CoDAS
ISSN 2317-1782 (Online version)

Original Article
Artigo Original

Vocal profile of 46,XX individuals with congenital adrenal hyperplasia

Perfil vocal de indivíduos 46,XX com hiperplasia adrenal congênita

Paloma Cristina Rodeiro Neves[1]
Maria Betânia Pereira Toralles[1]
Renata D´arc Scarpel[1]

Keywords

Congenital Adrenal Hyplerplasia
Disorders of Sex Development
Voice
Voice Quality
Auditory Perception

ABSTRACT

Purpose: Describe the vocal profile of 46,XX congenital adrenal hyperplasia (CAH) patients followed up at the Genetics Outpatient Clinic of the Federal University Bahia (GOC-UFBA). **Methods:** This is a descriptive, exploratory, cross-sectional study. The study sample consisted of 28 volunteers: 14 individuals diagnosed with CAH, followed up by the multiprofessional team of the GOC-UFBA, and 14 46,XX individuals without vocal changes and endocrine and/or genetic pathologies. Voice sample collection was performed individually in a quiet environment with participants properly seated. Acoustic (PRAAT program) and auditory-perceptual (Consensus Auditory-Perceptual Evaluation of Voice - CAPE-V) analyses were conducted. **Results:** In the qualitative assessment of pitch, eight (61.54%) patients in the CAH group showed low vocal pattern and eight (61.54%) individuals in the group without CAH presented high vocal pattern. There were statistically significant differences between the groups only for the following vocal attributes of the CAPE-V: overall severity (p=0.01), roughness (p=0.00), and pitch (p=0.01). No statistically significant difference was observed in the other acoustic parameters investigated (p>0.05). **Conclusion:** The present study demonstrated that 46,XX CAH individuals, even when submitted to hormone therapy, present rough, low, deviant voice.

Palavras-chave

Hiperplasia Adrenal Congênita
Transtornos do Desenvolvimento Sexual
Voz
Qualidade Vocal
Percepção Auditiva

RESUMO

Objetivo: Descrever o perfil vocal de indivíduos 46,XX com hiperplasia adrenal congênita, acompanhados no Ambulatório de Genética da Universidade Federal da Bahia (UFBA). **Método**: Trata-se de um estudo descritivo e exploratório, com corte transversal. A amostra foi de conveniência e participaram do estudo 28 voluntários, 14 diagnosticados com hiperplasia adrenal congênita, acompanhados pela equipe multiprofissional do Ambulatório de Genética da UFBA, e 14 indivíduos 46,XX sem alterações vocais e ausência de patologia de cunho endócrino e/ou genético. A coleta das vozes foi realizada individualmente, em um ambiente silencioso, com as participantes devidamente sentadas. Realizaram-se análises perceptivo-auditiva (CAPE-V) e acústica. **Resultados:** Em relação ao julgamento qualitativo do *pitch*, verificou-se que oito (61,54%) pacientes do grupo com hiperplasia adrenal congênita apresentaram um padrão vocal agravado e 8 (61,54%) do grupo sem a doença apresentaram um padrão vocal agudizado. Houve diferença estatisticamente significante entre os grupos apenas para as medidas da análise perceptivo-auditiva (CAPE-V) grau geral (p = 0,01), rugosidade (p = 0,00) e *pitch* (p = 0,01). Os demais parâmetros investigados na análise acústica não diferiram significativamente (p > 0,05). **Conclusão:** O presente estudo demonstrou que indivíduos 46,XX com hiperplasia adrenal congênita, mesmo submetidos à terapêutica hormonal, apresentam qualidade vocal rugosa, *pitch* agravado e voz desviada.

Correspondence address:
Paloma Cristina Rodeiro Neves
Programa de Pós graduação em Processos dos Órgãos e Sistemas Interativos – PPGPIOS, Universidade Federal da Bahia– UFBA
Av. Reitor Miguel Calmon, s/n - Canela, Salvador - BA, Brasil, CEP: 40231-300.
E-mail: fgapalomaneves@gmail.com

Received: December 09, 2018
Accepted: September 13, 2019

Study conducted at Universidade Federal da Bahia – UFBA - Salvador (BA), Brasil.
[1] Universidade Federal da Bahia – UFBA, Salvador (BA), Brasil.

Financial support: nothing to declare.
Conflict of interests: nothing to declare.

INTRODUCTION

Human oral communication is complex. Through words, we transmit a message that, impregnated with feelings, establishes a communicative relationship with the other. Our voice is the protagonist, and represents our emotions and reveals our identity and intentions. Our voice is considered one of the strongest expressions of our personality[1].

One of the organic factors that promote changes in an individual's voice is hormonal influence. Due to the influence of different sex hormones, there is a differentiation between the vocal pattern of men and women. These vocal changes are more common during puberty and will extend into adulthood. Changes in the levels of sex steroid hormones throughout an individual's development will be responsible for anatomophysiological changes in their target organs and/or tissues. Hormones, especially estrogens and androgens, will be determining in the development of the larynx, as well as in vocal physiology[2,3].

Recent studies have pointed to the presence of sex steroid hormone receptors (androgenic and estrogenic) in the larynx, vocal muscle, and mesenchymal tissues[3]. High levels of androgens, then, can lead to increased mass of laryngeal tissues, modifying the opening and closing cycle of the vocal folds, as well as reducing the fundamental frequency[4,5].

There is also evidence that the concentrations of sex hormones with anthropometric factors (height, body mass index, body weight, chest-abdomen ratio, testosterone, estradiol, dehydroepiandrosterone, and luteinizing and follicle-stimulating hormones) influence vocal quality. A study conducted in Germany analyzed 2,381 individuals aged 40 to 79 years, matched for sex and age, and found a correlation of anthropometric factors with sound pressure levels and fundamental frequency in both men and women. The greater the exposure to androgens, especially in women, the more evident the virilization process.

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disease resulting from deficiency of one of the five enzymes needed for the synthesis of cortisol. Because this pathology causes the adrenal gland to overproduce androgen, women (46,XX individuals) present female pseudohermaphroditism and are the most affected, with worsening of the voice as a result of virilization (masculinization)[4-6].

Acquisition of the male vocal pattern causes numerous losses in the biopsychosocial sphere of 46,XX individuals. Constant exposure to androgens intensifies the virilization process and can worsen prognosis; therefore, multi-professional treatment and monitoring since childhood are important[7-9]. Auditory-perceptual and acoustic assessments are important clinical instruments for the monitoring and follow-up of these patients.

Studies[10-12] have reported the importance of multidimensional voice analysis, understood as a set of complementary methods. The analyses can be subjective and/or objective, depending on the needs of the evaluator. In clinical practice, the auditory-perceptual analysis is the most used, considered as the reference standard and often sovereign in the vocal evaluation, despite its subjectivity and limitations. It provides essential data on the anatomy and physiology of the larynx, which allow characterization of the degree and type of vocal perceived deviance, when present. Acoustic analysis generates objective, quantified data that are free and easy to handle based on computer software, such as the PRAAT program, which provides measures on fundamental frequency (F_o), voice intensity, noise measures, and frequency and intensity perturbation measures, as well as information regarding changes in vocal patterns linked to laryngeal changes[13]. It is also possible to obtain a qualitative description of visual patterns of the vocal signal through spectrographic analysis, similar to the auditory-perceptual analysis, because of its subjective character[13-16].

Despite the discussions on the risks of early virilization in 46,XX individuals, in the past ten years, there has been a lack of studies addressing the voice in this population. To provide a more integrated multi-professional intervention, the present study aimed to describe the vocal profile of 46,XX CAH patients followed up in a genetics outpatient clinic.

METHODS

This study was approved by the Research Ethics Committees of the Institute of Health Sciences, Federal University of Bahia (UFBA), and Magalhães Neto Outpatient Clinic (AMN). It was carried out in accordance with the current rules for research involving human beings (Resolution no. 466/12, National Health Council) under protocol no. 5.662/2016.

This is a descriptive, exploratory, cross-sectional study. The data were collected between February and June 2017. All patients with CAH were invited, according to the research inclusion criteria, to participate in the sampling process, but only 14 individuals signed the Informed Consent Form (ICF). Thus, this study was conducted with a convenience sample of 28 volunteers: 14 46,XX CAH patients followed up by the multidisciplinary team of the GOC-UFBA and 14 46,XX healthy individuals without CAH. Both groups were matched for age.

The inclusion criteria for the CAH group were as follows: 46,XX individuals diagnosed with CAH aged 12 to 45 years, not undergoing hormone therapy, literate, under multi-professional health follow-up, who accepted to participate in the research and signed an ICF or presented a consent form signed by the parents and/or legal guardians (individuals aged <18 years).

The following non-inclusion criteria for the CAH group were adopted: presence of neurological and/or psychiatric changes that would prevent data collection, as well as of vocal changes resulting from vocal abuse, smoking, alcoholism, and other endocrine and/or congenital syndromes. Participants with CAH who interrupted the treatment adopted, withdrew the study at any time, were not available to collect data for vocal assessment, and/or presented irregularities in the multi-professional follow-up were excluded from the study.

The following inclusion criteria were used for the group without CAH: 46,XX individuals aged 12 to 45 years; with absence of vocal complaints resulting from vocal abuse, smoking, alcoholism or other endocrine and/or congenital syndromes; without report of vocal changes due to menstruation, premenstrual

tension, or pregnancy, as well as of the flu and/or respiratory allergies on the day of data collection; literate; who accepted to participate in the research and signed an ICF or presented a consent form signed by the parents and/or legal guardians (individuals aged <18 years).

To characterize the sample, the following data were collected from the participants' medical records: age, gender identity adopted, clinical classification, cases in the family (genetic inheritance), type of treatment (therapeutic and/or surgical), use of medication (regular or irregular), serum levels of steroid hormones (T, 17OHP, LH, and FSH), karyotype, date of diagnosis, and multi-professional intervention.

Participants interested in the study were contacted by the researcher to schedule the vocal assessments. The importance of vocal rest on the day of the vocal evaluation and the contraindications to the procedure (presence of heartburn/reflux, cold, sore throat, and any pathology of the respiratory tract) were highlighted.

The voice samples were collected individually in a quiet environment (<45 dB) with the participants properly seated using the PRAAT program. The emissions were captured by a Karsect HT9 microphone coupled to the PureAudioTM USB-AS adapter, positioned 4 cm from the mouth with a 45º directional pickup angle, which converts the integrated sound of the Lenovo notebook (model: Ideapad 320) into a high-quality sound, eliminating noise. Participants were asked to sustain the vowel /Ɛ:/ at habitual frequency and intensity; sustain the vowel /Ɛ:/ from the lowest to the highest pitch possible; count from 1 to 30; produce the sentences proposed by the Consensus Auditory-Perceptual Evaluation of Voice - CAPE-V (ASHA, 2003)[17] and spontaneous speech (How is your voice?). The CAPE-V protocol was adapted using the vowel /Ɛ:/ to facilitate posterior acoustic analysis.

The CAPE-V protocol was chosen for the auditory-perceptual analyses. This protocol comprises six predetermined voice attributes: overall severity, roughness, breathiness, strain, pitch, and loudness, whose degree of perceived deviance from normal are evaluated using a visual analog scale (VAS) (0-10 cm). The parameters resonance, pitch, and loudness are also assessed qualitatively.

Three speech-language pathologists specialized in the field of voice, working in computer-based acoustic analysis, with three to eight years of experience in the application of the CAPE-V assessed the study participants. The PRAAT 5.2.0 program was used to analyze the acoustic measures: fundamental frequency (F_0), vocal extension, perturbation measures of local jitter (%) and local shimmer (%), and harmonics-to-noise ratio (HNR) (dB). The F_0 rate used to analyze the speech samples was 8,000 Hz. Local jitter <1% and local shimmer <3% were considered as the normal values for women. The vocal extension was obtained from the lowest and highest F_0 range achieved during sustained vowel phonation. Spectrographic analysis[18] (trace shape, dark voice timbre degree, trace stability, and presence of noise and subharmonics) was also carried out. One of the limitations of the acoustic analysis was the lack of correlation between the acoustic and spectrographic measures.

The same speech-language pathologists who performed the spectrographic analysis of the voice samples were invited to conduct the auditory-perceptual analysis. The material was sent by email, in PDF (Form and Initial Instructions) and WAV (Voices) formats, and the judges were blinded to the age range and vocal complaints of patients, being informed only of the objectives of the study and oriented to listen to the voices as many times as needed in a quiet environment (<45 dB) following the adapted CAPE-V protocol.

After voice assessment by the judges, a descriptive statistical analysis was performed on the STATA 12.0 software (Stata Corporation, College Station, Texas) using mean, median, and simple percentage values. Categorical (overall severity, roughness, breathiness, strain, pitch, and loudness) and numeric (F_0, vocal extension, jitter and shimmer perturbation measures, and HNR) variables were statistically analyzed using the non-parametric Mann-Whitney test adopting a significance level of 5% (p<0.05).

The kappa coefficients between 0 and 1 were analyzed as follows: K <0.4, poor; 0.4 ≤ K <0.75, satisfactory to good; K ≥0.75, excellent (FLEISS, 1981). The inter-rater reliability between the three judges was 0.6, which is considered good. Based on the three analyses, a mean was obtained for each parameter on the CAPE-V scale.

To classify the degree of perceived deviance on the CAPE-V scale, an option was made for the Brazilian standard[17], in which scores of 0-35.5% = adequate; 35.6-50.5% = mildly deviant; 50.6-90.5% = moderately deviant; ≥90.6% = severely deviant.

RESULTS

Twelve (85.71%) patients with classic CAH and two (14.29%) with salt-wasting CAH were studied. Among the 14 46,XX CAH

Table 1. Clinical characteristics of the patients with congenital adrenal hyperplasia evaluated (n=14)

CAH*	Yes	No
Change of civil registration	2(14.28)	12(85.72)
Family inheritance	9 (64.28)	5 (35.72)
Psychological follow-up	8(57.14)	6(42.86)
Surgical intervention	11(78.57)	3(21.43)
Regular use of medication	13(92.85)	1(7.15)
Normal serum levels of steroid hormones	13(92.85)	1(7.15)
Diagnosis period (childhood)	13 (92.85)	1 (7.15)

*CAH: congenital adrenal hyperplasia.

Table 2. Clinical characteristics of the patients without congenital adrenal hyperplasia evaluated (n=14)

Without CAH*	Yes	No
Vocal complaint	-----	14(100)
Smoking	-----	14(100)
Ingestion of alcoholic beverages	10 (71.42)	4(28.58)
Presence of endocrine changes	-----	14(100)
Regular use of anabolic substances (steroids)	-----	14(100)
Regular physical activity	8 (57.14)	6(42.86)
Regular use of testosterone	-----	14(100)
Presence of GERD	-----	14(100)
Presence of respiratory changes	-----	14(100)

CAH: congenital adrenal hyperplasia; GERD: gastroesophageal reflux disease.

Table 3. Descriptive results of the auditory-perceptual and acoustic assessments of the voice in both groups (n=28)

Measures	With CAH	Without CAH
	n (%)	n (%)
Overall severity		
Adequate	2 (15.38)	2 (15.38)
Mildly deviant	9 (69.23)	11 (84.62)
Moderately deviant	2 (15.38)	-
Roughness		
Adequate	5 (38.46)	8 (61.54)
Mildly deviant	7 (53.85)	5 (38.46)
Moderately deviant	1 (7.69)	-
Breathiness		
Adequate	5 (38.46)	3 (23.08)
Mildly deviant	8 (61.54)	10 (76.92)
Strain		
Adequate	10 (76.92)	12 (92.31)
Mildly deviant	3 (23.08)	1 (7.69)
Pitch		
Adequate	5 (38.46)	9 (69.23)
Mildly deviant	6 (46.15)	3 (23.08)
Moderately deviant	2 (15.38)	1 (7.69)
Loudness		
Adequate	13 (100.00)	12 (92.31)
Mildly deviant	-	-
Moderately deviant	-	1 (7.69)
Pitch (qualitative)		
Low	8 (61.54)	2 (15.38)
High	4 (30.77)	8 (61.54)
Adequate	1 (7.69)	3 (23.08)
Loudness (qualitative)		
Loud	3 (23.08)	2 (15.38)
Soft	10 (76.92)	11 (84.62)
Resonance		
Normal	1 (7.69)	4 (30.77)
Laryngopharyngeal	3 (23.08)	2 (15.38)
Pharyngeal	2 (15.38)	2 (15.38)
Closed rhinophony	3 (23.08)	3 (23.08)
Hypernasal	1 (7.69)	2 (15.38)
Laryngopharyngeal with nasal compensation	3 (23.08)	-
Spectrographic trace shape		
Regular	10 (76.92)	11 (84.62)
Irregular	3 (23.08)	2 (15.38)
Dark voice timbre degree		
Weak	3 (23.08)	2 (15.38)
Normal	9 (69.23)	9 (69.23)
Strong	1 (7.69)	2 (15.38)
Spectrographic trace stability		
Stable	4 (30.77)	7 (53.85)
Unstable	9 (69.23)	6 (46.15)
Noise		
Present	8 (81.54)	11 (84.62)
Absent	5 (38.46)	2 (15.38)
Presence of subharmonics		
Yes	4 (30.77)	6 (46.15)
No	9 (69.23)	7 (53.85)

Table 4. Comparison of the median values related to auditory-perceptual analysis (CAPE-V) and acoustic (PRAAT) analyses of the voice in patients with and without CAH according to the Mann-Whitney test (p<0.05)

Measures	With CAH	Without CAH	p-value
	Median (IQR)	Median (IQR)	
CAPE-V			
Overall severity	37 (24;38)	20 (16; 22)	**0.01***
Roughness	35 (13;38)	0 (0;14)	**0.00***
Breathiness	14 (30;38)	15 (16;18)	0.15
Strain	0 (0)	0 (0)	0.76
Pitch	13 (28;38)	0 (0;16)	**0.01***
Loudness	0 (3;8)	0 (0)	0.06
PRAAT			
F_o (Hz)	200.66 (177.52 ;225.6)	236.34 (185.1;252.08)	0.34
Jitter	0.31 (0.23; 0.40)	0.35 (0.22; 0.51)	0.68
Shimmer	2.71 (2.07; 3.70)	2.73 (2.40; 3.26)	0.90
HNR (dB)	19.87 (17.04; 21.14)	17.74 (16.71; 18.45)	0.17
Minimum F_o (Hz)	180.92(100.49;187.31)	182.96(170.25;201.05)	0.10
Maximum F_o (Hz)	376.35 (300.25; 411)	413.35(364.55;459.85)	0.08

IQR: interquartile range; F_o: fundamental frequency; HNR: harmonics-to-noise ratio.

participants, two (28%) were aged 12-18 years, seven (50%) were between 19 and 30 years old, and five (35.72%) were over 30 years old. The tables 1 and 2 summarize the clinical characteristics of the participants with and without CAH in this study.

The descriptive results of the perceptual-auditory (CAPE-V) and acoustic (spectrographic analysis) vocal evaluations performed by the three speech-language pathologists are shown in Table 3. To statistically analyze the previously mentioned variables, it was necessary to isolate one patient who used of medication regularly to avoid interference in auditory-perceptual and acoustic evaluations of glottic sources.

Deviance was observed in the CAPE-V parameters - overall severity, roughness, breathiness, strain, pitch, and resonance - in the group with CAH. As for the PRAAT, spectrographic trace instability and presence of noise were predominant in these individuals.

Table 4 shows that there was statistically significant difference between the groups only for the measures of overall severity (p=0.01), roughness (p=0.00), and pitch (p=0.01). As for the acoustic analysis, no statistically significant differences were found between the groups with and without CAH for any of the measures.

DISCUSSION

The results found in the auditory-perceptual analysis (CAPE-V) showed greater deviance in patients with CAH compared with healthy patients. The parameters of overall severity, roughness, and pitch were statistically significant.

Despite the countless discussions on hormonal influence on the vocal quality of 46,XX individuals, there is a lack of publications addressing the vocal pattern in CAH. Studies involving transsexual men undergoing hormonal harmonization and their reflexes in the human voice are common in the literature, although women with CAH are compared with this group. It was chosen to conceptually confront the findings with those of existing studies in the area. The larynx is a hormone-dependent organ, a fact that makes it susceptible to hormonal changes throughout an individual's development. Testosterone is one of the androgenic hormones responsible for the anterior-posterior growth of the larynx, lowering and increasing the size and volume of the vocal folds. This change is more evident in boys during vocal change[19,20].

Early puberty in girls with CAH contributes to the appearance of laryngeal and vocal changes. A study[7] compared the larynx of a child with CAH at four years of age with that of a healthy 10-year-old female, and highlighted the similarity in size due to hormonal influence, showing the presence of secondary androgenic male characteristics (pubic hair, increased muscle mass, and low pitch). According to the literature, there is no difference in the vocal pattern of boys and girls during childhood[21-23]. After puberty, under hormonal influence, the larynx undergoes anatomophysiological changes and transitions from infant to adult[24].

In 46,XX individuals with CAH, even after hormone therapy, there is a tendency to virilization and, consequently, to voice worsening, due to androgenic action. Late diagnosis contributes to greater exposure of patients to androgens. Most participants in the CAH group showed changes in the auditory-perceptual parameters of voice, mainly in the qualitative analysis of pitch, which is in agreement with findings of previous studies[2-6]. Most patients in the CAH group presented low pitch, whereas the majority of healthy patients showed high pitch.

In clinical practice, auditory-perceptual analysis is considered the gold standard, therefore sovereign in relation to the others[1,25]. Through an essentially auditory phenomenon, it is possible to identify and differentiate a normal voice from an extremely compromised one, a fact that contributes to the findings of this study. In the auditory-perceptual analysis of the CAH group, the parameters overall severity, roughness, breathiness, and pitch were mildly deviant, differently from loudness and strain, which presented values within the normal voice variability.

The vocal resonance system consists of a set of elements of the phonatory system that are closely related to each other, aimed at vocal projection and amplification[1,25]. The balanced use of this system provides voice emission with perfect fit and diffuse sound quality, giving the feeling that the voice belongs to the speaker. Predominance of a resonant focus compromises the source-filter interaction, making it less efficient due to the excessive concentration of energy in a specific area of the phonatory system. Amplification becomes poor and there is no presence of defined harmonics[1,25]. In the voice samples of patients with CAH, changes in the resonant focus were found, with consequent reflexes in vocal quality.

In the literature[1,25], patients with the laryngopharyngeal focus present tense-strangled, compressed vocal quality with little projection as a result of tensioning of the larynx and pharynx group. This is mostly found in individuals who have difficulty expressing feelings of aggression. Nasal compensation can occur in cases of intense low vertical focus[1].

A study addressing disorders of sex development (DSD)[7] pointed out problems related to hormone therapy, such as treatment abandonment due to its effects, lack of resources to purchase medications or delay in obtaining them in the Brazilian Unified Health System (SUS), inadequate medication administration (parents or caregivers), and non-literacy. This fact, associated with early puberty in most girls with CAH, causes vocal changes and generates conflicts regarding body image. Of the 14 patients followed up in this study, only one did not use medication regularly. All auditory-perceptual parameters showed moderate deviance and, as for the acoustic analysis, the mean F_o was 120 Hz.

The change in the vocal pattern of transsexual men after hormone therapy is similar to that observed in patients with CAH after exposure to androgens. A prospective study[26] analyzed the reflexes on the vocal quality of seven transsexual men after hormone therapy with testosterone for 12 months and found a decrease in F_o after six months.

Although perceptual-auditory analysis of voice is the gold standard in this area, computer programs have been used to provide quantifiable and more objective data, through acoustic analysis. The acoustic parameters can vary and are influenced by the instruments used in the assessment, environmental noise, sex, and age of the speaker. They assist the clinician with understanding the phonation mechanism in different vocal realities but, despite being an objective and non-invasive analysis, it is still considered a complementary assessment in relation to the auditory-perceptual analysis. It enables description of the human voice almost completely through the analysis of F_0 and perturbation (shimmer and jitter), and noise (HNR) measures[27-29].

Fundamental frequency represents the number of glottic cycles performed by the vocal folds per second[1]. It results from the interaction of the length, strain and mass of the vocal folds during phonation. A longer and larger vocal tract, such as that of males, reaches bass sounds with ease.

The voice of men and that of women are the results of anatomical and physiological characteristics particular to each vocal apparatus. In general, a more elongated vocal tract has long vocal fold fibroblasts (VFF) and produces vocal extension at low pitch, whereas a shorter tract has short VFF and vocal extension at high pitch.

Studies[27,30] have shown that the expected mean F_0 values for adult men and women are around 113 and 205 Hz, respectively. Although the qualitative auditory-perceptual analysis of the pitch highlights the presence of a severe vocal pattern in patients with CAH, in the acoustic analysis, the median of the group presented expected values for normality (Md: 200.66). The values found for the CAH group are within the normal range, although the group without CAH had a higher median compared with that of the CAH group.

It should be emphasized that the number of participants was a limiting aspect to the present study. As it is a convenience sample, based on a non-probabilistic sample, it is not possible to make generalizations regarding the population studied. However, to reduce confounding variables, an option was made for the use a comparison group matched for age. In addition, it was not possible to perform an otorhinolaryngological evaluation, as well

as to apply the Voice Handicap Index (VHI), complementary to a more reliable multidimensional analysis of the voice and larynx, thus allowing identification of possible laryngological changes and their repercussions on the vocal quality of the patients, which is essential to multi-professional intervention.

CONCLUSION

The present study demonstrated that 46,XX individuals with congenital adrenal hyperplasia (CAH), even when submitted to hormone therapy, present a tendency to worsen their voice, possibly due to androgenic influence. Individuals with CAH presented rough, low, deviant voice. Further studies addressing not only vocal analysis should be conducted, considering that vocal changes interfere with the quality of life of individuals.

REFERENCES

1. Behlau M, Azevedo R, Pontes P. Conceito de voz normal e classificação das disfonias. In: Behlau M. Voz: o livro do especialista. Rio de Janeiro: Revinter; 2004.
2. Laureano JM, Romão GS, de Sá MFS, Ferriani RA, dos Reis RM, Ricz LNA. Atualização sobre a influência dos esteróides sexuais na qualidade da voz. Femina. 2006;34(11):735-41.
3. Abitbol J, Brux G, Millot M, Masson O, Mimoun H, Pau B, et al. Does a hormonal vocal cord cycle exist in women? Study of vocal premenstrual syndrome in voice performers by videostroboscopy-glottography and cytology on 38 women. J Voice. 1989;3(2):157-62. http://dx.doi.org/10.1016/S0892-1997(89)80142-0.
4. Nygren U, Södersten M, Falhammar H, Thorén M, Hagenfeldt K, Nordenskjöld A. Voice characteristics in women with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Clin Endocrinol (Oxf). 2009;70(1):18-25. http://dx.doi.org/10.1111/j.1365-2265.2008.03347.x. PMid:18727710.
5. Nygren U, Nyström HF, Falhammar H, Hagenfeldt K, Nordenskjöld A, Södersten M. Voice problems due to virilization in adult women with congenital adrenal hyperplasia due to 21- hydroxylase deficiency. Clin Endocrinol (Oxf). 2013;79(6):859-66. http://dx.doi.org/10.1111/cen.12226. PMid:23600848.
6. Tsuji DH, Senes LU, Badana SC, Pinho SMR. Manejo da frequência fundamental da voz na Hiperplasia por meio da tireoplastia tipo IV de Issihiki. Arq Int Otorrinolaringol. 2003;7(3)
7. Galli DO. Olhar fonoaudiológico sobre as anomalias de diferenciação sexual: um estudo exploratório [mestrado]. São Paulo: Pontifícia Universidade Católica de São Paulo; 2009.
8. Furtado PS, Morae's F, Lago R, Barros LO, Toralles MB, Barroso U. Gender dysphoria associated with disorders of sex development. Nat Rev Ural Mature Publishing Group. 2012;9(11):620-7.
9. Apostolos RAAC. Identidade de gênero, função sexual e qualidade de vida em indivíduos com hiperplasia adrenal congênita e cariótipo 46, xx registrados no sexo masculino [dissertação]. Salvador: Escola Bahiana de Medicina e Saúde Pública; 2017.
10. Pimenta RA. Uso da avaliação multidimensional da voz na caracterização vocal de pacientes com paralisia unilateral de pregas vocais [doutorado]. Faculdade de Medicina, Universidade de São Paulo, 2017. http://dx.doi.org/10.11606/T.82.2017.tde-03102017-084615.
11. Barcelos CB, Silveira PAL, Guedes RLV, Gonçalves AN, Slobodticov LDS, Angelis EC. Multidimensional effects of voice therapy in patients affected by unilateral vocal fold paralysis due to cancer. Braz J Otorhinolaryngol. 2018;84(5):620-9. PMid:28882539.
12. Lopes LW, Cavalcante DP, Costa PO. Intensidade do desvio vocal: integração de dados perceptivoauditivos e acústicos em pacientes disfônicos. CoDAS. 2014;26(5):382-8. http://dx.doi.org/10.1590/2317-1782/20142013033. PMid:25388071.
13. Vaz-Freitas S, Pestana PM, Almeida V, Ferreira A. Acoustic analysis of voice signal:Comparison of four applications software. Biomed Signal Process Control. 2018;40:318-23. http://dx.doi.org/10.1016/j.bspc.2017.09.031.
14. Lopes LW, Alves GÂS, Melo ML. Evidência de conteúdo de um protocolo de análise espectrográfica. Rev CEFAC. 2017;19(4):510-28. http://dx.doi.org/10.1590/1982-021620171942917.
15. Batalla FN, Gonzalez MR, Pelaez Gonzalez MB, Gonzalez Laborda I, Fernandez Fernandez M, Morato Galan L, et al. Acoustic voice analysis using the Praat programme: Comparative study with the Dr. Speech Programme. Acta Otorrinolaringol Esp. 2014;65(3):170-6. PMid:24679848.
16. Souza BO, Gama ACC. Apoio visual do traçado espectrográfico: impacto na confiabilidade da análise perceptivo-auditiva da voz por avaliadores inexperientes. Distúrb Comun. 2015;27(3):479-86.
17. Yamasaki R, Madazio G, Leão SHS, Padovani M, Azevedo R, Behlau M. Auditory-perceptual Evaluation of Normal and Dysphonic Voices Using the Voice Deviation Scale. J Voice. 2017;31(1):67-71. http://dx.doi.org/10.1016/j.jvoice.2016.01.004. PMid:26873420.
18. Côrtes MG, Gama ACC. Análise visual de parâmetros espectrográficos pré e pós- fonoterapia para disfonias. Rev Soc Bras Fonoaudiol. 2010;15(2):243-9. http://dx.doi.org/10.1590/S1516-80342010000200016.
19. Behlau MS, Rehder MI, Valente O. Disfonias endócrinas. In: Behlau MS, organizadores. Voz: o livro do especialista. 2. ed. Rio de Janeiro: Revinter; 2005.
20. Abitbol J. Normal voice maturation: hormones and age. In: Benninger MS, editor. The Performer's Voice. San Diego: Plural Publishing; 2006.
21. Cartei V, Bond R, Reby D. What makes a voice masculine:Pysiological and acoustical correlates of women´s ratings of men´s vocal masculinity. Horm Behav. 2014;66(4):569-76. http://dx.doi.org/10.1016/j.yhbeh.2014.08.006. PMid:25169905.
22. Braga J, Oliveira D, Sampaio T. Frequência fundamental da voz de crianças. Rev CEFAC. 2009;11(1):119-26. http://dx.doi.org/10.1590/S1516-18462009000100016.
23. Ramos L, Souza B, Gama A. Análise vocal na infância: uma revisão integrativa. Revista Distúrb. Comum. 2017;29(1):20-32.
24. Smillie I, McManus K, Cohen W, Lawson E, Wynne DM. The paediatric voice clinic. Arch Dis Child. 2014;99(10):912-5. http://dx.doi.org/10.1136/archdischild-2013-305683. PMid:24872383.
25. Gökdoğan Ç, Gökdoğan O, Tutar H, Aydil U, Yılmaz M. Speech Range Profile Findings in Mutational Falsetto. Speech Range Profile (SRP) Findings Before and After Mutational Falsetto (Puberphonia). J Voice. 2016;30(4):448-51. http://dx.doi.org/10.1016/j.jvoice.2015.05.014. PMid:26106069.
26. Irwig MS, Childs K, Hancock AB. Effects of testosterone of testosterone on the transgender male voice. J Voice. 2017;5(1):107-12. PMid:27643399.
27. Barsties B, De Bodt M. Assessment of voice quality: current state-of-the-art. Auris Nasus Larynx. 2015;42(3):183-8. http://dx.doi.org/10.1016/j.anl.2014.11.001. PMid:25440411.
28. Tenório LM. Discordâncias de gênero na HAC clássica: Análise secundária de dados [monografia]. Bahia: Faculdade de Medicina, Universidade Federal da Bahia; 2013.
29. Lopes LW, Alves GÂS, Melo ML. Evidência de conteúdo de um protocolo de análise espectrográfica. Rev CEFAC. 2017;19(4):510-28. http://dx.doi.org/10.1590/1982-021620171942917.
30. Vaz-Freitas S, Pestana PM, Almeida V, Ferreira A. Acoustic analysis of voice signal:Comparison of four applications software. Biomed Signal Process Control. 2018;40:318-23. http://dx.doi.org/10.1016/j.bspc.2017.09.031.

Authors' contributions

PCRN was responsible for the project conception, study design, collection, tabulation and analysis of data, and writing of the manuscript; MBPT supervised the collection, tabulation and analysis of data and provided general guidance on the writing of the manuscript; RDS assisted with the project conception, study design, and general guidance on the writing of the manuscript.