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ORIGINAL RESEARCH

Demographic, Clinical and Management Characteristics of Newly Diagnosed COPD Patients in Turkey: A Real-Life Study

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Purpose: In order to determine the clinical and sociodemographic characteristics of newly diagnosed treatment-naïve asthma and COPD patients in Turkey, a multicenter study in 2012 was initiated . We aimed to investigate the characteristics and therapies of COPD patients in the original study in more detail.

Patients and Methods: This nation-wide, multicentric, non-interventional, prospective, real-life observational cohort study was conducted in 122 centers. The newly diagnosed patients were not receiving any treatment before the recruitment. Their general characteristics, the combined GOLD 2011 COPD categories and exacerbation histories were noted. The patients were followed up with 3 voluntary visits for 1 year. Their adherence to the inhaled treatment according to GOLD 2011 was evaluated during follow-up visits.

Results: The study included 776 COPD patients. Their mean age was 59.4±9.1 years, and 11.9% of the patients were female. 35.1% of the patients were in the GOLD 2011 C and D category. 12.6% are frequent exacerbators, and 52.8% had at least one comorbid condition. 71.8% overtreatment rate was detected. Their attendance rates for three follow-up visits became 55.9%, 32.9% and 18.7%, respectively. The adherence rate to the treatment was measured as 81.9%.

Conclusion: Although these patients were diagnosed for the first time, the GOLD C and D categories and frequent exacerbator phenotype were found at a high rate. They were usually prescribed an overtreatment regimen. We think that newly diagnosed COPD patients should be evaluated carefully, and best effort should be made to treat these patients in accordance with the recommendations of the major COPD guidelines.

Keywords: COPD, newly diagnosed, treatment naïve, exacerbations

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of mortality and morbidity worldwide.[1,2] The population-based surveys of chronic obstructive pulmonary disease (COPD) have confirmed that COPD underdiagnosis is universally high and significant airflow obstruction is often present at the first diagnosis.[3,4] However, the newly diagnosed patients are expected to be in the early stages. The studies for understanding of different characteristics of newly diagnosed COPD patients are almost lacking. The newly diagnosed COPD patients are presumably to be different from usual COPD patients due to the perception of symptoms and adherence to treatment.

Turkey is among the countries with the highest prevalence of COPD. In the BOLD-Adana Turkey study, the prevalence of COPD was found 19.1% (28.5% in

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men and 10.3% in women) with a fixed ratio (FEV1/FVC <70%) in adults over 40 years of age.[5] We published the clinical, therapeutic features and treatment adherence of newly diagnosed treatment-naïve Turkish asthma and COPD patients in an observational multi-centric cohort study.[6] In this study, since the clinical and demographic characteristics of asthma and COPD patients were presented by comparison, the data of COPD patients could not be presented and discussed in detail. In this study, we aimed to analyze the clinical and therapeutic characteristics of COPD patients in this cohort in detail.

Materials and Methods

Study Design

This study is a nation-wide, multi-centric, prospective and non-interventional study focusing on the general characteristics, diagnosis and treatment approaches for newly diagnosed patients with COPD under real-life conditions for 1 year. Written informed consent was obtained from all subjects. The protocol, which was in accordance with the Declaration of Helsinki, was approved by the ethics committee of Erciyes University, Faculty of Medicine (February 10, 2012). The study was conducted between June 2012 and March 2014 in 122 centers (university hospital, public hospital and private hospital) in Turkey. All participants in the study were chest disease specialists.

COPD patients were enrolled on the basis of the GOLD (Global Initiative for COPD) 2011.[7] A standard web-based questionnaire including items related to demographics, clinical, laboratory and treatment parameters was applied to the patients. All procedures were administered by the investigators (pulmonary physicians) at 122 centers and supervised by the authorized Executive Board consisting of 11 academics for this research organization.

Study Population

To select the study patients and to avoid bias, the physicians screened all patients consecutively and all eligible patients were informed about the study. Outpatient COPD patients meeting the inclusion criteria below were included in the study:

- Age of diagnosis: ≥40 years to ≤80 years.
- Diagnosis of COPD within the previous 3 months or after the initiation visit.
- Diagnosis of COPD was based on a post-bronchodilator forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratio of <0.7, in the absence of a primary diagnosis of bronchiectasis, asthma or any other significant respiratory disease. The patients also had a smoking history of at least 10 packs/year, or occupational exposure to irritant or toxic gases or biomass exposure.
- Patients (or their legal representatives) who accepted to sign the informed consent form.

Procedures and Measures

All procedures were supervised by the authorized Executive Board of 11 academics for this research organization. A web-based "Case Report Form" was prepared by the Executive Board and contract research organization. The Case Report Form included previous and current medical history, demographics (the region of life spent longest, the region of life spent in last 3 months, height, body weight, body mass index and education status), risk factors (smoking, occupation, and biomass using), spirometry, disease severity (combined GOLD 2011 criteria for COPD), and the treatment prescribed.

At the first visit, the patients were taken medical history and examined. Spirometry tests were performed, chest radiographs were examined, treatments were arranged and the Case Report Form were completed. After the initial visit, all patients were followed-up for 12 months. Intended timing for the visits was 0–1 month for visit-1, 1–3 months for visit-2 and 3–12 months for visit-3; however, the frequency of the visits was not determined strictly, and the physicians were completely free to plan the follow-up procedures. Data collected during the follow-up visits included the information on exacerbations and assessment of adherence to the treatment. Two or more exacerbations within 1 year were considered to be "frequent exacerbation."

The physician evaluated patients' adherence to the medication at each visit using a scale. According to this scale, "high compliance" defines the patients who use medications regularly, "medium compliance" and "low compliance" terms define those who use medications with partial or significant interruptions, respectively. And finally, "non-compliance" defines the patients who did not use medication at all. The assessment for patients' adherence to the medications was completely based upon their statement.

Data Management

Physicians were blind to patients of other centers. All lower/upper limits regarding the laboratory test results, decimals, birth dates, etc. were identified in the software

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and entries out of limits were not allowed. System retrieved and weekly updated the package information (name, dosage, pharmaceutical form) of all the medications from the list at the website of Turkish Drug and Medical Device Institution (www.iegm.gov.tr) and allowed physicians to choose the correct and valid name of medication.

To improve data quality, the audit visits were performed at 20 centres (15% of all) which included 450 patients (22% of all) and data were compared with the source documents. Data were protected at high capacity servers located at data center of Türk Telekom (communication and substructure provider company). System equipments were designed binary so as to provide back-up in case of any breakdown. Security of the system was provided with software like firewall, antivirus, antispam, IPS (Intrusion Prevention System) and VPN (Virtual Private Network). SSL/VPN (Secure Socket Layer/Virtual Private Network) technology was used for encryption of database. To ensure the secure data transfer, a "https://" (Hyper Text Transfer Protocol Secure) link was used.

Statistical Analysis

Patients' demographics and disease characteristics were presented as mean ± SD for continuous variables and described as percentages for categorical variables.

Results

A total of 776 newly diagnosed treatment-naïve COPD patients from 122 centers were included. 11.9% of the patients were female. Their mean age was 59.4±9.1 years, and more than 50% of the patients were below 60 years. Current smoker rate was 56.3%. Education level of the study group was low, and approximately 80% of the patients had less than high school education. 23.4% of the patients were obese (BMI≥30). 60% of the whole COPD group was living in the cities. Table 1 demonstrates detailed data about the demographic and different characteristics of the patients included in the analysis.

Disease severity assessed during the initial visit using the combined GOLD 2011 criteria revealed the rates from A to D categories 25.7%, 39.2%, 28.5% and 6.6%, respectively. More than one-third of the patients (35.1%) were in the GOLD 2011 C and D categories despite their being newly diagnosed and treatment-naïve COPD patients. The detailed past history pointed out that 12.6% of the patients were frequent exacerbators (≥2 exacerbations in the preceding year), and 4.3% had hospitalization due to an exacerbation. More than half of the patients (52.8%) had at least one comorbid condition. The most frequent comorbidities were hypertension (21.1%), coronary artery disease (13.6%) and diabetes mellitus (10.1%) (Figure 1).

Table 1 Demographic and General Characteristics of the Patients

Parameters	
Age (years)(mean±SD)	59.4±9.1
Female/Male (%)	11.9/88.1
Age groups (years) (%)	
40–49	15.5
50–59	36.9
60–69	32.3
≥70	15.3
Smoking status (current/ex) (%)	56.3/38.1
Biomass exposure (%)	7.2
BMI (kg/m2) (%)	
<25	44.4
25–29.9	32.2
≥30	23.4
Education (%)	
Illiterate	11.1
Elementary school	55.5
Secondary school	11.7
High school	15.5
University	6.2
Living area (%)	
Urban	59.3
Rural	27.0
Mixed	13.7

Distribution of the preferred inhaled drug regimens according to the GOLD categories is shown in Table 2. Considering the study group as a whole, the most frequently prescribed drug regimen was ICS+LABA+LAMA combination (54.9%). The adherence of the physicians to GOLD 2011 medication recommendations is shown in Table 3. Considering the GOLD 2011 treatment strategy criteria, the overall overtreatment rate was determined as 71.8%. Overtreatment rates were 66.1%, 78.7%, 81.6% and 10.6% according to the GOLD 2011 COPD categories A, B, C and D, respectively.

The rates for visits 1, 2 and 3 in the 1-year follow-up were 55.9%, 32.9% and 18.7%, respectively. According to the patients' statements, 81.9% of the patients had high adherence to the treatment prescribed. The compliance rates were partially stable between visits in the GOLD groups.

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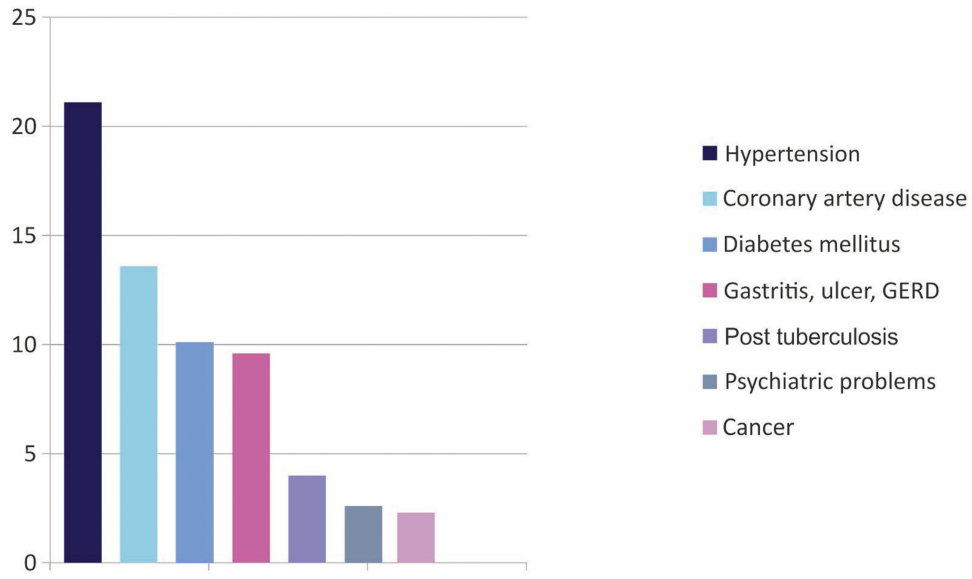


Figure 1 Frequency of comorbidities in newly diagnosed COPD patients.

Discussion

This multicentre, non-interventional, prospective, real-life observational study demonstrated the demographical, clinical and management characteristics of the newly diagnosed COPD patients in our country. To our knowledge, this is the first prospective study conducted on newly diagnosed and treatment-naïve COPD patients. Since COPD is closely related to age and is very rare among subjects below 40 years of age and elderly patients have difficulty performing spirometry correctly,[8–10] patients 40 years and over and 80 years and under were included in the study. The important findings of the study were that approximately one-third of newly diagnosed COPD patients had the GOLD stage C or D disease severity, and more than 70% of the patients were over treated. The detailed past history pointed out that 12.6% of our patients were frequent exacerbators before COPD diagnosis. This high exacerbation rate in newly diagnosed COPD patient group is a very important finding because COPD exacerbations are a major cause of morbidity and mortality.

Generally mild to moderate COPD patients are underdiagnosed and the diagnosis of COPD is usually made in moderate or severe stages.[11] Delay in diagnosis of COPD is a global and multifactorial problem.[4] In a Spain study, COPD prevalence was found 10% and only 27% of these patients had COPD diagnosis before.[12] In a Norway study, only 20% of male patients and 30% of female patients were diagnosed COPD by a physician.[8] The rate of underdiagnosed COPD patients in Turkey is much higher than European countries. In the BOLD-Adana study, 8.4% patients had COPD diagnosis.[5] The most important reason of delay in COPD diagnosis is the slowly progressive nature of COPD.[1] Therefore, the disease usually remains undetected, and a large number of patients are first determined during the exacerbation period. Another important reasons for the late diagnosis are the lack of awareness about COPD in health care providers,[13] underuse of

Table 2 Distribution of the Preferred Inhaled Drug Regimens According to the GOLD COPD Categories in Newly Diagnosed COPD Patients

Inhaled Drug Regimens (%)	GOLD Categories			
	A	B	C	D
ICS/LABA/LAMA	23.8	54.3	76.2	87.4
ICS/LABA	27.6	23.9	18.0	10.5
LABA + LAMA	5.5	8.3	1.5	2.1
LAMA	24.5	10.4	1.5	–
LABA	5.4	2.6	1.0	–
Others	13.2	0.5	1.8	–

Table 3 Adherence to GOLD 2011 Treatment Recommendations of Physicians

	Total	GOLD Categories			
		A	B	C	D
Appropriate	27.8	33.9	20.9	17.4	89.4
Overtreatment	71.8	66.1	78.7	81.6	10.6
Undertreatment	0.4	–	0.4	1.0	–

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spirometry in health care centers[14,15] and low awareness of COPD among the general population.[16,17]

Only 5.6% of the patients were nonsmokers. 7.2% of patients had biomass fuels use in their history. In low-income countries, exposure to biomass fuels for cooking and heating is an important cause of COPD in rural areas of developing and the least developed countries.[18,19] Biomass smoke is an important contributing factor to the development of chronic airway diseases in non-smoker females in the Central, East, and South Eastern Anatolian Regions of Turkey.[20,21] Underdiagnosis of COPD was frequent in women with exposure biomass fuels due to a lack of knowledge of hazards of biomass smoke, the low level of socioeconomic status and the ignorance of the health care providers.[22]

In the same period with this study, another study called the ALPHABET with a similar methodology was conducted on usual COPD outpatients (n:1610).[23] In both studies, the demographic characteristics of the patients were similar. However, the mean age of our study groups was found approximately 3 years younger than the usual COPD outpatients. Our findings have shown that 35.1% of the patients were labeled as GOLD C and D category. Interestingly, the ALPHABET study also yielded that 38.2% of the usual outpatients were identified as in the GOLD C and D categories.[23] These figures from newly diagnosed treatment-naïve outpatients and usual outpatients were quite similar.

COPD patients have a large number of comorbidities, and these comorbidities can also be seen in newly diagnosed patients.[24] The comorbidities of COPD may increase the risk of morbidity and mortality.[25] We found that at least one comorbidity was present in 52.8% of the patients. Although the comorbidity rate in our study was found comparably less than the previous studies (65-97%), their rank order was almost the same.[26,27]

Our analysis demonstrated that the majority of COPD patients with the GOLD stage A, B and C disease severity are overtreated. Although the patients in the present study were newly diagnosed and treatment-naïve ones, the over-treatment rate was found as 71.8%. The most frequently prescribed medication was triple regimen (ICS+LABA +LAMA) with an overall frequency of 54.9%. The current studies show that very high over-treatment rates in COPD are a major global problem.[28] In a study conducted in 2010 in Turkey, overtreatment was determined in 100% of the GOLD stage 1 and 91.1% of the GOLD stage 2 contrary to GOLD recommendations.[29] In the ALPHABET study, over-treatment was also noted in >70% of GOLD 2013 A, B, and C patients.[23] Compliance with COPD guidelines has been shown to be globally low in several studies, and adherence to the GOLD treatment strategy is not sufficient.[30–32] Other reasons for nonadherence in treatment may be the inability of physicians to perceive the severity of illness and the maintenance of ICS use habits.

The patients' adherence to the visits during 1-year of follow-up is poor in our population. We planned 3 voluntary follow-up visits for our patients during 1-year after the initial visit. Considering the 1-year follow-up visits, the attendance rates of our patient groups were moderate, 55.9%, 32.9% and 18.7%, respectively. Based upon the patients' statements, the adherence rate to the prescribed inhaled regimens was reportedly very high (81.9%). Adherence rates in COPD are known to vary from 22% to 78%.[33–35] Good adherence is associated with reduced exacerbation rates in patients with COPD.[36] A subgroup analysis of the TORCH (Towards a Revolution in COPD Health) study showed that good compliance to study medication in patients with COPD was associated with lower mortality rates compared with poor compliance (11.3% vs 26.4%).[37] Our study showed that adherence rates to the treatment decrease as the category becomes more severe from the GOLD stage A to D. This general trend is reasonable since less severe patients get more benefit from the prescribed therapy, and thus become comparably more adherent to the treatment.

In this study, 56% of COPD patients were active smokers. In a study to identify subgroups of COPD using cluster analysis in ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints), the rate of active smokers was between 25% and 42% (mean 36%).[38] In a previous study by Gunen et al, the smoking rate in COPD was found to be unexpectedly high in the Malatya region of Turkey.[20] In this study, 25.5% of the women and 57.2% of the men in the general population were current smokers. The prevalence of COPD was 18.1% in current smokers over 40 years of age, and 77.5% of the participants with COPD were current smokers.

This study has several limitations. The major limitation of the study is that the follow-up of patients was not regular due to the study design. Second, the determination of treatment adherence during a 1-year follow-up has some limitations. Selection bias could be a problem because surprisingly high adherence rates were obtained from the patients who attended the follow-up visits. Additionally, since the determination of treatment adherence was

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completely based upon the patients' statements, some misleading statements might have increased our adherence rates significantly. On the other hand, we believe that the general trends of treatment adherence revealed and the distributions according to the GOLD categories were less affected by this relatively subjective approach.

Conclusion

To our knowledge, this is the first prospective real-life study on newly diagnosed and treatment-naïve COPD patients. Although these patients were diagnosed for the first time, the GOLD C and D categories and frequent exacerbator phenotype were found at a high rate. Our data have shown that although this subgroup of patients is younger than the usual COPD patients with fully established disease, their comorbidity rates are high and 35% of these patients have a high risk for exacerbations (the GOLD categories C and D). They were usually prescribed an overtreatment regimen. In conclusion, every tool should be used to increase the awareness of COPD and the effective early detection program for COPD in our community. The newly diagnosed, treatment-naïve COPD patients should be evaluated carefully, and best effort should be made to treat these patients in accordance with the recommendations of the major COPD guidelines.

Disclosure

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