may reduce the lubrication and leads to difficulty in the phonation. Neuropathy may impact the small muscles of the larynx leading to improper generation of the voice. Sensory neural hearing loss is a common feature in advanced diabetes and all these patients tend to speak in a higher pitch to compensate for the loss. Few authors have shown that the laryngopharyngeal reflux disease (LPRD) is more common in diabetes.<sup>[28]</sup> LPRD is seen in about one-fifth of the study population and is associated with poor glycemic control, autonomic neuropathy, obesity and use of drugs that impact the lower esophageal sphincter. The LPRD resulted in increased prevalence of laryngeal symptoms in diabetes like throat clearing, lump in throat and annoying dry cough in diabetes patients.

## VOICE AND HORMONAL PREPARATIONS

The use of oral contraceptives, estrogen, androgen preparations also influence the changes similar to the pathological conditions as described above. Long standing use of androgens may have permanent masculinizing effects on the female voice. Hormone therapy results in significant lowering of the fundamental frequency, hoarseness in voice quality, difficulty in projecting the speaking and singing voices.<sup>[29]</sup> The vocal symptoms reverse partially after the withdrawal of the offending drug. The permanent changes are attributed to the muscle tissue

changes, coordination dysfunction, and proprioceptive dysfunction. The implicated drugs include danazol, testosterone, and decadurabolin.<sup>[30]</sup> Oral contraceptive pills inhibit the ovulation and have multiple effects on the voice quality. Estrogens lead to hypertrophy of the laryngeal mucosa and increased secretions of the laryngeal glandular cells. Progesterone leads to dryness and congestion of the vocal folds just before the menstruation.

## CONCLUSION

The human voice is intricately linked with the endocrine system of the individuals. Gonadal and thyroid hormones play a major role in voice alterations, and all other hormonal axes do have a minor role in the production of the voice. The hormonal influence on voice persists throughout the lifespan of an individual and is different in males and females. The changes are important in certain professionals such as teachers and singers. The clinicians should have a high index of suspicion to identify an endocrine abnormality with an unexplained change in the voice.

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