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Asthma severity identification from pulmonary acoustic signal for computerized decision support system

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Abstract

Objective: Breath sound has information about underlying pathology and condition of subjects. The purpose of this study is to examine asthmatic acuteness levels (Mild, Moderate, Severe) using frequency features extracted from wheeze sounds. Further, analysis has been extended to observe behavior of wheeze sounds in different datasets.

Method: Segmented and validated wheeze sounds was collected from 55 asthmatic patients from the trachea and lower lung base (LLB) during tidal breathing maneuvers. Segmented wheeze sounds have been grouped in to nine datasets based on auscultation location, breath phases and a combination of phase and location. Frequency based features F_{25}, F_{50}, F_{75}, F_{90}, F_{99} and mean frequency (MF) has been calculated from normalized power spectrum. Subsequently, multivariate analysis has been performed for analysis.

Result: Generally frequency features observe statistical significance ($p < 0.05$) for the majority of datasets to differentiate severity level $\Lambda = 0.432\text{-}0.939$, F(12, 196-1534) = 2.731-11.196, $p < 0.05$, $\eta^2 = 0.061\text{-}0.568$. It was observed that selected features performed better (higher effect size) for trachea related samples $\Lambda = 0.432\text{-}0.620$, $F(12, 196\text{-}498) = 6.575\text{-}11.196$, $p < 0.05$, $\eta^2 = 0.386\text{-}0.568$.

Conclusion: The results demonstrate that severity levels of asthmatic patients with tidal breathing can be identified through computerized wheeze sound analysis. In general, auscultation location and breath phases produce wheeze sounds with different characteristics.

Keywords: Asthma, Breath Sounds, Wheeze Detection, Airway Obstruction, Severity Level

Introduction

During breathing, acoustic signals are produced in lungs due to oscillations from turbulent flow at the bronchial walls. Respiratory acoustic signals have meaningful information about lung condition. Under normal circumstances, normal breath sounds are produced from lungs, while pathological disorders or airway obstructions return abnormal sounds. In the case of airway obstruction in asthmatic patients, whistling sounds are produced, termed as wheeze (1).

Previously, a few studies have conducted analysis on the correlation between change in lung function values and spectra of respiratory sounds (1-3). But in those studies, data was collected from asthmatic patients with tidal breathing. Baughman et al. found the ccorrelation between lung function values and ratio of time expended with wheeze to total recording time (T_w/T_{tot}) (2). collected data from ten asthmatics (mild to severe) patients with forced breathing from the trachea and chest. Analysis was done using quartile frequencies F_{50}, F_{75} and average power (AP). Only F_{50} recorded at trachea was found to be significant with the force expiratory volume in one second (FEV_1) values (1). Malmberg et al. collected data from 12 asthma (moderate to severe) patients with forced breathing through the trachea. This author investigated acoustic characteristics of wheeze in normal, stable and nonstable asthma patients. It was found that mean frequency (MF) in normal subjects is different from asthmatic patients (3). However, these works did not address the statistical analysis within the various auscultation locations, breathing phases and severity levels. Further, computerized wheeze sound analysis is an active field of research. Similarly, studies performing review on computerized wheeze sound analysis have also reported that most of the authors in the field of computerized wheeze sound analysis are working with detection or classification of wheeze sound (4-5).

The available research, when considered together, indicated several important insights. Firstly, there is sufficient indication that intensity of asthma can be identified using wheeze sound spectra. Secondly, while studies have collected data from different severity levels of asthmatic patients and conducted various analysis (4), very few have inferred back their findings to the severity levels of asthma. This gap is crucial given the fact that according to the World Health Organization (WHO), 235 million individuals are suffering from asthma. These statistics have driven researchers towards developing computerized devices for self-monitoring and self-management of asthma which are becoming more necessary and important. To this effect, physician assisted devices which are currently being used are spirometers and peak flow meters. However, these devices are predominantly utilized during supervised forced respiratory maneuvers which could pose a problem when dealing with children, manipulation for the long term and continuous observation of patients, very severe asthmatic conditions and unsupervised sessions. On another note, wheezing during forced exhalation was not always correlated to the degree of airway obstruction in asthmatic patients which reveals that FEV_1 values obtained using spirometry may not always correlate with intensity of asthma (6).

The aim of this study is to investigate behavior of frequency related features in three severity levels of asthma patients (mild, moderate and severe) through a multivariate statistical (MANOVA) approach. We further extend our analysis and observations according to location (Trachea and lower lung base (LLB)), phase (inspiratory (Inspir) and expiratory (Expir) and a combination of both (trachea inspiratory (T-Inspir), trachea expiratory (T-Expir), LLB inspiratory (LLB-Inspir) LLB expiratory (LLB-Expir)). Such an approach would be beneficial in the development of an automated portable monitoring system which is required for the self-management or treatment of patients (7). Previously, a few studies have investigated the correlation of sound spectra and lung function values (1-3) using statistical analysis. However, these studies did not use a multi variable approach between and in-between severity levels. Furthermore, in these studies, analysis with respect to auscultation location and breathing phase has not been performed. In addition, few works have focused on wheeze generated during normal breathing maneuvers which is essential in unsupervised sessions.

Methodology

Data was collected from two hospitals in Pakistan – District Headquarters Teaching Hospital, Gujranwala and Al-Mustafa Chest Clinic, Wazirabad. Ethical approval was taken from the ethical committee of both hospitals individually, with the principles of the Declaration of Helsinki. Written informed consent and clinical report forms were filled by all subjects that participated in this study. The study period began in June 2016 and end in July 2018. Details of data collection are also given in (8). Furthermore, data was collected according to CORSA standard (9).

In this study, a wireless digital stethoscope, WISE (10) is used to acquire data, few other studies have also used same device (11-13). Respiratory sounds were collected from the trachea, right and left lower lung base (LLB) (14). Short-term recording between 60 to 90 seconds were done in the sitting position with hands on the lap. Subjects were asked to breath by way of mouth. Recordings were done in a sound proof room with environmental conditions and subject's posture identical for all patients, hence ambient noise was minimal and negligible between patient to patient as described in literature (1).

Sample Size: Using conventional, since there was no study found in literature that dealt with the characterization of wheeze sounds in regard to asthmatic severity levels (mild, moderate and severe) using a frequency based feature vector, therefore, the sample size was determined on the basis of information obtained from the current study itself. The minimum number of individuals in the sample was determined using the G*Power software at a 95% confidence interval (CI), effect size (η^2) = 0.60, α = 0.05, power analysis = 0.80 (80%), number of groups = 3 and response variables = 6, same practice has been noted in (15). Given these input parameters, the minimum sample size for this work stood at 21 individuals. In this study almost similar number of subjects were selected as calculated by G*Power. But these number of samples are less than the existing population within Pakistan. A total of 55 asthmatic only subjects, male:female – 34:21, age:mean(SD) – 55(12.2) participated. Ground truth of severity levels was confirmed by minimum two physicians as follows 1) Mild – 17, male:female – 9:6, age:mean(SD) – 50(12.1), 2) Moderate – 18, male:female – 12:6, age:mean(SD) – 51.5(13.7) and 3) Severe – 20, male:female – 13:7, age:mean(SD) – 50(11.5).

Inclusion and Exclusion Criteria: The patients were diagnosed according to the available standards (16), and the asthma severity levels (mild, moderate and severe) were identified according to the National Asthma Education and Prevention Programme – Expert Panel Report 3 (7, 16). The diagnosis of asthma was based on shortness of breath, wheezing history (frequency of hospitalization or visits to the ED), and general condition of the patient. Such practices have also been observed in other studies (17, 18). Given these details, the subjects were recruited based on suggestions from senior medical officers at both hospitals. Children and geriatric patients were not considered in this study.

The selected subjects were non-smokers who were not addicted to drugs. In addition, the selected subjects were those diagnosed as asthmatic patients without any other lung, heart or bowel region disease, and none of the patients had taken any medication for a few hours prior to data collection.

Preprocessing and Filtering: Respiratory sounds were sampled at 8000 Hz. The dominant frequency of respiratory sounds, between 100-1600 Hz (4, 19), was obtained using a fourth order band-pass Butterworth filter. Wheeze sounds and breath phase was identified and segmented by physicians through audio-visual inspection of the recordings and with the aid of spectrograms. Wheeze sounds has been segmented by its manifestation in the spectrogram and with the criteria: increase in intensity by 20dB, duration longer or equal to 100 ms and frequency greater or equal to 100Hz (20). The combination of these procedures produced wheezes labeled according to severity level, phase and location. Detail of segmented wheeze samples is given in Table 1.

Analysis: The wheeze segments were analyzed using Fast Fourier Transform (FFT). FFT with 512 points hamming window with 50% overlap was applied to obtain power spectrum density within the range of 100-1600 Hz (17, 18). Hamming window is a smooth window with an acceptable leakage (17, 18).The amplitude of the power spectrum was interpreted as a probable distribution of frequencies (the sum of absolute power spectrum values normalized to one). Using this method, the distribution of frequencies of all recordings is comparable regardless of the loudness of lung sounds (17, 18) and lung capacity. From the characterized frequency spectra, quartile frequencies such as – F_{25}, F_{50}, F_{75}, F_{90}, F_{99} in Hz was obtained. Further, mean frequency (MF) in Hz has been calculated from power spectrum. MANOVA was performed to identify significant difference between mild, moderate and severe samples by considering 1) All wheeze samples without any discrimination of location and phase, 2) Location – trachea and LLB, 3) Phase – Inspir and Expir and 4) Combination of location and phase – T-Inspir, T-Expir, LLB-Inspir and LLB-

Expir. MANOVA statics, Cohen's effect size (η^2) and all subsequent post-hoc analysis was also investigated. A 95% confidence level was considered significant ($p < 0.05$) for all statistical analysis. Eta squared (η^2) is used to determine effect size as follows – 0.02 small, 0.13 medium and 0.26 large.

Results

Figure 1 provides the μ(SD) of frequencies in nine databases sequentially. Further, Table 2 indicates the summary of results of MANOVA statistics results. In table 2 the results for all wheeze samples, samples grouped by location and phase, and samples combination of location and phase.

Analysis of variance in all wheeze samples (Table 2, 2nd row) indicate significant difference in severity levels $\Lambda = 0.892$, $F(12, 1534) = 7.547$, $p < 0.05$, $\eta^2 = 0.108$. Further, Post hoc result also prove significant difference in three groups *a*, *b* and *c*. In Figure 1, it can be noticed that μ(SD) of all features is different for mild, moderate and severe.

When auscultation location was used (Table 2, 3rd and 4th row) as a basis of comparison, at the trachea features show significant difference with large effect size $\Lambda=0.620$, $F(12,498) = 11.196$, $p < 0.05$, $\eta^2 = 0.461$. Further, post hoc also discriminated three groups *a*, *b* and *c*. Further, clear difference in μ(SD) values for mild, moderate and severe also can be noticed from Figure 1. At the LLB (Table1, 4th row), frequency feature proved to have significant difference $\Lambda = 0.939$, $F(12, 1020)=2.731$, $p < 0.05$, $\eta^2 = 0.061$. However, in post hoc only groups *a* and *b* has been discriminated. These results also can be verified from Figure 1, which indicates small difference in mild, moderate and sever μ(SD) values.

In the case of breath phases (Table2, 5th and 6th row), inspiratory samples indicate significant difference $\Lambda = 0.855$, $F(12, 750) = 5.109$, $p < 0.05$, $\eta^2 = 0.145$. Similarly for expiratory phase significant difference observed $\Lambda = 0.877$,

$F(12, 768) = 4.359$, $p < 0.05$, $\eta^2 = 0.123$. In post hoc, inspiratory samples indicated significant difference for three groups, however, expiratory samples were discriminated by groups *a* and *b*. Further, differences for three severity levels by Inspir and Expir dataset can be noticed from Figure 1.

Table2 (last 4 rows), provides the results for samples as a combination of location and phase. Further, presentation of μ(SD) of features for mild, moderate and severe can be realized in Figure 1. For T-Inspir, features indicated significance with large effect size $\Lambda = 0.432$, $F(12, 196) = 8.504$, $p < 0.05$, $\eta^2 = 0.568$. For T-Expir, frequency feature produced significant difference with large effect size $\Lambda = 0.614$, $F(12, 286) = 6.575$, $p < 0.05$, $\eta^2 = 0.386$. Further, in post hoc, three groups discriminated by T-Inspir, however, groups *a* and *b* indicated significant difference for T-Expir. It has been observe that frequency features were statistically significant for LLB inspiratory samples $\Lambda = 0.862$, $F(12, 538) = 3.446$, $p < 0.05$, $\eta^2 = 0.138$. Similar result obtained in form of $p < 0.05$ for three groups. However, for LLB-Expir features indicated $p > 0.05$.

Discussion

Results of this study indicated that the set of selected features have good performance for all the tested hypothesis as shown in Tables 2, $\Lambda = 0.614$-0.939, $F(12, 196\text{-}1534) = 2.731$-$11.196$, $p < 0.05$, $\eta^2 = 0.061$-0.568. Further, post hoc results also discriminated with in severity levels (group *a*, *b* and *c*). MANOVA results discriminated the severity levels for most of the datasets related to locations (trachea and LLB) and phase (Inspir and Expir). Reason could be that the strength to features has been improved due to MANOVA test. This approach is necessary, as breath sounds manifest from a very complex human respiratory system. Breath sounds originate from a complicated breathing system which consists of up to 23 generations with a total of almost 17 million tubes (21).

There have been also some studies that have used other or related features in a similar kind of work. Correlation with severity levels has been observed in (21) by using power spectrum bins of breath cycles, (1) through MF of non-wheeze segments, (3) using MF of wheeze segments and number of wheezes, and in (2) using the ratio of time expended with wheeze to total recording time (T_w/T_{tot}). However, wheeze data in (3, 21) was obtained from forced breathing maneuvers. According to another study, wheeze can also be generated in normal subjects with forced breathing (6). Hence, such wheezes are not always related to the degree of acuteness of asthma (6). On the other hand, asthma was induced in selected subjects under medication (1, 21). But, there is evidence that medication effects the change in frequencies of breath sounds and induced wheeze sounds may also be different from spontaneous wheeze sounds. Compared to these studies, our work demonstrated that severity levels of asthmatic patients can be differentiated with tidal breathing through spontaneous and non-induced wheeze sounds.

This work has investigated the characteristics of wheeze spectra according to severity levels obtained from two auscultation locations, trachea and LLB. (1, 3) have found good correlation between spectral features (mean frequency) and lung function values using a univariate approach using tracheal sounds. Another study, collected data from the trachea and LLB, conducted a similar analysis and found correlation only for tracheal breath sounds (1). These findings concur with our results. For the trachea, we found that the frequency feature produced larger effect size Λ = 0.432-0.620, F(12, 196-498) = 6.575-11.196, $p < 0.05$, η^2 = 0.386-0.568. Also, can be noticed higher variance represented by trachea related datasets in Figure 1. While these studies, and ours, provide good correlation results for the trachea, we found that a multivariate approach is suitable for the LLB, which is predominantly the location of auscultation by physicians for asthmatic patients, as it provides direct information on the physical identification and severity of pathology. Our findings revealed that the discriminatory power in the LLB samples is Λ = 0.862-0.939, F(12, 538-1020) = 2.731-3.446, $p < 0.05$, η^2= 0.061-0.138. Nevertheless, the overall analysis reveals that trachea has better performance than LLB due to the different characteristics in the acoustic filter that appears at these locations (22).

Correlation between severity levels and frequency feature set were also investigated within breath phases. It can be observed that the selected features performed for LLB-Inspir but show statistical insignificance for LLB-Expir. Further, in post hoc test, inspiratory and expiratory samples performed differently. It can be noticed that three groups *a*, *b* and *c* has been discriminated by all of the Inspir related samples. However, Expir related samples indicated significant difference for only *a* and *b* group. These findings concluded that inspiratory and expiratory wheeze samples exhibit different characteristics, which concurs with results from (23). Furthermore, it was also demonstrated that breath sounds attained during the Inspir and Expir phases showed different characteristics (22). This is largely due to dissimilarity in the physiology of the airway passage (i.e. long and short airways) experienced by the airflow during the inspiratory and expiratory phases.

It has been found that frequency parameters are higher in Inspir related samples than Expir related datasets, it can be noticed in datasets related to combination of phase and location (Figure 1). Interestingly, in normal subjects, tidal breathing sounds Inspir sounds are louder and higher than Expir sounds (vesicular breath sounds). Findings of the study indicated that Inspir related wheeze samples have stronger relation to severity level with respect to Expir related wheeze sounds. This difference was most likely due to the fact the inspiratory wheeze sounds are more prominent or Inspir sounds can be recorded better than Expir wheeze sounds in this study settings. Similarly, frequency values are higher in trachea related wheeze samples with respect to LLB related wheeze samples. This could be due to the fact that breath sounds are filtered

LLB. These differences in location and phase also can be due to different physiology, filters and severity levels.

In this study, the severity level of asthmatic patients has been correlated with wheeze spectra through frequency dependent features. The findings indicated that the frequency $\Lambda = 0.432\text{-}0.939$, $F(12, 196\text{-}1534) = 2.731\text{-}11.196$, $p < 0.05$, $\eta^2 = 0.061\text{-}0.568$ have performed well for all the tested hypothesis as shown in Tables 2 to 5 (9 datasets). We observed evidence of correlation to physiology, similar to another study, where airway thickness (wall area) was calculated and correlated to normal, mild, moderate and severe asthmatic subjects using computed tomography, where it was concluded that increase in wall thickness increased the severity level of asthmatic patients (24). Similarly, another study (17) noted that high-pitch sounds are produced when the calibre of air becomes narrow leading to the fluttering of airway walls and fluids (17) which produce wheeze sounds. These works indicated that changes in lung airways inevitably cause changes in the frequency of breath sounds so much so that in severe patients, this becomes conspicuous where wheezes appear to be louder than the underlying breath sounds and can be clearly heard without a stethoscope. Results of this study concurred with other studies, which revealed that obstruction in lung airways effect the frequencies of breath sounds from which wheeze manifest (2, 17).

Limitations

In the future, this study can be extended to an analysis of the characteristics of wheezes in other diseases with similar symptoms, e.g., COPD and pneumonia, and their behaviour in other related populations in which the monitoring and management of asthma is a priority, such as children and the elderly. An accurate and low-computation-cost solution could indeed provide a strategy for the development of a much needed portable and affordable computerized decision support system (CDSS) for asthmatic patients. Such an application must be easily tailored to individual patients and should be aligned to the current practices of physicians and patient ergonomics.

Conclusion

The results of frequency feature vector demonstrated that severity levels of asthmatic patients (mild, moderate and severe) can be identified through analysis of wheeze sound obtained with tidal breathing maneuver. Findings of the study also indicated that overall frequency features discriminated the severity level in all the datasets except LLB expiratory (LLB-Expir). In post hoc test pair *a* and *b* discriminated all datasets. However, pair c was discriminated by all datasets related to trachea location and inspiratory phase. Selected features indicated different characteristics according to severity levels, location and breath phases. Inspiratory and expiratory breath phases indicated different behavior according to severity level. It was also found both phases are equally informative for severity level of asthma patients. With the comparison of location related datasets, trachea related data sets indicated higher effect size than the LLB related datasets. Overall comparison of datasets also indicated that trachea related datasets are more specific and good predictors. However, trachea is not under the practice of physician. Because it does not provide location of obstruction. Furthermore, the set of selected features and results of this study could play role for the discrimination/classification of the severity level for computerized decision support system (CDSS). In addition, the findings of this study could be generalized to overall population of the Pakistan and whole world. As, sounds generated during respiration are not effected by area or location of the subjects. In future features can be selected which are more suitable for LLB location.

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Table 1: Summary of datasets used in this study

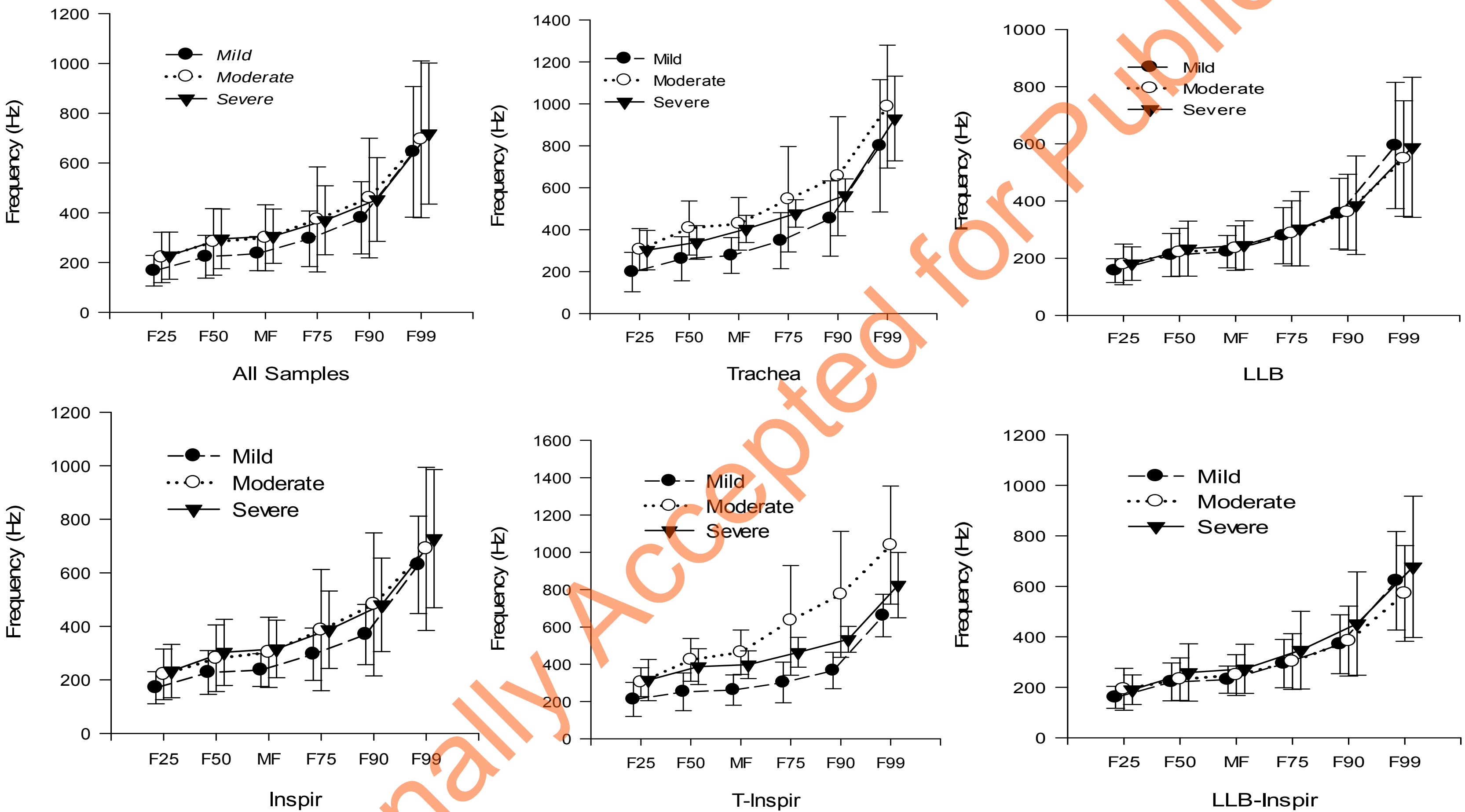
	Total subjects	Male	Female	All Samples	Trachea	LLB	Inspir	Expir	T-Inspir	T-Expir	LLB-Inspir	LLB-Expir
Mild	17	9	8	199	49	150	98	101	20	29	78	72
Moderate	18	12	6	254	85	169	127	127	32	53	95	74
Severe	20	13	7	322	123	199	158	164	54	69	104	95
Total	55	34	21	775	257	518	383	392	106	151	277	241

Table 2: Summary of MANOVA statistics on various datasets –details of post hoc – *a* (mild and moderate), *b* (mild and severe), *c* (moderate and severe)

Dataset	Wilks's Lambda (Λ)	F	df	Error	ρ-value	Effect Size (η^2)	Post hoc

All Samples	0.892	7.547	12	1534	**0.000**	0.108	***a,b,c***
Trachea	0.620	11.196	12	498	**0.000**	0.461	***a,b,c***
LLB	0.939	2.731	12	1020	**0.001**	0.061	***a,b***
Inspir	0.855	5.109	12	750	**0.000**	0.145	***a,b,c***
Expir	0.877	4.359	12	768	**0.000**	0.123	***a,b***
T-inspir	0.432	8.504	12	196	**0.000**	0.568	***a,b,c***
T-Expir	0.614	6.575	12	286	**0.000**	0.386	***a,b***
LLB-inspir	0.862	3.446	12	538	**0.000**	0.138	***a,b,c***
LLB-Expir	0.935	1.324	12	466	0.201	0.065	*b*

**bold font indicates statistical significance, $p < 0.05$.*


Frequency (Hz)
Mild
Moderate
Severe
F25
F50
MF
F75
F90
F99
All Samples
Trachea
LLB
Inspir
T-Inspir
LLB-Inspir

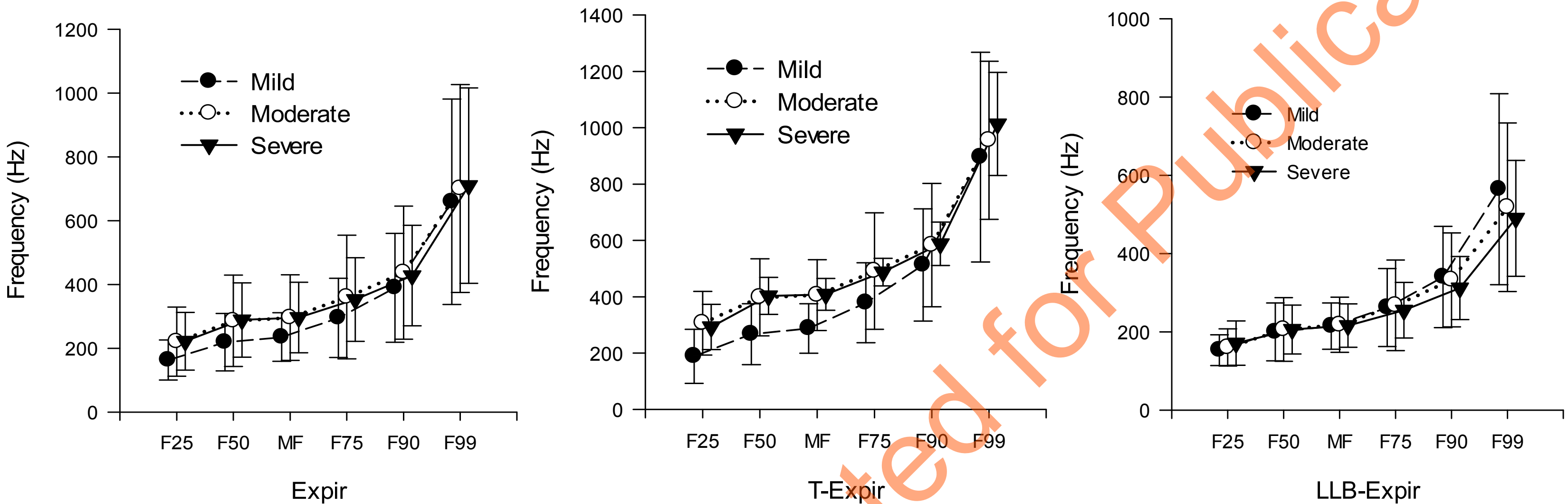


Figure 1: Results of MANOVA analysis with µ(SD) values of selected frequency parameters in nine data bases. Variance of mild, moderate and severe patients can be noticed datasets.