

ASSESSMENT OF QUALITY OF LIFE, COMPLIANCE AND ADVERSE DRUG REACTIONS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS**Dr. Basavanna P. L.*, Joicy James, Kadeejath Sayitha, Mohammed Musthafa K. and Mohammad Rowghani**

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ABSTRACT

Background: Chronic obstructive pulmonary disease is a common condition and is characterised by limitation in airflow, which is not fully reversible. It is one of the most common causes of disease burden both globally and in India. Multiple drugs used in the treatment of COPD may increase the risk of ADR in these patients. So it is very important to monitor ADR in these patients to rationalise drug therapy. Since COPD is a chronic condition and not fully curable, it is necessary to assess the medication adherence and quality of life. Objectives: The main objective of the study was to assess the quality of life, compliance and adverse drug reactions in chronic obstructive pulmonary disease patients. Materials and Methods: Study was carried at pulmonology department, in PKTB hospital, Mysore, Karnataka, from November 2018 to April 2019. A total of 252 patients were enrolled in the study as per the inclusion and exclusion criteria. Patients demographics data were collected using data collection form and quality of life were assessed by using St. George's questionnaire. The adverse drug reactions were analysed by using Naranjo causality assessment scale and Hartwig's scale and medication adherence were analysed by Morisky Green Levine 4-Item (MGL-4) Medication Adherence Scale. The domains associated with each objective were identified and correlated with multiple factors. Results: Out of 252 candidates, males show dominance over females .75 were presented with ADRs (29.8%). Stomach upset was the most commonly reported ADR .53.33% of ADRs were mild and 46.66% were moderate. 63% of ADRs were probable and 37% were in the possible category. In our study, medium adherence (52%) has superiority over low (35.3%) and high adherence (12.7%). Among the study population, QoL is highly impaired in terms of all the 3 domain such as symptom, activity and impact component. The activity component is most affected and symptom component is least affected. Conclusion: The study was conducted to enhance the overall quality of life among the COPD patients. It can be improved by providing education and awareness about the disease and importance of medication adherence among the study population.

KEYWORDS: Adverse drug reaction (ADR), Chronic Obstructive Pulmonary Disease (COPD), MGL-4 medication adherence scale (Morisky Green Levine 4-Item), Quality of life (QoL).

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common respiratory condition characterised by progressive airflow limitation which is partially reversible.^[1] COPD occurs when the pulmonary system has a permanent blockage and by interfering with the transfer of vital gases. COPD can be easily diagnosed by the obstruction in a portion of alveoli or bronchi, which reduces the volume of air within the lungs. Thus, this process may lead to reduced exchange of gases.^[2] COPD can also restrict the daily activities due to the imbalance in pulmonary functions, dyspnoea and limitations in exercise tolerance. Hence it is associated with poorer health status. Physical aspect of health is greatly affected than mental aspects of health.^[3]

According to WHO estimates, currently 210 million

people have COPD and 3 million people of COPD in 2005. Now COPD is the 4th leading cause of death worldwide and WHO has predicted that COPD will become the 3rd leading cause of death by 2030.^[4] In US, COPD is the third leading cause of mortality. About 12-16 million people get affected by COPD in US.^[5] Now it is estimated that more than 210 million people have detected with the disease globally.

About 251 million cases of COPD were present in worldwide in 2016 and 3.15 million deaths per year were reported due to COPD. In 2016, it is estimated that three out of five death was due to non communicable disease whereas the second leading cause of death is COPD in India today.^[7]

Quality of Life

A variety of studies claim to assess the quality of life. However there is only less agreement about the fundamental concepts that the measures represent. Clinical symptoms (like pain, nausea, vomiting), functional disability (Katz activities of daily living), health status measures (RAND health status measures, sickness impact profile), and measures of life satisfaction and psychological well-being are the measures so included for assessing QoL.^[8]

Medication Adherence

Adherence is defined as the behaviour of a person in taking medications by following diets and lifestyle changes. Adherence is associated with both the patients and health care providers. Usually COPD patients are poorly adherent and may result in the high risk of morbidity, healthcare expenditures, hospitalizations and mortality, and reduced quality of life. Adherence is mainly affected by the patients intention about their disease, treatment types and patient providers communication and social environment. Patients adhere to the treatment when they have hope about the disease management and when they understand seriousness of the non-adherence. Providers plays a major role in making patients aware about the seriousness of non-adherence.

According to the WHO, the adherence of patients to the long term treatment in chronic diseases is 50% in developed countries. Low adherence is seen in the patients who have been prescribed with the COPD treatment.

The term compliance has been used as the extent to which a patient undertakes the prescribed medications by following medical instructions. Patients who ignore the doctor's orders are said to have low compliance. Patient adherence in chronic obstructive pulmonary disease is multifactorial and is influenced by the patient, the physician and society(9) .

Adverse Drug Reaction

According to WHO, ADR is defined as "a response to a drug which is noxious and unintended, which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiological function".^[10]

A type of ADE is an ADR, whose cause is assigned to a drug and its physiologic properties. The NCC MERP defines ADE as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient or consumers". ADR and ADE can be differentiated as, ADRs are presented with appropriate prescribing and dosing pattern, while ADE can be occurred with the inappropriate use of the drug during the drug therapy. ADE can also caused by

medication errors.

The management of ADRs are complicated one as they increases the costs due to increased hospitalization, prolongation of hospital stay, additional investigations, and drug therapy in more serious cases. So it is necessary to detect the ADRs and the risk associated with the use of drugs earlier, during the ADR monitoring and reporting program. Thus, Pharmacovigilance Programme of India has launched in June 2010 to ensure the safety of the drug and to promote ADR data in Indian patients.^[11]

METHODS AND METHODOLOGY

This is a hospital based prospective observational study. It was conducted at PKTB hospital, Mysore. The study was carried out at pulmonology department of Chronic Obstructive Pulmonary Disease patients and the study duration was the period of six months from November 1st 2018 – April 30th 2019. The data were collected from the patient medication history and their by standers respectively after getting informed consent. During the study period we attended 252 patients who are above 18 years old. The patients who were referred for consultation and those who are not willing are excluded from the study.

Ethical approval was obtained from the Institutional Ethical Committee of Mysore Medical College and Research Institute, K R Hospital; Mysuru.

Importance of the study was explained to the participants and informed consent was taken from the patients or their bystander. SGRQOL questionnaire was used to investigate the quality of life of people living with COPD. And it is filled by patient itself and recorded the same. The data collected from the patients from questionnaire and data collection form. The statistical analysis was done by using SPSS and analyzed using the statistical like ANOVA and two-tailed t-test and the results were compared.

RESULTS

Demographic details of the study population

Table 1. Gender distribution of the study.

Gender	Frequency	Percentage
Male	214	84.9%
Female	38	15.1%
Total	252	100.0%

Table 2: Age categorization in the study population.

Age Group	Frequency	Percentage
25-34 yrs	2	0.8%
35-44yrs	2	0.8%
45-54yrs	43	17.1%
55-64yrs	79	31.3%
>64yrs	126	50.0%
Total	252	100%

Adverse Drug Reactions

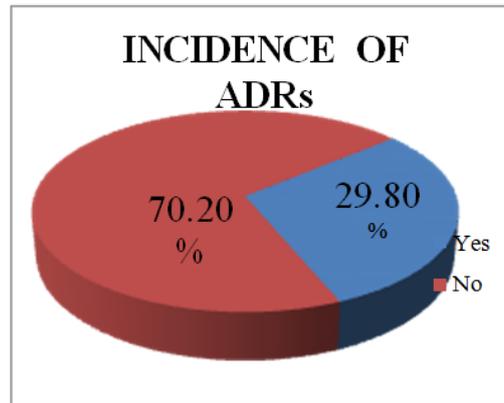


Figure 2: Incidence of ADRs.

Table 4: Suspected ADR in the study population.

SUSPECTED ADR	FREQUENCY	PERCENTAGE
Pruritus	2	2.66%
Hoarseness	2	2.66%
Swelling of limbs	2	2.66%
Sleeping Trouble	4	5.33%
Frequent Urination	2	2.66%
Vomiting	5	6.66%
Stomach Upset	12	16.0%
Dryness Of Mouth	7	9.33%
Headache	10	13.33%
Mouth Sores	3	4.00%
Injection Site Swelling	3	4.00%
Dyspepsia	2	2.66%
Constipation	2	2.66%
Mood Change	2	2.66%
Tremor	9	12.0%
Nausea	4	5.33%
Tachycardia	4	5.33%
Total	75	100%

Table 5. Suspected medication in the study population.

Suspected Medication	Frequency	Percent age
Hydrocortisone	21	28.0%
Acetylcysteine	2	2.66%
Doxofylline	11	14.66%
Benidipine	2	2.66%
Salbutamol+Triotropium	3	4.00%
Levosalbutamol+ipratropium+Budesonide	11	14.66%
salmeterol+fluticasone	2	2.66%
Budesonide	7	9.33%
bromohexine+Guaifenesin+menthol+Terbuta line	2	2.66%
Azithromycin	2	2.66%
Metoprolol	2	2.66%
Levothyroxine	2	2.66%
Levosalbutamol+ipratropium	4	5.33%
Furosemide	4	5.33%
Total	75	100

Table 6. Causality assessment of ADR in the study population.

Naranjo causality assessment Scale.	Frequency	Percent
Probable	47	63%
Possible	28	37%
Total	75	100%

Table 7: Hartwigs severity assessment scale.

Severity	Frequency	Percentage
Mild	40	53.33%
Moderate	35	46.66%
Total	75	100%

MEDICATION ADHERANCE

Table 6. Medication adherence.

MGL medication adherence	Frequency	Percent
Low adherence	89	35.3%
Medium adherence	131	52.0%
High adherence	32	12.7%
Total	252	100%

QUALITY OF LIFE

Table 8. Quality of life with their scores.

Scores	Mean	Std.Deviation
Symptom Score	30.30	08.862
Activity score	51.92	19.835
Impact Score	43.45	15.753
Total Score	42.04	13.037

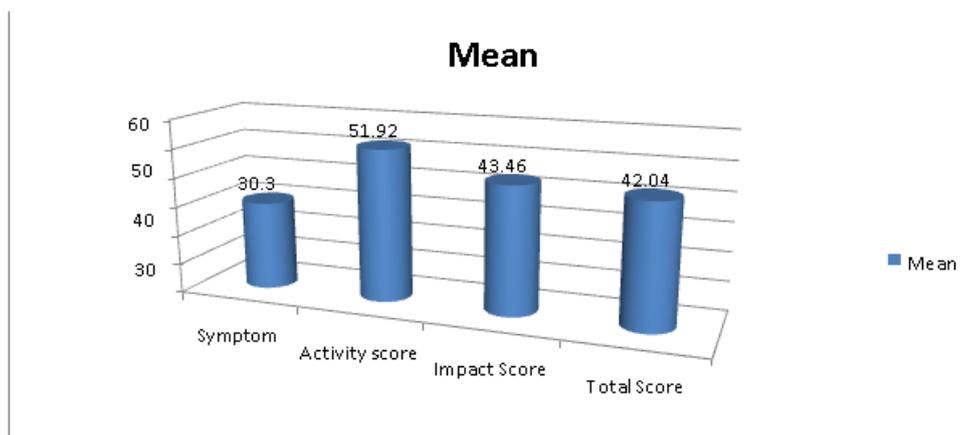


Figure 2: Quality of life with their scores.

Table 10: Correlation of qol (oneway anova method).

Factors	Significance (P< 0.05)			
	Symptom Score	Activity Score	Impact Score	Total score
Gender	0.644	0.62 2	0.981	0.731
Age Group	0.015	0.000	0.000	0.000
Education	0.020	0.085	0.141	0.084
Annual Income	0.214	0.471	0.309	0.300
Cigarette/Day	0.027	0.000	0.000	0.000
Co-Morbidities	0.320	0.000	0.035	0.017
Patient with ADR's	0.006	0.000	0.004	0.000

Table 1 shows greater dominance of males over females in the study population. Among 252 patients included in the study, 214 were males (84.90%) and 38 were females (15.10%). Table 2 point out that the 50% of the COPD

patients are in the age group of > 64 years and the least were in the age group between 25-44 years.

Out of 252 patients, 75 patients (29.80%) are observed

with ADR and 177 patients (70.20%) are without ADR. The details are represented in the figure 1. From the table 3, it is understood that the most commonly reported ADR is Stomach upset (16.0%), followed by headache (13.33%), tremor (12.0%) and dryness of mouth (9.33%). Among the study population, the mostly suspected drug causing ADR is hydrocortisone 28.00% (n=21), followed by 14.66% doxofylline (n=11) and 14.66% levosalbutamol+ipratropium+budesonide (n=11). The details of the suspected drugs are given in the table 4. Among 75 ADR found in the study population, the Naranjo scale assessment provides 63% of ADRs are probable and 37% are possible. The details are represented in the Table 5. Table 6 shows that out of 75 ADR, 53.33% of ADRs were mild and 46.66% were moderate.

Out of 252 patients, 35.30% patients (n=89) have low adherence, 12.70% patients (n=131) have medium adherence, and 12.70% patients (n=32) have high adherence to the medications provided. It shows a very few patients are highly adherent. The details are depicted in table 7.

In our study, the current health statuses of 43.30% of the patients are fair and of 7.50% patients are very poor. Using St George's Respiratory Questionnaire for COPD, we found that the mean symptom, activity, impact and total score were 30.30, 51.92, 43.45 and 42.04 respectively. The scores showed significant impairment in all three domain scores, i.e., symptoms, activity and impact. The details are represented in the Table 8 and figure 2. The study also observed that age, smoking status and the incidence of ADR had a statistically significant positive correlation with QOL scores across all domains. Education status and co morbidities also had significant positive correlation with QOL scores except in impact and symptom domain respectively. The details are depicted in table 10.

DISCUSSION

Demographic

The present study set out to assess the Quality of Life, medication adherence and adverse drug reaction in patients with COPD. The study was carried out in the pulmonology department of PKTB hospital, Mysore over a period of 6 months.

Out of 252 patients reviewed, we found that male patients (84.9%) were predominant while comparing to female patients (15.1%). This was concordant with the study results of Varughese JD *et al.*^[12] In this study, 100 patients were involved in which, 78% were male and 22% were female. The study also correlated with the study of Mishra VR *et al.*^[13]

In our study, majority of the patients (50%) belongs to the age group of >64 years and the least number (0.8%) of patients is in the age group of 25-34 years and 35-44 years. The result pointed out the increased incidence of

COPD among older patients. This result is consistent with the study of Shahab L *et al.*, which reported a linear increase in the prevalence of COPD with age. The mean age in the study population was found to be 62.5.^[14]

The education status revealed that the 51.6% of the patients were uneducated and only 1.6 % of the patients had higher education in our study population.

On the review of the social history of the study population, it is found that 40.10 % of the patients had the habit of smoking, 8.70% were alcoholics and 36.1% of the patients had both habits. It is evident that among the total study population, 76.2 % patients had the habit of smoking. Among smokers, 2 patients take <5 cigarette (0.80%) per day, 26 patients takes >5 cigarettes (10.31%) per day, 84 patients take 1packet (33.33%) per day and 80 patients take >1packet (31.74%) per day. This indicates that smokers are more prone to develop COPD. This result is supported by the study conducted by Varughese JD *et al*, in which 70% of the total population diagnosed with COPD had the habit of smoking (48%- ex smokers, 22%- current smokers).^[12]

Our study showed that the most patients with COPD have one or more co morbidities. Among the total study population, 138 patients (54.8%) were found with the co-morbidities such as hypertension (32.50%), diabetes mellitus (8.7%), ischemic heart disease (4.0%), atrial fibrillation (1.60%), peripheral vascular disease (0.4%), hypothyroidism (0.80%), tuberculosis (1.60%), lower respiratory tract infection (2.40%), urinary tract infection (1.20%) and right indirect inguinal hernia (1.60%). This shows hypertension to be the most commonly occurring co morbidity followed by diabetes mellitus, IHD and atrial fibrillation. The frequency of other co morbidities is less in the population. This result was comparable with a study by Crisafulli *et al.* Out of 316 patients, 51% were affected with at least one co morbidity. The most prevalent co morbidities were hypertension, diabetes mellitus, coronary disease, chronic heart failure, dyslipidaemia and osteoporosis.^[15]

Adverse Drug Reaction

People with COPD are usually in advanced ages and also pharmacotherapy in COPD commonly involve polypharmacy. Hence they are at high risk of developing ADR.

Out of 252 patients, 75 patients (29.80%) reported ADR, in which 67 are male patients and rest are female. This is concordant with the result of study conducted by Purushothaman S *et al.*, which reported higher prevalence of ADR among male patients with COPD. This association was found to be statistically significant.^[16]

In our study, nervous system (45.31%) is mostly affected due to reported ADR, which is followed by alimentary canal (21.32%) and then other system (26.64). A very

few allergic reaction (6.66%) were also reported. A similar result is shown in the study conducted by

Petrova G et al, in which the nervous system was most affected by ADR in the study population.^[17]

Among the reported ADR, reactions associated with nervous system were vomiting (6.66%), headache (13.33%), sleeping trouble (5.33%), mood change (2.66%), tremor (12%) and nausea (5.33%). Stomach upset (16%), dyspepsia (2.66%) and constipation (2.66%) were the adverse reaction which affected digestive system and others include frequent urination (2.66%), hoarseness of voice (2.66%), tachycardia (5.33%), dryness of mouth (9.33%), mouth sores (4%) and swelling of limbs (2.66%). Reported allergic reactions include pruritus (2.66%) and injection site swelling (4%).

Drug contributing majorly to ADRs is hydrocortisone (28.00%). Other major drugs causing ADRs are doxofylline (14.66%), levosalbutamol+ ipratropium+ budesonide (14.66%) and Budesonide (9.33%). This is similar to a study carried out by puroshothaman S et al (16), in which the most common drug contributing to the ADR are systemic steroids (69%).

Our study results which were observed by Naranjo Causality assessment scale shows that 18.70% were “probable” and 11.10% were “possible” ADRs. A similar finding was observed in a study conducted by Khan A et al(18). In their study Naranjo algorithm, showed 55% “probable”.

Hartwig’s severity assessment scale shows 53.33% of the total ADRs are mild and 46.66% are moderate. A similar result is reported in a study conducted by Petrova G et al, in which most of the reported ADRs were considered to be mild or moderate. About 59% of ADRs were mild in their study [32.6% -level 1 and 26.4 % level 2].^[17]

An association is found between the education and smoking status with the ADR, whereas the association of gender, age, economic status, marital status and co morbidity with ADR is not significant.

Medication Adherence

To optimise the management of COPD, the patient adherence to the treatment is very essential. As COPD is a chronic disease, the patients with high adherence to the treatment will be less.

Among 252 study patients, 35.3% patients have shown low adherence towards the drugs, 52% patient were presented with medium adherence and 12.7% were high adherent to the COPD treatment . This was contrast to the study results conducted by Duarte-De-Araujo, here out of 319 patients, 94 patients (31.3%) were poorly adhered and 50 patients (16.7%) were non adherent to inhaled medications.^[19]

COPD patients usually have low adherence pattern due to several conditions. But the prevalence of poor adherence is unexpectedly low in our study results. However a study conducted by Tottenborg SS et al.,^[20] explained variability in the prevalence of poor adherence, when using different methods or instruments or in a different population.

Gender, age, economic status and education status had found a significant association with medication adherence. In our study, gender of the patients shows association with medication adherence with a p-value of 0.010. And age shows association with a p- value of 0.000. Education and annual income are also associated with medication adherence with p-values of 0.003 and 0.001 respectively.

Male patients were poorly adhered to the treatment than female patients in our population, indicating a significant association of gender with medication adherence. A significant association between gender and medication adherence is also seen in the study conducted by Humenberger M et al.^[21]

We found a significant association between age and medication adherence. In our study medication adherence is poor in aged patients. A study conducted by Agh T et al., also showed a significant association between age and medication adherence among the study population.^[22]

Medication adherence is also seen to have association with economic status among the study population. However socioeconomic inequalities have been associated with a risk of poor adherence in a study conducted by Tottenborg et al.^[20]

Education status also plays a role in medication adherence, where in our study low adherence is mostly seen in illiterate patients when compared with the others. This association may be because education plays an important role on modifying beliefs; patients are likely to modify the recommended therapy based on how they feel or their level of dyspnoea. Similar association between education and medication adherence is reported in the study result of Restrepo RD.^[23]

Quality of Life

According to studies, COPD is one of the major public health threats in India. The patients with COPD are facing many health problems and are challenged with restricted physical activities and reduced HRQOL. Poor QOL is mainly due to dyspnoea and co morbidities. In our study the mostly seen symptom is dyspnoea.

The study showed an impaired QOL among 252 COPD patients using a disease- specific Questionnaire (SGRQ-C). The mean symptom, activity, impact and total score were 30.30, 51.92, 43.45 and 42.04 respectively. QOL

was impaired across all the components i.e. symptom, activity and impact component. In our study the activity component is most affected while symptom component is least affected. A study conducted By Malhotra M et al showed a similar result in which the symptom, activity, impact and total score were 54.25, 67.26, 54.27 and 58.16 respectively. In this study, the activity component was most affected and symptom component and activity components was affected almost similarly (24). However, in another study conducted by Ahmed MS et al showed that the mostly effected domain in the study population was symptom domain and the least affected was activity domain.^[25]

We found the age has a statistically significant positive correlation with QOL scores across all domains. With increasing age, QOL worsened. It indicates that age has a significant impact on QOL. Some studies had shown the similar results to us.^[26,27] with many reporting no correlation between age and QOL.^[28] Some studies also reported that worse health status is observed in younger patients.^[29]

There exists a statistically significant positive correlation between the education status and symptom, activity and total score in our study. While the correlation between the impact score and education status is non significant. Similar to us, a study showed that education status had significant impact on QOL.^[24]

In our study an association is also found between the quantity of cigarette consumption and QOL. Cigarette consumption worsens QOL. Increase in the number of cigarette causes decrease in the QOL. An association of smoking index with QOL is found to be significant in the study conducted by Ahmed MS et al. This study showed poor HRQOL with increased quantum of smoking.^[25]

Co morbidities are common in COPD patients. The mostly occurring includes hypertension, diabetes mellitus and ischemic heart disease. In our study, co morbidity has significant association with all the QOL score except with the symptom score. The activity component has stronger association than impact and total score. In general, presence of co morbidity reduces the quality of life. A similar result is observed in the study of Huber MB et al. This study clearly showed that co morbidities in COPD are associated with poorer generic HRQOL.^[30] A study by Pati S et al., also supported our result in which QOL score was high in the COPD patients with co morbid condition indicating their poor health status.^[31]

The association between ADR and all the QOL scores i.e., symptom, impact, activity and total score is statistically significant. The poor quality of life is seen in the patients observed with ADR than in the patients without ADR.

Gender and economic status did not impact QOL in a

significant manner. However a study conducted by Ferrer M et al reported that gender shows impact on QOL with females reporting poor QOL.^[32] Similar to us, a study conducted by Engstrom CP has shown that gender has no role in the QOL of COPD patients.^[33]

In our study, no association was found between the economic status and QOL. But many study showed that low economic status is linked to poor QOL. An association between economic status and QOL is seen in the study of Pati et al. Study found the mean score of the patients with low income to be 62.9. This indicates the high impairment of QOL in this group (34). Similar to our result, a study conducted by Uppal M et al., reported that there is no significant correlation between economic status and QOL.^[35]

CONCLUSION

COPD is a leading respiratory disease affecting both the length and quality of life. As on 2016, three out of five leading causes of mortalities constitute non-communicable diseases whereas COPD is the second biggest cause of death in India today. In addition, it is among the top eight leading causes of disabilities in India.

In our study, male patients were more in number when compared with females. One major reason for COPD among male is higher prevalence of smoking in this gender, and also males are more exposed to smoking than females. Also majority of the patients is above 64 years of age and illiterate. Hypertension is the most common associated co morbidity in the COPD patients.

ADRs are associated with considerable morbidity, mortality and high medical cost. Polypharmacy is common in patients with COPD. So they are at high risk of developing ADR. Careful therapeutic monitoring and dose individualisation is necessary to minimize the incidence of ADR. In our study out of 252 patients, 75 patients are observed with ADR, in which 67 are male patients and 8 are female. The most common reported ADR is stomach upset. Tremor is also observed in 12% of the patients. Hydrocortisone is the major drug contributing to ADR. All the reported ADRs are categorized as mild and moderate. Naranjo causality assessment provides all the reported ADRs come under probable and possible. The association of education status and quantity of cigarette per day is found to be statistically significant in our population.

Poor adherence in patient with COPD is a significant concern. In our study, most of the patients had medium adherence towards the drugs. Socio-demographic variables such as gender, age, education status, and economic status have shown association with medication adherence. Male patients were mostly non adherent when compared to females. Increasing age, illiteracy, and low annual income led to poor adherence. Marital status, co-morbidity and quantity of cigarette consumption had no

association with medication adherence.

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