ORIGINAL ARTICLE

Factors Responsible for Depression in Patients with Chronic Obstructive Pulmonary Disease

YASIR AHMED[1], SAADIA ASHRAF[2], TAIMUR ZEB[3], WAQAS AHMAD[4], SHAHID ZIA[5], MUHAMMAD FAYAZ[6]
[1]Experiential Registrar, Department of Pulmonology, Khyber Teaching Hospital Peshawar, KPK.
[2]Professor, Department of Pulmonology Khyber Teaching Hospital Peshawar, KPK.
[3]Registrar, Pulmonology Alkhidmat Hospital Charsadda, KPK.
[4]Assistant Professor, Pulmonology Department, Lady Reading Hospital Peshawar, KPK.
[5]Trainee Registrar, Department of Pulmonology, Khyber Teaching Hospital Peshawar, KPK.
[6]Post Graduate Resident, Department of Pulmonology, Khyber Teaching Hospital Peshawar, KPK.
Corresponding author: Yasir Ahmed, Email: Dr.yasirimtiaz@gmail.com

ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a neglected but important health problem, accounts for significant morbidities and mortalities worldwide. By year 2030, it is expected to be the third leading causing of mortality. COPD patients with associated depression can affect disease progression, high healthcare resource utilization, more frequent exacerbations and increased mortality.

Objectives: To determine the frequency of factors leading to depression in patients with COPD presenting to tertiary care hospital at Peshawar.

Material & Methods: It was descriptive Cross-Sectional Study conducted at Pulmonology unit,Khyber teaching hospital Peshawar from 12th November 2019 to 12th May 2020.Patients with COPD fulfilling the inclusion criteria were assessed for depression. A total of 43 patients were selected according to Hamilton Depression Rating Scale (HDRS 21) for Depression. Factors leading to depression like Gold stage of COPD, smoking, socio economic status, mMRC grades of dyspnea and C reactive proteins level were assessed. Frequency was calculated for each of these factors causing depression. These factors were further stratified on basis of age, gender, duration of COPD and no of hospitalization. SPSS version 22 was used for analyzing of the collected data. P value less than 0.05 was marked as statistically significant.

Results: Among these 43 COPD patients with depression, 19 (44.2%) were males and 24 (55.8%) were females. Mean age was 61.93 years (45-80) ± 10.30 SD. Frequency of Gold stage of COPD was stage II (16.3%), stage III (58.1%) and stage IV (25.6%). Frequency of smoking was 37.2%. CRP level was raised in 58% of patients. mMRC grades of dyspnea were grade II (18.6%), grade III (44.2%) and grade IV (37.2%) and 67.4% of the patients were poor. On post stratification of smoking on the basis of gender, and Gold stages of COPD on the basis of number of hospitalization, p value was 0.02 and 0.01 which was significant statistically.

Conclusion: It concludes that GOLD stage of COPD, smoking, increased CRP level, increased Dyspnea (MMRC scale) and poverty are the factors leading to depression in patients with COPD, affecting quality of life and progresion of COPD.

Keywords: Chronic obstructive pulmonary disease, depression, GOLD.

INTRODUCTION

As a leading cause of mortality, chronic obstructive pulmonary disease (COPD) exacts a heavy and increasing social and financial toll[1]. In the next decade, chronic obstructive pulmonary disease (COPD) will overtake stroke as the third leading cause of death [2]. Medication therapy for COPD have made very little improvement, so patients still deal with frequent acute exacerbations, lengthy hospital stays, low survival rates, and impaired physical performance and quality of life[3]. Patients with chronic obstructive pulmonary disease (COPD) have a significantly higher rate of depression than the general population (10-42% vs. 0-5%)[4]. Patients with COPD often go undiagnosed and untreated for depressive disorders in both primary and secondary care[5], despite evidence that some interventions, such as antidepressant medicines, pulmonary rehabilitation, or counseling, can improve quality of life.

The impact of COPD on mortality and disability-adjusted life years (DALYs) in India is substantial, with estimates ranging from 6.6% to 7.7%. Previous studies found that anywhere from 6-56% of people with COPD also experienced depressive symptoms[6,7]. Other factors outside the medical burden contribute to the overall impact of COPD on the lives of those who suffer from it. Conditions, anticipations, coping strategies, and mental health of the patients all factor significantly. Depressive symptoms are strongly linked to declines in functional status, QoL, disease progression, and mortality in COPD[8].

Patients suffering from depression are at risk of not completing their prescribed management programs, such as pulmonary rehabilitation[9] and quitting smoking. Therefore, clinical outcomes may be negatively affected by depression. Patients admitted to the emergency room due to depression have a higher admission and relapse rate[10]. Patients with COPD who also

suffer from depression place a greater financial strain on healthcare systems.

In addition to being an independent predictive factor for death in individuals with COPD, depression is linked to frequent hospital readmission for acute exacerbation [11]. Reduced functionality due to COPD may contribute to the development and maintenance of depression[12]. Age, gender, employment status, living alone, and steroid use are just few of the characteristics that have been linked to depression in COPD patients in previous research [13].

Due to the irreversible nature of COPD, the goal of treatment is not to cure the disease but to alleviate symptoms, boost functioning, and boost quality of life.[14] Patients with COPD, who often experience substantial physical disability and unpleasant symptoms including dyspnea and productive cough, have long been hypothesized to suffer from depression. Depression has a negative impact on quality of life since it can affect a person's emotional, social, and even physical well-being. While some research has linked COPD patients to higher rates of depression, others have not found this to be the case.[15]

MATERIALS AND METHODS

It was a descriptive cross sectional study conducted at pulmonology unit Khyber teaching hospital Peshawar between 12th November 2019 to 12th May 2020. Sample size was 43 keeping 87.5%6 proportion of heavy smoking as risk factor of depression in patients with COPD with 95% confidence interval, 7% margin of error. Consecutive non probability sampling technique was used. COPD patient fulfilling the inclusion criteria (as per GOLD criteria based on spirometry findings that is post-bronchodilator fixed FEV1/FVC < 0.70 with post bronchodilator FEV1 reversibility of < 12% measured on spirometer) were included. Patients of both gender & age between 40 to 80 years

were included. Depression was defined as any patient having a score of more than 7 according to 21-Scale on Hamilton Depression Rating Scale (HDRS). Patients with intellectual cognitive impairment or mental illness other than depression i.e. anxiety, obsessive compulsive disorder, bipolar disorders and patients with history of other pulmonary diseases i.e. asthma, bronchiectasis, interstitial lung diseases , cardiac failure and hypothyroidism were excluded.

After ethical approval from hospital ethical and research committee & appropriate management of the patients, written informed consent was obtained from all patients intended to be included in the study. Patients were assessed according to 21-Scale Hamilton Depression Rating Scale (HDRS) for presence of depression. All the information pertaining to age, gender, factors of depression such as low socioeconomic status, stage of COPD, grade of dyspnea, smoking history, quantitative CRP levels were recorded. The patient's duration of COPD (in years) and number of hospitalizations per year are the potential effect modifiers were also be recorded in a pre-designed structured performa. Age and gender were stratified in analysis to see any effect modification.

Data Analysis: Data was entered and analyzed using Statistical Package for Social Sciences (SPSS) version 22.0. Mean +SDs were calculated for quantitative variables including age, serum CRP levels, duration of COPD and number of hospitalizations. Percentages and Frequencies were calculated for 92 gender, socioeconomic status, smoking history, stage of COPD and grade of dyspnea. Factors leading to depression were stratified with age, gender, duration of COPD and number of hospitalizations (which are the potential effect modifiers) in order to exclude bias from the study. Post stratification chi square test was applied by keeping P Value < 0.05 as significant. All results will be presented in the form of graphs and tables.

RESULTS

In this study, 43 COPD patients with depression were included. Minimum age in this study was 45 years while maximum age was 80 years. Among these 43 patients, 19 (44.2%) were male patients and 24 (55.8%) were females. (Figure # 7). Mean age was 61.93 years (45-80) ± 10.30 SD while median age was 60 years. On the basis of age, these 43 patients were divided into two groups. 25 patients (58.1%) were in Group 1 (age 40 to 60years) while 18 patients (41.9%) were included in group B(60-80yrs).COPD mean duration was 9.79 years (2-24) ± 4.78 SD while median for duration of COPD was 10 years. Among these 43 patients, 29 patients (67.4%) had 1 to 10 years duration of COPD while 14 (32.6%) were having more than 10yrs duration of copd. Patients were also distributed on the basis of number of hospitalization. Among these 43 patients, 13 patients (30.2%), 16 patients (37.2%), 11 patients (25.6%) and 3 patients (7%) were having history of 1, 2, 3 and 4 times hospitalization respectively.

Patients were also stratified on the bases of spirometric grade/stage of COPD as well. Among these 43 patients, 07 patients (16.3%) were in stage II of COPD , 25 patients (58.1%) presented in stage III of COPD while 11 patients (25.6%) were found in stage 1V of COPD.

Stages of COPD was stratified on basis of duration of COPD. Among 29 patients with disease duration of 1 to 10 years, 6 (20.6%), 18 (62.1%) and 5 (17.3%) were having stage II, stage III and stage IV COPD respectively. While the remaining 14 patients, 2 (11.2%), 11 (61.2%) and 5 (27.6%) were documented as stage II, stage III and stage IV of the disease respectively However, on post stratification it was not significant statistically i.e. p value was 0.38 (Table # 5). COPD was further stratified among gender with smoking. Among males 12 (63%) and 7 (37%) were smokers and non smokers respectively. While among females , 4 (16.7%) and 20 (82.3%) were smokers and non smokers respectively. On post stratification chi square test was applied and p value was statistically significant i.e. p= 0.02 (Table # 7).

2. SMOKING Among these 43 patients, 16 (37.2%) and 27 (62.8%) were smokers and nonsmokers respectively. (Figure #

10). Smoking was also stratified on the basis of age of patients,duration of copd and number of hospitalization

3. SOCIO-ECONOMIC STATUS Among these 43 COPD patients with Depression, 29 (67.4%) were poor, that is, their monthly income was less than PKR 20,000 per month while 14 patients (32.6%) were having satisfactory monthly income i.e. more than PKR 20,000 per month. (Figure # 11). Socio economic status was stratified 98 on the basis of gender, age of the patent, duration of copd & number of hospitalization

4. MMRC GRADES OF DYSPNEA These 43 COPD patients with depression were also divided on the basis of grades of dyspnea. Among them 8 (18.6%), 19 (44.2%), 16 (37.2%) were 99 suffering from mMRC grade II, grade III and grade IV respectively (Figure # 12).

MMRC grades of dyspnea was stratified on the basis of gender of patients

5. CRP LEVEL Among these 43 patients, 25 (58%) patients had raised CRP, while 18 (42%) had normal or low CRP level. (Figure # 13) Mean CRP was 16.28 mg/dl (1-66) ± 15.58 SD. Mean high CRP level was 24.36 mg/dl ± 16.46 SD. Mean normal CRP level was 3.39 mg/dl ± 1.29 SD

CRP level was also stratified on the basis of number of hospitalization. Five patients (38.5%) and 8 (61.5%) were documented to have high and normal level of CRP respectively with history of one-time hospitalization in the last year. While patients having history of two times hospitalization were having 12 (75%) and 4 (25%) raised and normal CRP level respectively in their blood. Patients with three times of hospitalization were 6 (54.5%) and 5 (45.5%) raised and normal CRP respectively. Among patients with history of four times hospitalization, 2 (66.6%) and 1 (33.4%) were having raised and normal CRP level respectively. P value was not significant statistically i.e. p=0.25 (Table #22).

Table 1: Distribution of patients on the basis of duration of COPD (n=43)

	Duration of COPD	Frequency
Group 1	1- 10 years	29 (67.4%)
Group 2	> 11 years	14 (32.6%)
Total	2-24 years	43 (100%)

Table 2: Stratification of stages of COPD on the basis of gender (n=43)

Stages of COPD	Gender of patients Frequency (%age)		Total	P-value 0.55
	Male	Female		
Stage II	2 (10.5%)	5 (20.8%)	7 (16.3%)	
Stage III	11 (57.8%)	14 (58.3%)	25 (58.1%)	
Stage1V	6 (31.7%)	5 (20.9%)	11 (25.6%)	
Total	19 (100%)	24 (100%)	43 (100%)	

Table 3: Stratification of stages of COPD on the basis of age (n=43)

Stage of COPD	Age of patient Frequency (%)					
					Total	
	Age	40-60yrs	Age	>	60	P- Value 0.74
Stage II	5 (20%)		2 (11.2%)			7 (16.3%)
Stage III	14 (56%)		11 (61.2%)			25(58-1%)
Stage IV	6 (24%)		5 (27.6%)			11(25.6%)
Total	25 (100%)		18 (100%)			43 (100%)
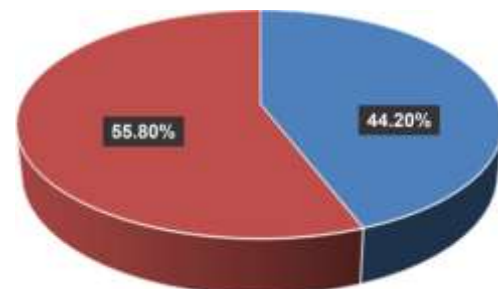
Figure 1:
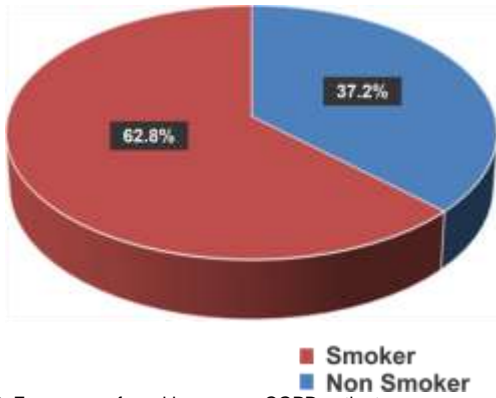
Figure 2: Frequency of smoking among COPD patients

Monthly Income < 20k PKR per month
Monthly Income > 20k PKR per month

Fig 3: Distribution of patients on the basisof socio economic status

Table 4: Stratification of socio economic status on the basis duration of COPD (n=43)

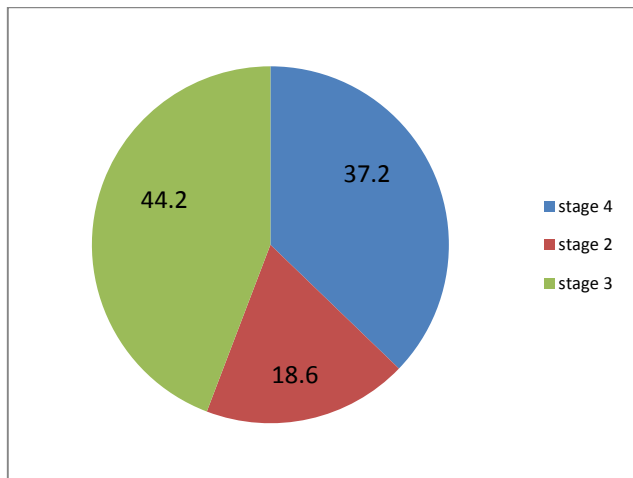| Duration of COPD	Monthly socio economic status		Total	P value 0.38
	POOR PKR<20k	Satisfactory PKR>20k		
1-10 years	19 (65.5)	10 (34.5)	29 (100%)	
>10 years	10(71.4%)	4 (28.6%)	14(100%)	
Total	29(67.4%)	14 (32.6%)	43 (100%)	

Figure 4: Distribution of patient on the bases of Grades of dyspnea

Table 4: Stratification of MMRC grades of dyspnea on basis of no of hospitalization (n=43)

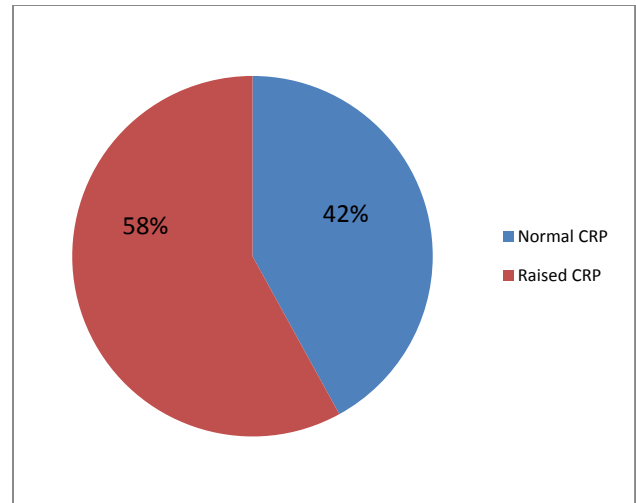| No of hospitalization	mMRC grade of dyspnea frequency			Total	P value 0.63
	Grade 2	Grade 3	Grade 4		
1 Times	4 (30.8%)	5 (38.4%)	4 (30.8%)	13 (100%)	
2 Times	2 (12.5%)	9 (55%)	5 (32.5%)	16 (100%)	
3 Times	1 (9.1%)	4 (36.3%)	6 (54.6%)	11 (100%)	
4 times	1 (33.3%)	1 (33.3%)	1 (33.4%)	3 (100%)	
Total	8 (18.6%)	19 (44.2%)	16 (37.2%)	43 (100%)	

Figure 5: Frequency of raised CRP in COPD patients with depression

Table 5: Stratification of CRP level on the basis duration of COPD (n=43)

Duration of COPD	CRP level Frequency(%)		Total	P value 0.58
	High CRP	Normal CRP		
1-10 years	17 (58.6%)	12 (41.4%)	29 (100%)	
>10 years	8 (57%)	6 (43%)	14 (100%)	
Total	25 (58.3%)	18 (41.8%)	43 (100%)	

Table 6: Stratification of CRP level on the basis of no of hospitalization (n=43)

Number of hospitalization	C reactive protein level Frequency (%)		Total	P Value 0.25
	High CRP	Normal CRP		
1 Time	5 (38.5%)	8 (61.5%)	13(100%)	
2 Times	12 (75%)	4 (25%)	16(100%)	
3 Times	6 (54.5%)	5 (45.5%)	11(100%)	
4 Times	2 (66.6%)	1 (33.4%)	3 (100%)	
Total	25 (58.3%)	18 (41.8%)	43(100%)	

DISCUSSION

A study done by Jose AK et al concluded that number of hospitalizations in previous year and mMRC grades of dyspnea were important factors for depression in patients with COPD. This is consistent with the results of our study. We also emphasized that dyspnea is an important factor for re hospitalization. Similar results for mMRC grades (level) of dyspnea were also reported by Tse HN et al.[16,17] Our study concludes that 68.4% of the COPD patients were having low monthly income. And low socio economic status was an important factor for depression. Similar results were also given by Kumbhare SD et al .[17] Another study conducted by Lotfaliany et al concluded that low socio economic status was associated significantly with depression in chronic diseases including COPD. The results of our study were also supported by the conclusion of Stellefson et al that low socio economic status is an independent important factor leading to mentalstress[18].

In our study 37.2% of the patients were smokers which was statistically significant on the basis of gender (p <0.02). Diamond M et al concluded that smoking was also an independent risk factor for depression which is consistent with the results of our study· While Paine et al gave the direct relation of anxiety, depression and cumulative smoking, which also supports our results.[19]

Khan S et al concluded that Gold stage of COPD and smoking were among the important factors leading to depression which is consistent with the results of our study. We concluded that Gold stage III and IV and smoking were associated with depression. Xu K et al concluded in their study that heavy smoking and high serum CRP were the most important factors for depression in COPD patients, the latter was the strongest responsible factor for it. Riveria CM et al and Lee SH concluded that increased dyspnea was asscoiated with depression, which

supports the results of our study.[20]

Dyspnea was one of the most important factor for depression in our study. In our study, 44.2% of the patients were having mMRC grade III dyspnea while 37.2% of patients were reported with mMRC grade IV dyspnea. A study conducted by Rivera CM et al concluded that the patients with depression were found to have greater grades of dyspnea and poor exercise capacity which is consistent with the results of our study[21]. Similarly, Trevisan C et al conducted on study on the association of depression and dyspnea in patients with COPD. They followed the patients for four years and concluded that patients with worsened dyspnea were more found to be depressed than the other counterparts which is also consistent with the results of our study[22].

In our study, 58% of the patients were having raised level of CRP and we concluded it one of the most important independent risk for depression in patients with COPD. Xu K et al studied the risk factors for depression in COPD patients and concluded that CRP was the strongest factor for depression in COPD patients which is consistent with the results of our study.[23].

CONCLUSION

This study concludes that low socio economic status, GOLD stage of COPD, smoking history, increased CRP level and increased dyspnea (MMRC scale) are the factors leading to depression and any one of them acts as an independent and clinically important factor for depression and thus affects quality of life and outcome of the disease.

Recommendations: Further studies comprising of large sample size are recommended to elaborate the contributions of each of these risk factors. Future work to correlate each of these factors with depression is also recommended. Number of hospitalization in COPD is an important factor leading to depression and its consideration for further work up is recommended as well. Socio economic status of a patient is also important risk factor for depression in many of chronic diseases in developing countries including Pakistan and further studies are recommended keeping in view its different aspects in our population.

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