

## The Burden of Chronic Obstructive Lung Disease Disease on the Health System

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**Aim:** To analyze the cost of patients hospitalized in secondary and tertiary hospitals due to the diagnosis of Chronic Obstructive Lung Disease (COPD) and to draw attention to the cost of COPD and the reasons that increase the cost in our country.

**Method:** This research was carried out to chest diseases clinic in second and third level hospitals affiliated to the ministry of health, between 1 January 2018-31 December 2018. Demographic features, smoking, duration of hospitalization, length of hospitalization in intensive care, antibiotics used, number of outpatient apply, total hospitalization cost, total costs and duration of antibiotics used were recorded. Costs were stated in Turkish Lira and converted into dollars. Cost data of patients with more than one hospitalization were entered separately.

**Results:** The numbers of men and women were equal in both 2nd level and 3rd level patients. Looking at patients with COPD in both the secondary and tertiary, total hospital cost in patients was significantly higher than those who did not. When the length and number of hospitalization increased, the total cost of the hospital increased significantly. Significant differences were not found between age groups, gender, smoking status, comorbidities, antibiotic use, number of outpatient clinic admissions, and the number of hospitalizations in the last two years in terms of total hospital cost.

**Conclusion:** The elimination and prevention of the both of internal and external factors that cause the disease, especially without the need for medication, is of great importance in terms of both financial and labor loss prevention and reduction.

**Keywords:** Chronic Obstructive Lung Disease, COPD, Burden of COPD, Hospital cost, Hospital cost in the health system

**Short Title in English:** The Burden of COPD

## **Introduction**

The Chronic Obstructive Lung Disease (COPD) is defined as a general preventable disease characterized with frequent respiratory symptoms and airflow limitation by The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 (1).

The COPD leads an important challenge for the health care provider and it is the third leading cause of death in the United States in 2014 (2). Also the COPD is the fourth leading cause of death all around the World (3). Risk factors for the development of COPD include occupational exposures (chemical agents, fumes) and dust, indoor air pollution (Wood burning stove, biomass fuel), asthma and airway hyperresponsiveness (4,5).

Countries use a significant portion of their Gross Domestic Product, and individuals' income, for health expenditures. As a result of this, the cost of healthcare services is one of the important issues that are constantly on the agenda (6). It was announced that the COPD has created a significant financial burden of approximately \$ 50 billion in the spending of the US government in 2010 (7).

COPD is a common health problem that causes both labor loss and financial loss. In particular, the increase in the frequency of hospital admissions, the increase in hospitalization and the increase in the drugs used create great burdens on the health system of governments. For this reason, it is great importance to take measures for reduction of hospital admissions and management of the disease including non-pharmacological treatment options whenever possible.

In the current study, we aim to analyze the cost of patients hospitalized in 2<sup>nd</sup> and 3<sup>rd</sup> hospitals due to the COPD and to draw attention to the cost of COPD that increase the cost in our country.

## **Patients and Method:**

This research was carried out the chest diseases clinic in second and third level hospitals affiliated to the ministry of health in Konya province, between 1 January 2018 - 31 December 2018. The data of 100 patients (fifty men and fifty women) who were hospitalized and followed up with COPD diagnoses over the years were analyzed.

The study was conducted with the permission and approval of Konya Provincial Health Directorate commission with the following date and numbered (Date: 05/07/2018/ Number:16-03). The patients admitted to the hospital for other reasons than COPD were not included in the current study. For this purpose, approximately ....patients were excluded in the current study.

The study was done retrospectively. As the limitations of the study, it can be given that it is conducted only in one center and it covers the last two years.

Demographic data such as age and gender of the patients, smoking, duration of hospitalization, length of hospitalization in intensive care, diseases in addition to COPD, antibiotics used, number of outpatient apply in the last two years, total number of hospitalizations in the last two years, total hospitalization cost, total hospitalization cost of intensive care, daily costs of antibiotics used, total costs of antibiotics used, duration of antibiotics were recorded. Costs were stated in Turkish Lira (TL). It was converted into dollars as a currency using the exchange rate from which the data was taken. Cost data of patients with more than one hospitalization were entered separately.

### **Statistical Analysis**

The research data were uploaded and analyzed via "SPSS (Statistical Package for Social Sciences) for Windows 22.0 (SPSS Inc, Chicago, IL)". Descriptive statistics were presented as median (interquartile range), frequency distribution and percentage. Pearson Chi-Square Test and Fisher's Exact Test were used to evaluate categorical variables. The suitability of variables to normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov / Shapiro-Wilk Test). The Mann-Whitney U Test was used as a statistical method for statistical significance between two independent groups, and the Kruskal Wallis Test between three independent groups, for variables that were found to be inconsistent with the normal distribution. When a significant difference was detected between three independent groups, Bonferroni correction was applied in post-hoc paired comparisons to determine the source of the difference. Statistical significance level was accepted as  $p < 0.05$ .

### **Results:**

Within the scope of the research, a total of 200 patients with a diagnosis of COPD, 100 of whom were from the 2nd hospital and 100 from the 3rd hospital patients, were examined.

The median age of the second level patients was 69 (IQR: 67-78), and the numbers of men and women were equal. 9.0% of the patients were still smoking, 7.0% cessation of smoking and the remaining 84.0% had never smoked. 78.0% of the second level patients diagnosed with COPD had at least one additional disease. In these diseases; hypertension took the first place with 41.0%, followed by diabetes mellitus with 32.0% and heart failure and asthma with 14.0%. The

least common additional diseases were hyperlipidemia (20%), chronic renal failure (4.0%) and bronchitis (7.0%) (Table 1).

When looking at the 3rd level patients examined within the scope of the research; while the median age was 56 (IQR: 53-58), the numbers of men and women were equal. 66.0% of the patients were smoking, while the remaining 34.0% were not. 47.0% of the patients with COPD had additional disease. Among the existing additional diseases, hypertension took the first place with 18.0%, diabetes mellitus with 14.0% and heart failure with 10.0%. The least common additional diseases were bronchitis (1.0%), chronic renal failure (3.0%) and hyperlipidemia (4.0%) (Table 1).

The median number of outpatient clinic apply in the last two years was 11 (IQR: 5.2-17.0), while the median number of hospitalizations in the last two years was 2 (IQR: 1-3) in the 2nd level patients with COPD. The patients were hospitalized for a median of 6 (IQR: 4-9) days. 25.0% of the 2nd patients diagnosed with COPD had stayed in the intensive care unit (ICU). The median length of stay in the ICU was 3 (IQR: 1.0-10.5) days. The median length of hospital stay in all patients with COPD was 7 (IQR: 5-11) days.

The median number of outpatient clinic apply of patients with 3rd level COPD in the last two years was 5 (IQR: 2-9), while the median number of hospitalizations in the last two years was 1 (IQR: 0-2). The median length of stay in the service was 7 (IQR: 5-10) days. 29.0% of the patients with a diagnosis of 3rd level COPD that were remained in the ICU. The average length of stay in the ICU was 3 (IQR: 2-7) days. The median length of hospital stay in all patients with level 3 COPD was 8 (IQR: 5.0-11.8) days.

Hospital costs of the patients examined within the scope of the study were calculated as USD. According to this; the median cost of the ICU of 25 of the patients with 2nd level COPD who stayed in the ICU was 448.6 (IQR: 181.5-1416.7) USD. While the median hospital cost of the 2nd level patients hospitalized in the ICU was USD 701.7 (IQR: 306.9-1526.2), the median hospital cost of the patients not hospitalized in the ICU was USD 274.7 (IQR: 196.1-490.2). The median total cost of the hospital for the 2nd level patients was 305.0 (IQR: 216.2-593.5) USD (Figure 1a,b,c and d).

The median ICU cost of 29 of the patients with a diagnosis of 3rd level COPD who stayed in the ICU was 602.7 (IQR: 383.2-1073.4) USD. The median hospital cost of the 3rd level patients staying in the ICU was 1780.3 (IQR: 1057.9-2201.0) USD, while the median hospital cost of the 3rd level patients not staying in the ICU was 318.0 (IQR: 191.1-469.7) USD. The median

total cost of the hospital for 3rd level patients was 424.9 (IQR: 257.8-1000.0) USD (Figure 1a,b,c and d).

While antibiotic treatment was applied to 50.0% of the 2nd level patients examined within the scope of the study, it was applied to 71.0% of the 3rd level patients. The median duration of antibiotic use was 6.5 (IQR: 4-10) days for 2nd level patients, while it was 6.0 (IQR: 4-10) days for 3rd level patients. Looking at the antibiotics used; while cefuroxime was applied to 36.0% of the 2nd level patients and ceftriaxone was applied to 14.0% of the 2nd patients, the ceftriaxone was applied in the first place with 40.0% of 3rd patient, followed by moxifloxacin with 23.0% of 3rd patient and cefuroxime with 16.0% of 3rd patient (Table 2).

The median total antibiotic cost of 50 patients who received antibiotic treatment among the 2nd level patients was 17.9 (IQR: 11.5-25.8) USD, while the median total antibiotic cost of 71 patients who received antibiotic treatment among the 3rd level patients was 65.4 (IQR: 34.5-155.5) USD ( Table 3).

Among patients who applied to 2nd level health care institutions and hospitalized in ICU, total hospital cost was significantly higher than those who did not ( $p < 0.001$ ). In addition, as the length of hospitalization increased, the total cost of the hospital increased significantly ( $p < 0.001$ ) (Table 4). On the other hand, no statistically significant differences were found between the age groups, gender, smoking status, comorbidities, antibiotic use, number of outpatient clinic admissions, and the number of hospitalizations in the last two years in terms of total hospital cost ( $p > 0.05$ ) ( $p > 0.05$ ) ( Table 4). Looking at patients with tertiary COPD diagnosis; hospital total cost was significantly higher among men than women, those who were hospitalized in the ICU than non- hospitalized in the ICU, those who did use antibiotics than those who did not use antibiotics, and those with more than 10 outpatient apply from less than 5, and those between 5-10 ( $p = 0.025$ ;  $p < 0.001$ ;  $p < 0.001$ ;  $p < 0.001$ ). Also when the number of admissions and length of hospital stay increased in the last two years, the total cost of the hospital increased significantly ( $p < 0.001$  for both) (Table 4).

On the other hand, no statistically significant difference was found between the age groups, smoking status and comorbidities of the patients with COPD who applied to the 3rd level hospital in terms of the total cost of the hospital ( $p > 0.05$ ) (Table 4).

Distribution of age, comorbidity, smoking status, antibiotic use, and length of stay at the healthcare institution level of patients with COPD according to sex and smoking status were given in the table 5 and 6.

## **Discussion:**

According to the GOLD 2017 report; COPD is a common, preventable and treatable disease characterized by persistent airflow restriction and respiratory symptoms due to airway and / or alveolar abnormalities, usually caused by severe exposure to harmful particles or gas. COPD is one of the most important causes of illness, death and disability worldwide (1).

COPD is a very common and heterogeneous disease with increasing morbidity and mortality worldwide, placing a significant burden on healthcare providers. Although pharmacological and non-pharmacological treatment options are abundant, smoking cessation continues to be the most effective therapeutic and preventive intervention in the care of these patients (4).

Since patients with COPD are mostly smokers or have used smokers, additional diseases such as cardiovascular system, circulatory system and central system diseases may be developed because of smoking. In addition to the primary effects of COPD on the lung in these patients, these systemic effects and accompanying diseases also require treatment and increase the cost of the disease (8).

In our study, when the additional diseases to be considered in both 2<sup>nd</sup> and 3<sup>rd</sup> level patients, hypertension took the first place, followed by diabetes mellitus, heart failure and asthma. The least common additional diseases were hyperlipidemia, chronic renal failure and bronchitis.

It was reported that women with COPD were younger and their number of pack years was considerably lower than it was among men. Also in COPD patients, men had increased risk for comorbidities or tended to be and greatly higher among mortality men than women (9). Interestingly, it was reported that. COPD is still mainly a “men’s disease” (10). Also, while COPD mortality is especially decreasing among men, similar pronounced change has not been observed among women, and it may be said that COPD mortality in women will surpass or is surpassing that in men (11, 12).

According to our results, the man had higher smoking status than women. In the 3<sup>rd</sup> level patients with COPD; hospital total cost was significantly higher among men than women, those who were hospitalized in the ICU than non- hospitalized in the ICU, those who did use antibiotics than who did not use antibiotics, and those with more than 10 outpatient apply from less than 5, and those between 5-10, respectively. In addition, as the number of admissions and length of hospital stay increased in the last two years, the total cost of the hospital increased significantly, too.

COPD is a major public health problem and will remain a challenge for clinicians within the 21st century. COPD puts enormous pressure on healthcare systems due to its high prevalence, morbidity and mortality. The prevalence of COPD in the population has significant effects in daily life compared to other chronic conditions, and serious resources are required. Therefore it is important to allocate minimum resources and reduce the relative impact of COPD (13).

According to our results, the median total antibiotic cost of 50 patients who received antibiotic treatment among the 2nd level patients studied was 17.9 USD, while the median total antibiotic cost of 71 patients who received antibiotic treatment among the 3rd level patients was 65.4 USD. Accordingly, the cost of the 3rd level patients using antibiotics was higher than the 2nd level patients. We think that this is due to the fact that the prognosis of patients admitted to 3rd hospitals is more severe compared to 2nd hospitals.

According to hospital costs of the patients, the median cost of the ICU of the patients with 2nd level COPD who stayed in the ICU was 448.6 USD. While the median hospital cost of the 2nd level patients hospitalized in the ICU was 701.7 USD, the median hospital cost of the patients not hospitalized in the ICU was 274.7 USD. The median total cost of the hospital for the 2nd level patients was 305.0 USD. Also, the median ICU cost of 29 of the patients with COPD who stayed in the ICU of 3rd level hospital was 602.7 USD. The median hospital cost of the 3rd level patients staying in the ICU was 1780.3 USD, while the median hospital cost of the 3rd level patients not staying in the ICU was 318.0 (IQR: 191.1-469.7) USD. The median total cost of the hospital for 3rd level patients was 424.9 USD. Among patients who hospitalized in ICU, total hospital cost was significantly higher than those who did not. In addition, as the length of hospitalization increased, the total cost of the hospital increased significantly. It can be said that when the number and duration of patients hospitalized in the ICU increased, the total cost of the hospital increased, too.

COPD is an extremely common heterogeneous disease all over the world. This disease affects people at different levels, causing serious costs over the state from hospitals and also loss of workforce. The frequency of hospital admissions, the length of stay in the intensive care unit, the bad prognosis of the disease and the drugs used cause serious financial burdens and loss of healthcare personnel time. There are pharmacological and non-pharmacological treatment options for the disease. For this reason, the elimination and prevention of the both of internal and external factors that cause the disease, especially without the need for medication, is of great importance in terms of both financial and labor loss prevention and reduction.

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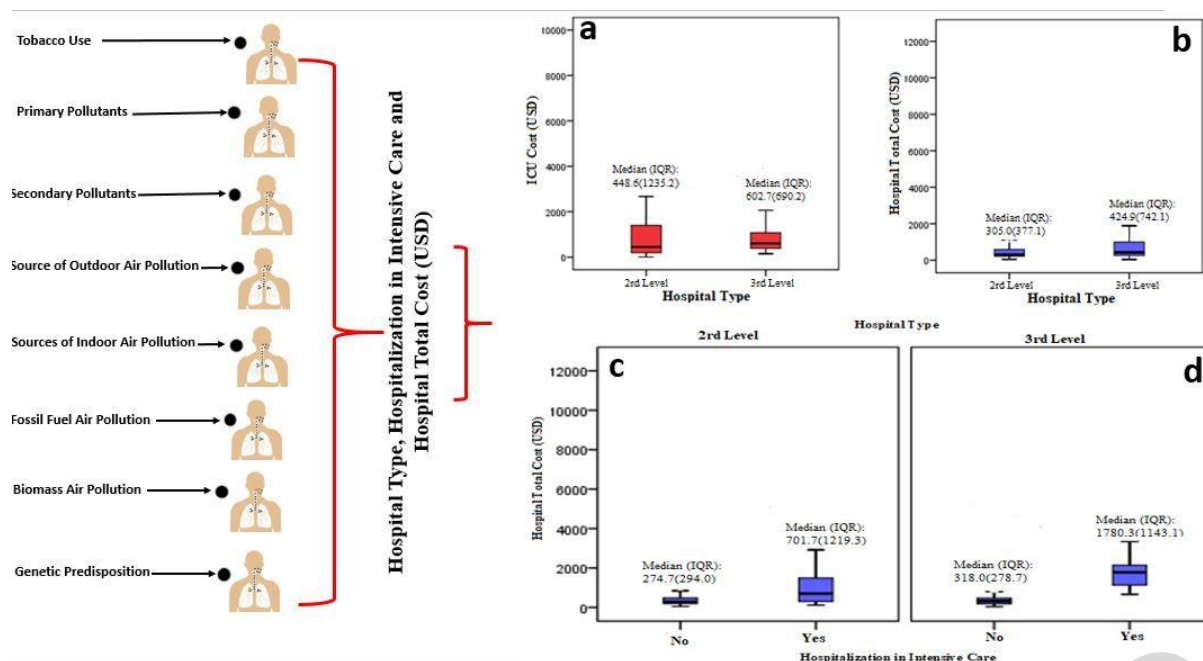


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**Figure 1:** Risk factors for COPD (Tobacco Use, Source of Outdoor Air Pollution, Primary and Secondary Pollutants, Fossil Fuel Air Pollution, Sources of Indoor Air Pollution, Biomass Air Pollution, Genetic Predisposition). Patients are divided into 3 groups as follows. Distribution of total hospital cost and ICU cost according to the health institution level applied by COPD patients (a and b) and Distribution of the total cost of the hospital according to the hospitalization status in the ICU at the health institution levels applied by the patients with COPD (c and d)

### **Table Legends:**

**Table 1.** Some descriptive and clinical features of patients with COPD according to the level of health institution

**Table 2.** Antibiotic use status and duration according to the health institution level applied by COPD patients

**Table 3.** Distribution of total costs of antibiotics used by patients with COPD according to the level of healthcare institution

**Table 4.** Distribution of total hospital costs according to some descriptive and clinical characteristics at the health institution levels where COPD patients apply

**Table 5.** Distribution of age, comorbidity, smoking status, antibiotic use, and length of stay at the healthcare institution level where COPD patients apply according to sex

**Table 6.** Distribution of age, presence of comorbidities, antibiotic use and length of stay at the healthcare institution level where COPD patients apply according to smoking status

**Table 1.** Some descriptive and clinical features of patients with COPD according to the level of health institution

	2rd level (n=100)	3rd level (n=100)
<b>Age (year), median (IQR)</b>	69 (61-78)	56 (53-58)
<b>Sex, n (%)</b>		
Male	50 (50.0%)	50 (50.0%)
Female	50 (50.0%)	50 (50.0%)
<b>Smoking Status, n (%)</b>		
Still using	9 (9.0%)	66 (66.0%)
Stopped smoking	7 (7.0%)	0(0%)
Never used	84 (84.0%)	34 (34.0%)
<b>Presence of Additional Diseases, n (%)</b>	78 (78.0%)	47 (47.0%)
<b>Existing Diseases, n (%)</b>		
HT	41 (41.0%)	18 (18.0%)
DM	32 (32.0%)	14 (14.0%)
HF	14 (14.0%)	10 (10.0%)
Asthma	14 (14.0%)	8 (8.0%)
Bronchitist	7 (7.0%)	1 (1.0%)
CHR	4 (4.0%)	3 (3.0%)
HL	2 (2.0%)	4 (4.0%)
Other	16 (16.0%)	29 (29.0%)

n: Number of patients; %: Column percentage; IQR: Interquartile range (25% -75%); \*Mann-Whitney U Test; <sup>b</sup>Ki-Square Test; <sup>c</sup>Fisher's Exact Test

**HT:** Hypertension

**DM:** Diabetes Mellitus

**HF:** Heart failure

**CHR:** Chronic Renal Failure

**HL:** Hyperlipidemia

**Table 2.** Antibiotic use status and duration according to the health institution level applied by COPD patients

	2rd level (n=100)	3rd level (n=100)
<b>Antibiotic Use Status, n (%)</b>		
No	50 (50.0%)	29 (29.0%)
Yes	50 (50.0%)	71 (71.0%)
<b>Antibiotic Use Time (day), median (IQR)</b>		
	6.5 (4-10)	6.0 (4-10)
<b>Antibiotics Used, n (%)</b>		
Ceftriaxone	14 (14.0%)	40 (40.0%)
Cefuroxime	36 (36.0%)	16 (16.0%)
Moxifloxacin	0(0)%	23 (23.0%)
Piperacillin	0(0)%	8 (8.0%)
Ampicillin	0(0)%	6 (6.0%)
Ciprofloxacin	0(0)%	6 (6.0%)
Meropenem	0(0)%	6 (6.0%)
Clarithromycin	0(0)%	6 (6.0%)
Cefazolin	0(0)%	4 (4.0%)
Imipenem	0(0)%	4 (4.0%)
Levofloxacin	0(0)%	3 (3.0%)
Teicoplanin	0(0)%	3 (3.0%)
Vancomycin	0(0)%	3 (3.0%)
Tigecycline	0(0)%	2 (2.0%)
Fusidic acid	0(0)%	2 (2.0%)
Amoxicillin	0(0)%	1 (1.0%)
Colistin	0(0)%	1 (1.0%)
Linezolid	0(0)%	1 (1.0%)
Caspofungin	0(0)%	1 (1.0%)
Rifamycin	0(0)%	1 (1.0%)
Metronidazole	0(0)%	1 (1.0%)

%; Percent; IQR: Interquartile range (%25-%75);

**Table 3.** Distribution of total costs of antibiotics used by patients with COPD according to the level of healthcare institution

	2rd level (n=50)	3rd level (n=71)
	median (IQR)	median (IQR)
<b>Total Antibiotic Cost (USD)</b>	17.9 (11.5-25.8)	65.4 (34.5-155.5)

n: Number of patients; %: Column percentage; <sup>a</sup>Mann-Whitney U Test; <sup>b</sup>Ki-Square Test

**Table 4.** Distribution of total hospital costs according to some descriptive and clinical characteristics at the health institution levels where COPD patients apply

	Hospital Total Cost (USD)			
	2rd level		3rd level	
	n	median (IQR)	n	median (IQR)
<b>Age group</b>				
<55 yaş	11	271.8 (181.8-514.3)	33	499.5 (253.3-893.4)
55-65 yaş	33	376.2 (212.5-627.7)	67	366.6 (257.3-1141.2)
>65 yaş	56	291.5 (227.8-593.5)	0	-----
<i>p</i>		0.572 <sup>a</sup>		0.608 <sup>b</sup>
<b>Sex</b>				
Male	50	292.8 (205.9-526.0)	50	718.9 (291.5-1780.3)
Female	50	343.7 (222.0-701.7)	50	347.4 (233.0-643.8)
<i>p</i>		0.176 <sup>b</sup>		0.025 <sup>b</sup>
<b>Cigaret</b>				
Yes	16	365.3 (232.2-790.0)	66	450.1 (233.0-1175.4)
No	84	305.0 (209.0-582.8)	34	359.4 (279.1-835.9)
<i>p</i>		0.625 <sup>b</sup>		0.558 <sup>b</sup>
<b>Additional Diseases</b>				
Yes	78	302.1 (207.0-596.9)	47	366.6 (259.4-1278.0)
No	22	333.7 (228.5-482.4)	53	457.4 (245.8-991.5)
<i>p</i>		0.897 <sup>b</sup>		0.814 <sup>b</sup>
<b>ICU admission</b>				
Yes	25	701.7 (306.9-1526.2)	29	1780.3 (1057.9-2201.0)
No	75	274.7 (196.1-490.2)	71	318.0 (191.1-469.7)
<i>p</i>		<0.001 <sup>b</sup>		<0.001 <sup>b</sup>
<b>Antibiotic Use</b>				
Yes	50	319.1 (210.6-600.0)	71	638.3 (341.6-1499.5)
No	50	291.5 (216.5-584.8)	29	235.0 (147.4-347.4)
<i>p</i>		0.615 <sup>b</sup>		<0.001 <sup>b</sup>
<b>Outpatient clinic applications number</b>				
<5	18	418.9 (233.4-843.9)	41	280.8 (173.6-616.1)
Between 5-10	31	294.0 (216.2-452.9)	38	463.6 (300.7-852.8)
>10	51	291.5 (204.9-600.2)	21	1789.5 (772.6-2426.0) <sup>xy</sup>
<i>p</i>		0.154 <sup>a</sup>		<0.001 <sup>a</sup>
<b>Hospitalizations number in the last 2 years</b>				
Never	7	600.2 (312.6-1935.2)	49	280.8 (185.7-388.9) <sup>yz</sup>
1-2	56	295.0 (198.3-641.8)	27	538.8 (304.0-974.5) <sup>z</sup>
≥3	37	285.2 (211.9-548.1)	24	1707.5 (875.9-2080.7)
<i>p</i>		0.163 <sup>a</sup>		<0.001 <sup>a</sup>
<b>Length of stay in the hospital</b>				
≤5 day	29	183.7 (131.6-271.7) <sup>yz</sup>	27	180.6 (119.7-235.0) <sup>yz</sup>
6-10 day	44	291.5 (247.1-417.2) <sup>z</sup>	44	388.9 (307.5-768.5) <sup>z</sup>
≥11 day	27	627.7 (549.2-1593.3)	29	1780.3 (718.9-2201.0)
<i>p</i>		<0.001 <sup>a</sup>		<0.001 <sup>a</sup>

<sup>a</sup>Kruskal Wallis Test; <sup>b</sup>Mann-Whitney U Test

**Table 5.** Distribution of age, comorbidity, smoking status, antibiotic use, and length of stay at the healthcare institution level where COPD patients apply according to sex

	2rd level			3rd level		
	Sex		P	Sex		P
	Male (n=50)	Female (n=50)		Male (n=50)	Female (n=50)	
<b>Age (year), median (IQR)</b>	70.5 (61-78)	69 (59.8-80.0)	0.975	56 (53.8-58.0)	56 (53-58)	0.972
<b>Additional Diseases, n (%)</b>	36 (72.0)	42 (84.0)	0.148	17 (34.0)	30 (60.0)	<b>0.009</b>
<b>Smoking, n (%)</b>	15 (30.0)	1 (2.0)	<b>&lt;0.001</b>	37 (74.0)	29 (58.0)	0.091
<b>Hospitalization (days), median (IQR)</b>	7.5 (4.8-10.2)	7 (5-13)	0.570	8 (6.0-16.2)	7 (5-10)	0.064
<b>Use of Antibiotics, n (%)</b>	21 (42.0)	29 (58.0)	0.110	40 (80.0)	31 (62.0)	<b>0.047</b>

n: Number of patients; %: Column percentage; IQR: Interquartile range (25% -75%); <sup>a</sup>Mann-Whitney U Test; <sup>b</sup>Ki-Square Test;



**Table 6.** Distribution of age, presence of comorbidities, antibiotic use and length of stay at the healthcare institution level where COPD patients apply according to smoking status

	2rd level			3rd level		
	Smoking		p	Smoking		p
	Yes (n=16)	No(n=84)		Yes(n=66)	No(n=34)	
<b>Age (year), median (IQR)</b>	63.5 (55.5-75.0)	70.5 (61.0-79.8)	0.165	56 (53-58)	57 (53-58)	0.615
<b>Additional Diseases, n (%)</b>	9 (56.3)	69 (82.1)	<b>0.043<sup>c</sup></b>	31 (47.0)	16 (52.9)	0.993
<b>Smoking, n (%)</b>	7.5 (5.2-9.0)	7 (5-11)	0.883	8 (5.0-12.2)	7 (4.8-11.2)	0.574
<b>Hospitalization (days), median (IQR)</b>	5 (31.3)	45 (53.6)	0.102	51 (77.3)	20 (58.8)	0.054

n: Number of patients; %: Column percentage; IQR: Interquartile range (25% -75%); <sup>a</sup>Mann-Whitney U Test; <sup>b</sup>Ki-Square Test; <sup>c</sup>Fisher's Exact Test