RESEARCH ARTICLE

Validation of portable Bluetooth enabled smart spirometer (Alveoair™) for the measurement of various lung functions in healthy subjects

Pranjali Sameer Shinde, Rohan Ravindra Kulkarni, Ganesh Vilas Kulkarni

Department of Physiology, ACPM Medical College, Dhule, Maharashtra, India

Correspondence to: Pranjali Sameer Shinde, E-mail: drpranjaliss@gmail.com

ABSTRACT

Background: Alveoair™ is a fully indigenously developed turbine operated handheld and portable Bluetooth enabled smart spirometer. Affordable Bluetooth enabled smart spirometers like Alveoair™ have been designed and developed to meet the challenges of patients with lung tissue disorders with aims to provide constant monitoring of the lung conditions and identify the degree of prognosis of the diseases before and after treatment. During the current pandemic of coronavirus disease 2019, lung function is severely affected. Spirometry is one of the most important tools in the investigation and monitoring of the patients with respiratory pathology and helps establish diagnosis for various lung diseases through the evaluation of lung functions and curves. **Aims and Objectives:** The objective of the present study is validation of Alveoair™ spirometer accuracy with Food and Drug Administration 510K Notified and CE approved spirometer NuvoAir in measuring lung capacity with various parameters limited to forced vital capacity (FVC), forced expiratory volume (FEV)1, peak expiratory flow (PEF), and FEV1/FVC measurement readings. **Materials and Methods:** The present study was done on 60 healthy subjects without any risk factors affecting pulmonary functions and all the necessary precaution taken during the period of study. Pulmonary function test was performed by both Alveoair™ and NuvoAir devices on each of the subjects for result comparisons. **Results:** It is evident that measurements parameters FVC, FEV1, PEF, and FEV1/FVC by the Alveoair™ have demonstrated parity with NuvoAir measurement with high Pearson and interclass correlation coefficient >90%, r^2 value of FVC, FEV1, and PEF >90% and for FEV1/FVC ratio >80% and P-value for all the parameters <0.0001 as compared to NuvoAir device. Using Bland-Altman plots, it was seen that the mean difference was small and well over 95% of measurements were within the limits of agreement. **Conclusion:** Alveoair™, Bluetooth enable low-cost spirometer, used for the measurements of FEV1, FVC, PEF rate, and FEV1/FVC in healthy subjects, is found to be compatible with any other smart devices with regard to its sensitivity, accuracy, and reproducibility.

KEY WORDS: Bluetooth Enabled Smart Spirometer; Spirometry; Validation; Monitoring; Asthma; Chronic Obstructive Pulmonary Disease, Coronavirus Disease 2019, Respiratory Diseases

INTRODUCTION

Pulmonary function test (PFT) is a crucial method in diagnosis of respiratory illness and associated symptoms. In addition, it is a monitoring tool for patients with prior history of respiratory conditions.[1-3] Respiratory diseases affect a large set of population, in total 300 million people globally suffer from asthma and by 2025, this number is expected to reach 400 million.[4] While asthma prevalence is higher in high-income countries, most asthma-related mortalities occur in low-middle-income countries.[4]

In addition to this, the prevalence of chronic obstructive pulmonary disease (COPD) was estimated at around 7.6%.[5] COPD imposes significant health-care costs and on

the standard of life of the patients.[6] This is going to increase further as the world ages and there is a rise in pollution.[7] However, the perception is that the exact prevalence of this disease is unknown.[5]

Even though spirometry is an important tool which helps in respiratory disease diagnosis,[1-3,8] it is still finding a corner place or is unutilized in the primary care settings,[9,10] Some of the reasons for lesser adoption of spirometry by the clinicians could be due its operational attributes such as size of spirometer, cost of procurement, higher maintenance cost with repeated calibration, and dedicated resources or technicians. From an interpretation point of view, most physicians require specialized training for performing and its interpretation.[11] As a result, this promotes physicians to refer the patients to either a superspecialist or a larger health-care setting where this spirometry facility is available.[11] As the world is moving toward digitalization of health-care services, few portable smart diagnostic devices emerged in the market which includes digital portable spirometers run on mobile phones or tablets. Given the high prevalence, there is a great need for a portable/handheld spirometer which needs to be low cost, but still able to perform precise and systematic spirometry measurements, with functions comparable to laboratory spirometers.[12]

Here, digital spirometer devices work as capturing data samples and analyze and transfer these samples to mobile phones for further interpretation and display to end users (physicians). Use of other digital mediums in association with digital devices reduces the burden of processing of complex data and provides a much more enhanced and powerful interface for display and analysis at low cost.

Keeping the same idea at front to develop a highly accurate and low-cost spirometer, Alveoair™ is a fully indigenously developed turbine operated handheld and portable Bluetooth enabled smart spirometer that can be deployed in primary care settings and at family physician offices easily. Early detection and constant monitoring of lung volume and capacities facilitates the healthy lung conditions and may reduce hospitalization costs.[13] Conventional spirometers have been a challenge in terms of portability, cost of software and hardware vis-à-vis pulmonary diagnosis, setup requirement, and feasibility of test before and after treatment.[14,15] Affordable Bluetooth enabled smart spirometers like Alveoair™ have been designed and developed to meet the challenges of patients with lung tissue disorders with aims to provide constant monitoring of the lung conditions and identify the degree of prognosis of the diseases before and after treatment. Alveoair™ enables the physician to efficiently diagnose lung conditions even in remote areas and during emergency scenarios with a highly affordable and maximum achievable accuracy and reproducibility. Handheld, flow-sensing spirometers have several advantages over traditional volume sensing, desktop spirometers for clinical and epidemiological purposes including portability, utility in the field or home settings, lesser risk of cross-contamination, battery power, and ease of cleaning.[9]

The objective of the present study was undertaken to validate its measurements limited to forced vital capacity (FVC), forced expiratory volume (FEV)1, and peak expiratory flow (PEF) with compatible device under the trade name "NuvoAir." Alveoair™ is ISO 26782:2009, ISO 23747:2015 certified spirometer and also calibrated using 3L syringe. Accuracy of the results is of the 3L syringe test which is within ±2.5% which is in accordance with the ISO standards accuracy of volume.[9]

NuvoAir spirometer is Food and Drug Administration (FDA) 510K Notified and CE approved spirometer hence selected for validating the measurements and diagnostic compatibility.[9] Recent study conducted a systematic search and review of commercially available portable electronic spirometers designed for asthma patient use and observed that accuracy of most of the devices was not publicly available but there were very few devices which demonstrated volume accuracy of 3% or 50 ml and flow accuracy of 5% or 200 ml.[16] Although, Alveoair™ meets the requisite standards prescribed by FDA, we have undertaken the present study in tertiary care hospital:

1. To determine mean value and SEM of FVC, FEV1, and plug flow reactor (PFR) measurements of healthy subjects by "Alveoair™" as well as "NuvoAir" spirometer
2. To establish compatibility of measurement of FVC, FEV1, and PFR with another Bluetooth enabled smart "NuvoAir" spirometer in healthy matched subjects
3. To compare and determine % errors of measurements and correlation between FVC, FEV1, and PFR measurements by two devices
4. To provide cost-effective Bluetooth enabled smart Indian device Alveoair™ with the same standards of Sweden made NuvoAir which will be useful to the community in the current pandemic of coronavirus disease 2019 (COVID-19).

MATERIALS AND METHODS

Materials and Methods used.[15] A cross-sectional prospective study was conducted in the respiratory medicine department of the tertiary care center. Sixty subjects for the study were drawn randomly among the medical and paramedical students voluntarily without any risk factors affecting pulmonary functions. The subjects were requested to give written consent and were screened for blood pressure and lung tissue abnormalities. The height and weight of the subjects were recorded to calculate the predicted values of lung volume and capacities measurement of the subjects.

Alveoair™ is a handheld digital spirometer that connects to smart mobile phones over the Bluetooth low-energy (BLE) protocol. Weight of the device is approx. 78 g with batteries and it uses AAA batteries to power up sensors. Lifespan of

the batteries is around 1200 spirometry tests or 1.5 years. Alveoair™ works on turbine mechanisms (Flow MIR disposable turbines used) with disposable nozzles.

To conduct successful spirometry, in standing position, the subjects were asked to blow the air into the Flow MIR disposable turbine connected to Alveoair™ device and upon forceful exhalation devices capture the data and send reading to the mobile app over BLE protocols. In the application, data gathered and Alveofit™/alveoMD app check the quality of test conducted and values interpretation. Alveoair™ device used NHANES III study to calculate the percentage of FEV1 and FVC along with z score and LLN values. The device allows users to perform minimum three maneuvers and can be extended to six maneuvers and it chooses the one that has obtained the best FEV1 and FVC, but it also allows users to perform individual maneuvers and visualize each curve independently. Please refer Figure 1 for alveoair digital spirometer device and mobile application.

1. The subjects were tested on both Alveoair™ and NuvoAir spirometers under expert guidance randomly
2. Sufficient rest time as per spirometry methodology was provided to the subjects for each iteration of the test. Hourly testing rate on an average was 6 patients/h
3. Sterilized turbine was used to conduct spirometry
4. Data have been collected using the alveoMD application (both mobile/Tablet and Web Application) so that data can be used for future references
5. Data have been stored on HIPAA compliant Alveofit™ servers
6. The patient lung values (FVC, FEV1, and FVC/FEV1 ratio) were compared with the standard values as published by GLI 2012, NHANES III, Quanjer 1993 and the patient diagnosis was performed accordingly
7. Statistical analysis was carried out to determine mean values with standard deviation (SD). The *P*-value, Pearson correlation coefficient, and the intraclass correlation coefficient (ICC) were also calculated to evaluate degree of agreement and relation between the values obtained by Alveoair™ and NuvoAir devices for same patients using SPSS statistics, version 24. Moreover, Bland and Altman plots were created to depict the bias between the mean differences for the values obtained by the two spirometry devices.

Inclusion Criteria

Healthy individuals without any respiratory disorder or any related history between the age group of 15 and 45 years were included in the study.

Exclusion Criteria

Followings are exclusion criteria[17,18]
1. Any history of painful ear infection
2. Eye surgery in the past 3 months
3. Chest/abdominal surgery in the past 3 months
4. Any history of tuberculosis, COPD, asthma, collapsed lungs, and aneurysm
5. History of detached retina
6. Stroke or heart attack in the past 3 months
7. History of blood in cough in last month
8. Pregnant woman
9. Subjects who were COVID-19 positive and undergoing treatment
10. Subjects who had heavy meal just before the scheduled test
11. Subjects suffering with cough during the test.

Ethics Approval and Consent to Participate

The study was approved by the ACPM Medical College, Dhule, Maharashtra meeting 20.IEC/ACPMMC/Dhule, topic Research proposal of entitled "Validation of portable Bluetooth enabled smart spirometer (Alveoair) for the measurement of various lung functions in healthy subjects" (December 8, 2020). Each participant was informed about the study and provided written informed consent.

RESULTS

A total of 60 participants were screened and selected for the study according to pre-defined inclusion and exclusion criteria. All selected participants performed spirometry with both the devices. The observations obtained from both the devices were analyzed and mean values with SD are depicted in Table 1. It is evident that measurement by the Alveoair™ spirometry demonstrated parity with NuvoAir measurement with minimum SD as compared to NuvoAir device. However, difference in mean value and SD between the measurements of both devices is statistically insignificant.

We also calculated Pearson correlation, r^2, ICC, and *P*-value to evaluate the difference of recorded data by both the smart spirometry devices and shown in Table 2. It is observed that both matrices for FEV1, FVC, PEF rate (PEFR), and FEV1/FVC are significantly high and for some parameters are still higher and suggest that Alveoair™ is compatible as regard the accuracy and sensitivity of measurements. These matrices also validate the measurement and performance of Alveoair™ spirometers with such other Bluetooth enabled smart devices marketed by other manufacturers like NuvoAir.

The correlation plots using all the parameters measured by both the spirometric devices are depicted in Figure 2 for visual presentation of difference between the results recorded from the same patient random order. The correlation plots for FEV1, FVC, PEF, and FEV1/FVC demonstrate high degree of statistically significant agreement between the Alveoair™ and NuvoAir measurements done on all the 60 healthy subjects, thus confirm the hypothesis of the present study.

Table 1: Observations obtained from both the devices								
Parameter	Alveoair™				NuvoAir			
	FEV1 (L)	FVC (L)	PEF (L/m)	FEV1/FVC Ratio	FEV1 (L)	FVC (L)	PEF (L/m)	FEV1/FVC ratio
Mean	2.65	3.12	420.07	0.87	2.73	3.31	407.3	0.85
Minimum	1.17	1.3	164	0.61	1.10	1.29	142.8	0.57
Maximum	4.43	4.92	844	1	4.63	5.18	814.8	1
SD	0.64	0.75	138.49	0.06	0.70	0.82	135.52	0.07

FEV: Forced expiratory volume, FVC: Forced vital capacity, PEF: Peak expiratory flow

Bland-Altman Analysis

Bland-Altman plots are also drawn for observations recorded from Alveoair™ and NuvoAir device to assess reproducibility of the observations and shown in Figure 3. These plots provide the visual analysis of mean difference of the measurements carried out by Alveoair™ and NuvoAir. It is observed that all the parameters measured by both devices demonstrate close conformity to each value and insignificant difference between the mean values of measurements, suggesting reproducibility of measurements by the Alveoair™ spirometer [Table 3].

DISCUSSION

In the present study, the results of the PFTs measured by portable Bluetooth enabled spirometer Alveoair™ and NuvoAir spirometer were compared.

It is evident that measurement by the Alveoair™ spirometer demonstrated parity with NuvoAir measurement with less SD as compared to NuvoAir device. However, the difference in mean value and SD between the measurements of both devices is statistically insignificant. The correlation plots for FEV1, FVC, PEF, and FEV1/FVC demonstrated a high degree of statistically significant agreement between the Alveoair and NuvoAir measurements which confirms accuracy and sensitivity of apparatus.

Bland-Altman plots of both the devices demonstrated close proximity to each value and statistically insignificant difference between the measured values, with more than 95% values within the limits of the agreement.

In a recent study,[15] CE Class 2A and FDA 510K Notified NuvoAir showed all spirometric parameters in significant correlation with conventional spirometer and Alveoair™ showed significant correlation with NuvoAir.[3]

For a clinical trial for validation studies of a particular device/method with a standard device, following statistical techniques are used to measure the correlation and agreement between the readings. Similar techniques were used in the studies performed for validating other such spirometer devices.[15, 19-22]
a. Bland-Altman analysis
b. Pearson correlation

Table 2: Pearson and ICC				
Parameter	Pearson correlation coefficient (r)	r²	ICC	*P*-value
FEV1	0.988	0.977	0.966	<0.0001
FVC	0.986	0.978	0.952	<0.0001
PEFR	0.951	0.905	0.947	<0.0001
FEV1/FVC ratio	0.91	0.835	0.91	<0.0001

FEV: Forced expiratory volume, FVC: Forced vital capacity, PEF: Peak expiratory flow, ICC: Intraclass correlation coefficient, PEFR: Peak expiratory flow rate

Table 3: Comparison of parameters	
Parameter	# of readings whose difference is within the limits of agreement (i.e., within 2 SDs)
FVC	Difference of 98% of all the readings were within the limits of agreement
FEV1	Difference of 98% of all the readings were within the limits of agreement
FEV1/FVC Ratio	Difference of 95% of all the readings were within the limits of agreement
PEF	Difference of 97% of all the readings were within the limits of agreement

FEV: Forced expiratory volume, FVC: Forced vital capacity, PEF: Peak expiratory flow

c. Intraclass coefficient
d. *P*-value.

In general, the values of Pearson correlation and ICC values should be >0.7 to indicate a good to very good correlation between values measured by the two methods.[21,22]

Moreover, to demonstrate high agreement in the readings, according to the Bland-Altman analysis, the difference of majority of the readings should be within 2-SD of the mean of the difference between the values which are considered as limits of agreement.[20]

Similar studies were conducted for other portable spirometers such as Vital Flo[19] and Air MD (NuvoAir spirometer)[15] on a comparable number of patients and the statistical analysis of the above-mentioned four spirometry parameters was done. The study, validations, and the results were tabulated in a similar form as our current study.
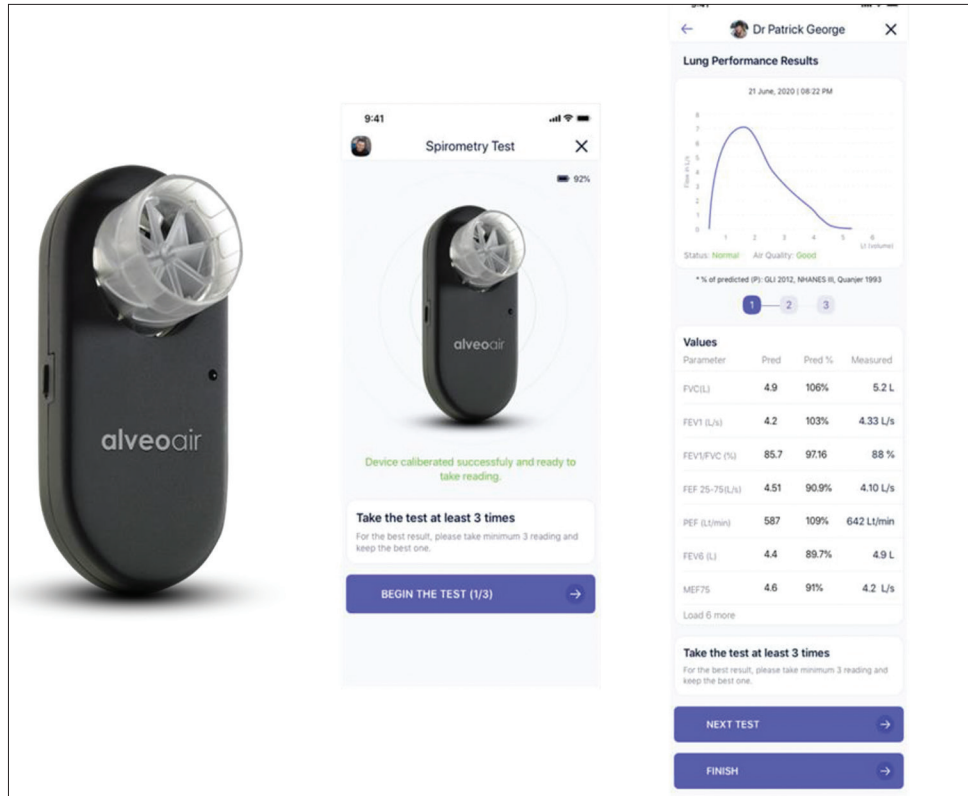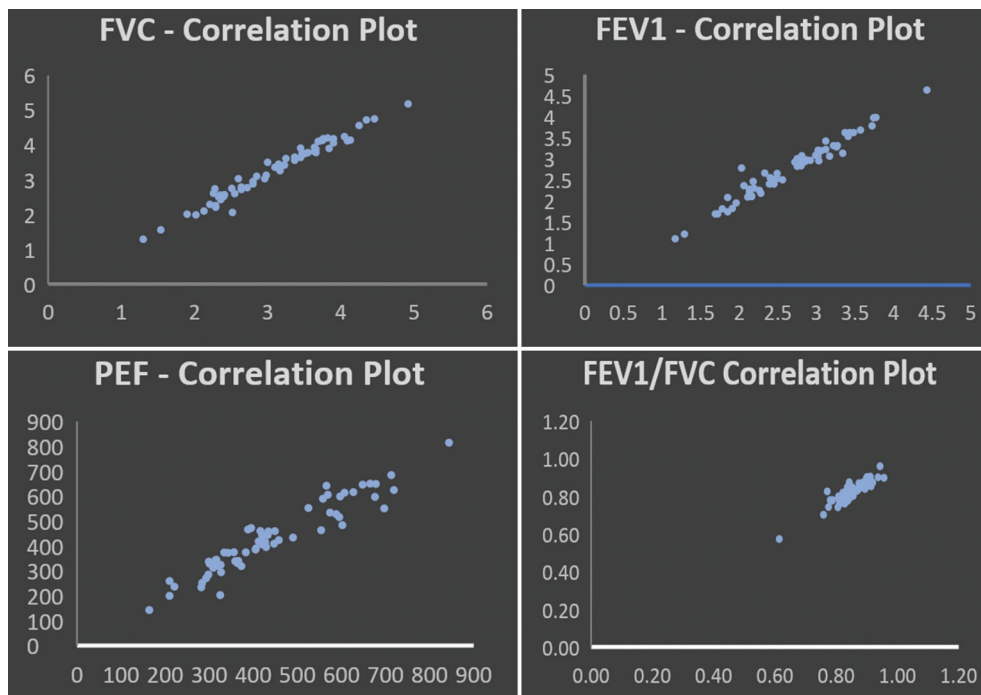
Figure 1: Alveoair™ spirometer

Figure 2: The correlation plots using all the parameters measured by both the spirometric devices

Vital Flo study was conducted on pre-diagnosed asthma patients while our study was conducted on healthy subjects. The reason for not involving asthma patients in the study was the wariness of respiratory patients to visit the hospitals during the COVID-19 pandemic.

Similarly, for Air MD, subjects with no pre-diagnosed respiratory conditions and patients with pre-diagnosed conditions were taken as part of the study.

As can be seen from these studies, the correlation of the readings of the four parameters under consideration are
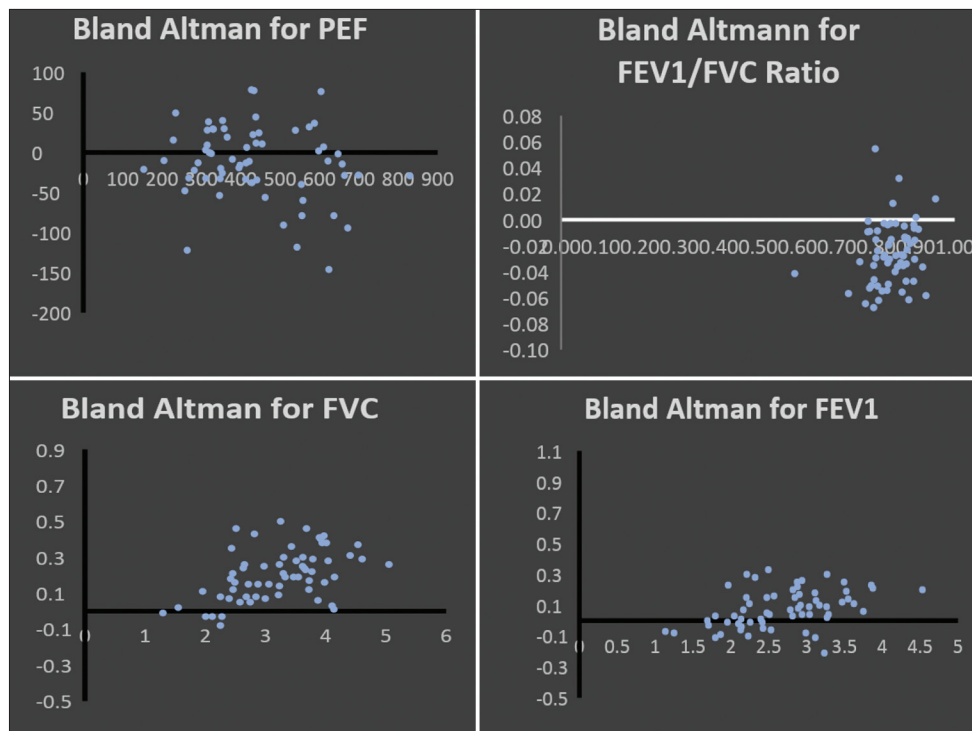
Figure 3: Bland-Altman plots for observations recorded from Alveoair™ and NuvoAir device to assess reproducibility

>0.90 as is the case with our current study and as well as in the Bland-Altman analysis, the difference between the readings of these parameters is within the 95% (2-SD) limits of agreement.[15,19]

According to the manufacturer, Alveoair™ digital spirometer offers easy handling and nozzles are disposable and of individual use. It can be connected to any smartphone device after downloading the app Alveo MD Lite. It also allows the visualization of spirometry loop, history of respiratory diseases, allergies, difference before and after medication, and diagnosis of pathologies. The device itself detects errors in acceptance criteria that it reports in the display of the results.[23]

NuvoAir is made in Sweden while Alveoair™ is completely designed and made in India and cost of hardware and software along with its further subscriptions is very low. Potentially millions of people have respiratory disease but remain undiagnosed[5] only because of low accessibility to conventional spirometers.[10] The biggest strength of this study is that Alveoair™ is a handheld, affordable, easily accessible spirometer which can be used anywhere, anytime by patients, paramedical workers, and medical professionals of primary health-care providers to tertiary care hospitals.

Recent ongoing work has explored the potential role for home spirometry to monitor disease\progression and would allow more frequent measurements that could promote early detection of changes in disease status in individual patients.[24]

Validation of measurements of volume and capacities using smart portable devices could be utmost support in health-care system, if performed by the patients/nurses themselves without technical or medical training, as measure of constant monitoring of lung functions in certain chronic pulmonary diseases at primary care center or in rural health-care center.[25]

There are few limitations of the present study: (1) It requires internet access to conduct the test after downloading the app. (2) The present study is conducted only on healthy subjects so further research is needed in patients with respiratory diseases.

CONCLUSION

Alveoair™ is a Bluetooth enabled, highly portable, low-cost spirometer, used for the measurements of FEV1, FVC, PEFR, and FEV1/FVC in healthy subjects. It can be operated easily with use of mobile application and does not need repeated recalibration.

It was found to be compatible with any other smart devices with regard to its sensitivity, accuracy, and reproducibility. The results of portable spirometer demonstrate validation with measurements of same parameters using "NuvoAir" portable spirometer, suggesting that "Alveoair™" is a reliable portable spirometer for the assessment of lung function with least setup requirements, low cost, high performance, and reproducibility of spirogram.

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