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Research Article

Factors Associated with Lung Function Tests Indices in Adult Asthmatics Attending a Tertiary Hospital in South-Western Nigeria

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ABSTRACT

The prevalence of asthma has continued to increase globally and despite new guidelines and drugs, there is still a failure of control. The aim of this study was to assess the determinants of Lung Function test indices among adult asthmatics attending the Tertiary hospital. The study was a cross-sectional study conducted at the University College Hospital, Ibadan, Nigeria. A simple random sampling technique with computer-generated random numbers was used to recruit 355 patients. Spirometry was done with handheld Spirobank II (Medical International Research USA, Inc) after withholding a short-acting inhaled beta-agonist for at least six hours before the test. With each of the patients sitting comfortably, and after an initial familiarisation with the machine, the spirometry was carried out. Data were analysed using SPSS version 23. The Chi-square test was used to analyse association between categorical variables and correlation analyses was used to analyse relationships between continuous variables. Linear regression and ordinal logistic regressions were used to determine the predictors of lung function tests. A p-value of ≤ 0.05 was considered to indicate statistical significance. Three hundred and fifty-five patients who met the criteria for recruitment were interviewed. The mean age of the respondents was 39.04 (SD+ 11.335) years. For every 1 unit increase in age, there was a statistically significant increase in Forced expiratory volume per second (FEV1) % predicted by about 0.318 units (95%CI=0.116-0.520, p=0.002). Also, after adjusting for other variables, the predictor of FEV1 % predicted was sex and occupation. Females were about 2.5 times less likely to have severe asthma than males (OR= 0.397; 95% CI= 0.253-0.621). For every 1 unit increase in body mass index (BMI), there was a statistically significant increase in peaked expiratory flow rate (PEFR)% predicted by about 0.714 units (95%CI= 0.118-1.314, p=0.019). Also, for every 1 unit increase in age, there was a statistically significant increase in PEFR% predicted by about 0.354 units (95%CI= 0.153-0.555, p=0.001). In conclusion, after adjusting for other variables, lung function test indices increased with age and body mass index. The female sex and the Professionals were less likely to have severe asthma than males and unskilled workers respectively.

Keywords: *Factors, Lung Function Tests, Adult Asthmatics*

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INTRODUCTION

Pulmonary function assessment is very important in the diagnosis and management of patients with asthma. Spirometry can be used for early detection of ventilatory dysfunction before the onset of symptoms. It could also be used to follow the natural history of disease over time. In a case-control study of 240 subjects in Benin, Nigeria, it was reported that there was no significant difference between Spirometric and peak-flow meter values. Thus, the peak-flow meters which are less bulky and cheaper could be used in place of spirometer, especially in the rural settings (Oni *et al*, 2014). The asthma control test was reported to have significant correlations with FEV1 and serum magnesium levels. It can therefore be used to monitor response to treatment in resource-limited settings where there is no peak flow meter (Yanamadala *et al*, 2021). The PEFR of healthy medical students of the Benue State University was 405.97 ± 77.59 L/min (437.32 ±60.11L/min in the males and 316.01 ±44.76L/min in the females) with height being the best predictor of PEFR among the studied subjects (Ogli and Agaba, 2014). The prevalence of asthma among respiratory unit patients was 6.6% and higher in the first three decades of life in a study conducted in Nigeria(Oni *et al*, 2010). It was reported that Helicobacter pylori protect children from asthma and also reduces the severity in those children with asthma (Fouda *et al* 2017).

Cigarette smoking and exposure to unclean fuel used for cooking were reported to be associated with an increased prevalence of asthma in a study conducted in India (Singh *et al*, 2020). Also, cigarette smoking was associated with lower mean values of FEV1 and the ratio of FEV1/FVC according to Isah *et al* (Isah *et al*, 2017). Asthma severity and control were strongly related to the quality of life of children with asthma in an Egyptian study (Enaldy *et al*, 2019). Interleukin-25 was found to be associated with severe asthma in a study conducted in Warsaw to assess the relationship between interleukin-25 and asthma control (Paplinska *et al*, 2019). There has been an increasing prevalence of asthma in Africa over the past two decades and there is a need to investigate the predisposing factors to reduce its burden (Adeloye *et al*, 2013). Desalu *et al* reported the adult prevalence of asthma in Urban Nigeria to be 3.3% and in rural Nigeria to be 1.5% respectively in a study conducted in Ilorin, Nigeria (Desalu *et al*, 2021). However, the prevalence of physician-diagnosed asthma and clinical asthma among all subjects was 2.5% and 6.4% respectively according to another nationwide prevalence study carried out in Nigeria (Ozoh, 2019).

Forced expiratory volume per second is more reliable than Peak expiratory flow rate in the assessment of lung function (GINA, 2022). The lower the values of Forced expiratory volume in one second (FEV1) and the Peaked expiratory flow rate (PEFR), the higher the asthma severity. Asthmatics harbor an unusual type of inflammation in the airways that make them more reactive than non-asthmatics to a wide range of stimulants, leading to extreme bronchial wall reduction resulting in wheezing and dyspnoea. Narrowing of the bronchial wall is typically reversible, but in some patients with chronic asthma, the bronchial wall may not be reversible (Mcfadden, 2005). The predictors were height and age according to the results of a study conducted in Nigeria by Fawibe *et al*. The values of spirometric indices decrease with age in both sexes but increase with stature. (Fawibe *et al*, 2017). Workers in the spinning and weaving areas of a textile company had lower lung function test indices compared with workers in other areas. Additionally, respiratory symptoms (rhinitis, cough, and breathlessness) were more prevalent in the dusty areas of the company (Nagoda *et al*,2012). Teachers exposed to chalkboards are at increased risk of occupational-related lung damage compared to those who were not and there is a need to shift from chalkboards to whiteboards. The aim of this study was to assess the determinants of lung function test indices among asthmatics attending the University College Hospital, Ibadan, Nigeria.

MATERIALS AND METHODS

The study was carried out at the Medical outpatient clinic of the University College Hospital (UCH), Ibadan Oyo State in the South Western area of Nigeria from 1st of April 2010 to 31st of March 2011. Ibadan is the largest city in West Africa South of Sahara and has a population of about 3.6 million inhabitants; it is cosmopolitan in nature in which the Yorubas are the predominant ethnic group. The study was cross-sectional and was conducted over a period of 12 months to complete the sample size.

Sampling techniques

A simple random sampling technique with computer generated random numbers was used for selection. Asthma clinic holds weekly at the Medical Outpatient Clinic. An average of 74 patients were seen per month (an average of 888 in 12 months) at the asthma clinic during the period. Random numbers within the range of the number of registered asthmatics was generated using the random number function of Microsoft Excel 2007. The numbers were sorted from the smallest to largest and on each clinic day, eight patients with serial numbers corresponding to the random numbers generated were selected for recruitment until the calculated sample size of 355 was achieved.

Study population: this was composed of adults age between 18years and 55years with an established diagnosis of asthma and already on treatment and follow up.

Definition of asthmatic patients: Physician diagnosed asthma, or patients treated for asthma attack and the use of asthma medications.
Patients with history of recurrent cough worse at night, recurrent wheeze, recurrent breathlessness at least partially reversible (with or without the use of bronchodilators) and chest tightness. On examination, they might have hyper-expansion of the thorax, chest deformity, dyspnoea and rhonchi.

Inclusion criteria: consenting patients 18 to 55years; patients with established diagnosis of asthma and history of the use of inhalers (dry powder and metered dose inhalers).

Exclusion criteria: included non-consenting patients, subjects with asthmatic attacks, those with smoking history of more than 5 pack-years because they were more likely to have chronic obstructive pulmonary disease. Patients with chronic illness that may affect their functional status (such as ischaemic heart disease or cardiac failure).

Sample size estimation: Sample size was estimated using the formula

$$n = \frac{(Z_\alpha + Z_\beta)^2 pq}{d^2}$$

Quoting prevalence rate of asthma, 13% for Nigeria according to the International Study of Asthma and Allergies in Childhood (Wjs M and Boakye D, 2007).

n= minimum sample size
Z_α=the standard normal deviate, usually set at 1.96, which corresponds to the 95% confidence level.
p=the prevalence rate of asthma for Nigeria =13%.
q=1.0- p
d=degree of accuracy desired usually set at 0.05.
β=20%, Power is 80%

$$n = \frac{(1.96+0.84)^2(0.13)(1-0.13)}{(0.05)^2} = 355$$

For the purpose of this study, a minimum 355 patients were recruited.

Height: The heights of the subjects were measured using a stadiometer manufactured by Seca Corporation Columbia, Maryland, United States of America. The heights were measured to the nearest 0.01meter(m). The patients were asked to remove their headwear and the hair was flattened temporarily with a hard-flat surface making it perpendicular to the wall. Zero error was adjusted for after each subject for accuracy.

Weight measurement: The patient had an instruction of a 12-hour overnight fast **(so** that breakfast would not interfere with weight) and an emptied bladder. The weight was measured with Elgil Medical, England. Then, they were requested to stand on the platform looking straight but still. After the first measurement, the process was repeated and the mean recorded.

Measurement of lung function: Lung function assessment was done with handheld Spirobank II(Medical International Research USA, Inc) after withholding short-acting inhaled beta-agonist for at least six hours before the test. With each of the patients sitting comfortably, and after an initial familiarisation with the machine, the spirometry was carried out. The best of three efforts of Forced expiratory volume in one second (FEV_1) and Peaked expiratory flow rate (PEFR) were recorded. The FEV_1% as percentage predicted and the PEFR% as a percentage predicted were calculated for the respondents and these were entered into the records. The spirometry was performed by trained personnel and the equipment meet ATS standard for accuracy and reproducibility.

Categorisation of lung function tests results: FEV_1% predicted was used to classify patients into three asthma categories of severity. Patients with FEV_1% greater than 80% were classified as having Intermittent/M ild persistent asthma, those with FEV_1% between 60%-80% were classified as having Moderate persistent asthma while those with FEV_1% less than 60% were classified as having Severe asthma. PEFR% predicted was also used to classify patients into three asthma categories of severity. Patients with PEFR% greater than 80% were classified as having Intermittent/Mild persistent asthma, those with PEFR% between 60%-80% were classified as having Moderate persistent asthma while those with PEFR% less than 60% were classified as having Severe asthma.

Occupational classification: Occupational status was classified according to the groupings by Borroffka and Olatawura, used by Eze *et al*(Eze *et al*, 2009) in their work: Class I (doctors, lawyers, teachers, scientists, high government officers); Class II(teachers, administrators, supervisory personnel, large-scale farmers, entrepreneur and armed forces officers); Class III (clerks, motor vehicle officers, mechanics, tailors, butchers, soldiers, policeman, small-scale entrepreneurs); Class IV (cooks, barbers, domestic servants, gas station attendants, goldsmiths, palm wine tappers, small-scale farmers); Class V (labourers and petty traders) and class VI (housewives, unemployed educated youths and apprentices). Professionals belonged to classes I and II, Skilled workers were classses III and IV, unskilled workers were classes V and VI.

Data Analysis: The data were analysed using SPSS software version 23. Frequency tables and diagrams in form of charts were used for relevant variables. Correlation analysis was used for continuous variables and chi-squared tests were used to assess association of Lung Function Tests indices with other variables. Linear regressions and ordinal logistic regressions were done to determine the predictors of Lung Function Tests indices. A p-value ≤ 0.05 was considered to indicate statistical significance.

Ethical Consideration: The Approval of Ethical Review Committee of the University of Ibadan/University College Hospital, Ibadan was obtained after permission was sought from the Heads of Departments of Medicine and Chest unit of the University College Hospital Ibadan. Informed consents were obtained from eligible patients before administration of the questionnaires and examination. Privacy and confidentiality of the respondents were guaranteed by anonymity of respondents.

RESULTS

Socio-demographic characteristics of respondents: Socio-demographic characteristics of the respondents is shown in table 1. Three hundred and fifty-five patients who met the criteria for recruitment were included in the study and interviewed. The mean age of the respondents was 39.04 (SD$\pm$ 11.335) years. About half of the respondents had tertiary education and about half of the respondents, 189(53.2%) belonged to occupational class III, followed by those in class VI, 81 (22.8%) and class II, 53 (14.9%).

Table 1:
Socio demographic characteristics of respondents n=355

	Variable	Frequency	Percentages (%)
Age group (years)	<30	89	25.1
	30-39	66	18.6
	40-49	102	28.7
	50+	98	27.6
Sex	Male	188	53.0
	Female	167	47.0
Marital status	Single	94	26.5
	Married	244	68.7
	Others	17	4.8
Educational level	No formal education	54	15.3
	Primary education	63	17.7
	Secondary education	65	18.3
	Tertiary education	173	48.7
Occupation	Class I	14	3.9
	Class II	53	14.9
	Class III	189	53.2
	Class IV	14	3.9
	Class V	4	1.3
	Class VI	81	22.8

Relationship of Lung Function Tests indices with selected variables: The relationship of (FEV1%) with age was positive, weak in strength and statistically significant (r = 0.147, p-value=0.005). For BMI, there was no relationship.

Relationship of Lung Function Tests indices with selected variables: The relationship of (FEV1%) with age was positive, weak in strength and statistically significant (r = 0.147, p-value=0.005). For BMI, there was no relationship.

Linear regression for FEV_1 expressed as %Predicted on significant variables: For every 1 unit increase in age, there was a statistically significant increase in FEV_1 by about 0.318 units (95%CI= 0.116-0.520, p=0.002).

Linear regression for PEFR expressed as % Predicted on significant variables

As shown in table 3, for every 1 unit increase in body mass index, there was a statistically significant increase in PEFR% predicted by about 0.716 units (95%CI= 0.118-1.314, p=0.019). Also, for every 1 unit increase in age, there was a statistically significant increase in PEFR% predicted by about 0.354 units (95%CI= 0.153-0.555, p=0.001.

Association of FEV_1 expressed as %Predicted with selected variables: Table 5 shows association of FEV_1 expressed as %Predicted with selected variables. A higher proportion of patients who were males (73.3%) had <60% predicted while a lower proportion of those who were females (54.6%) had <60% predicted. The association was statistically significant (χ^2= 15.83, p=0.0001)

Ordinal logistic regression analysis of FEV_1 % predicted on selected variables: Table 6 shows the Ordinal Logistic Regression analysis of FEV_1 % predicted on selected variables. After adjusting for other variables, the predictor of FEV_1 % predicted were sex and occupation. Females were about 2.5 times less likely to have severe asthma than males (OR= 0.397; 95% CI= 0.253-0.621). Professionals were about 2.5 times less likely to have severe asthma than unskilled workers (OR= 0.401; CI= 0.206-0.783).

Association of PEFR expressed as %Predicted with selected variables: Table 7 shows association of PEFR expressed as %Predicted with selected variables. A higher proportion of patients who were males 120(72.3%) had <60% predicted while a lower proportion of those who were females 100(54.6%) had <60% predicted. The association was statistically significant (χ^2= 15.83, p=0.0001).

Table 2:
Correlation of lung function tests with selected variables

	Forced expiratory volume per sec expressed as percentage predicted (FEV_1%)	**Peaked exploratory flow rate expressed as percentage predicted (PEFR%)**
Monthly income		
Pearson correlation	0.024	0.014
p-value	0.699	0.822
Age		
Pearson correlation	0.147	0.195
p-value	0.005	0.0001
BMI		
Pearson correlation	0.063	0.128
p-value	0.239	0.019

Correlation is significant at 5% level of significance(2-tailed)

Table 3:
Linear regression for FEV_1 expressed as % Predicted on significant variables

ANOVA TABLE					
Model	Sum of squares	Degree of freedom	Mean square	F	Significant
1 Regression	8816.24	2	4408.12	9.247	0.0001*
Residual	167.809	352	476.732		
Total	176625.90	354			
Linear regression for FEV_1%Predicted on significant variables					
Variable	**Regression coefficient(B)**	**Standard Error for B**	**95% CI for B**	**T**	**p-value**
Age	0.318	0.103	0.116-0.520	3.095	0.002*

Dependent variable: FEV_1 expressed as %Predicted *Predictors: Age* **Significant at 5% level of significance*

Table 4:
Linear regression for PEFR expressed as % Predicted on significant variables

ANOVA TABLE					
Model	Sum of squares	Degree of freedom	Mean square	F	Significant
1 Regression	7103.867	2	3551.93	8.05	0.0001*
Residual	155359.151	352	441.361		
Total	162463.017	354			
Linear regression for PEFR expressed as % Predicted on significant variables					
Variable	**Regression coefficient(B)**	**Standard Error for B**	**95% CI for B**	**T**	**p-value**
Age	0.354	0.102	0.153-0.555	3.469	0.001*
BMI	0.716	0.304	0.118-1.314	2.356	0.019

Dependent variable: PEFR expressed as % Predicted; *Predictors: Age, BMI* **Significant at 5% level of significance*

Table 5:
Association of FEV_1 expressed as %Predicted with selected variables

	Variable	Intermittent/Mild persistent (n)	Moderate(n)	Severe (n)	x^2	p-value
Education	**No formal education**	10(18.5%)	16(29.6%)	28(51.9%)	5.21	0.52
	Primary	8(12.7%)	14(22.2%)	41(65.1%)		
	Secondary	5(7.7%)	16(24.6%)	44(67.7%)		
	Tertiary	21(12.1%)	39(22.5%)	113(65.3%)		
Occupation	**Professional**	19(16.4%)	25(21.6%)	42(62.1%)	9.62	0.047*
	Skilled	21(12.7%)	47(28.3%)	98(59.0%)		
	Unskilled	4(5.5%)	13(17.8%)	56(76.7%)		
Sex	**Male**	11(6.6%)	33(19.8%)	123(73.3%)	15.83	0.0001
	Female	33(17.6%)	52(27.7%)	103(54.8%)		

**Significant at 5% level of significance*

Table 6:
Ordinal logistic regression analysis of FEV_1 % predicted on selected variables

Variable	Odd Ratio	95% CI	p-value
Intermittent Mild Asthma	0.015	0.006-0.041	0.0001*
Moderate Asthma	0.066	0.026-0.168	0.0001*
Occupation			
Professional	0.401	0.206-0.783	0.007*
Skilled	0.423	0.226-0.791	0.007*
Unskilled	1		
Sex			
Female	0.397	0.253-0.621	0.0001*
Male	1		

Dependent variable: FEV_1 % predicted
Predictors: Occupation, Sex
**Significant at 5% level of significance*

Ordinal logistic regression analysis of PEFR %Predicted on selected variables: Table 7 shows the Ordinal Logistic Regression analysis of PEFR %Predicted on selected variables. After adjusting for other variables, the predictor of PEFR %Predicted were sex. Females were about 2.45 times less likely to have severe asthma than males (OR= 0.408; 95% CI= 0.264-0.631).

Distribution of Body Mass indices of the respondents: Figure 1 shows the distribution of Body Mass Indices of the respondents. The majority 241 (66.9%) of the respondents had normal weight, 76(21.1%) were overweight and 17(4.9%) were obese.

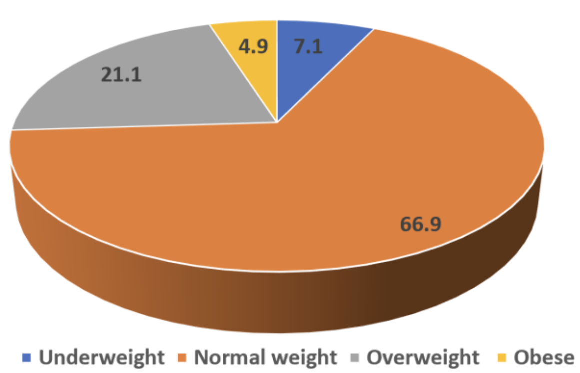

Figure 1:
Distribution of Body Mass indices of the respondents

Table 7:
Association of PEFR expressed as %Predicted with selected variables

Association of Asthma severity with selected variables

Variable	Intermittent/ Mild persistent (n)	Moderate(n)	Severe (n)	x^2	p-value
No formal education	12(22.2%)	15 (27.8%)	27 (50.0%)	7.67	0.263
Primary	9(14.3%)	13 (20.6%)	41 (65.1%)		
Secondary	5(7.8%)	18 (28.1%)	41 (64.1%)		
Tertiary	20(11.6%)	42 (24.3%)	111 (64.2%)		
Occupation					
Professiona	13(11.6%)	30 (26.1%)	72(62.3 %)	2.98	0.561
Skilled	23(13.9%)	45 (27.1%)	98(59.0 %)		
Unskilled	10(13.7%)	13 (17.8%)	50(68.5 %)		
Sex					
Male	10(6.0%)	36 (21.7%)	120 (72.3%)	18.13	0.0001*
Female	36(19.1%)	52 (27.7%)	100 (53.2%)		

Table 8:
Ordinal logistic regression analysis of PEFR %Predicted on selected variables

Variable	Odd Ratio	95% CI	p-value
Intermittent Mild Asthma	1.096	0.824-1.456	0.529
Moderate Asthma	4.688	3.311-6.638	0.0001*
Sex			
Female	0.408	0.264-0.631	0.0001*
Male	1		

DISCUSSION

This study showed that the higher the age of the patients and BMI, the higher the FEV_1. In addition, lung function test indices were lower in the males than females, and in the unskilled than skilled and professionals. This might be due to exposure of the unskilled to irritants that precipitate asthma attacks and the inability to purchase their drugs leading to poor adherence. Consequently, the control would be poor. The determinants of lung function test indices in this study were age, BMI, sex, and occupation. Forced Expiratory Volume per second increases with BMI since it is proportional to body size. Men have longer airways than women causing increased resistance in the respiratory tract in a review of literature conducted by Barosso and colleagues (Barosso *et al*,2018). Okwute and colleagues reported that the peak expiratory flow values were higher in males than females but a sample size of 40 subjects used might not achieve the objectives of their study (Okwute *et al*, 2022). This was contrary to the findings of this study where the PEFR was higher in females. Asthma control was reported to be poor among patients with metabolic syndrome according to Adeyeye and colleagues hence there is a need to screen patients with asthma for metabolic syndrome (Adeyeye *et al*, 2012). In a study conducted in Nigeria, males had higher respiratory volumes than females; age, height, weight, and percentage of body fat had significantly low correlations with lung function test parameters (Ogunlana *et al*, 2021). The correlations were equally weak in this study in concordance with Ogunlana and colleagues' report.

The degree of symptoms and anti-asthmatic treatment correlated with asthma severity according to Calcaciano and colleagues in a multi-center study in Italy (Calcaciano *et al*, 2017). Elevated interleukin-25 was also reported to be associated with increased asthma severity in another study conducted in Warsaw, Poland (Paplinska *et al*, 2019). Forced Expiratory Volume per second increased with BMI according to the findings of a study conducted in Nigeria and other anthropometric measurements were related to lung function indices (Nene *et al*, 2022). The peaked expiratory flow rate was higher in males than females and increased with age. It was also found that Peaked expiratory volume increased with BMI which was similar to the findings of this study (Hossain *et al*, 2022).

Patients' social problem-solving was reported to be a key contributor to asthma control and asthma-related quality of life according to McCormic and colleagues. Behavioural strategies focused on adaptation to solve such problems are necessary (McCormic *et al*, 2014). Frequent wheezing and B-agonist use may be a sign of unrelieved air trapping which could be diagnosed with spirometry and lung volume measurements. Chest pain is common in persistent asthma according to Vempilly *et al* (Vempilly *et al*, 2020). Contrary to the findings of this study, lung function indices were lower in females than in males. In another study conducted at the University of Benin Teaching Hospital, Nigeria, it was found that a positive correlation existed between asthma severity and BMI. This was in contrast to the findings of this study which showed that the lower the BMI, the lower the lung function test results, and the higher the asthma severity. However, there was a strong negative correlation between the quality of life and duration of asthma (Oni *et al*, 2013). Lung function indices were associated with body weight, height and age according to the results of a study conducted by Nku and others in South-South Nigeria (Nku *et al*, 2006). This was similar to the findings of this study which showed a positive correlation of BMI and age with lung function test indices.

The lung function test indices which were lower in the lower age groups and BMI in this study could show that the severity of asthma was worse in the younger patients with lower BMI than heavier older patients. The lung function test indices were also lower in the males and unskilled workers than females and professionals. It showed that asthma severity was worse in the males and the unskilled workers than females and professionals.

In conclusion, from this study, peaked exploratory flow rate expressed as percentage predicted were lower among the younger age groups compared with older age groups and among patients with lower body mass indices compared with overweight and obese patients. Also, peaked exploratory flow rate expressed as percentage predicted were lower among the males compared with females. Forced expiratory volume per sec expressed as percentage predicted were lower among the younger age groups. Additionally, FEV1 expressed as %predicted were lower in males than females and in the unskilled compared with skilled and professionals.

The study was a cross-sectional study, therefore causal relationship could not be established. There are needs for experimental studies to establish causal relationships. The study is hospital-based which might not reflect the true picture in the community, hence secondary generalisation is difficult

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