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PREVALENCE OF AIRFLOW OBSTRUCTION IN AN APPARENTLY HEALTHY POPULATION SAMPLE: A PRELIMINARY ITALIAN STUDY.

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Letter

Chronic obstructive lung diseases are are characterised by the presence of airflow obstruction. Airflow obstruction (AO) is usually progressive, and may be partially reversible[1]. Types of obstructive lung disease (OLD) include 5 clinical phenotypes were identified: 1) severe and markedly variable airflow obstruction with features of atopic asthma, chronic bronchitis, and emphysema; 2) features of emphysema alone; 3) atopic asthma with eosinophilic airways inflammation, 4) mild airflow obstruction without other dominant phenotypic features and 5) chronic bronchitis in nonsmokers[2]. Spirometry is accepted as the diagnostic test to assess AO and classify the severity of OLD based on the reduction in the pre-bronchodilator (pre-BD) ratio of forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) and FEV1 as percentage of the predicted value. In spite of spirometry standards for diagnosis, a high proportion OLD in the community remains undiagnosed. Our aim was to evaluate the distribution of AO in an apparently healthy general population sample (volunteer blood donors). The authors report a retrospective study. Data were collected from May 2011 to May 2022. All subjects who presented for blood donation to the Associazione Volontari Italiani del Sangue (AVIS) in Milan were eligible. Subjects received a brief questionnaire from the clinic receptionist that determined age, smoking history. They were asked for informed consent to participate. Since the data did not contain personal identifiers, this study was considered exempt from review by an Ethics Committee in accordance with the Declaration of Helsinki. The inclusion criterion was acceptance of participation in the study. Patients excluded were those who did not give informed consent, and with previously diagnosed and treated OLD. Baseline data collection were: questionnaires including questions about smoking, respiratory symptoms and physician-diagnosed respiratory diseases. Spirometry was performed in the practice building by trained research assistants using an office spirometer. Tests were performed according to ERS/ATS criteria[3]. All spirometric tests were reviewed by an independent senior pulmonologist to ensure acceptability.The criterion for prevalence of AO was a baseline pre-bronchodilatador forced expiratory volume in 1s/forced vital capacity (FEV1/FVC) ratio < 0.7, regardless of age, sex, height and ethnicity . Subjects with spirometric defect resulting as pre-bronchodilator FEV1/FVC ratio greater than 0.70 and FVC less than 70% of the predicted value were excluded, although the presence of an OLD cannot be excluded .The following risk factors for AO were analysed: age, sex, body mass index (BMI) and smoking habit. Non-smokers were defined as never smoker, and former- smokers those who had smoked regularly up to 6 months before the study.Results were expressed as mean (SD) for quantitative variables and as percentage for qualitative variables. Quantitative variables were analysed by Student's t-test or Mann-Whitney U-test, and qualitative variables by X^2 or Fisher's test. 4462 subjects (3910 males 87.6% and 552 females 12.4%) were included into the study; 73 were excluded because of reporting previously treated OLD, and 119 due to absence of informed consent. 4270 patients were included and 4258 concluded the study (12 were excluded owing to not acceptable or not reproducible spirometry). The mean age of the subjects was 44.3 ± 13.8 years. A history of smoking was reported in 1687 participants (38.61%) (40.6% former and 59.4 % active smokers) while 2482 were no-smokers (58.29%). Among the active smokers 1548 smoked <20 cigarettes per day (91.76%) and 139 > 20 cigarettes per day (8.24%). One hundred and six subjects had AO (2.48%). Among the subjects with OA, disease severity was mild (FEV1>70% predicted), 14.1%, moderate (FEV1 50-69%) and 9.4% severe (FEV1<50%). Severe AO was found in eleven patients of the total sample. A history of smoking was present in 53% of the subjects with AO and in 38% of those without OA ($p<0.01$). Regarding respiratory comorbidities, allergic rhinitis was found in 503 non-smokers and in 37 smokers subjects. A history of untreated bronchial asthma was present in 15 subjects (14.8%) with AO and in 3%

without AO (p<0.001). However, the two groups were not significantly different in age, gender and BMI. Table 1 summarises the anthropometric characteristics and smoking habit in the study population, stratified by the presence of AO and its severity. Table 2 shows the spirometric measurements stratified by the presence of AO and its severity.Table 3 shows the respiratory comorbidities stratified by the presence of AO and its severity. Among 4258 healthy asymptomatic subjects, we found that prevalence of AO was 2.48%. We found a severe AO in 9.4% of AO subjects, but only in 0.24% of overall sample of asymptomatic subjects. Women represent only the 15.5% of our cohort, but these data match that women are under-represented among blood-donors in Italy. Finally, we have found a lower prevalence than previous reports. Our prevalence of AO (2.5%) differs from that founded in previous similar studies (ranging 7.5% to 22.2%)[4,5]. Also considering only subjects with FEV1 < 80% of predicted, our prevalence of AO (0.8%) is lower than that found by a previous study by Guo Xu (2.6%)[6]. This discrepancy may be due to the fact that our study was performed on a blood-donor population, that is not a random sample of the general population: people with serious health problems usually are not blood-donors, and our sample consisted of relatively young subjects who are assumed to be healthy. Therefore, the prevalence and incidence rates of disease in blood-donors may be lower than in the general population and does not represent the risk levels of the general population. On the other hand, our study highlights that even in a relatively young and apparently healthy population there are subjects with AO. However, the value assigned to screening for OLD requires judgments about the evidence for the benefit of earlier identification balanced against the harms of missed cases, false-positive diagnostic workups, and treatment harms. In conclusion, we agree with current guidelines that an OLD is diagnosed when symptoms are confirmed by appropriate functional tests. However, if such a statement represents the basis of our daily clinical practice, diagnosis may be not so straightforward when the disease is at its initial stage.

All the authors read and approved the final version of the manuscript

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Agata Lax: wrote the paper and analyzed data

performed research/study

Antonello Nicolini and Francesca De Chiara: collected data and analyzed data

Gialuca Ferraioli: collected data and analyzed data

Teresa Diaz de Teran: analyzed data

Paolo Banfi, Elena Compalati,Fagetti Laura, Agata Lax: designed the study

Monica Gonzales: English revision and editing

Paolo Solidoro: analyzed data

All the authors read and approved the final version of the manuscript

Competing interests

Agata Lax, Antonello Nicolini, Paolo Banfi, Gianluca Ferraioli, Teresa Diaz de Teran, Monica Gonzales, Elena Compalati, Laura Fagetti, and Paolo Solidoro report no conflict of interest.

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Table 1 - Anthropometric characteristics and smoking habit of study population stratified by the presence of airway obstruction and its severity.

	Subjects with AO (FEV1/FVC < 0.7)	**Subjects with AO (FEV1/FVC < 0.7) and FEV1 < 80%pred**	**Subjects with AO (FEV1/FVC < 0.7) and FEV1 ≥ 80%pred**	**Subjects without AO (FEV1/FVC ≥ 0.7)**
Age (years), mean + SD	49.0 ± 9.0	50.1 ± 0.5	48.4 ± 9.4	44.2 ± 11.0
Sex, % female	6.3	9.5	4.8	15.7
BMI (kg/m^2), mean + SD	24.8 ± 3.6	25.0 ± 3.8	24.7 ± 3.6	25.1 ± 3.4
Ever smoke, %	62.3	47.6	70.0	44.2

Table 2 - Number and spirometric characteristics of study population stratified by the presence of airway obstruction and its severity.

	Subjects with AO (FEV1/FVC < 0.7)	**Subjects with AO (FEV1/FVC < 0.7) and FEV1 < 80%pred**	**Subjects with AO (FEV1/FVC < 0.7) and FEV1 ≥ 80%pred**	**Subjects without AO (FEV1/FVC ≥ 0.7)**
Subjects, N (%)	106 (2.48%)	64 (1.5%)	42 (0.98%)	4152 (97.52%)
FEV1/FVC, mean + SD	64.9 + 5.5	63.0 + 7.7	65.8 + 3.7	85.5 + 5.7
FEV1 (% predicted), mean + SD	82.0 + 18.4	62.1 + 16.3	91.8 + 9.3	102.4 + 14.8

Table 3 Respiratory comorbidities stratified by the presence of airway obstruction and its severity

	Subjects with AO (FEV1/FVC < 0.7)	**Subjects with AO (FEV1/FVC < 0.7) and FEV1 < 80%pred**	**Subjects with AO (FEV1/FVC < 0.7) and FEV1 ≥ 80%pred**	**Subjects without AO (FEV1/FVC ≥ 0.7)**
Bronchial asthma	11 (16.41%)	5 (7.46%)	6 (8.95%)	56 (83.58%)
Allergic rhinitis	22 (4.37%)	8(1,59%)	14(2.78%)	491 (97.61%)
Chronic bronchitis	73 (4.32%)	21 (1.24%)	52 (3.08%)	1614 (95.67%)