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Changes on Electrocardiographic Patterns and Associated Factors among Chronic Obstructive Pulmonary Disease Patients

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ABSTRACT

Background
Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by airflow limitation that is not fully reversible. The lungs and the heart are so closely interrelated organs that diseases of the one results in impaired functioning of the other. COPD induced cardiovascular diseases (CVDs) are diagnosed by electrocardiogram (ECG) and other instruments. ECG is one of the basic diagnostic tools that uses in early screening of COPD associated systemic effect of CVDs. However, concomitant CVDs among COPD patients are not usually assessed by ECG in routine medical practice at the setup.

Objective
The present study aimed to explore and detect changes of ECG pattern, and determine the associated risk factors among COPD patients.

Materials and Methods
The study was conducted among COPD patients visiting chest clinic of Jimma Medical Center (JMC), Southwest Ethiopia; from May 18 to August 18, 2017 G.C. A hospital based cross-sectional study was conducted among 80 COPD patients; and investigations for 12 lead resting supine ECG as well as measurements of other variables were performed. The results of ECG patterns and other variables were entered into Epidata (3.1) and exported to statistical package for the social sciences (SPSS) 20 for further analysis.

Results
Eighty COPD patients were enrolled in the study and the prevalence of abnormal ECG was 83.75% where arrhythmia accounted for 50%, atrial enlargement 48.8%, myocardial infarction (MI) 41.3%, axis deviation 35%, other ECG abnormalities (poor R-wave progression and low QRS amplitude) 35% and ventricular hypertrophy 15%. The identified associated factors with the abnormal ECG were less monthly income, smoking, hypoxia, male gender and severity of COPD with their specific adjusted odds ratio (AOR) and 95% CI of 2.1(1.6-7.9), 2.2(1.5-8.6), 2.9(1.2-6.9), 3.1(1.5-23) and 3.2(2.0-8.4) respectively.

Conclusion
Routine ECG investigation should be performed at the setup to initiate early management of CVDs comorbidity for better prognosis among COPD as abnormal ECG is inevitable among them.

Keywords
ECG pattern; Minnesota ECG criteria; COPD; Six minute walk distance test (6MWDT); Associated factors.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease with some significant extra pulmonary effects that is characterized by a progressive/persistent airflow limitation, associated with an abnormal inflammatory response of the lung and airways to noxious particles or gases which

is not usually fully reversible.[1]

The risk factor for COPD results from a gene-environment interaction; related in more complex ways by which one risk factor influences another factor.[2] Even though, cigarette smoking is the most commonly encountered risk factor for COPD, there are also many identified risk factors of COPD like the genetic deficiency of alpha-1 antitrypsin (AAT),[3,4] frequent exposure to occupational dusts and chemicals (vapors, irritants, and fumes),[5-7] indoor air pollutions (wood, animal dung, crop residues, and charcoal) by burning as biomass fuel in confined spaces especially among women living in rural parts and outdoor air pollutions (fossil fuel combustion and motor vehicle emissions) in industrialized countries.[8-12]

Following triggers from different risk factors there is a characteristic pattern of inflammation in the lungs of COPD patients (increased numbers of neutrophils, macrophages and CD8+ lymphocytes)[13]; results in abnormal inflammatory response that induce parenchymal tissue destruction and impairs defense mechanisms due to imbalance between released inflammatory mediators and anti-inflammatory mediators from inflammatory cells,[14,15] and/or with an amplified effect of oxidative stress over anti-oxidative and an excess of proteases against anti-proteases in the lung.[16] Pathophysiological changes as characteristic of the disease are manifested in both pulmonary and as well as extra pulmonary/systemic effects. Pulmonary pathophysiology includes mucus hyper secretion, airflow limitation and air trapping (leading to hyperinflation), gas exchange abnormalities, pulmonary hypertension and corpulmonale.[17,18] Systemic/extra pulmonary effects of COPD, particularly in patients with severe disease include skeletal muscle wasting,[19] risk of cardiovascular diseases (CVDs),[20] anemia,[21] osteoporosis[22] and other systemic effects[23-25] (diabetes, sleep-disorders, glaucoma, depression and etc.) with a major impact on survival and prognosis of COPD patients.

The CVDs developed among COPD patients as systemic effect can be diagnosed by different instruments including electrocardiogram (ECG). ECG is the graphic records of time-varying bio-electric potential generated by the electrical activity of heart which used to measure and monitor the structural and functional activity of the heart for its ease of usage and non-invasiveness. The ECG changes observed among heart of COPD patients are high amplitude of P wave, vertical P wave axis, vertical QRS axis, prolonged PR and QT interval as cardiac markers of CVDs suggesting abnormal ECG (arrhythmia, axis deviation, heart chamber enlargement and hypertrophy).[26]

Even though, mechanism of COPD induced development of CVDs evidenced with abnormal ECG is complex and unclear; their correlation was expected *via* the effect of abnormal systemic inflammatory response[27,28] resulting in progression of pathologic atherosclerosis, biological (hypoxemia, endothelial dysfunction, increased platelet activation, arterial stiffness) with the mutual classical risk factors[1] (smoking, pollution, free radicals and aging) that ends in pulmonary vascular dysfunction, pulmonary hypertension, right and left heart dysfunction and arrhythmia. The anatomical and physiological similarity of two vital organs also affect each other[29] and may be adverse effects of drugs used to treat COPD can directly induce cardiac problems with acute exacerbation of COPD.[30]

In general, there were very limited studies that determine the factors associated with ECG changes than exploring the magnitude of various ECG findings. The identified factors for ECG changes were amount of systemic C-reactive proteins (CRP) as markers of inflammation, hypoxia, duration and severity of COPD which was exacerbated by mutual risk factors smoking and aging.[26-33]

Thus, the current study aimed to explore and detect changes of ECG pattern by using the 12 lead ECG which is not routinely performed especially in developing countries including Ethiopia and the study area due to economic constraints and determine the associated risk factors among COPD patients.

MATERIALS AND METHODS

Study Design and Setting

The study was conducted at JMC, located in Oromia regional state, at southwest Ethiopia which is one of the largest teaching referral hospitals in the country, providing the health service at inpatient and outpatient level for the catchment area of 15 million populations in dwelling in the southwest of the country. The health service is delivered by specialists, medical residents, medical interns and other health professionals. The study was conducted from May 18 to August 18, 2017 G.C among COPD patients attending chest clinic of JMC employing a hospital based cross-sectional study design.

Participants and Recruitment

The study populations were all COPD patients attending chest clinic of JMC who were available during data collection period. The sample size was determined based on the total annual number of COPD patients attending chest clinic of JMC. According to the data used in the study conducted for assessment of osteoporosis and associated factors among COPD patients, the hospital had a total of 100 COPD patients in the year 2013/14 G.C. By considering this annual flow of the cases as a target population, the total sample size of 80 patients was obtained by using Yamane Taro, 1967 equation [$n=N/(1+Ne^2)$], where n-sample size, N-target population (100) and e-level of precision (0.05).[34]

Data Collection (Instrument and Technique)

The data was collected by trained Diploma Nurses employed from the chest and cardiac clinic of JMC. Data collectors were briefly oriented about the objectives and purpose of the study to respondents and took informed verbal and written consent prior

to data collection. Then, face-to-face interview was conducted using structured questionnaires to assess COPD related and socio-demographic variables.

Body mass index (BMI) was computed from client's height and weight measured with validated tape meter and weight scale at standing position.

Six minute walk distance test (6MWDT) was obtained by measuring the total distance the patient walked/covered in meter within six minutes to evaluate the severity of the disease as the indicator of exercise tolerance capacity of the COPD patients.

Dynamic pulmonary function test was carried out to diagnose and grade severity of COPD based on post bronchodilator result of forced expiratory volume in one second (FEV1) % predicted, forced vital capacity (FVC) and (FEV1/FVC) ratio as per the guideline of Global Initiative for Chronic Obstructive Lung Disease (GOLD)[1] by using dry digital spirometry (Care Fusion, Germany).

Hypoxic status was measured by digital pulse oximeter (Lifebo, Germany) indicating percentage of SPO_2 by placing the probe on non-polished/bare finger of the clients.

Finally the patients underwent ECG investigation after other variables (anthropometry and COPD related) were measured. Standard 12-lead supine resting ECG (NIHON KOHDEN Cardiofax S) was used with machine calibrated on 1 mV for a 10 mm (0.1 mV/mm) at speed of 25 mm/s, where each small box and large box represents 0.04 sec and 0.2 sec respectively. 10 electrodes (4 limb electrodes at right and left arms & legs +6 chest electrodes (V1-V6)) were placed on clients' arms, legs and chest after orientation and gel applied, yielding a total of 12 leads that measures the potential difference of movement of electrical activity of the heart.

Each ECG paper was visually analyzed for recording errors, manually interpreted by investigator in liaison with the cardiologist and classified according to the Minnesota coding criteria, merged and thematised to different main and sub-categories.

Data Processing and Analysis

Data was checked, categorized, coded and entered into EpiData version 3.1 after template formed and finally exported to SPSS version 20 for further analysis. Descriptive statistics like frequencies, percentages, mean and standard deviations were used to describe the findings. In bivariate analysis, simple-crosstab/chi–square test and binary logistic regression were conducted to explore the association between ECG pattern status& the associated factors. Those variables with p-value <0.25 were taken as a candidate for the final model. In multivariate analysis, the confounders were controlled and adjusted to odds ratio (AOR) with 95% confidence interval (CI) to express the strength of the association between ECG pattern and p-value less than 0.05 was considered as statistically significant.

ETHICAL CLEARANCE

Implementation of the proposal was carried out after getting approval letter from the ethical clearance committee/ethical review board of Jimma University (IRB/699/2017). An official letter of collaboration and permission request to chest and cardiac clinic of JMC was obtained from Department of Physiology and Internal Medicine prior to study conduction. Informed verbal and written consent was taken from the respondents/clients after explaining the objectives and purpose of the study. The participants were assured that they have full right to participate or withdraw from the study and the collected data/information were kept confidentially. Any abnormal finding of the ECG pattern was required consultation of physicians of chest clinic for further interventions.

Operational Definitions

- Hypoxia is refers to result of SPO_2 less than 90% post 6MWDT.[35]
- Severity of COPD was categorized by using the result of six minute walk distance test (6MWDT) which is the total distance covered/walked in meter within six minutes by taking the initial and last result of saturation pressure of oxygen (SPO_2) with Pulse oximetry. Based on distance covered within six minutes, the severity of COPD can be classified as mild (≥350 m), moderate (250-349 m), severe (150-249 m) and very severe (≤149 m).[36]
- Abnormal ECG–refers to any change deviated from normal sinus ECG based on Minnesota ECG coding criteria.[37]

RESULTS

Results of Socio-demographic and Economic Status of COPD Patients

Out of the total sampled 80 COPD patients attending chest clinic of JMC from May 18 to August 18, 2017 G.C, the mean age was 55.1 (±13.66) that ranges from 26-90 years by which majority of them (32.5%) belongs to interval of 51-60 years. Majority of the analyzed 80 COPD patients were males (53.8%), married (85%), farmers (38.7%), not attend formal education (63.8%), Oromo (73.8%), Muslims (56.3%), dwellers of rural (53.8%) and had monthly income of less than 2000 ETB (63.75%) (Table 1).

Results of Anthropometric Measurements of COPD Patients

The (mean,±SD) of height, weight and BMI of the sampled and analyzed 80 COPD patients were (1.64±0.089 meter, 53.5±10.55 kg and 19.98±3.43 kg/m^2) respectively (Table 2).

Table 1. *Socio-demographic and Economic Status of COPD Patients Attending Chest Clinic of JMC from May 18 to August 18, 2017 G.C, n=80*

Variables	Categories	Frequency	Percentage (%)
Age in years	<30	4	5.0
	31-40	9	11.3
	41-50	18	22.5
	51-60	26	32.5
	61-70	15	18.6
	71-80	5	6.3
	>81	3	3.8
	Total	80	100.0
Sex	Male	43	53.8
	Female	37	46.2
	Total	80	100.0
Marital status	Unmarried	3	3.8
	Married	68	85.0
	Widowed	7	8.7
	Divorced	2	2.5
	Total	80	100.0
Occupation	Gov't employee	13	16.2
	Private	5	6.3
	House wife	28	35.0
	Farmer	31	38.7
	Other	3	3.8
	Total	80	100.0
Educational status	No formal educ.	51	63.8
	Primary school	20	25
	Secondary school	3	3.8
	College & above	6	6.7
	Total	80	100.0
Ethnicity	Oromo	59	73.8
	Amhara	8	10.0
	Dawuro	6	7.5
	Others	7	8.7
	Total	80	100.0
Religious status	Orthodox	22	27.5
	Muslim	45	56.3
	Protestant	11	13.8
	Others	2	2.5
	Total	80	100.0
Residence	Urban	37	46.2
	Rural	43	53.8
	Total	80	100.0
Monthly Income in ETB	<2000	51	63.75
	>2000	29	36.25
	Total	80	100.0

In ethnicity others refers to Tigre (2), Wolaita (3) and Kefa (1), ETB-Ethiopian birr/ national curreny, currently exchange for 1 dollar=27 ETB

Table 2. *Results of Variables Related with COPD among COPD Patients Attending Chest Clinic of JMC from May 18 to August 18, 2017 G.C, n=80*

Variables	Categories	Frequency	Percentage (%)
Smoking Status	Smoke cigarette	51	63.75
	Non smokers	29	36.25
	Total	80	100.0
Exposure to Biomass	Exposed	48	60.0
	Not exposed	32	40.0
	Total	80	100.00
Results of 6MWD in Meter	350-750	11	13.8
	250-349	17	21.2
	150-249	22	27.5
	<149	30	37.5
	Total	80	100.0
Duration of the Illness	<5 years	57	71.25
	>5 years	23	28.75
	Total	80	100.00
Hypoxia status (Result of SPO_2 post 6MWDT)	>90%	20	25.0
	<90%	60	75.0
	Total	80	100.0

Results of Variables Related with COPD

Among the total observed 80 COPD patients during 3 month study period, majority of the COPD patients were smokers (63.75%), also exposed to non-smoking risk factors/biomass exposure (60%), and walked a distance of less than 149 meter (37.5%) within six minutes. Majority of the patients were classified to stage 4/ very severe category of COPD (37.5%) based on the result of 6MWDT who were developed the disease within five years (71.25%) and hypoxic based on the result of their SPO_2 percentage less than 90(75%).

Results of ECG patterns among COPD patients

Out of the total analyzed and interpreted ECG papers from the sampled 80 COPD patients by investigator in liaison with the cardiologist, about 67 patients had abnormal ECG pattern (83.75%) while a few 13 patients had normal sinus ECG pattern (16.25%). Among the abnormal ECG pattern categorized based on the Minnesota coding criteria; arrhythmia accounted for (50%), atrial enlargement (48.8%), Myocardial infarction (MI)/coronary artery diseases (CADs) (41.3%), axis deviation (35%), other abnormalities (35%) like (poor progression of R-wave and low QRS amplitude), and ventricular hypertrophy (15%) were observed as one patient may have more than one types of abnormal ECG. Among arrhythmias as one types of abnormal ECG, different sub types were evaluated as per the Minnesota coding criteria. From this, sinus origin arrhythmia, conduction block, ectopic arrhythmia and pre excitation syndrome (PES)/Wolf Parkinson syndrome (WPWS) were interpreted with frequency of 30%, 23.8%, 17.5% and 2.5% respectively. The results of sub types of arrhythmias were listed under Table 3 in detail.

Table 3. *Results of ECG patterns among COPD patients attending chest clinic of JMC from May 18 to August 18, 2017 G.C, n=80*

Variables	Categories	Frequency	Percentage (%)
General ECG pattern	Normal	13	16.25
	Abnormal	67	83.75
	Total	80	100.00
Abnormal ECGs			
1. Arrhythmia 40 (50%)	Sinus origin (SOA)	24	30.0
	Sinus tachycardia (ST)	7	8.8
	Sinus bradycardia (SB)	13	16.3
	Sinus arrhythmia (SA)	4	5.0
	Ectopic (EA)	16	20.0
	Atrial flutter (Af)	1	1.3
	Atrial fibrillation (AF)	5	6.3
	Multi focal atrial tachyc.(MAT)	1	1.3
	Premature atrial contr.(PAC)	3	3.8
	Premature ventr. Contr.(PVC)	6	7.5
	Conduction block (CBA)	19	23.8
	AVB	1	1.3
	BBB	14	17.5
	CRBBB/complete	3	3.8
	IRBBB/incomplete	6	7.5
	CLBBB/complete	4	5.0
	ILBBB/incomplete	1	1.3
	Hemi fasicular block (HFB)	4	5.0
	LAHFB	2	2.5
	LPHFB	2	2.5
	PES or WPWS	2	2.5
2. Axis deviation (AD) 28 (35%)	RAD	11	13.5
	LAD	15	18.8
	EAD/Indefinite	2	2.5
3. Atrial enlargement (AE) 39 (48.8%)	RAE/ P-Pulmonale	23	28.8
	LAE	9	11.3
	BAE/ biatrialenlargt	7	8.8
4. Ventr. Hypertrophy (VH) 12 (15%)	RVH	5	6.3
	LVH	7	8.8
5. Myocardial infaction (MI)/ CADs 33 (41.3%)	Qwave abnormality	3	3.8
	ST-Twave changes	23	28.8
	Prolonged QTc interval	7	8.8
6. Other abnormality 28 (35%)	Poor Rwave progression	12	15.0
	Low QRS amplitude	16	20.0

One patient may have more than one abnormal ECG, AVB-Atrioventricular block, BBB-Bundle branch block, CBBB-Complete bundle branch block (right-R and left-L), IBBB-Incomplete bundle branch block (right and left), PES-Preexcitation syndrome, WPWS-Wolf Parkinson white syndrome, RAD-Right axis deviation, LAD-Left axis deviation, EAD-Extreme axis deviation, RAE-Right atrial enlargement, LAE-Left atrial enlargement, BAE-Biatrial enlargement, RVH-Right ventricular hypertrophy, LVH-Left ventricular hypertrophy.

Another interpreted abnormal ECG was axis deviation which was seen among 28 COPD patients (35%) from which LAD responsible for 18.8%, RAD 13.8%, and EAD 2.5% as interpreted by the hexaxial reference system.

The ECG also diagnosis enlargement and hypertrophy of heart champers as RAE accounted for 28.8%, LAE 11.3% and bi atrial enlargement/BAE contributed 8.8% from the total 48.8% of atrial enlargement while RVH and LVH responsible for 6.3% and 5.8% respectively to ventricular hypertrophy.MI/ CADs (ST-T-wave changes 28.8%, prolonged QTc interval 8.8% and Q-wave abnormality 3.8%) and other ECG abnormalities (low QRS amplitude 20% and poor R-wave progression 15%) were also observed.

Changes on ECG pattern and factors associated with ECG changes

Among evaluated 80 ECG papers of COPD patients, the prevalence of abnormal ECG pattern was 83.75% where the

high prevalence was observed among urban dwellers 32.4%, rural 51.3%, male 48.8%, smokers 60%, Muslims 48.8%, Oromo 63.8%, farmers 37.5% and also it was higher among COPD patients with age less than the mean/<55 years 50%, who had no formal education 55%, who engaged 72.5%, who earned less than 2000 ETB 58.75%, among underweight patients 50% and among patients with SPO_2 level less than ninety/hypoxic (70%).

Table 4. *ECG Pattern Changes and Associated Factors by Bivariate Logistic Regression and chi square/ X^2 test among COPD Patients Attending Chest Clinic of JMC from May 18 to August 18, 2017 G.C, n=80*

Dichotomous Variables	Categories	Status of ECG pattern			COR(95% CI)	X^2	*p*-value
		Normal	Abnormal	Total			
Residence	Urban	11(13.8)	26(32.4)	37(46.2)	1	9.2	0.008 *
	Rural	2(2.5)	41(51.3)	43(53.8)	8.6(1.8-42)		
	Total	13(16.25)	67(83.75)	80(100.00)			
Sex	Male	4(5.0)	39(48.8)	43(53.8)	3.1(1.8-11)	3.3	0.079 *
	Female	9(11.2)	28(35.0)	37(46.2)	1		
	Total	13(16.25)	67(83.75)	80(100.00)			
Age in years	>55	2(2.5)	40(50.0)	42(52.5)	8.1(1.6-39)	8.6	0.009 *
	<55	11(13.8)	27(33.7)	38(47.5)	1		
	Total	13(16.25)	67(83.75)	80(100.00)			
Educational Status	No formal educ	7(8.7)	44(55.0)	51(63.8)	1.6(0.5-50)	0.66	0.42
	Others (educated)	6(7.5)	23(28.7)	29(36.2)	1		
	Total	13(16.25)	67(83.75)	80(100.00)			
Religious stat	Muslim	6(7.5)	39(48.8)	45(56.3)	1.6(0.5-5.36)	0.64	0.425
	Others	7(8.7)	28(35.0)	35(43.7)	1		
	Total	13(16.25)	67(83.75)	80(100.00)			
Ethnicity	Oromo	8(10.0)	51(63.8)	59(73.8)	1.9(0.57-6.9)	1.2	0.28
	Others	5(6.2)	16(20.0)	21(26.2)	1		
	Total	13(16.25)	67(83.75)	80(100.00)			
Occupation	Farmer	1(1.3)	30(37.5)	31(38.8)	1	6.3	0.033 *
	Others	12(15.0)	37(46.2)	49(61.2)	0.1(0.013-0.84)		
	Total	13(16.25)	67(83.75)	80(100.00)			
Marital status	Married	10(12.5)	58(72.5)	68(85.0)	1	0.79	0.379
	Others	3(3.8)	9(11.2)	12(15.0)	0.5(0.1-2.2)		
	Total	13(16.25)	67(83.75)	80(100.00)			
Monthly income (EBR)	<2000	4(5.0)	47(58.75)	51(63.75)	8(2-28)	3	0.003 *
	>2000	9(11.25)	20(25.0)	29(36.25)	1		
	Total	13(16.25)	67(83.75)	80(100.00)			
Severity of BMI	Under weight	5(6.25)	40(50.0)	45(56.25)	5.5(1.7-44)	3	0.113 *
	Others	8(10.0)	27(33.75)	35(43.75)	1		
	Total	13(16.25)	67(83.75)	80(100.00)			
Smoking status	Smoke	3(3.8)	48(60.0)	51(63.75)	8.4(2-33)	11	0.003 *
	Not smoke	10(12.5)	19(23.75)	29(36.25)	1		
	Total	13(16.25)	67(83.75)	80(100.00)			
Exposure to biomass	Exposed	2(2.5)	46(57.5)	48(60.0)	12(2.5-59)	12	0.002 *
	Not exposed	11(13.75)	21(26.25)	32(40.0)	1		
	Total	13(16.25)	67(83.75)	80(100.00)			
Severity of COPD	Mild	7(8.75)	4(5.0)	11(13.75)	1	15	0.000 *
	Others	6(7.5)	63(78.75)	69(86.25)	18(4-81)		
	Total	13(16.25)	67(83.75)	80(100.00)			
Duration of disease	<5 years	12(15.0)	45(56.25)	57(71.25)	1	4.1	0.099 *
	>5 years	1(1.3)	22(27.5)	23(28.75)	5.8(1.7-48)		
	Total	13(16.25)	67(83.75)	80(100.00)			
Hypoxia (SPO_2 level)	>90%	9(11.2)	11(13.8)	20(25.0)	1	14	0.000 *
	<90%	4(5.0)	56(70.0)	60(75.0)	11.4(2.3-43)		
	Total	13(16.25)	67(83.75)	80(100.00)			

**-candidate variables for multivariate analysis (p-value<0.25), others in dichotomous variables were expressed in Table 1 in detail.*

Table 5. *ECG Pattern Changes and Associated Factors by Multivariate Logistic Regression among COPD Patients Attending Chest Clinic of JMC from May 18 to August 18, 2017 G.C, n=80*

Dichotomous Variables	Categories	Status of ECG pattern		AOR(95% CI)	*p*-value *≤0.05
		Normal	Abnormal		
Residence	Urban	11(13.8)	26(32.4)	1	0.274
	Rural	2(2.5)	41(51.3)	2.4(0.08-7.45)	
Sex	Male	4(5.0)	39(48.8)	3.1(1.5-23)	0.027 *
	Female	9(11.2)	28(35.0)	1	
Age in years	>55	2(2.5)	40(50.0)	2.4(0.1-4.1)	0.527
	<55	11(13.8)	27(33.7)	1	
Occupation	Farmer	1(1.3)	30(37.5)	0.2(0.1-3.6)	0.106
	Others	12(15.0)	37(46.2)	1	
Monthly income (EBR)	<2000	4(5.0)	47(58.75)	2.1(1.6-7.9)	0.047*
	>2000	9(11.25)	20(25.0)	1	
Severity of BMI	Under weight	5(6.25)	40(50.0)	0.7(0.06-8.4)	0.802
	Others	8(10.0)	27(33.75)	1	
Smoking history	Yes	3(3.8)	48(60.0)	2.2(1.5-8.6)	0.046 *
	No	10(12.5)	19(23.75)	1	
Nonsmoking exposure status	Yes	2(2.5)	46(57.5)	1.8(0.1-8)	0.124
	No	11(13.75)	21(26.25)	1	
Severity of COPD	Mild	7(8.75)	4(5.0)	1	0.021 *
	Others	6(7.5)	63(78.75)	3.2(2-8.4)	
Duration of disease	<5 years	12(15.0)	45(56.25)	1	0.345
	>5 years	1(1.3)	22(27.5)	4.8(1.8-12.9)	
Hypoxia (SPO_2 level)	>90	9(11.2)	11(13.8)	1	0.037 *
	<90	4(5.0)	56(70.0)	2.9(1.2-6.9)	

**-statistically significant variable (p-value<0.05), others value was known from Table 1.*

In the bivariate analysis, the candidate variables having *p*-value<0.25 were selected for the final model. Accordingly about eleven variables (residence, sex, age, occupation, monthly income, severity of BMI, smoking status, status of exposure to nonsmoking risks, severity of COPD based on 6MWDT results, duration of the illness and hypoxia status) were identified as the expected factors associated with the development of abnormal ECGs with their specific chi square, COR with 95% CI and *p*-values also explained in Table 4 in details.

Further, multivariate analysis (binary logistic regression with enter methods) were used to identify the main predictor variables by controlling the confounders with AOR and showed by dichotomous variables.

Finally the five variables (sex, monthly income, smoking history, severity of COPD and hypoxia) with *p*-value less than 0.05 fitted the final model with AOR (95% CI) and identified as the associated factors with abnormal ECG pattern among COPD patients.

By making all other variables constant; the likelihood of developing abnormal ECG pattern among COPD patient was 3.1 times among males than females, 2.1 times among those who earned less than 2000 ETB than earned more than 2000 ETB, 2.2 times among smokers than nonsmokers, 3.2 times among other stages of COPD than mild stage and 2.9 times among hypoxic patients (SPO_2 less than 90) than more than 90 (Table 5).

DISCUSSION

Among 80 COPD patients assessed, their mean age was greater than 50 years (55.1±13.66) which is also in line with other studies that revealed the mean age of more than 50 years from minimum mean 52.56±11 to maximum mean 59±7[12,38-41] while majority of the patients (32.5%) classified at interval of 51-60 years which is also in harmony with the study of Banker H who reported that majority of patients (35%) were grouped in this age interval.[42] The male dominance (53.8%) observed in the present study is in agreement with other studies.[12,36,38,40-62] But the odd female dominance (54.2%) was observed among COPD patients conducted in India.[38] The frequency of underweight BMI category (56.25%) was dominant over other groups as it is in harmony with study of Tariku et al[22] but the pattern of severity of COPD was against the study of Tariku et al[22] because different approach of severity classification was used while the prevalence of COPD by its stages was matched with the study conducted by Lokendra et al[41] where the frequency of patients were increased through the stages from mild to very severe (13.8%-37.5%) and (12%-36%) in the present study and Lokendra et al study respectively.[41] The dominance of smokers (63.75%) than nonsmokers was also in line

with other studies as it confirms that majority of COPD patients (50-80%) were smokers.[1]

Abnormal ECG pattern was interpreted among 67(83.75%) of COPD patients which is consistent with other studies[32,36,41,46,48,58-62] that reported the prevalence of abnormal ECG among COPD patients >50% ranges 50%[46,62]-81.5%.[60] But, the prevalence of abnormal ECG <50% was only reported by study of Agarwal R (35.7%).[49]

Based on Minnesota ECG coding criteria for classification, the observed abnormal ECG were:

1. Arrhythmia (50%) due to global hypoxia in COPD patients manifested in high alveolar wall resistance, alveolar, and capillary destruction and air trapping that result in under ventilated/alveolar hypoxia which is compensated by vascular remodeling (hypoxia induced pulmonary vasoconstriction (HIPVC), intimal hyperplasia, smooth muscle hypertrophy/ hyperplasia, endothelial cell dysfunction and loss of the pulmonary capillary bed) resulting in pulmonary hypertension that increases work load on the heart reflected as arrhythmia.

2. Heart chamber enlargement (atrial enlargement 48.8% like RAE/P-pulmonale 28.8% and ventricular hypertrophy 15%) due to HIPVC as compensatory of alveolar hypoxia in COPD patients resulting in pulmonary hypertension with increased burden of heart to overcome pulmonary pressures ends with chamber enlargement specially on the right side the heart; seen on ECG as p-pulmonale.

3. Axis deviation 35% due to hyperinflation and hyper expansion of the lungs of COPD patients that compresses the heart and pushes diaphragm downwards and resulting in the heart to be elongated, and vertically oriented and rotated clockwise in the transverse plane as the heart has fixed attachments to the great vessels. This causes displacement of the right ventricle anteriorly and the left ventricle posteriorly.

4. Signs of MI/CADs (41.3%) also observed on ECG secondary to global hypoxia among COPD patients.

5. Low QRS amplitude 20% and poor progression of R-wave 15% due to dampening effect/insulating effect of hyper inflated lungs and lowered position of the heart (tubular) with respect to electrodes.

The determined associated factors with abnormal ECG by their specific AOR with 95% CI were:

1. Hypoxia/SPO_2 level less than 90% post 6MWDT with [AOR 2.9(1.2-6.9)] as it induces pulmonary vasoconstriction as compensatory mechanism and further increases work load of heart results in abnormal ECG like p-pulmonale, RVH, axis deviation and MI/CADs. This is in line with study conducted by Shah V et al as the hypoxia is the independent risk factor in inducing abnormal ECG especially atrial fibrillation with [AOR 1.76(1.64-1.89)].[33]

2. Severity of COPD: by making the mild stage of COPD reference, other stages are 3.2 more likely to develop abnormal ECG/AOR 3.2(2.0-8.4) as it is consistent with the study conducted by Sin & Man with [AOR 2.18(1.46-3.27)] and Nilson U et al with [AOR 1.89 (1.2-2.99)].[27,31] This is mainly due to the exacerbation of the disease resulting in systemic comorbidities including CVDs as evidenced by ECG.

3. Smoking [AOR 2.2(1.5-8.6)] as a mutual risk factor for COPD and CVDs also in harmony with study conducted by Shah V et al as one of the determined risk factor [AOR 2.2(1.5-3.1)] for the development of abnormal ECG indicating CVDs due to COPD systemic comorbidity.[33]

4. Gender male [AOR 3.1(1.5-23)] is another identified risk factor for development abnormal ECG among COPD patients because all the male patients were exposed to smoking and they were relatively elders (the two mutual risk factors (smoking and aging)). This is also in agrrementwith study conducted by Larssen MS et al who revealed that being male was risk for developing abnormal ECG with [AOR 1.864(0.39-3.57)].[26]

5. COPD patients with low monthly income less than 2000 ETB are also the risk factor for abnormal ECG among COPD patients by [AOR 2.1(1.6-7.9)] but it was not determined among other reviewed studies. Because low socioeconomic status is multi component factor for poverty and malnutrition affecting birth weight that impairs growth, maturation & development of vital organs and as well as frequent exposures to respiratory infection that later develops CVDs.

In nutshell, the present study revealed higher prevalence of abnormal ECG than any previous studies. The possible justification for this difference might be absence of routine screening for systemic comorbidities including CVDs in the setting and the treatmentis also limited to the primary compliant of the patients (COPD).

STUDY LIMITATION

The present study is limited to a small sample size, thus further research is needed with inclusion of more patients, preferably at multicenter level to validate our findings.

CONCLUSION

Among 80 COPD patients enrolled in the present study, maximum numbers of patients were in the age range of 51-60 years, with high prevalence among males, with low economic status, living in rural areas, farmers, smokers and underweight. The prevalence of abnormal ECG was 83.75%. As the classification was based on Minnesota ECG coding criteria, the identified abnormal ECG were: arrhythmia 50%, atrial enlargement 48.8%, MI/CADs 41.3%, axis deviation 35%, other ECG abnormalities (poor R-wave progression and low QRS amplitude) 35% and ventricular hypertrophy 15% .

The identified associated risk factors with the abnormal ECG were hypoxia, sex, low monthly income, smoking history and severity of COPD.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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