ORIGINAL ARTICLE *UDK: 616.24-002.2:316.34]:303.62(497.7)*

www.doi.org/

SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH NEWLY DIAGNOSED CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN PRIMARY HEALTH CARE

Kovachevikj K.[1], Janevska S.[1], Kovachevikj M.[2], Kondova Topuzovska I.[3]

[1]*PHI, Family medicine practice "Vita Katerina", Skopje, Republic of N. Macedonia*

[2]*Biotechnical Faculty, University of Ljubljana, Ljubljana, Slovenia*

[3]*University Clinic for Infectious Diseases and Febrile Conditions, Faculty of Medicine, University of "Saints Cyril and Methodius", Skopje, Republic of N. Macedonia*

Abstract

Introduction. Chronic obstructive pulmonary disease (COPD) is one of the most common respiratory diseases. However, it remains significantly unrecognized and undiagnosed in clinical practice. The aim of this study is to investigate the association between sociodemographic and clinical characteristics of patients with newly diagnosed chronic obstructive pulmonary disease in a population aged ≥ 40.

Materials and Methods. A one-year cross-sectional study was conducted in a family medicine practice in Skopje, including individuals aged 40 to 75 years without respiratory complaints. Sociodemographic questionnaires and six screening tests for COPD were evaluated. COPD diagnosis is established by spirometry, defined as a postbronchodilator FEV1/FVC ratio <0,70.

Results. The total number of participants was 175, of which 18 participants (9%) had newly diagnosed COPD. These participants were significantly older (p=0.003), male (p=0.03), with a low level of education (p=0.008), mainly workers (p=0.045), heavy smokers ≥30 pack/years (p=0.0007), or were exposed to biomass fuels (p=0.036). Tuberculosis (p=0.028), arterial hypertension (p=0.045), family history of respiratory disease (p=0.0135), chronic respiratory disease in childhood (p=0.001) and one lower respiratory tract infection in the last year (p=0.0447) were identified as significant risk factors for COPD.

Conclusion. A considerable proportion (9%) of asymptomatic adults aged ≥40 years had previously undiagnosed COPD. Older age, male sex, lower level of education, heavy smoking, biomass exposure, tuberculosis, hypertension, family history of respiratory disease, and recurrent childhood infections were significantly associated with newly diagnosed COPD.

Keywords: *Chronic obstructive pulmonary disease; primary health care; questionnaires; risk factors; sociodemographic characteristics.*

Introduction

Chronic obstructive pulmonary disease (COPD) is increasingly becoming one of the most common causes of morbidity, mortality, and disability worldwide. COPD is currently the third lead-

ing cause of death globally, and 90% of deaths occur in low- and middle-income countries (1). The global prevalence of COPD is estimated to be 10.3% and is projected to increase by 23% by 2050 (2). COPD is also the fifth leading cause of years of life lost due to disability DALYs (the Disability- Adjusted Life Years) (3). Despite this and the identification of the disease as a serious public health problem that requires an urgent solution, COPD often remains unrecognized and undiagnosed. COPD is a chronic, progressive disease, that progresses gradually over time. It is as a result of long-term, complex interactions between various endogenous and exogenous risk factors that damage the lungs and disrupt their normal development and aging process. While tobacco smoking is the leading risk factor for the disease, other factors also play a role in the development of COPD. Inhalation of toxic particles and gases from the environment (smoke from burning solid fuels, inorganic dust, chemical agents and/or vapors, and air pollution), delayed and impaired lung development in childhood, frequent respiratory infections in adult patients, family predisposition, presence of comorbidities, and low socioeconomic status additionally contribute to the development of the disease (1,4,5). The clinical and biological expression of these exposures differs substantially among individuals and is influenced by the age at exposure and the cumulative burden of interacting risk factors over time (6).

Macedonia has a relatively high reported prevalence of COPD (7.16%) (7), accompanied by a rising prevalence of smoking among people aged 15-64 (from 43% in 2002 to 46% in 2017) (8). A 2022 population-based study by Minov et al. in the Skopje region, reported a COPD prevalence of 4.6%, increasing with age, and identified active smoking and occupational exposure as key risk factors (9). Notably, nearly half of participants without a prior COPD diagnosis demonstrated persistent airflow obstruction. These findings strongly suggest that a substantial proportion of COPD cases in our setting remain unrecognized and undiagnosed (9). According to the 2019 World Health Organization (WHO) report, *Primary Health Care Organization, Performance and Quality in North Macedonia,* COPD ranks first in hospitalizations, second in referrals to secondary-level care and third among the most common reasons for visits to general practitioners (8). Together, these indicators reflect important gaps in early detection and optimal disease management, with many patients being diagnozed only at advanced stages. This unmet need for earlier recognition and intervention provided the rationale for conducting this present study.

The purpose of this paper is to investigate the association between sociodemographic and clinical characteristics of patients with newly diagnosed COPD in a population aged ≥ 40, in the primary health care setting.

Materials and Methods

A one-year cross-sectional study was conducted in a family medicine practice in Skopje, Republic of North Macedonia. Individuals aged 40 to 75, who presented for examination without respiratory symptoms were included. Individuals with previously diagnosed COPD or asthma, cognitive disorders, neurodegenerative diseases, inability to perform spirometry, contraindications to spirometry, acute lower respiratory tract infections, hypersensitivity to salbutamol and pregnant/breastfeeding individuals, were excluded from the study. The research was conducted by one family physician. Sociodemographic questionnaires and six COPD screening tests were administered. For spirometry tests, participants were referred to a reference outpatient clinic at secondary health care level. COPD was diagnosed based on post-bronchodilator

spirometry demonstrating a forced expiratory volume in one second to forced vital capacity ratio (FEV_1/FVC) <0,70. Spirometry was performed by a specialist who was not involved in the initial screening. The Ethics Committee for Research Involving Human Subjects, Faculty of Medicine, University of "Saints Cyril and Metodius" Skopje, Republic of North Macedonia gave approval for performing the study and publishing the results obtained (03-1208/5, 14.03.2023). All participants were informed about the study and provided written informed consent.

The sociodemographic questionnaire consisted of three sections. The first section included demographic characteristics: age, sex, body mass index (BMI), educational level, current occupation, socioeconomic status, place of residence, and exposure to passive smoking. The second section addressed smoking status and smoking intensity. Smoking status was defined as: current user of tobacco (smoking at least one cigarette per day for a minimum of six months), former user of tobacco (previously smoked at least one cigarette per day for at least six months, but does not currently smoke), non-smoker. Smoking intensity was calculated using the pack-years formula. This section also included questions regarding occupational or household exposure to harmful particles or chemicals, as well as exposure to fuels used for heating, cooking, and other household needs. The third section referred to the participants' health status. Information on family history of respiratory disease, chronic respiratory diseases in childhood, and frequency of common cold, bronchitis, or pneumonia during the previous year was collected. These variables were also incorporated within the COPD screening questionnaires (CDQ (10), CAPTURE (11), COPD SQ (12), SBQ(13,14)).

Statistical analysis of the data was performed using SPSS software (version 25.0; IBM SPSS, USA). The Kolmogorov-Smirnov test and Shapiro-Wilk test were used to assess the normality of data distribution. Categorical variables were presented as absolute numbers and percentages. Numerical variables were expressed as mean, standard deviation, minimum and maximum values, median, and interquartile range. For comparison between the COPD and non-COPD groups, Fisher's exact test and the chi-square test were used for categorical variables. For quantitative variables, depending on data distribution, Welch's test or the Mann-Whitney U test was applied.

Results

A total of 200 participants were included in the study, with a mean age of 53.5 ± 8.4 years. The sample consisted of 96 men (46%) and 104 women (52%). The study was completed by 175 participants, of whom 18 were diagnosed with COPD by spirometry. The frequency of COPD was 9%. Sex was significantly associated with COPD, with 72.78% of participants diagnosed with COPD being male, while only 27.78% were female (p=0.03). Participants with COPD were significantly older (59.2 ± 7.9 years) compared to those without COPD (52.6 ± 8.0 years) (p=0.003) (Table 1).

Table 1. Sociodemographic and other characteristics of the study's participants according to COPD status

Variables	Sample size n=175	COPD		p-value	difference test
		yes (n=18)	no (n=157)		
Sex n (%)					
Male	84 (48%)	13 (72.22%)	71 (45.22%)	X^2=4.72 *p=0.03	
Female	91 (52%)	5 (27.78%)	86 (54.78%)		

Variables	Sample size n=175	COPD		p-value	difference test
		yes (n=18)	no (n=157)		
Age (years) mean+SD)	53.2 ± 8.2	59.2 ± 7.9	52.6 ± 8.0	t=3.35 **p=0.003	
BMI (kg/m2) mean+SD	28.99 ± 5.3	28.56 ± 5.9	29.04 ± 5.2	t=0.36 p=0.72	
Ethnic groups n (%)					
Macedonian	66 (38.15%)	5 (27.78%)	61 (39.35%)	Fisher's exact p=0.554	
Albanian	105(60.69%)	13(72.22%)	92 (59.35%)		
Serbian	2 (1.16%)	0	2 (1.29%)		
Education n (%)					
No qualification	4 (2.29%)	3 (16.67%)	1 (0.64%)	Fisher's exact **p=0.008	p<0.0001
Primary school	75 (42.86%)	4 (22.22%)	71 (45.22%)		*p=0.046
High school	45 (25.71%)	6 (33.33%)	39 (24.84%)		p=0.435
Higher education	3 (1.71%)	0	3 (1.91%)		p=0.55
Bachelor's degree	36 (20.57%)	5 (27.78%)	31 (19.75%)		p=0.42
> higher than a Bachelor's degree	12 (6.86%)	0	12 (7.64%)		p=0.22
Profession n (%)					
Administrative workers	34 (19.43%)	5 (27.78%)	29 (18.47%)	Fisher's exact *p=0.045	p=0.344
Health care workers	38 (21.71%)	0	38 (24.2%)		*p=0.018
Housewives	42 (24%)	4 (22.22%)	38 (24.2%)		p=0.85
Manual workers	61 (34.86%)	9 (50%)	52 (33.12%)		p=0.15
Place of residence n (%)					
Urban	61 (34.86%)	5 (27.78%)	56 (35.67%)	X^2=0.68 p=0.411	
Rural	114(65.14%)	13(72.22%)	101(64.33%)		
Family history of respiratory disease n (%)					
Yes	38	8 (44.44%)	30 (19.11%)	X^2=6.1 *p=0.0135	
No	137	10(55.56%)	127(80.89%)		
Chronic respiratory diseases in childhood n (%)					
Yes	14	5 (27.78%)	9 (5.73%)	X^2=10.7 **p=0.001	
No	161	13(72.22%)	148(94.27%)		

X^2(Chi-square test); Welch's t-test *sig p<0.05, **sig p<0.01

There was a statistically significant association between educational level and COPD status (Fisher's exact test, p=0.008). This difference was primarily driven by the markedly higher proportion of participants without formal education in the COPD group (16.78%) compared to the non-COPD group (0.64%) (p<0.0001). Primary education was more frequent among

participants without COPD (45.22%) than among those with COPD (22.22%) (p=0.046). No statistically significant differences were observed across the remaining educational categories (Table 1). Profession was also significantly associated with COPD status (Fisher's exact test, p=0.045). However, this association appeared to be largely influenced by the absence of COPD among health care workers (0% vs 24.2%, p=0.018). Although manual workers constituted a higher proportion of the COPD group (50% vs 33.13%), this difference did not reach statistical significance (p=0.15). Similarly, no significant differences were observed among administrative workers (p=0.344) or housewives (p=0.85). No significant association was found between place of residence and COPD occurrence (p=0.411), although a higher proportion of participants lived in rural areas. This finding should be interpreted cautiously, as the overall study sample included approximately twice as many rural as urban residents (Table 1).

There was a statistically significant difference between the participants with and without COPD regarding family history of respiratory disease (p=0.0135), with 44.44% of participants with COPD reporting a positive family history compared to 19.11% of those without COPD. Similarly, chronic respiratory diseases in childhood were significantly (p=0.001) more common among participants with COPD (27.78%) than among those without COPD (5.73%) (Table 1).

Table 2. Smoking status, passive exposure to smoking in the household, and intensity of tobacco use according to COPD status

Variables	Sample size n=175	COPD		COPD
		yes (n=18)	no (n=157)	
Smoking n (%)				
0 Non-smoker	74 (42.53%)	5 (27.78%)	69 (44.23%)	Fisher's exact p=0.376
1 Former user of tobacco	20 (11.94%)	3 (16.67%)	17 (10.9%)	
2 Current user of tobacco	80 (45.98%)	10 (55.56%)	70 (44.87%)	
Passive exposure to smoking in the household n (%)				
Daily	86 (49.14%)	13 (72.22%)	73 (46.5%)	Fisher's exact p=0.079
Weekly	13 (7.43%)	1 (5.56%)	12 (7.64%)	
Monthly	7 (4%)	2 (11.11%)	5 (3.18%)	
Less than monthly	23 (13.14%)	1 (5.56%)	22 (14.01%)	
Never	44 (25.14%)	1 (5.56%)	43 (27.39%)	
Does not know	2 (1.14%)	0	2 (1.27%)	
Intensity of tobacco use (pack/years)				
0	75	5 (27.78%)	70 (44.59%)	Fisher's exact *p=0.017
1-14.9	26	1 (5.56%)	25 (15.92%)	
15-29.9	26	1 (5.56%)	25 (15.92%)	
≥30	48	11 (61.11%)	37 (23.57%)	

The smoking status of the participants (current, former, non-smoker) had no statistically significant association with COPD diagnosis (Fisher's exact test, p=0.376) (Table 2). Although current

smokers and former smokers were more prevalent in the COPD group, these differences did not reach statistical significance. Conversely, non-smokers were more common among participants without COPD (44.23%) than among those with COPD (27.78%), but again without statistical significance. Passive smoking exposure had no statistically significant association with COPD diagnosis (Fisher's exact test, p=0.079). However, daily exposure to passive smoking was more frequently reported among participants with COPD (72.22%) compared to those without COPD (46.5%). In contrast, smoking intensity demonstrated a statistically significant association with COPD (Fisher's exact test, p=0.079). Participants with a smoking history of ≥30 pack/years were overrepresented in the COPD group (61.11%) compared to the non-COPD group (23.57%) (p=0.0007) (Table 2).

Table 3. Exposure to air pollutants according to COPD status

Variables	Sample size n=175	COPD		p-value
		yes (n=18)	no (n=157)	
Cooking fumes n (%)				
No, never	126 (72%)	14 (77.78%)	112 (71.34%)	Fisher's exact p=0.91
Yes, currently	37 (21.14%)	3 (16.67%)	34 (21.66%)	
Yes, in the past	12 (6.86%)	1 (5.56%)	11 (7.01%)	
Biomass fuel n (%)				
No, never	66 (37.71%)	3 (16.67%)	63 (40.13%)	Fisher's exact *p=0.036
Yes, currently	77 (44%)	8 (44.44%)	69 (43.95%)	
Yes, in the past	32 (18.29%)	7 (38.89%)	25 (15.92%)	
Vapors from various substances n (%)				
No, never	161 (92%)	16 (88.89%)	145 (92.36%)	Fisher's exact p=0.3
Yes, currently	5 (2.86%)	0	5 (3.18%)	
Yes, in the past	9 (5.14%)	2 (11.11%)	7 (4.46%)	
Gases n (%)				
No, never	155 (88.57%)	14 (77.78%)	141 (89.81%)	Fisher's exact p=0.197
Yes, currently	6 (3.43%)	1 (5.56%)	5 (3.18%)	
Yes, in the past	14 (8%)	3 (16.67%)	11 (7.01%)	
Dust n (%)				
No, never	72 (41.14%)	6 (33.33%)	66 (42.04%)	Fisher's exact p=0.589
Yes, currently	84 (48%)	9 (50%)	75 (47.77%)	
Yes, in the past	19 (10.86%)	3 (16.67%)	16 (10.19%)	
Chimney/exhaust systems n (%)				
Yes	138 (86.25%)	17 (100%)	121 (84.62%)	Fisher's exact p=0.132
No	22 (13.75%)	0	22 (15.38%)	

Variables	Sample size n=175	COPD		p-value
		yes (n=18)	no (n=157)	
Years of exposure median (IQR)	30 (20 – 40)	33.5 (28.5 – 40)	30 (20 – 40)	Mann-Whitney U test Z=0.92 p=0.358

Exposure to biomass fuel was significantly associated with COPD (Fisher's exact test, p=0.036), with a higher proportion of participants with COPD reporting past exposure to biomass fuel compared to those without COPD (38.89% vs 15.92%, p=0.017) (Table 3). No statistically significant differences were observed between participants with and without COPD regarding exposure to cooking fumes (p=0.91), vapors from various substances (p=0.30), gases (p=0.197), dust (p=0.589), or chimney/exhaust systems (p=0.132). The duration of exposure did not differ significantly between groups (Mann-Whitney U test, p=0.358). The median duration of exposure was 33.5 years (IQR 28.5 – 40) in the COPD group and 30 years (IQR 20 – 40) in the non-COPD group (Table 3).

The overall proportions of participants with at least one comorbidity were similar in both groups, 77.78% in the COPD group and 76.43% in the non-COPD group, with no statistically significant difference (Fisher's exact test, p=1.0) (Table 4). Among individual comorbidities, arterial hypertension was significantly more prevalent in participants with COPD (77.78%) compared to those without COPD (51.59%) (p=0.045). Tuberculosis was also significantly more frequent in the COPD group (11.11% vs 0.64%, p=0.028). No statistically significant differences were observed between the groups with or without COPD for the other listed comorbidities (Table 4).

Table 4. Prevalence of comorbidities according to COPD status

Comorbidities	Sample size n=175	COPD		p-value
		yes (n=18)	no (n=157)	
Carcinoma	5 (2.86%)	1 (5.56%)	4 (2.55%)	p=0.423
Diabetes mellitus	27 (15.43%)	3 (16.67%)	24 (15.29%)	p=1.0
Arterial Hypertension	95 (54.29%)	14 (77.78%)	81 (51.59%)	*p=0.045
Angina pectoris, Myocardial infarct	4 (2.29%)	0	4 (2.55%)	p=1.0
Heart failure	0	0	0	0
Cerebrovascular accident	0	0	0	0
Nasal allergy	18 (10.29%)	1 (5.56%)	17 (10.83%)	p=1.0
Skin allergy	9 (5.14%)	0	9 (5.73%)	p=0.6
Food allergy	6 (3.43%)	0	6 (3.82%)	p=1.0
Insect sting allergy	5 (2.86%)	0	5 (3.18%)	p=1.0
Tuberculosis	3 (1.71%)	2 (11.11%)	1 (0.64%)	p=0.028
Osteoarthritis	10 (5.71%)	1 (5.56%)	9 (5.73%)	p=1.0
Rheumatoid arthritis	0	0	0	0

Comorbidities	Sample size n=175	COPD		p-value
		yes (n=18)	no (n=157)	
Osteoporosis	4 (2.29%)	1 (5.56%)	3 (1.91%)	p=0.355
Depression	19 (10.86%)	3 (16.67%)	16 (10.19%)	p=0.4199
Anxiety	18 (10.29%)	1 (5.56%)	17 (10.83%)	p=0.698
Eczema	5 (2.86%)	0	5 (3.18%)	p=1.0
Other allergies	6 (3.43%)	0	6 (3.82%)	p=1.0

Participants with COPD had a significantly higher number of common colds, bronchitis, or pneumonia in the 12 months preceding the study compared with participants without COPD (p=0.026) (Table 5).

Table 5. Frequency of respiratory infections in the past 12 months according to COPD status

Variables	Sample size n=175	COPD		p-value
		yes (n=18)	no (n=157)	
Common cold, Bronchitis or Pneumonia in the last 12 months n (%)				
0	80	3 (16.67 %)	77 (49.04%)	Fisher's exact *p=0.026
1	60	10 (55.56%)	50 (31.85%)	
2+	35	5 (27.78%)	30 (19.11%)	

Discussion

In this cross-sectional study, we investigated the association between sociodemographic and clinical characteristics, and newly diagnosed COPD in adults aged ≥40 years in primary health care. Our findings demonstrate that several sociodemographic and clinical factors were significantly associated with newly diagnosed COPD.

The study included 175 participants, of whom 52% were female and 48% male. Although both sexes were similarly represented in the overall sample, male sex was significantly more associated with COPD (77.22% vs. 27.7%, p=0.03). This finding is consistent with results from the Burden of Obstructive Lung Disease (BOLD) study, which reported a higher prevalence of stage II or higher COPD in men (11.8%) than in women (8.5%) (15). Similarly, the ELISABET study conducted in France showed higher COPD prevalence among men, despite comparable sex representation in the overall study (1,5,16). We have also identified age as a significant risk factor (p=0.003), confirming the well-established relationship between aging and COPD. The PLATINO study, conducted in five Latin American regions, demonstrated a strong positive association between age and COPD prevalence (17). Comparable findings were reported in a general adult population from the Skopje region, where COPD prevalence was four times higher in individuals older than 45, when compared with younger participants (6.7% vs. 1.6%, p=0.0000) (9).

Another important sociodemographic characteristic is educational level, which, in our study, was also significantly associated with COPD (p=0.008). A markedly higher proportion of pa-

tients with COPD had no formal education, which is widely recognized as an indicator of socioeconomic disadvantage. Lower socioeconomic status is associated with increased exposure to environmental pollutants, occupational hazards and limited access to preventive healthcare. Occupational exposure to dusts, fumes, and chemical agents has long been established as an independent contributor to chronic airflow limitation (18). Workers exposed to occupational hazards were reported to have a twofold higher COPD prevalence, emphasizing the role of occupational hazards in the Skopje region (19). Our findings therefore support the broader evidence linking socioeconomic vulnerability and lower educational levels with increased COPD risk (1,20,21). Importantly, approximately one-fifth of individuals with COPD worldwide have never smoked, underscoring the contribution of non-tobacco-related risk factors, including workplace exposures (22).

Exposure to biomass fuel was another significant factor in our study, particularly among participants with past exposure, suggesting that prolonged past exposure to these fuels has delayed health effects. A meta-analysis by Hu et al., including studies from several countries where biomass fuel is widely used, demonstrated a two- to threefold increased risk of COPD among individuals exposed to biomass smoke (23). Our findings are consistent with this global evidence and highlight the continued relevance of indoor air pollution as a preventable risk factor.

Smoking tobacco remains the most important and extensively studied risk factor for COPD in the past five decades, as evidence has been provided that COPD is much more common in smokers and former smokers compared to non-smokers (1). The disease occurs in 15-20% of current smokers, whereas 60-70% of individuals affected by COPD are current or former smokers (7). Nevertheless, it is also well documented that only a portion of smokers develop COPD, and that a substantial fraction of COPD cases can be attributed to additional environmental, occupational and early life factors (22,24).

Although we did not find a statistically significant association between smoking status and COPD in our cohort, smoking intensity showed a clear relationship (p=0.017). Participants with ≥30 pack/years were significantly more likely to have COPD, indicating that cumulative exposure may be more informative than smoking status alone. Similarly, in the Minov et al. study from the same region, smoking intensity of ≥20 pack/years was significantly associated with COPD (9). While many studies use ≥10 pack/years as an inclusion threshold, recent evidence suggests that even lower smoking intensity increases the 5-year risk for COPD development in middle-aged adults. Passive smoking is also recognized as a major global health risk. The Global Burden of Disease Study ranked it among the top ten leading risk factors for mortality worldwide (3). In terms of the DALYs, which measure the total burden of a disease, COPD was the fifth leading cause of years of life lost due to disability (25). Lifelong exposure to passive smoking doubles the risk of developing COPD, and the duration of exposure to passive smoking negatively affects lung development at the earlier stages of life, also leading to higher risks for developing COPD (26). Although we did not observe a statistically significant association (p=0.079), daily exposure to passive smoking was considerably more common among individuals with COPD (72.22% vs 46.5%), while participants who were never exposed to passive smoking in the household were more common in the group without COPD (27.3% vs. 5.5%). It is important to note that our assessment focused primarily on passive smoke exposure within the household. However, given the high prevalence of smoking in our country, passive exposure outside of the home environment is likely widespread. Such exposure may have reduced the variability between groups and potentially attenuated the observed association between passive smoking and COPD.

Genetic susceptibility and early-life influences also appear to play an important role. A positive family history of respiratory disease was significantly more common among smoking siblings with COPD, suggesting inherited or shared environmental vulnerability (27). In our study, family history of respiratory diseases and chronic respiratory diseases in childhood were significantly associated with COPD in adulthood. Impaired lung development due to asthma, allergies, infections, or other risk factors, during intrauterine development or childhood, can result in reduced peak lung function and increased COPD risk later in life (28–30).

COPD is often accompanied by other chronic diseases and conditions, sharing common risk factors and pathophysiological mechanisms. In our study, arterial hypertension was the most prevalent comorbidity and was significantly associated with COPD (p=0.045). Cross-sectional analysis of data from the U.S. National Health and Nutrition Examination Survey (1999-2018) also demonstrated a significant association between COPD and hypertension (OR=1.18, 95% CI 1.05–1.31), with a strong correlation observed in adults younger than 60 with high smoking intensity (31). Undiagnosed COPD is common among hypertensive individuals aged ≥40 in Brazil, further underscoring the need for targeted screening (32). Tuberculosis was also significantly more frequent among the participants in our study with COPD (p=0.028). Feng et al. confirmed a bidirectional association between tuberculosis and COPD, with increased risk of COPD among individuals with a history of tuberculosis (pooled OR=2.46, 95% CI: 1.95–3.10), and increased tuberculosis risk among individuals with COPD (pooled OR=2.21, 95% CI: 1.57–3.11) (33). These findings support integrated screening strategies, particularly in endemic regions. According to data from the Center for Public Health in Skopje (2023), the Skopje region remains among the four regions with the highest tuberculosis incidence (34), highlighting the local public health relevance of this association. Finally, frequent lower respiratory infections are an important clinical indicator associated with COPD development. This is consistent with the GOLD 2025 recommendations and the national guideline for COPD prevention, diagnosis, and management in primary care in North Macedonia, both of which emphasize early identification of high-risk individuals (1,5).

Limitations of the Study

Although this study provides important insight into the association between sociodemographic and clinical characteristics and newly diagnosed COPD, several limitations should be considered. The sample size was relatively small and restricted to a single geographic region, with data collected over a one-year period and limited to one family medicine practice. Therefore, the findings cannot be generalized to all adults aged ≥40 years in the Republic of North Macedonia.

Nevertheless, this study represents one of the first efforts to support the development of a structured COPD screening approach in primary care aimed at identifying individuals at increased risk who should be referred for spirometry. The research was conducted in accordance with current recommendations, using standardized spirometry based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) lung function criteria for defining and staging COPD. Importantly, spirometry confirmation of COPD was performed by a specialist who was not involved in the initial screening process and was unaware of participants' questionnaire responses, thereby reducing the risk of potential diagnostic bias. Although regionally conducted, the sample included participants from both urban and rural settings.

The results may contribute to strengthening preventive activities, promoting timely diagnosis and treatment, improving patients' quality of life, and reducing the overall burden of disease. We be-

lieve these findings may serve as a foundation for developing a national COPD screening strategy.

Conclusion

Nearly one in ten asymptomatic adults aged ≥40 had previously undiagnosed COPD, underscoring the substantial burden of unrecognized disease in primary care. Older age, sex, lower educational level, heavy smoking, biomass fuels exposure, tuberculosis, hypertension, family history of respiratory disease, and recurrent childhood infections were independently associated with newly diagnosed COPD. These findings highlight the need for systematic risk assessment and targeted spirometry screening of high-risk individuals in primary care. Early identification of COPD in apparently asymptomatic adults may enable timely intervention, reduce disease progression, and ultimately decrease the long-term clinical and socioeconomic burden of COPD.

Ethical approval: The Ethics Committee for Research Involving Human Subjects, Faculty of Medicine, University of "Saints Cyril and Metodius" Skopje, Republic of North Macedonia gave approval for performing the study and publishing the obtained results (03-1208/5).

Consent for publication: Written informed consent was obtained from all patients prior to inclusion in the study.

Conflict of interest: The authors report no conflicts of interest.

Funding: This work did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

Declaration of interest: All authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the work reported.

Author contribution statement: Kovachevikj Katerina conceived and designed the study, developed the research protocol, conducted data collection, performed statistical analysis, interpreted the findings, and drafted the manuscript. Janevska Sashka contributed to participant recruitment and data collection and provided technical and organizational support during the implementation of the study. Kovachevikj Miona contributed to the statistical analysis, data interpretation, and participated in the preparation, refinement and revision of the manuscript. Kondova Topuzovska Irena supervised the study, contributed to the study design and methodological framework, provided critical revisions, and approved the final version of the manuscript

Use of Artificial Intelligence (AI) tools: The authors declare that no artificial intelligence tools were used in the preparation of this manuscript.

Acknowledgments: Acknowledgment: We would like to thank our patients who participated in the study and the staff who supported our work.

References:

1. Минов Ј (ур.). Хронична опструктивна белодробна болест. Скопје: Медицински факултет Универзитет „Св Кирил и Методиј", 2023.

2. Global Initiative for Chronic Obstructive Lung Disease; Global Strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2025 Report). Published online 2025. Accessed February 10, 2026. https://goldcopd.org/2025-gold-report/

3. Adeloye D, Song P, Zhu Y, et al. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. Lancet Respir Med. 2022 ;10(5):447-458. doi:10.1016/S2213-2600(21)00511-7

4. Ferrari AJ, Santomauro DF, Aali A, et al. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. The Lancet. 2024;403(10440):2133-2161. doi:10.1016/S0140-6736(24)00757-8

5. Министерство на здравство на Република Северна Македонија, Упатство за практикување на медицина заснована на докази за третман на пациент со хронична обструктивна белодробна болест-ХОББ на ниво на примарна здравствена заштита . Accessed February 10, 2026. https://portal.mdt.gov.mk/post-body-files/upatstva-za-praktikuvanje-na-medicina-zasnovana-na-dokazi-file-fVVX.pdf

6. Agustí A, Melén E, DeMeo DL, et al. Pathogenesis of chronic obstructive pulmonary disease: understanding the contributions of gene–environment interactions across the lifespan. Lancet Respir Med. Elsevier Ltd. 2022;10(5):512-524. doi:10.1016/S2213-2600(21)00555-5

7. Soriano JB, Abajobir AA, Abate KH, et al. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med. 2017;5(9):691-706. doi:10.1016/S2213-2600(17)30293-X

8. Marti T. Primary Health Care Organization, Performance and Quality in North Macedonia. 2019. Accessed February 10, 2026. https://www.who.int/europe/publications/i/item/WHO-EURO-2019-3609-43368-60838

9. Minov J, Stoleski S, Stikova E, et al. COPD in a sample of the general adult population from the Skopje region. Academic Medical Journal. 2022;2(1):47-58. doi:10.53582/amj2221047m

10. Stanley AJ, Hasan I, Crockett AJ, et al. COPD Diagnostic Questionnaire (CDQ) for selecting at-risk patients for spirometry: A cross-sectional study in Australian general practice. NPJ Prim Care Respir Med. 2014;24. doi:10.1038/npjpcrm.2014.24

11. Martinez FJ, Mannino D, Leidy NK, et al. A new approach for identifying patients with undiagnosed chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2017;195(6):748-756. doi:10.1164/rccm.201603-0622OC

12. Zhou YM, Chen SY, Tian J, et al. Development and validation of a chronic obstructive pulmonary disease screening questionnaire in China. International Journal of Tuberculosis and Lung Disease. 2013;17(12). doi:10.5588/ijtld.12.0995

13. Price DB, Tinkelman DG, Halbert RJ, et al. Symptom-based questionnaire for identifying COPD in smokers. 2006;73(3):285-295. doi:10.1159/000090142

14. Zhang Q, Wang M, Li X, et al. Do symptom-based questions help screen COPD among Chinese populations? Sci Rep. 2016;6. doi:10.1038/srep30419

15. Buist S, Mcburnie MA, Vollmer WM, et al. International Variation in the Prevalence of COPD (The BOLD Study): A Population-Based Prevalence Study. Vol 370. 2007. www.thelancet.com

16. Quach A, Giovannelli J, Chérot-Kornobis N, et al. Prevalence and underdiagnosis of airway obstruction among middle-aged adults in northern France: The ELISABET study 2011-2013. Respir Med. 2015;109(12):1553-1561. doi: 10.1016/j.rmed.2015.10.012

17. Menezes AMB, Perez-Padilla R, Jardim JRB, et al. PLATINO Study: Chronic obstructive pulmonary disease in five Latin American cities. Lancet. 2005; 366:1875-1881. doi: 10.1016/S0140-6736(05)67632-5

18. Lytras T, Kogevinas M, Kromhout H, et al. Occupational exposures and 20-year incidence of COPD: the European Community Respiratory Health Survey. Thorax. 2018;73(11). doi:10.1136/thoraxjnl-2017-211158ï

19. Stoleski S, Minov J, Mijakoski D, et al. COPD prevalence and characteristics among sample of working population. Front Public Health. 2025;13. doi:10.3389/fpubh.2025.1598290

20. Beran D, Zar HJ, Perrin C, et al. Burden of asthma and chronic obstructive pulmonary disease and access to essential medicines in low-income and middle-income countries. Lancet Respir Med. Lancet Publishing Group. 2015. 3(2):159-170. doi:10.1016/S2213-2600(15)00004-1

21. Gershon AS, Warner L, Cascagnette P, et al. Lifetime risk of developing chronic obstructive pulmonary disease: A longitudinal population study. The Lancet. 2011. 378(9795):991-996. doi:10.1016/S0140-6736(11)60990-2

22. Colak Y, Løkke A, Marott JL, et al. Low smoking exposure and development and prognosis of COPD over four decades: a population-based cohort study. Eur Respir J. Published. 2024. 64(3). doi:10.1183/13993003.00314-2024

23. Hu G, Zhou Y, Tian J, et al. Risk of COPD From Exposure to biomass smoke: a meta-analysis. CHEST journal. 2010;138 (1): 20-31. doi: 10.1378/chest.08-2114

24. Rennard SI, Vestbo J. COPD: the dangerous underestimate of 15%. Lancet. 2006. 367: 1216-1219. doi: 10.1016/S0140-6736(06)68516-4

25. Forouzanfar MH, Alexander L, Anderson HR, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet. 2015;386(10010):2287-2323. doi:10.1016/S0140-6736(15)00128-2

26. Eisner MD, Balmes J, Katz PP, et al. Lifetime environmental tobacco smoke exposure and the risk of chronic obstructive pulmonary disease. Environ Health. 2005;4. doi:10.1186/1476-069X-4-7

27. McCloskey SC, Bipen PD, Hinchliffe SJ, et al. Siblings of patients with severe chronic obstructive pulmonary disease have a significant risk of airflow obstruction. Am J Respir Crit Care Med. 2001; 164:1419-1424. doi:10.1164/rccm2105002

28. Stick S. Paediatric origins of adult lung disease c 1 The contribution of airway development to paediatric and adult lung disease. Thorax. 2000

29. Lange P, Celli B, Agustí A, et al. Lung-Function Trajectories Leading to Chronic Obstructive Pulmonary Disease. New England Journal of Medicine. 2015;373(2):111-122. doi:10.1056/nejmoa1411532

30. Svanes C. What has the ECRHS told us about the childhood risks of asthma, allergy and lung function? Clin Respir J. 2008;2 Suppl 1:34-44. doi:10.1111/j.1752-699X.2008. 00082.x

31. Liang X, Chou OHI, Cheung BMY. The association between systemic arterial hypertension and chronic obstructive pulmonary disease: results from the U.S. National Health and Nutrition Examination Survey 1999–2018: a cross-sectional study. Chronic Obstr Pulm Dis (Miami). 2023;10(2):190-198.

32. Martins SM, Dickens AP, Salibe-Filho W, et al. Accuracy and economic evaluation of screening tests for undiagnosed COPD among hypertensive individuals in Brazil. NPJ Prim Care Respir Med. 2022;32(1). doi:10.1038/s41533-022-00303-w

33. Feng J, Hu M, Duan H. Bidirectional association between tuberculosis and chronic obstructive pulmonary disease: a systematic review and meta-analysis. J Clin Med. 2025;14(21):7639. doi:10.3390/jcm14217639.

34. Јанковска А, Симоновска В, Крстев Б. Анализа на состојбата со туберкулоза за 2023 година за Скопскиот регион споредено со периодот од 2010-2022 година. ЈЗУ Центар за јавно здравје – Скопје; 2024.