JMD
https://doi.org/10.14802/jmd.21010 / J Mov Disord 2021;14(3):226-230
pISSN 2005-940X / eISSN 2093-4939

BRIEF COMMUNICATION

Phonatory Characteristics of Male Patients with Classic Essential Tremor

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ABSTRACT

Objective Voice tremor (VT) is one of the characteristics of essential tremor (ET). This study was designed to describe the group and phonatory characteristics of classic ET patients with VT.

Methods This retrospective case-control study compared classic ET patients with age and sex-matched controls. The ET population was subgrouped based on auditory perceptual voice analysis. Electroglottography and acoustic voice samples obtained from both groups were analyzed for contact quotient (CQ) and multidimensional voice program parameters, i.e., fundamental frequency (F_0), perturbation, noise, and tremor parameters.

Results The CQ, F_0, perturbation, noise, and tremor characteristics significantly increased from the moderate VT group to the severe VT group.

Conclusion The CQ, F_0, and noise characteristics reflected the vocal folds' functionality. The perturbation and tremor parameters variation were reasoned considering the tremor-related changes occurring in the laryngeal, vocal tract, and expiratory muscles in patients with ET. Thus, phonatory analysis may help in monitoring the progression of ET.

Keywords Acoustics; Essential tremor; Phonation; Voice; Voice tremor.

Essential tremor (ET) is a heterogeneous, progressive neurodegenerative disorder characterized by an action tremor of 4–12 Hz.[1] The cardinal feature of ET is a postural and/or kinetic tremor of the head, neck, voice, jaw, and other regions of the body.[1] ET also affects the oropharyngeal, laryngeal, and respiratory subsystems of speech production[2,3] causing rhythmic fluctuations in the frequency and/or intensity of one's voice,[4,5] termed essential voice tremor (EVT). EVT is reported in 10–25% of the people with ET.[6] Individuals with EVT experience voice disturbances, such as modulations in pitch and loudness, struggle while speaking, dysphonia, voice breaks, and diminished intelligibility.[2,3,5] The pathophysiology of ET emerges from an extensive central oscillatory network (CON)[7] involving the laryngeal motor cortex in the primary motor cortex and its projections to the corticobasal ganglia and thalamocortical loop, which play a significant role in voluntary control of phonation.[8]

Acoustic voice analysis provides a window to understand speech subsystem physiology.[9] Acoustic analysis of voice in EVT has shown increased frequency and amplitude perturbation,[5] along with a higher extent of fundamental frequency (F_0) and extent of amplitude.[10] The measurement of voice tremor (VT) frequency in EVT patients is reported to be between 4.1–5.1 Hz.[6] Machine learning is being devised to estimate pitch contours and for the analysis of spectral characteristics.[11,12] Although the utilization of these measures has helped in EVT diagnosis,[4,6] monitoring of symptoms following pharmacological treatment,[5,11] and administration of

Received: January 30, 2021 **Revised:** April 22, 2021 **Accepted:** June 8, 2021
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botulinum toxin,[3] no studies have attempted to classify ET based on the severity of EVT. In addition, there is a lacuna in the literature regarding the description of the clinical characteristics of EVT.[13] Hence, the present study aims to describe the group characteristics and determine the phonatory characteristics of patients with EVT with varying severity of VT by employing standard methods to record and analyze voice data.

MATERIALS & METHODS

Participant selection

The present research is a retrospective case-control study approved by the Institutional Ethics Committee of National Institute of Mental Health and Neurosciences, Bengaluru, India. Recorded speech and voice samples of all individuals diagnosed with neurological disorders, referred for routine voice evaluation, were retrieved from the voice database of the Department of Speech Pathology and Audiology at National Institute of Mental Health and Neurosciences, Bengaluru, India. The data were extracted between 2008 and 2017 and served as a source for the experimental group. All the subjects included had a confirmed diagnosis of ET as per the Consensus statement of the Movement Disorder Society on Tremor and clinical examinations.[14] Inclusion criteria for the experimental group consisted of age between 45–65 years; the first symptom was upper limb tremor or simultaneous onset of the upper limb, head tremor and/or VT; < 10 years duration of ET, no isolated head and VT; 'off' medication at the time of voice evaluation; no structural abnormality of vocal folds (VFs) on laryngoscopy; and no history of stroke or any other neurological condition.

Healthy control (HC) data consisted of recorded voice samples used to establish clinical normative. The data were from both sexes of individuals aged between 18–70 years who were screened and found to have no neurological, otolaryngological, or psychiatric disorders before recording. From this data pool, we selected controls who were matched in age, sex, and language with the experimental group, thus maintaining homogeneity.

The voice samples were recorded for sustained phonation of vowel /a/ on Computerized Speech Labs 4500 (KAYPENTAX, Lincoln Park, NJ, USA) at a sampling rate of 44,100 Hz using a high-fidelity microphone (SHURE SM-48; Shure Inc., Niles, IL, USA) placed at a 10 cm distance from the mouth.[9] Simultaneous electroglottography (EGG) recordings (model 6103, KAYPENTAX, Lincoln Park, NJ, USA) were obtained with two surface electrodes; an electrode was placed on each of the alae of the thyroid cartilage.[2] Sustained phonation was considered per the standard protocols for the assessment of EVT.[4,5,11]

Subgrouping ET

Five speech-language pathologists with over ten years of experience rated each sample of phonation on the Vocal Tremor Rating Scale (VTRS)[15] to reclassify the experimental group into subgroups of ET. Voice samples having an interrater agreement of 80% were considered when classifying the severity of VT among samples as follows: 1-no VT (NVT), 2-mild VT, 3-moderate VT, and 4-severe VT.

Measurement of phonatory characteristics

The classified phonation samples were trimmed at their onset and offset to obtain a 2-second-long duration of sustained phonation.[9] Parameters were computed using EGG and Multi-Dimensional Voice Program (MDVP) software (ver.5105, KAYPENTAX, Lincoln Park, NJ, USA). The contact quotient (CQ) was measured using EGG. F_0, frequency perturbation [jitter (Jitt), smoothened pitch period perturbation quotient (sPPQ), and coefficient of frequency variation (vF_0)], amplitude perturbation [shimmer (Shim), smoothened amplitude perturbation quotient (sAPQ), and coefficient of amplitude variation (vAm)], noise [noise to harmonic ratio (NHR) and soft phonation index (SPI)], and tremor parameters [rate of frequency tremor (Fftr), rate of amplitude tremor (Fatr), magnitude of frequency tremor (FTRI), and magnitude of amplitude tremor (ATRI)] were measured with MDVP. Each parameter is described in Supplementary Material 1 (in the online-only Data Supplement).

Statistical analysis

Data were analyzed using SPSS v22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were computed for all the parameters for the HC group and the ET subgroups. The Shapiro-Wilk test was performed to check the normal distribution of data. The Kruskal-Wallis H-test was used to compare the HC group and subgroups of ET patients. Bonferroni (post hoc) corrected *p*-values (< 0.05) were used for the interpretation during multiple comparisons.

RESULTS

A total of 308 patients with ET (204 males) were considered for inclusion in the study; of these patients, 69 male patients fulfilled the inclusion criteria. Out of 178 voice samples (102 males) considered as HCs, 69 males ($\overline{X}$: 56.9 ± 6.7 years) were matched in age, sex, and language with individuals in the ET subgroups. Table 1 depicts the group characteristics of the ET subgroups. The results of the Kruskal-Wallis H test are depicted in Figure 1. Parameters CQ, F_0, frequency perturbation, amplitude perturbation, and tremor showed a significant difference between ET subgroups and exhibited an increasing trend with VT severity. SPI

Table 1. Characteristics of ET and subgroups of ET

Group characteristics	ET as a group (n = 69)	Subgroups of ET: NVT (n = 14)	Mild VT (n = 15)	Moderate VT (n = 12)	Severe VT (n = 28)	p-value
Mean age (years)	56.9 ± 6.7	51.3 ± 6.9	55.3 ± 6.7	57.6 ± 7.1	60.4 ± 4.1	0.001*
Duration of essential tremor (years)	3.5 ± 1.9	4.7 ± 1.8	2.8 ± 1.7	3.8 ± 1.6	3.1 ± 1.1	0.019*
Age of essential tremor onset (years)	53.6 ± 7.1	46.7 ± 7.9	52.5 ± 7.3	53.8 ± 7.2	57.3 ± 4.9	0.001*
Duration of essential voice tremor (years)	2.3 ± 1.6	-	1.7 ± 0.7	2.6 ± 1.6	2.3 ± 1.7	-
Age of essential voice tremor onset (years)	57.6 ± 5.3	-	59 ± 3.7	55.9 ± 6.9	58.1 ± 4.8	-
Family history	40.5 (28)	50 (7)	60 (9)	41.6 (5)	25 (7)	-
Bilateral upper limb tremor (AE)	100 (69)	100 (14)	100 (15)	100 (12)	100 (28)	-
Bilateral lower limb tremor (AE)	73.9 (51)	28.6 (4)	46.7 (7)	100 (12)	100 (28)	-
Head tremor (AE)	37.9 (26)	-	14.3 (2)	41.7 (5)	67.9 (19)	-
Tongue tremor (AE)	26.1 (18)	7.1 (1)	20 (3)	33.3 (4)	35 (10)	-

Values are presented as mean ± standard deviation or n (%) unless otherwise indicated. *significant at 5% level of significance between all the subgroups of ET. ET: essential tremor, NVT: no vocal tremor, VT: vocal tremor, AE: at the time of evaluation.

values were reduced in NVT and gradually increased with the severity of VT. CQ showed a reduction in NVT and mild VT but an increase in moderate and severe VT. Post hoc analysis showed significant differences between subgroups of ET (Supplementary Table 1 in the online-only Data Supplement).

DISCUSSION

In this study, we tried to objectively measure the phonatory characteristics of voice in patients with ET with varying VT severity. The mean ages of NVT patients and severe VT patients were 51.3 and 60.4 years, respectively. Similar findings on EVT suggest that older individuals exhibit moderate to severe VT.[4-6,11] We considered the duration between the age of ET onset and EVT onset as the transition period (Table 1). The transition period was shorter for the moderate and severe VT groups than for the mild VT group.

Sustained phonation results from medialization of the VF by the cricothyroid (adductor) and thyroarytenoid with constant subglottal pressure.[16] The CQ reflects VF medialization (adduction), the SPI determines the completeness of VF closure, and NHR indicates noise (air escape) in the voice signal due to incomplete VF closure.[2,16-18] The CQ was reduced in NVT patients and mild VT patients and increased with the severity of VT. However, the SPI and NHR showed a reduction in NVT patients (< HCs) and reached HC values with tremor severity. We hypothesize that reduced values of the CQ, SPI, and NHR in NVT patients may indicate hypoadduction of the VF, as reported in cases with hypokinetic dysarthria.[2,16,17] Although the CQ was lower in patients with mild VT (compared to patients with NVT), SPI and NHR values were higher, which may indicate reduced contact time between VFs with complete closure (SPI) and negligible air escape (NHR). However, an increase in tremor severity caused VFs to hyperadduct (>CQ) but these patients had complete VF closure (normal SPI) and the least noise (NHR). Adduction of VFs and maintenance of subglottal pressure occurs due to activation of the prefrontal cortex, periaqueductal gray, nucleus retroambiguus, and motor neural pathway,[19] which are components of the CON.[7] Thus, the faulty neural impulse to the thyroarytenoid causes postural tremor, which may disrupt constant subglottal pressure to maintain sustained phonation.

A pitch (F_0) change is achieved by altering the length, mass, and tension of VFs caused by cricothyroid and thyroarytenoid muscles (CT-TA).[16] Frequency perturbation reflects VF vibration and respiratory aerodynamics, whereas amplitude perturbation reflects glottal closure during phonation.[18] Electromyography and pulmonary functions in EVT patients have shown deficits in CT-TA and expiratory (rectus abdominis and pectoralis) muscles of phonation,[2,20] respectively.

In our study, the increase in F_0 with the severity of VT suggests elongation of VFs, as substantiated by videostroboscopy studies,[4] in addition to a decrease in mass and increase in tension of CT-TA.[4] We also obtained higher values of frequency perturbation (Jitt, sPPQ, and vF_0) and amplitude perturbation (Shim, sAPQ, and vAm) in patients with moderate and severe VT, similar to findings in the literature.[5] We hypothesize that changes in muscle tone and stiffness of CT-TA in addition to an imbalance between subglottal and supraglottal pressure are the reason for abnormal frequency and amplitude perturbation values.

Modulation seen in phonation occurs due to activation of corticobulbar fibers that project to mouth, face, laryngeal, and pharyngeal motoneurons.[19] The tremor parameters (Fftr, Fatr, FTRI, and ATRI)[9] determine the strongest periodic modulation of frequency and amplitude in voice. Our study showed an increase in tremor parameters with the severity of VT. We hypothesize that the abnormal tremor parameters could be from oscillations in intrinsic and extrinsic laryngeal muscles, the vocal tract, and respiratory muscles (diaphragm, rectus abdominis, and pectoralis);[2] these oscillations may induce modulation in glottal airflow.

Our findings can help clinicians quantify patients' voice characteristics with ET rather than them having to rely on perceptual evaluation alone. This may help clinicians monitor the progres-

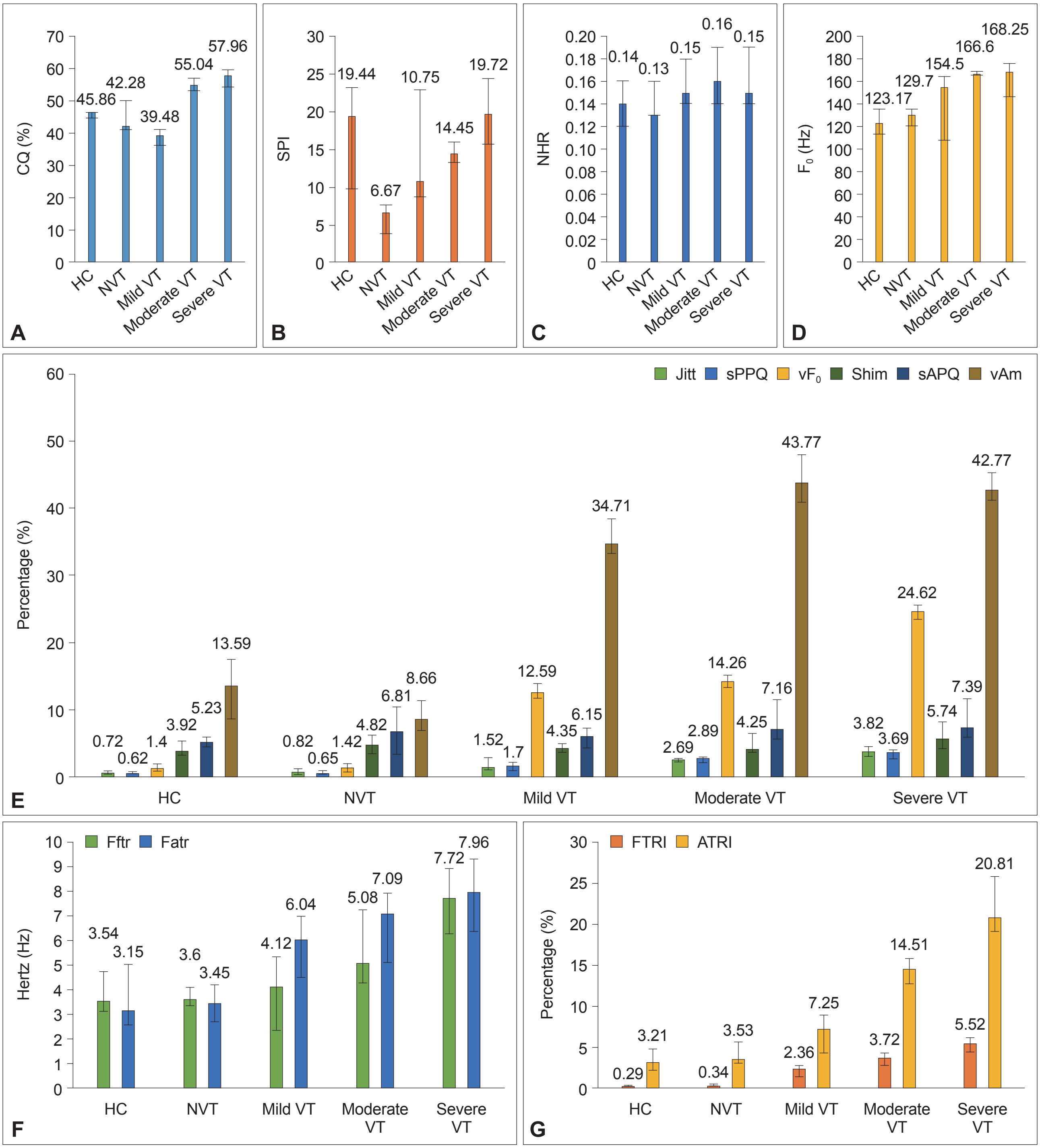

Figure 1. Median and interquartile range for the healthy control (HC) group and essential tremor subgroups (NVT: no vocal tremor, Mild VT: mild vocal tremor, Moderate VT: moderate vocal tremor, and Severe VT: severe vocal tremor). A: Contact quotient (CQ). B: Soft phonation index (SPI). C: Noise to harmonic ratio (NHR). D: fundamental frequency (F_0). E: Amplitude and frequency perturbation parameters [Jitter (Jitt), smoothened pitch period perturbation quotient (sPPQ), coefficient of frequency variation (vF_0), shimmer (Shim), smoothened amplitude perturbation quotient (sAPQ), coefficient of amplitude variation (vAm)]. F: Tremor parameters [rate of frequency tremor (Fftr), rate of amplitude tremor (Fatr)]. G: Tremor parameters [magnitude of frequency tremor (FTRI), magnitude of amplitude tremor (ATRI)]. Hz: hertz, %: percentage.

sion of the disorder by analyzing the deterioration of voice quality and may also serve as a baseline for intervention studies.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.14802/jmd.21010.

Conflicts of Interest

The authors have no financial conflicts of interest.

Funding Statement

None.

Acknowledgments

Authors thank Mr. Prashasti P. Poovaiah for his assistance.

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SUPPLEMENTARY MATERIAL 1

Parameters of phonatory characteristics (as per Computerized Speech Labs 4500, KAYPENTAX, Lincoln Park, NJ, USA)

Electroglottography (EGG; model 6103, KAYPENTAX, Lincoln Park, NJ, USA) parameter included

Contact quotient (CQ, %): The duration of contact at the closing phase of the phonatory cycle. The CQ measures the electrical impedance between the vocal folds during a glottal vibratory cycle.

Multi-Dimensional Voice Program (MDVP) (ver.5105, KAYPENTAX, Lincoln Park, NJ, USA) parameters included

1. Fundamental frequency (F_0, Hz): Average value of all period to period change in frequency in a voice sample.
2. Frequency perturbation parameters:
   1) Jitter percent (Jitt, %): Period to period variability of the pitch within the analyzed voice sample.
   2) Smoothened pitch period perturbation quotient (sPPQ, %): Pitch variations occurring between consecutive pitch periods.
   3) Coefficient of frequency variation (vF_0, %): Variations of F_0 for all period to period analyzed voice samples.
3. Amplitude perturbation parameters:
   1) Shimmer percent (Shim, %): Period to period variability of the peak to peak amplitude within the analyzed voice sample.
   2) Smoothened amplitude perturbation quotient (sAPQ, %): Amplitude variations occurring between consecutive pitch periods.
   3) Coefficient of amplitude variation (vAm, %): Amplitude variations within the analyzed voice sample.
4. Noise related parameters:
   1) Noise to harmonic ratio (NHR): Noise present in the analyzed signal.
   2) Soft phonation index (SPI): Indicates how completely or tightly the vocal folds adduct during phonation.
5. Tremor parameters:
   1) F_0 tremor frequency (Fftr, Hz): Most intensive low frequency F_0 modulating component, i.e., rate of periodic tremor of the frequency.
   2) Amplitude tremor frequency (Fatr, Hz): Frequency of the most intensive low frequency amplitude modulating component, i.e., rate of amplitude change.
   3) Frequency tremor intensity index (FTRI, %): Magnitude of the frequency tremor.
   4) Amplitude tremor intensity index (ATRI, %): Magnitude of the amplitude tremor.

Supplementary Table 1. Results of comparison between 'HC and ET subgroups' and 'within subgroups of ET' using Kruskal-Wallis H test for EGG and MDVP parameters of phonation

Parameters	HC	NVT	Mild VT	Moderate VT	Severe VT	Kruskal-Wallis H Statistics	*p*-value	Results of Post-hoc*: significant comparisons
CQ (%)	45.86 (44.81, 46.52)	42.28 (41.12, 50.15)	39.48 (36.33, 41.22)	55.04 (53.23, 57.08)	57.96 (54.32, 59.66)	85.33	< 0.001	HC and mild VT HC and moderate VT HC and severe VT NVT and moderate VT NVT and severe VT Mild and moderate VT Mild and severe VT
F_0 (Hz)	123.17 (113.44, 135.59)	129.70 (120.72, 135.83)	154.50 (107.60, 164.25)	166.60 (165.05, 168.96)	168.25 (146.36, 175.62)	58.57	< 0.001	HC and moderate VT HC and severe VT NVT and moderate VT NVT and severe VT Mild and moderate VT Mild and severe VT
Jitt (%)	0.72 (0.50, 0.98)	0.82 (0.38, 1.29)	1.52 (1.13, 2.93)	2.69 (2.29, 2.83)	3.82 (3.08, 4.59)	92.85	< 0.001	HC and mild VT HC and moderate VT HC and severe VT NVT and moderate VT NVT and severe VT Mild and severe VT
sPPQ (%)	0.62 (0.54, 0.85)	0.65 (0.45, 1.00)	1.70 (1.01, 2.24)	2.89 (2.13, 3.07)	3.69 (2.76, 4.07)	95.73	< 0.001	HC and mild VT HC and moderate VT HC and severe VT NVT and mild VT NVT and moderate VT NVT and severe VT Mild and severe VT
vF_0 (%)	1.40 (0.94, 1.98)	1.42 (0.79, 1.98)	12.59 (11.78, 13.92)	14.26 (13.35, 15.19)	24.62 (23.47, 25.60)	101.97	< 0.001	HC and mild VT HC and moderate VT HC and severe VT NVT and mild VT NVT and moderate VT NVT and severe VT
Shim (%)	3.92 (3.28, 5.39)	4.82 (3.50, 6.28)	4.35 (3.69, 4.99)	4.25 (3.67, 6.53)	5.74 (4.21, 8.25)	15.51	0.004	HC and severe VT
sAPQ (%)	5.23 (4.48, 5.96)	6.81 (3.42, 10.45)	6.15 (4.39, 7.28)	7.16 (5.68, 11.56)	7.39 (5.97, 11.68)	28.62	< 0.001	HC and moderate VT HC and severe VT
vAm (%)	13.59 (8.67, 17.51)	8.66 (6.96, 11.43)	34.71 (33.21, 38.38)	43.77 (40.89, 48.00)	42.77 (41.16, 45.25)	101.66	< 0.001	HC and mild VT HC and severe VT HC and moderate VT NVT and mild VT NVT and severe VT NVT and moderate VT Mild and moderate VT
NHR	0.14 (0.12, 0.16)	0.13 (0.13, 0.16)	0.15 (0.14, 0.18)	0.16 (0.14, 0.19)	0.15 (0.14, 0.19)	22.64	< 0.001	HC and mild VT HC and moderate VT HC and severe VT
SPI	19.44 (9.72, 23.18)	6.67 (3.90, 7.70)	10.75 (8.71, 22.83)	14.45 (13.21, 15.98)	19.72 (15.60, 24.39)	34.19	< 0.001	HC and NVT NVT and mild VT NVT and moderate VT NVT and severe VT
Fftr (Hz)	3.54 (3.11, 4.73)	3.60 (3.34, 4.09)	4.12 (2.34, 5.33)	5.08 (4.26, 7.24)	7.72 (6.26, 8.92)	33.55	< 0.001	HC and moderate VT HC and severe VT NVT and severe VT Mild and severe VT
Fatr (Hz)	3.15 (2.56, 5.02)	3.45 (2.68, 4.20)	6.04 (4.49, 6.99)	7.09 (5.10, 7.91)	7.96 (6.36, 9.30)	58.97	< 0.001	HC and mild VT HC and moderate VT HC and severe VT NVT and mild VT NVT and moderate VT NVT and severe VT
FTRI (%)	0.29 (0.19, 0.39)	0.34 (0.24, 0.54)	2.36 (1.39, 2.78)	3.72 (2.77, 4.32)	5.52 (4.44, 6.15)	105.03	< 0.001	HC and mild VT HC and moderate VT HC and severe VT NVT and mild VT NVT and moderate VT NVT and severe VT
ATRI (%)	3.21 (2.20, 4.82)	3.53 (3.07, 5.67)	7.25 (4.29, 8.92)	14.51 (12.74, 15.83)	20.81 (19.12, 25.78)	93.27	< 0.001	HC and mild VT HC and moderate VT HC and severe VT NVT and moderate VT NVT and severe VT Mild and severe VT

The median and interquartile range is reported for healthy control (HC), no vocal tremor (NVT), mild vocal tremor (mild VT), moderate vocal tremor (moderate VT), and severe vocal tremor (severe VT). *significant difference noted using Bonferroni corrected *p*-values checked at 5% level significance. EGG: electroglottography, MDVP: multidimensional voice program, CQ: contact quotient, F_0: fundamental frequency, Jitt: jitter, sPPQ: smoothened pitch period perturbation quotient, vF_0: coefficient of frequency variation, Shim: shimmer, sAPQ: smoothened amplitude perturbation quotient, vAm: coefficient of amplitude variation, NHR: noise to harmonic ratio, SPI: soft phonation index, Fftr: rate of frequency tremor, Fatr: rate of amplitude tremor, FTRI: magnitude of frequency tremor, ATRI: magnitude of amplitude tremor, Hz: hertz, %: percentage, ET: essential tremor.