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ORIGINAL RESEARCH

Prevalence of Chronic Obstructive Pulmonary Disease and Its Associated Risk Factors in Yunnan Province, China: A Population Based Cross-Sectional Study

Geyi Wen[1,*], Jinliang Meng[1,*], Puxian Peng[2,*], Yanyan Xu[1], Ruiqi Wang[1], Wenlong Cui[2], Aihan Wen[2], Guohong Luo[2], Yunhui Zhang[1], Songyuan Tang[2]

[1]Department of Pulmonary and Critical Care Medicine, the First People's Hospital of Yunnan Province, the Affiliated Hospital of Kunming University of Science and Technology, Kunming, Yunnan, People's Republic of China; [2]Institute of Health Studies, School of Public Health, Kunming Medical University, Kunming, Yunnan, People's Republic of China

*These authors contributed equally to this work

Correspondence: Yunhui Zhang, Department of Pulmonary and Critical Care Medicine, the First People's Hospital of Yunnan Province, No. 157 Jinbi Road, Xishan District, Kunming, Yunnan, 650032, People's Republic of China, Email yunhuizhang3188@126.com; Songyuan Tang, Institute of Health Studies, School of Public Health, Kunming Medical University, 1168 West Chunrong Road, Yuhua Street, Chenggong District, Kunming, Yunnan, 650500, People's Republic of China, Email tsythailand@hotmail.com

Purpose: Chronic obstructive pulmonary disease (COPD) is a significant disease impacting health and quality of life. Yunnan Province, a major tobacco producer, lacks comprehensive COPD studies. The purpose of this study is to describe the epidemic situation of COPD in Yunnan province and explore its influencing factors.

Methods: This study is a cross-sectional research conducted in a representative sample of adults aged 20 and older from 13 prefectures and cities in Yunnan Province, China. COPD was diagnosed using post-bronchodilator pulmonary function tests. Demographics were analyzed with descriptive statistics. The influencing factors of COPD were examined by using the multivariate logistic regression models.

Results: Our study found that high-risk individuals for COPD accounted for 20.30% of the screened population aged 20 and above, with a COPD prevalence of 27.18% among this high-risk group. Male had a higher prevalence (33.01%) than did female (16.35%; $p<0.001$ for sex difference). Additionally, the proportion of severe and extremely severe COPD cases in Yunnan Province was higher than the national average and other provinces. After considering the potential confounding variables, male (OR=2.291, 95% CI: 1.584–3.313), age (OR=1.501, 95% CI: 1.338–1.685), underweight (OR=1.747, 95% CI: 1.225–2.491), previous smoking (OR=1.712, 95% CI: 1.182–2.478), passive smoking (OR=1.444, 95% CI: 1.159–1.800), and a history of respiratory system diseases in childhood (OR=2.010, 95% CI: 1.346–3.001) were significantly associated with an increased risk of COPD. Conversely, being overweight (OR=0.636, 95% CI: 0.489–0.828), and residing in high-altitude counties (OR=0.445, 95% CI: 0.263–0.754) were negatively correlated with the risk of COPD.

Conclusion: There is significant prevalence of COPD (27.18%) among high-risk population aged 20 and above in Yunnan Province, China. Apart from male, smoking, BMI and other known risk factors for COPD. We found that high-altitude residence had a lower prevalence of COPD. There is no significant difference in COPD prevalence between Han and ethnic minority populations.

Keywords: chronic obstructive pulmonary disease, epidemiological characteristics, influencing factors, high-risk population, China

Introduction

Chronic obstructive pulmonary disease remains a major public health problem, associated significant social and economic burden worldwide because of its high prevalence and related disability and mortality.[1] In 2019, 212.3 million prevalent cases of COPD were reported globally, with COPD accounting for 3.3 million deaths and

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74.4 million DALYs.[2] WHO has declared COPD is the 3rd leading cause of death at the global level.[3] According to the China Pulmonary Health (CPH) study, the prevalence of COPD in the population aged 20 years or older is 8.6% and aged 40 years or older is 13.7% in China.[4] Based on the Global Burden of Disease (GBD) 2019 database, the disease burden of COPD in China is relatively heavy, and the number of affected individuals is still increasing.[5]

The prevalence and burden of COPD vary across different regions of China, influenced by factors including the economy, society, natural environment, population demographic patterns, and others.[6,7] For example, the prevalence of spirometry-defined COPD among the population 40 years or older was 11.6% in Fujian Province,[8] 9.8% in Anhui Province[9] and 9.3% in Shanxi Province.[10] Assessing the regional prevalence of COPD is of urgent significance for the development of regional public health policies and better allocating medical resources. Yunnan Province is relatively unique compared to other provinces in China, which is located in the mountainous plateaus of southwestern China, is recognized as one of the economically disadvantaged province in China. It possesses distinctive geographical features, diverse ethnic minority populations, and faces challenges related to tobacco epidemic prevalence. In short, as an undeveloped province in southwest China with a significant tobacco producing province, the substantial disease burden attributable to COPD warrants careful consideration. Despite the existence of numerous investigations concerning COPD within Yunnan province, their scope remains localized to specific geographic regions or demographic population. Thus, there is an urgent need to investigate the prevalence and explore the various risk factors associated with the condition in different regions of Yunnan Province, to promote specific prevention and control measures. To help fill the evidence gap, we conducted a cross-sectional survey, with the aim of including a large population and using screening questionnaire to identify high-risk population for COPD among participants. Then pulmonary function tests are performed on all identified high-risk individuals to estimate the prevalence of COPD and its associated risk factors among high-risk population in Yunnan Province. Furthermore, we collected and assessed the association between the prevalence of COPD and altitude as well as ethnicity.

Materials and Methods

Study Participants

Our study provides reliable estimates of the prevalence of COPD among high-risk populations in Yunnan Province. We used the COPD-PS questionnaire[11] (Chinese version) and COPD-SQ questionnaire[12] (Chinese version) to conduct initial screening for high-risk population from all study participants. High-risk individuals were defined as those with a COPD-SQ score of 16 or higher, or (and) a COPD-PS score of 5 or higher. The high-risk population consists of all high-risk individuals. Individuals with a COPD-PS score of less than 5 and a COPD-SQ score of less than 16 were classified as non-high-risk individuals. The COPD-PS questionnaire[11] (Appendix 1) and COPD-SQ questionnaire[12] mainly contain the following information:1) Self-reported chronic cough, chronic expectoration, dyspnea and other chronic respiratory symptoms; 2) Exposure to current or past smoking, indoor use of contaminated fuel and other risk factors; 3) Family history of chronic respiratory diseases. All these high-risk participants underwent a post-bronchodilator pulmonary function test.

We employed a multi-stage cluster sampling methodology to recruit a representative sample of adult residents aged 20 years and above in Yunnan Province. In the first stage, we randomly selected 13 prefectures out of the 16 prefectures in Yunnan Province. In the second stage, we randomly chose one county from each selected prefecture (with the exception of Kunming and Qujing, where 3 and 2 counties were selected, respectively, due to their larger populations) to serve as study sites, resulting in a total of 16 counties selected. Additionally, we selected 4 towns/villages located within the administrative boundaries corresponding to the selected counties. In the third stage, we stratified the final sampling by sex and age distribution based on 2020 China census data.[13] We selected only one participant from every household, without replacement. We got the contact information ie name, home address and contact phone number of each selected participant from the Residents' Health Records System[14] (every resident in Yunnan Province has a unique identity (ID) of Residents' Health Records) (Figure 1). Then village doctors informed every participant to go to the designated place for on-site investigation, when someone did not want to come, continued to carry out simple random sampling for another person to replace him.

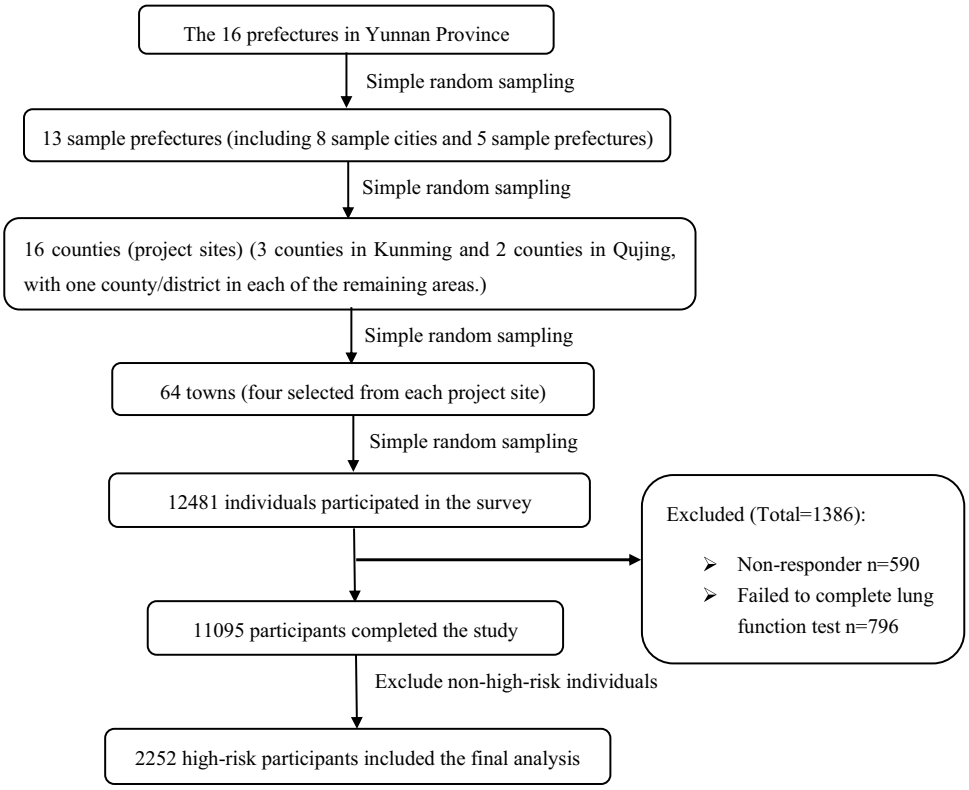

Figure 1 Flowchart of participants through the study.

The inclusion criteria for the study population in the sampling frame were as follows: 1) aged 20 years or above; 2) permanent residents within the study sites, with a minimum of 6 months of residency within the past year before the screening; 3) voluntary participation and signed informed consent. The exclusion criteria for enrollment were as follows (if any of the following conditions were met): 1) recent history (within the last 3 months) of myocardial infarction, stroke, or shock; 2) severe heart failure, severe arrhythmias, or unstable angina within the last 4 weeks; 3) massive hemoptysis within the last 4 weeks; 4) chest, abdominal, or ocular surgery within the last 3 months; 5) psychiatric disorders including hallucinations, delusions, use of antipsychotic medications, or epilepsy requiring medication; 6) cognitive impairment, including dementia or impaired comprehension; 7) uncontrolled hypertension (systolic blood pressure >200 mmHg, diastolic blood pressure >100 mmHg), heart rate >120 beats/minute, or aortic aneurysm; 8) severe hyperthyroidism; 9) pregnancy or lactation in females; 10) respiratory infectious diseases (such as tuberculosis or influenza) within the last month.

Based on a national cross-sectional study by the research team led by Wang Chen,[4] the prevalence of COPD was found to be 2.1% (in 2018) among individuals aged 20–39, and 13.7% (in 2018) among individuals aged 40 and above. We used the PASS software (NCSS, Kaysville, UT, USA)[15] to calculate the sample size. Additionally, considering the possibility of refusal during field surveys, we set a conservative visit success rate of 90% and applied a design effect of 1.2 to account for the multi-stage cluster sampling design. The final sample size was 1053 for the 20–39 age group and 6056 for the 40 and above age group.

Ethics

The study was initiated and led by the First People's Hospital of Yunnan Province and was approved by the Ethics Committee of the First People's Hospital of Yunnan Province (KHLL2022-KY141-C-1). Written informed consent has been obtained from all study participants.

Measures

Dependent Variable

The dependent variable is the presence of COPD. It is diagnosed based on the results of pulmonary function test. All high-risk participants were subjected to pulmonary function tests using the German Jaeger spirometer (MasterScreen Pneumo, Jaeger).[16] Technicians trained in pulmonary function testing and quality control performed pulmonary function tests on all high-risk individuals. Pulmonary function tests were performed strictly in accordance with the guidelines.[17,18] The specific operation of pulmonary function test is as follows: Step 1, turn on the pulmonary function instrument and calibrate the instrument. In the step 2, the pulmonary function testing technician explained the examination process to the subjects, demonstrated the examination action, and asked the subjects to practice the examination action, and then checked the essentials of the action. The step 3 is to measure the pulmonary function for pre-bronchodilator (the first pulmonary function test). Step 4, post-bronchodilator pulmonary function test (the second pulmonary function test): for individuals with a pre-bronchodilator $FEV_1/FVC < 0.7$, inhale bronchodilator (salbutamol 400 μg) through a 500 mL spacer, and wait for 15 minutes, a post-bronchodilator pulmonary function test was conducted to confirm the diagnosis of COPD. Individuals who had dyspnea, chronic cough or sputum production, a history of recurrent lower respiratory tract infections and/or a history of exposure to risk factors for the disease with a post- bronchodilator $FEV_1/FVC < 0.7$ were diagnosed as COPD patients.[1]

Independent Variable

All baseline covariates data were obtained by trained interviewers through standard questionnaires.[4] Age, gender, nationality, and education level are self-reported. Body mass index (BMI) is defined as weight (kg) divided by the square of height (m). Marital status is divided into in marriage and not in marriage. We define current smoking as the act of having consumed a minimum of 100 cigarettes throughout one's lifetime and presently continuing to smoke. Passive smoking is characterized as the inhalation of smoke by non-smokers in the presence of smokers. Family history of respiratory system diseases is designated by whether any individuals within the family have been diagnosed with conditions such as COPD, chronic bronchitis, or emphysema et al. Childhood history of respiratory system diseases is defined as having encountered pneumonia, asthma, bronchitis, or other respiratory system diseases at least once before the age of 14. Biomass fuel use is defined as the predominant utilization of wood fuel or animal dung for cooking or heating purposes for a period of six months or longer within the past. The counties in Yunnan Province have an altitude coefficient that varies greatly by location, ranging from 64.8 to 334.7. 16 counties in this study are categorized as high altitude (altitude>2500), middle altitude (altitude: 1500–2500), and low altitude (altitude<1500). Based on population reference values from China, we calculated the ratios of observed to predicted FEV_1 and utilized them to classify the degree of obstruction. This classification includes the following stages: GOLD stage I (≥80% predicted), GOLD stage II (≥50% to <80% predicted), GOLD stage III (≥30% to <50% predicted), and GOLD stage IV (<30% predicted).[19]

Statistical Analysis

Statistical significance evaluation for continuous variables was conducted using non-parametric test, whereas chi-square tests were used for categorical variables. The multivariable logistic regression analysis was conducted to investigate the risk factors for COPD among all high-risk populations and high-risk individuals who have never smoked. Due to the small sample size of GOLD stage IV (n=29), individuals with GOLD stage III and IV were merged for analysis. The SPSS software (Version 26) was used to carry out all statistical analyses. All statistical inferences were set as a two-tailed *p*-value less than 0.05.

Results

Demographic Characteristics and Risk Factors for COPD by GOLD Stage in the High-Risk Population

Between November 2022 and June 2023, a total of 12,481 eligible individuals (5841 males and 6640 females) were invited to participate in the survey. Of these, 11,095 individuals (including 5001 males and 6094 females) completed the

study (see Figure 1). The overall response rate was 88.90% (85.62% for males and 91.78% for females). Of them, there are 2252 high-risk individuals and 8843 non-high-risk individuals. After excluding individuals with incomplete pulmonary function test or missing key variables, a total of 2252 high-risk individuals (1463 males and 789 females) were included in the final analysis.

The general characteristics and risk factors of the study population, stratified by COPD severity, are presented in Table 1. The prevalence of COPD by GOLD stages I, II, and III–IV was, respectively, 9.99%, 11.10%, and 6.08% in the high-risk population. The distribution of patients in GOLD stages I, II, and III–IV showed a significant male predominance compared to females, with statistically significant differences ($P<0.05$). Additionally, as age increased, the proportion of patients in each stage gradually increased. Individuals with lower education levels had a higher proportion of disease prevalence. Moreover, in low and mid-altitude areas, there was a larger proportion of patients in each stage, with statistically significant differences (the *p*-values for all the mentioned associations are less than 0.05). The remaining characteristics of study population with COPD are shown in Table 1.

Table 1 Demographic Characteristics and Risk Factors for COPD by GOLD Stage in the High-Risk Population of Adults Aged 20 Years and Above in Yunnan Province, China in 2022

	Total (N=2252)	No COPD (N=1640)	GOLD Stage I(N=225)	GOLD Stage II(N=250)	GOLD Stage III–IV(N=137)	$\chi 2$/ t-value	*p for Difference*
Proportion of participants (%)	100	72.82	9.99	11.10	6.08		
Sex							
Male	1463(64.96)	980(59.76)	168(74.67)	194(77.60)	121(88.32)	79.225	<0.001
Female	789(35.04)	660(40.24)	57(25.33)	56(22.40)	16(11.68)		
Age (years)							
20–49	213(9.46)	194(11.83)	6(2.67)	6(2.40)	7(5.11)	81.045	<0.001
50–59	536(23.80)	407(24.82)	34(15.11)	51(20.40)	44(32.12)		
60–69	854(37.92)	622(37.93)	92(40.89)	92(36.80)	48(35.04)		
≥70	649(28.82)	417(25.43)	93(41.33)	101(40.40)	38(27.74)		
Nationality							
Han nationality	1738(77.18)	1255(76.52)	180(80.00)	196(78.40)	107(78.10)	1.693	0.638
Other ethnic minorities*	514(22.82)	385(23.48)	45(20.00)	54(21.60)	30(21.90)		
Education							
Primary school and below	1289(63.22)	913(61.73)	129(62.62)	162(69.83)	85(69.67)	12.900	0.045
Middle and high school	622(30.51)	460(31.10)	69(33.50)	62(26.72)	31(25.41)		
College and higher	128(6.28)	106(7.17)	8(3.88)	8(3.45)	6(4.92)		
Marital status							
Married	1916(85.08)	1390(84.76)	193(85.78)	215(86.00)	118(86.13)	0.508	0.917
Unmarried	336(14.92)	250(15.24)	32(14.22)	35(14.00)	19(13.87)		
Body-mass index (kg/m^2)							
<18.5	177(7.86)	104(6.34)	9(4.00)	41(16.40)	23(16.79)	73.154	<0.001
18.5–24.9	1421(63.10)	1011(61.15)	171(76.00)	153(61.20)	86(62.77)		
25.0–29.9	545(24.20)	436(26.59)	41(18.22)	46(18.40)	22(16.06)		
≥30.0	109(4.84)	89(5.43)	4(1.78)	10(4.00)	6(4.38)		
Smoking history							
Never-smoker	953(42.32)	764(46.59)	78(34.67)	79(31.60)	32(23.36)	81.222	<0.001
Former smoker	525(23.31)	321(19.57)	56(24.89)	88(35.20)	60(43.80)		
Current smoker	774(34.37)	555(33.84)	91(40.44)	83(33.20)	45(32.85)		

(*Continued*)

Table 1 (Continued).

	Total (N=2252)	No COPD (N=1640)	GOLD Stage I(N=225)	GOLD Stage II(N=250)	GOLD Stage III–IV(N=137)	$\chi 2$/ *t*-value	*p for Difference*
Smoking exposure (pack-years)							
0	953(42.42)	764(46.67)	78(34.67)	79(31.85)	32(23.53)	63.303	<0.001
1–14.9	179(7.98)	131(8.01)	17(7.56)	21(8.47)	10(7.35)		
15–29.9	371(16.53)	265(16.21)	35(15.56)	49(19.76)	22(16.18)		
≥30	742(33.07)	476(29.11)	95(42.22)	99(39.92)	72(52.94)		
Passive smoking at home							
Yes	742(34.88)	527(34.15)	78(35.94)	90(37.50)	47(37.01)	1.444	0.695
No	1385(65.12)	1016(65.85)	139(64.06)	150(62.50)	80(62.99)		
Family history of respiratory system diseases							0.008
Yes	422(18.74)	335(20.43)	29(12.89)	36(14.40)	22(16.06)	11.862	
No	1830(81.26)	1305(79.57)	196(87.11)	214(85.60)	115(83.94)		
History of respiratory system diseases during childhood							
Yes	131(6.16)	81(5.25)	17(7.83)	20(8.33)	13(10.24)	8.878	0.031
No	1996(93.84)	1462(94.75)	200(92.17)	220(91.67)	114(89.76)		
Biomass use							
Yes	946(42.01)	719(43.84)	84(37.33)	95(38.00)	48(35.04)	8.663	0.034
No	1306(57.99)	921(56.16)	141(62.67)	155(62.00)	89(64.96)		
Altitude							
Low-altitude counties	783(34.77)	576(35.12)	60(26.67)	94(37.60)	53(38.69)	23.847	0.001
Mid-altitude counties	1313(58.30)	936(57.07)	145(64.44)	151(60.40)	81(59.12)		
High-altitude counties	156(6.93)	128(7.81)	20(8.89)	5(2.00)	3(2.19)		
FEV_1 (L)#	2.30(1.73,2.84)	2.51(2.05,3.03)	2.16(1.71,2.59)	1.49(1.24,1.73)	0.88(0.71,1.05)	–	<0.001
FVC (L)#	3.11(2.49,3.80)	3.22(2.62,3.89)	3.52(2.81,3.99)	2.70(2.21,3.19)	2.04(1.71,2.47)	–	<0.001
Post-bronchodilator FEV_1: FVC ratio#	75.06 (66.81,80.28)	77.87 (73.99,81.94)	63.88 (60.32,66.94)	55.03 (48.76,62.63)	42.74(37.27,50.00)	–	<0.001

Notes: *Other ethnic minorities include Bai, Tibetan, Dai, Hani, Hui, Lahu, Naxi, Yi, Zhuang and so on. #FEV_1, FVC and Post-bronchodilator FEV_1: FVC ratio are not normal distributions. *M* (P_{25}, P_{75}) is used to describe the distribution, and non-parametric test is used to analyze the difference.

Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; FEV_1, Forced Expiratory Volume in 1 second; FVC, Forced Vital Capacity.

Prevalence of COPD in the High-Risk Population

Among the high-risk population aged 20 years and above in Yunnan, the overall prevalence of COPD diagnosed based on lung function was 27.18% (95% *CI* 25.35–29.06). The prevalence among males (33.01%, 95% *CI* 30.61–35.49) was higher than females (16.35%, 95% *CI* 13.84–19.12; $p<0.001$, significant gender difference). This gender difference was observed in all age groups of the high-risk population and never-smoking high-risk population (see Table 2). The prevalence of COPD increased with age, with rates of 8.29% (95% CI 5.46–13.58) among individuals aged 20–49 years, 24.07% (95% CI 20.51–27.92) among those aged 50–59 years, 27.17% (95% CI 24.21–30.28) among those aged 60–69 years, and 35.75% (95% CI 32.06–39.57) among individuals aged 70 years and above ($p<0.001$ for age difference). The prevalence of COPD in the underweight population (BMI<18.5 kg/m^2) was 41.24% (95% CI 33.91–48.87). In the normal weight population (BMI 18.5–24.9 kg/m^2), the prevalence of COPD was 28.85% (95% CI 26.51–31.29), in the overweight population (BMI 25.0–29.9 kg/m^2), the prevalence of COPD was 20.00% (95% CI 16.72–23.61), and in the obese population (BMI≥30.0 kg/m^2), the prevalence of COPD was 18.35% (95% CI 11.58–26.91). It can be observed that as BMI increased, the prevalence of COPD in high-risk populations decreased, and this difference was statistically significant (trend test p-value < 0.001). This difference is observed in both males and females, as well as in high-risk

Table 2 Prevalence of COPD in the High-Risk Population Aged 20 and Above Based on Spirometry in Yunnan Province in 2022

	Prevalence (%) in High-Risk Population (95% CI)			Prevalence (%) in Never-Smokers (95% CI) Among High-Risk Population		
	Male(n=1463)	Female(n=789)	Total(N=2252)	Male(n=196)	Female(n=757)	Total(N=953)
Total	33.01(30.61–35.49)	16.35(13.84–19.12)	27.18(25.35–29.06)	32.14(25.67–39.17)	16.64(14.06–19.49)	19.83(17.34–22.51)
Age (years)						
20–49	10.20(5.82–16.27)	6.06(1.68–14.80)	8.92(5.46–13.58)	33.33(7.49–70.07)	6.78(1.88–16.46)	10.29(4.24–20.07)
50–59	29.95(25.28–34.94)	11.63(7.25–17.39)	24.07(20.51–27.92)	25.71(12.49–43.26)	12.05(7.52–17.99)	14.43(9.88–20.06)
60–69	34.07(30.09–38.23)	15.11(11.32–19.58)	27.17(24.21–30.28)	26.98(16.57–39.65)	15.33(11.45–19.92)	17.36(13.60–21.65)
≥70	42.54(37.70–47.50)	24.17(18.89–30.09)	35.75(32.06–39.57)	38.20(28.10–49.11)	24.14(18.78–30.17)	28.04(23.19–33.29)
p for trend	<0.001	<0.001	<0.001	0.398	0.001	0.001
Nationality						
Han nationality	33.63(30.88–36.46)	16.78(13.88–20.01)	27.79(25.69–29.96)	32.00(24.63–40.10)	16.84(13.90–20.11)	19.92(17.09–22.99)
Other ethnic minorities*	30.89(25.92–36.20)	14.97(10.19–20.91)	25.10(21.40–29.08)	32.61(19.53–48.02)	15.98(10.80–22.39)	19.53(14.46–25.47)
p for trend	0.353	0.560	0.228	0.938	0.791	0.901
Body-mass index (kg/m^2)						
<18.5	50.00(40.32–59.68)	26.87(16.76–39.10)	41.24(33.91–48.87)	42.11(20.25–66.50)	26.87(16.76–39.10)	30.23(20.79–41.08)
18.5–24.9	34.87(31.81–38.02)	17.28(14.03–20.94)	28.85(26.51–31.29)	32.85(25.07–41.38)	17.45(14.12–21.19)	20.92(17.75–24.38)
25.0–29.9	24.00(19.62–28.83)	12.82(8.47–18.34)	20.00(16.72–23.61)	24.32(11.77–41.20)	13.26(8.68–19.08)	15.14(10.65–20.60)
≥30.0	26.47(16.50–38.57)	4.88(0.60–16.53)	18.35(11.58–26.91)	33.33(0.84–90.57)	5.13(0.63–17.32)	7.14(1.50–19.48)
p for trend	<0.001	0.010	<0.001	0.550	0.015	0.004
Education						
Primary school and below	36.41(32.95–39.98)	19.19(15.96–22.76)	29.17(26.70–31.74)	34.12(24.18–45.20)	19.46(16.14–23.13)	21.52(18.31–25.02)
Middle and high school	30.79(26.64–35.17)	11.26(6.70–17.41)	26.05(22.64–29.68)	25.37(15.53–37.49)	11.81(7.03–18.23)	16.11(11.42–21.78)
College and higher	21.36(13.90–30.53)	0	17.19(11.10–24.86)	35.71(12.76–64.86)	0	13.16(4.41–28.09)
p for trend	0.004	0.002	0.010	0.462	0.004	0.136
Marital status						
Married	33.15(30.58–35.80)	15.85(13.08–18.94)	27.45(25.46–29.51)	30.67(23.70–38.37)	16.12(13.28–19.29)	19.20(16.47–22.16)
Unmarried	32.02(25.24–39.42)	18.35(12.65–25.28)	25.60(21.01–30.61)	39.39(22.91–57.86)	18.79(12.87–26.00)	22.53(16.68–29.29)
p for trend	0.764	0.446	0.480	0.328	0.432	0.311
Smoking history						
Never-smoker	32.14(25.67–39.17)	16.64(14.06–19.49)	19.83(17.34–22.51)	–	–	–
Former smoker	39.30(35.05–43.67)	18.18(2.28–51.78)	38.86(34.67–43.18)	–	–	–
Current smoker	28.95(25.73–32.33)	4.76(0.12–23.82)	28.29(25.14–31.61)	–	–	–
p for trend	0.001	0.366	<0.001	–	–	–
Smoking exposure (pack-years)						
0	32.14(25.67–39.17)	16.64(14.06–19.49)	19.83(17.34–22.51)	–	–	–
1–14.9	28.74(22.01–36.24)	0	26.82(20.48–33.94)	–	–	–
15–29.9	29.25(24.59–34.25)	8.33(0.21–38.48)	28.57(24.03–33.46)	–	–	–
≥30	35.97(32.49–39.56)	25.00(3.19–65.09)	35.85(32.39–39.42)	–	–	–
p for trend	0.084	0.340	<0.001	–	–	–
Passive smoking at home						
Yes	36.30(31.90–40.88)	17.02(12.82–21.93)	28.98(25.73–32.39)	41.03(25.57–57.90)	17.29(12.95–22.38)	20.33(15.96–25.29)
No	31.70(28.70–34.82)	16.70(13.43–20.40)	26.64(24.33–29.05)	26.28(19.13–34.48)	17.04(13.68–20.82)	19.19(16.08–22.60)
p for trend	0.087	0.910	0.251	0.075	0.929	0.683

(*Continued*)

Table 2 (Continued).

	Prevalence (%) in High-Risk Population (95% CI)			Prevalence (%) in Never-Smokers (95% CI) Among High-Risk Population		
	Male(n=1463)	Female(n=789)	Total(N=2252)	Male(n=196)	Female(n=757)	Total(N=953)
Biomass use						
Yes	30.73(26.89–34.77)	14.65(11.31–18.52)	24.00(21.31–26.85)	26.76(16.94–38.59)	14.97(11.51–19.00)	16.85(13.49–20.66)
No	34.39(31.31–37.57)	18.07(14.39–22.23)	29.48(27.02–32.03)	35.20(26.87–44.25)	18.28(14.53–22.52)	22.44(18.88–26.32)
p for trend	0.149	0.194	0.004	0.224	0.222	0.031
Family history of respiratory system diseases						
Yes	26.72(21.31–32.70)	12.00(7.58–17.76)	20.62(16.86–24.79)	32.43(18.01–49.79)	12.50(7.91–18.47)	16.10(11.35–21.86)
No	34.29(31.62–39.04)	17.59(14.66–20.84)	28.69(26.62–30.82)	32.08(24.90–39.93)	17.83(14.82–21.16)	20.86(18.00–23.95)
p for trend	0.021	0.078	0.001	0.967	0.102	0.130
History of respiratory system diseases during childhood						
Yes	45.07(33.23–57.34)	30.00(18.85–43.21)	38.17(29.82–47.06)	25.00(5.49–57.19)	29.31(18.09–42.73)	28.57(18.40–40.62)
No	32.59(30.06–35.21)	15.67(13.04–18.61)	26.75(24.82–28.75)	29.88(22.99–37.51)	16.06(13.34–19.09)	18.81(16.20–21.65)
p for trend	0.030	0.004	0.005	1.000	0.010	0.048
Altitude						
Low-altitude counties	32.79(28.65–37.14)	15.75(11.77–20.45)	26.44(23.38–29.67)	32.47(22.23–44.10)	15.69(11.60–20.55)	19.37(15.37–23.90)
Mid-altitude counties	34.29(31.14–37.56)	17.79(14.35–21.67)	28.71(26.28–31.24)	33.33(24.43–43.20)	18.24(14.72–22.21)	21.19(17.81–24.89)
High-altitude counties	23.30(15.54–32.66)	7.55(2.09–18.21)	17.95(12.27–27.89)	21.43(4.66–50.80)	8.00(2.22–19.23)	10.94(4.51–21.25)
p for trend	0.080	0.153	0.014	0.764	0.160	0.146

Notes: *Other ethnic minorities include Bai, Tibetan, Dai, Hani, Hui, Lahu, Naxi, Yi, Zhuang and so on.
Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; CI, Confidence Interval.

populations who have never smoked (see Table 2). As education level increases, the prevalence of COPD decreases accordingly, with statistically significant differences ($P<0.05$).

The prevalence of COPD among never smokers was 19.83% (95% CI 17.34–22.51), among former smokers was 38.86% (95% CI 34.67–43.18), and among current smokers was 28.29% (95% CI 25.14–31.61), with statistically significant differences ($P<0.001$). This difference trend was also observed in males, while no such difference was observed in females. Furthermore, as smoking amount increases, the prevalence of COPD also increases accordingly, with statistically significant differences (trend test p-value < 0.001). Individuals with a history of respiratory system diseases during childhood have a significantly higher prevalence of COPD (38.17%, 95% CI 29.82–47.06) compared to those without a history of respiratory system diseases during childhood (26.75%, 95% CI 24.82–28.75), with statistically significant differences ($P<0.05$). This difference is observed in both males and females, as well as in high-risk populations who have never smoked.

The incidence rate of COPD exhibits a notable disparity among regions of varying altitudes. A comprehensive analysis reveals a heightened prevalence of COPD in low-altitude areas, estimated at 26.44% (95% CI 23.38–29.67), as well as in mid-altitude counties, approximated at 28.71% (95% CI 26.28–31.24). In contrast, high-altitude regions display a comparatively lower prevalence rate of 17.95% (95% CI 12.27–27.89), with statistically significant differences ($P<0.05$). This notable divergence is further evident within high-risk groups including both males and females (Figure 2).

In the Han Chinese population, the spirometry-defined prevalence of COPD was documented at 27.79% (95% CI, 25.69–29.96). Among this population subset, the prevalence among males was observed to be significantly higher at 33.63% (95% CI, 30.88–36.46) as compared to females with a prevalence rate of 16.78% (95% CI, 13.88–20.01). Similarly, among minority ethnic groups, the overall COPD prevalence was reported as 25.10% (95% CI, 21.40–29.08). Further stratification by gender revealed a higher prevalence among males at 30.89% (95% CI, 25.92–36.20), while among females, it was lower at 14.97% (95% CI, 10.19–20.91). Notably, the observed differences in COPD prevalence between genders were found to be statistically significant. These findings contribute valuable insights into the

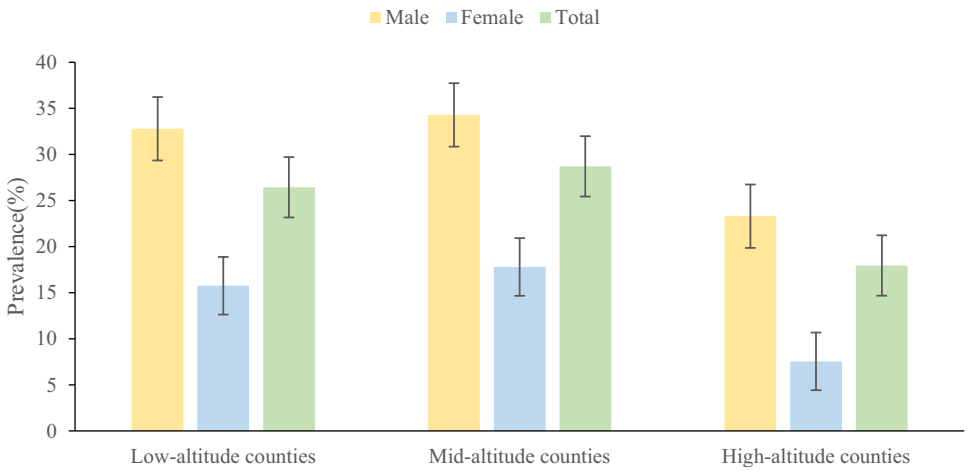

Figure 2 Prevalence of spirometry-defined COPD among high risk population aged 20 years or older in different altitude regions of Yunnan Province in 2022. Bars represent proportion and error bars 95% CI. COPD=chronic obstructive pulmonary disease.

epidemiology of COPD within the Han Chinese and minority ethnic populations, underscoring the importance of gender-specific considerations in disease management and prevention strategies (Figure 3).

Result of Multivariate Analysis of COPD

In the multivariable adjusted analysis, male gender (OR=2.291, 95% CI: 1.584–3.313), age (OR=1.501, 95% CI: 1.338–1.685), underweight (BMI<18.5kg/m^2) (OR=1.747, 95% CI: 1.225–2.491), previous smoking (OR=1.712, 95% CI: 1.182–2.478), passive smoking (OR=1.444, 95% CI: 1.159–1.800), and a history of respiratory system diseases in childhood (OR=2.010, 95% CI: 1.346–3.001) were significantly associated with an increased risk of COPD. Conversely, being overweight (BMI 25.0–29.9kg/m^2) (OR=0.636, 95% CI: 0.489–0.828), having a family history of respiratory system diseases (OR=0.722, 95% CI: 0.540–0.965), and residing in high-altitude counties (OR=0.445, 95% CI: 0.263–0.754) were negatively correlated with the risk of COPD (see Table 3). Furthermore, among never smokers, family history of respiratory system diseases and altitude showed no significant association with COPD, while the other influencing factors were consistent with the entire population.

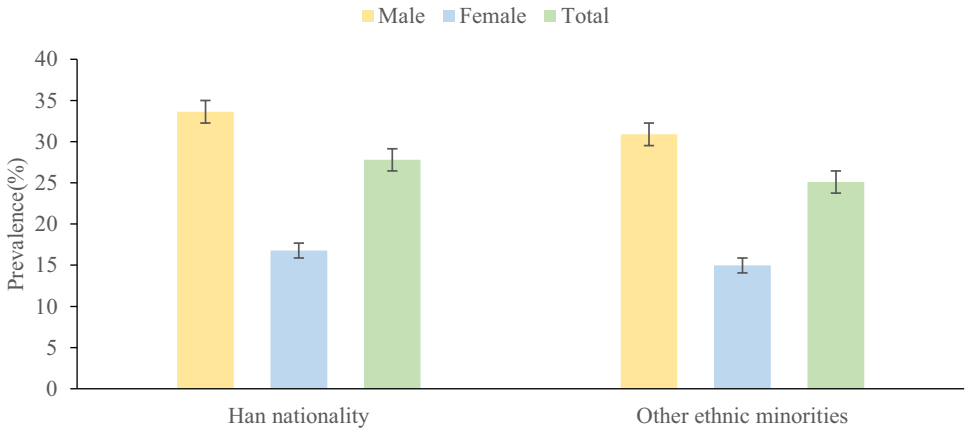

Figure 3 Prevalence of spirometry-defined COPD among high risk population aged 20 years or older in different ethnic groups of Yunnan Province in 2022. Bars represent proportion and error bars 95% CI. COPD=chronic obstructive pulmonary disease.

Table 3 Multiple-Adjusted ORs for COPD Associated with Risk Factors in the General Adult High-Risk Population Aged 20 Years or Older in Yunnan Province in 2022

	High-Risk Population		Never-Smokers Among High-Risk Population	
	OR	OR 95% CI	OR	OR 95% CI
Male sex	2.291*	1.584–3.313	2.094*	1.404–3.123
Age (every 10-year difference)	1.501*	1.338–1.685	1.482*	1.207–1.820
Body-mass index (kg/m^2)				
<18.5	1.747*	1.225–2.491	1.485	0.860–2.563
18.5–24.9	1.000(Ref)		1.000(Ref)	
25.0–29.9	0.636*	0.489–0.828	0.699	0.447–1.092
≥30.0	0.608	0.343–1.080	0.384	0.114–1.291
Smoking history				
Never-smoker	1.000(Ref)		–	–
Former smoker	1.712*	1.182–2.478	–	–
Current smoker	0.985	0.684–1.417	–	–
Passive smoking	1.444*	1.159–1.800	1.491*	1.020–2.181
Family history of respiratory disease	0.722*	0.540–0.965	–	–
A history of respiratory illness during childhood	2.010*	1.346–3.001	1.767*	1.003–3.115
Altitude				
Low-altitude counties	1.000(Ref)		–	–
Mid-altitude counties	0.999	0.800–1.247	–	–
High-altitude counties	0.445*	0.263–0.754	–	–

Note: *p<0.05, which has significant statistical significance.
Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; OR, Odds Ratio; CI, Confidence Interval.

Discussion

To the best of our knowledge, our study represents the largest survey of COPD in a representative sample of the general adult population in Yunnan Province, and it fills several knowledge gaps about the COPD epidemic in Yunnan. Our investigation utilized COPD-SQ and COPD-PS screening tools in a large-scale population and then used pulmonary function test to diagnose COPD. Most surveys on the prevalence of COPD use the method of pulmonary function test across the entire population, with few studies using a combination of screening questionnaires and pulmonary function test. There are three reasons why we adopt this approach. Firstly, the US Preventive Services Task Force recommended against screening for COPD in asymptomatic adults and stated that whole-population screening for COPD using spirometry has no net benefit.[20,21] Secondly, previous studies have shown that screening in primary care has been demonstrated to have a significant impact.[22,23] Finally, the economy of Yunnan Province is underdeveloped, and the level of economic development in different regions is uneven. A cross-sectional analysis demonstrated that screening instruments for COPD were feasible to administer in the low- and middle-income settings.[24] So, through the research implementation process, we have confirmed the feasibility of screening questionnaire combined with pulmonary function test in the early detection of COPD in Yunnan Province, especially in primary care of county hospitals and township health centers which are the cornerstones of Chinese medical system.

We found that high-risk individuals for COPD accounted for 20.30% of the screened population aged 20 years and older. And the prevalence of spirometry-defined COPD among the high-risk individuals was 27.18%. The research which used COPD-SQ combined with pulmonary function test from across the country showed that among the high-risk population who received pulmonary function test, 31.59% were screened and diagnosed as COPD patients.[25] This ratio is higher than that of our study, which may be related to different sampling methods. Another study in Fengning Manchu Autonomous County used COPD-PS combined with pulmonary function test, the prevalence of spirometry-defined COPD among the high-risk individuals was 24.27%.[26] The study also showed that for COPD high risk patients, receiving early screening has a cost-effective advantage over no screening.

Additionally, we observed a higher proportion of severe and extremely severe COPD patients in Yunnan Province than the national average and other provinces. The results of this study showed that severe and very severe COPD cases (GOLD stages III–IV) accounted for 22.4% of all COPD patients, which was much higher than the national level (7.4%)[6] and other provinces (2.4% in Gansu,[27] 4.9% in Guizhou,[28] and 7.0% in Zhejiang[29]). Yunnan Province is located in Yunnan-Guizhou Plateau, with special geographical environment and backward economic development, which leads to limited medical accessibility, and these severe and extremely severe COPD patients have not been diagnosed and treated in time. That may be a reason why the proportion of severe and extremely severe COPD patients in Yunnan is higher than that in other regions. Which indicates that the severity of COPD in Yunnan Province is relatively high, emphasizing the urgent need for early diagnosis and detection of COPD patients in Yunnan Province.

COPD is the result of the interaction of multiple factors such as genetics, environment, and growth and development. The risk factors causing COPD have diverse characteristics. Well known risk factors include tobacco and second-hand tobacco, biomass exposure, occupational exposure, low BMI, family history and childhood history of respiratory disease, socioeconomic status, etc.[30–32] Consistent with these, we also found that males, low BMI, childhood history of respiratory disease and smoking were risk factors. However, we did not find any family history of respiratory diseases or biomass exposure as risk factors. Against other studies,[33,34] this research demonstrates that individuals with a family history of respiratory system diseases (OR=0.722, 95% CI: 0.540–0.965) were negatively correlated with COPD. Our data demonstrates that a considerable percentage of males (66.4%) and those aged above 50 years (92.1%) in the high-risk category do not possess a family history of respiratory diseases. Further, among this group, there is a high incidence of smoking (59.1%). This observation may imply that a family history of respiratory diseases serves as a protective factor against developing COPD. This phenomenon may arise from individuals with a familial predisposition to respiratory ailments altering their personal habits, notably abstaining from smoking, as a proactive measure against respiratory afflictions. But we can explore it further on the pathophysiological mechanism for the argument that family history of respiratory disease may serve as a protective factor against developing COPD in the following research.

The analysis of this study revealed that the prevalence of COPD in high-risk male population was 33.01% (95% CI: 30.61–35.49%), which was significantly higher than the prevalence in females, which was 16.35% (95% CI: 13.84–19.12%). This difference was statistically significant ($P < 0.001$). Gender is an important factor influencing the risk of developing COPD, with multiple studies finding that males are at a higher risk for COPD, whereas females are associated with lower disease risk.[35] Both domestic and international studies[36–38] have shown a significant trend of higher COPD prevalence in males compared to females, and smoking, as the main risk factor for COPD,[39] has a significantly higher prevalence and smoking intensity in males compared to females,[4] which may be the main reason for the significant difference in COPD incidence between genders. Additionally, the incidence of COPD increases with age, which may be due to age-related declines in bodily function and organ function, as well as the increased rigidity of the chest wall, reduced lung elastic recoil, decreased airway diameter, and degeneration of elastic fibers around the alveolar ducts, leading to decreased lung function.[40] The incidence of COPD is also closely related to the duration of exposure to risk factors.

Smoking is a well-established risk factor for developing COPD.[4,41–43] Our data also reveals that former smokers (OR=1.712,95% CI 1.182–2.478) have a higher risk of COPD. Furthermore, in view of the high prevalence of passive smoking and COPD among non-smokers. Passive smoking has been associated with COPD in epidemiological studies.[44,45] Smoking prevention and cessation are important strategies for reducing the burden of COPD and related diseases in populations. But we are surprised that in the multivariate analysis, present smokers had a non-significant OR for COPD. The participants of this study is high-risk population. Besides smoking accidents, other risk factors such as age, family history of respiratory diseases and chronic respiratory diseases are also considered when screening high-risk population. Whether other risk factors dilute the influence of smoking on COPD needs further in-depth study. And we found the prevalence of COPD among never smokers was high 19.83%. This observation suggests that, in addition to smoking, alternative factors such as respiratory infections and environmental exposures may also contribute to the occurrence of COPD. Which is also reported by Rotterdam Study.[46]

This finding is consistent with Wang Chen's research on the influence of BMI on COPD,[4] which shows that underweight (body mass index < 18.5 kg/m^2) may be an important risk factor for individuals to develop COPD and

overweight and obese (BMI>25 kg/m^2) individuals are less likely to have COPD compared to those with normal weight. Meanwhile, Xingyao Tang et al[47] research on the relationship between BMI and lung function also showed the same finding. The interplay between BMI and COPD is intricate. Certain academics posit[48] that they mutually exacerbate each other. Firstly, the dysregulation between energy expenditure and dietary intake in COPD patients precipitates BMI decline. Conversely, diminished BMI instigates muscle protein degradation and alterations in muscle fiber architecture, culminating in respiratory muscle atrophy and weakened respiratory muscle strength. This diminishes immunoglobulin and complement production, impairing immune function and heightening susceptibility to respiratory infections, thereby exacerbating respiratory ailments. These findings underscore the importance of emphasizing nutritional support and ameliorating low body weight in COPD management.

Individuals with a history of respiratory system diseases in childhood (OR=2.010, 95% CI: 1.346–3.001) were significantly associated with an increased risk of COPD. Research suggests that during pregnancy, at birth, and during adolescence, any direct or indirect exposure factors that can affect lung growth and development have the potential to increase the risk of developing COPD. Poor lung growth and development are identified as independent risk factors for COPD.[49,50] The most crucial factors in this regard are low birth weight and childhood lower respiratory tract infections, which have significant impacts on the development of COPD.

We found that high altitude has a significant protective effect on the prevalence of COPD. Studies abroad show that the incidence of COPD is negatively correlated with altitude.[51,52] Some scholars believe that this may be related to the increase of airway diameter in plateau environment than the increase of lung volume. In addition, the air density in plateau area decreases, and the atmospheric pressure also decreases, which leads to the increase of FEV_1/FVC solid ratio, which eventually leads to the low incidence of chronic obstructive pulmonary disease in plateau.[28] Some scholars also believe that[53,54] with the passage of time and the development of generations, people in high altitude areas have undergone physiological and genetic adaptation in order to adapt to extreme heights and cope with chronic hypoxia and ordinary high-intensity exercise. However, the relationship between altitude and COPD is controversial. A pooled analysis of individual data from the PREPOCOL-PLATINO-BOLD-EPI-SCAN studies shows living at high altitude is not associated with a difference in COPD prevalence after accounting for individual risk factors. However, high altitude itself was associated with an increased risk of undiagnosed COPD.[55] A cross-sectional study based on Gansu population from China points out that high altitude is a risk factor for COPD.[56] Therefore, we need to conduct more research to explore the relationship between high altitude and COPD in the future. There are many ethnic minorities in Yunnan province, however this study shows that there is no statistical difference in the prevalence of COPD between Han nationality and ethnic minorities among high-risk population. But Brakema EA et al[57] showed that high COPD prevalence at high altitude, the household air pollution plays an important role in explaining the high prevalence of COPD at high altitude.

Our study has several limitations. Firstly, it is a cross-sectional study, which cannot establish a causal relationship between COPD and its influencing factors. However, the findings of this study are consistent with previous literature. Secondly, individuals with COPD-PS<5 and COPD-SQ<16 were not screened for pulmonary function, which may have resulted in the exclusion of some COPD patients. In future research, a sample from this subgroup will be screened for pulmonary function. Thirdly, air pollution as a vital risk factor for COPD. But our study only collected the information of biofuels used to indirectly and roughly assess the indoor air pollution. Despite the above limitations, our study suggested that it is necessary to carry out early screening, early diagnosis and early treatment of COPD in Yunnan Province. Identifying high-risk groups, carrying out publicity and education, pulmonary function screening and consulting services, and improving individual protection awareness and physical fitness are the keys to COPD prevention and treatment.

Conclusion

Our data indicate that COPD has a high prevalence (27.18%) among the adult high-risk population in Yunnan Province, China. The proportion of severe and very severe COPD patients in Yunnan Province is higher than the national average and other provinces. Male, age, underweight (BMI<18.5kg/m^2), previous smoking, passive smoking, and a history of respiratory system diseases in childhood were significantly associated with an increased risk of COPD. Conversely, high-

altitude residence has been found to be associated with a lower prevalence of COPD. There is no significant difference in COPD prevalence between Han and ethnic minority populations. Smoking is a major preventable risk factor for this disease. Prevention and early detection of COPD should be a public health priority in Yunnan Province to reduce the incidence and mortality rates associated with this disease.

Abbreviations

COPD, Chronic Obstructive Pulmonary Disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; FEV_1, Forced Expiratory Volume in 1 second; FVC, Forced Vital Capacity; OR=Odds Ratio; CI= Confidence Interval; BMI, Body mass index.

Data Sharing Statement

Data generated and/or analyzed during the study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study strictly complies with the Declaration of Helsinki. The study was initiated and led by the First People's Hospital of Yunnan Province and was approved by the Ethics Committee of the First People's Hospital of Yunnan Province (KHLL2022-KY141-C-1). Written informed consent has been obtained from all study participants.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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