Prevalence and Severity of Chronic Pulmonary Disease and Its Lifestyle Determinants in the Persian Cohort Study Mashhad: A Cohort Study Protocol

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A R T I C L E I N F O	A B S T R A C T
	Introduction: Asthma and Chronic Obstructive Pulmonary Disease (COPD) are prevalent respiratory disorders with significant societal and healthcare impacts. This study will be conducted on the participants of the Persian Cohort study at Mashhad University of Medical Sciences (POCM) to determine the prevalence of asthma and COPD and to explore their relationship with dietary patterns, urban structure, lifestyle, and the severity in Iran. **Methods:** A comprehensive assessment will be employed in this cohort study, including lifestyle factors, dietary patterns, anthropometry, spirometry, depression and stress levels, sleep quality, and physical activity. Individual-level analysis will utilize multivariate logistic regression to assess associations between outcome variables and potential predictors like air quality, smoking, occupation, socioeconomic status, and nutritional status. Adjustments for gender, age, chronic health conditions, and other potential confounders will be incorporated. **Results:** This study will investigate the most closely associated factors influencing the prevalence and severity of asthma and chronic obstructive pulmonary disease. **Conclusions:** The final outcomes will delineate the relationship between the prevalence of asthma and COPD and various lifestyle factors, including socioeconomic status, air pollution, and physical activity.

List of Abbreviations:
COPD: Chronic Obstructive Pulmonary Disease
POCM: PERSIAN Organizational Cohort study in Mashhad University of Medical Sciences
DALYs: Disability-Adjusted Life Years
VC: Vital Capacity
FEV1: forced expiratory volume in one second
FVC : forced Vital Capacity
FFQ: Food Frequency Questionnaire
DASS-21: Depression Anxiety and Stress Scale
PSQI: Pittsburgh Sleep Quality Index
BIA: bioelectrical Impedance Analysis
PA: physical Activity
DASH: Dietary Approaches to Stop Hypertension

Introduction

Presently, chronic lower airway diseases such as Chronic Obstructive Pulmonary Disease (COPD) and asthma rank as the third leading cause of mortality in the United States (1). COPD and asthma are aspiratory illnesses that pose a serious open well-being (2). The common characteristic of asthma and COPD is airway obstruction (3). The airflow obstruction in asthma is episodic and reversible and is characterized by symptoms like chest tightness, wheezing, coughing, and breathlessness. On the other hand, airflow obstruction in COPD is chronic and is diagnosed when there is a recurring chronic productive cough for at least three months in two or more consecutive years. Unlike asthma, airflow obstruction in COPD is not entirely reversible (1).

According to the 2017 Worldwide Burden of Disease Study, the disability-adjusted life years (DALYs) associated with chronic respiratory diseases rose from 97.2 million per year in 1990 to 112.3 million per year in 2017. It was also stated that although DALYs improved over time in patients with asthma, this indicator decreased in COPD. Similarly, global deaths from chronic respiratory diseases increased by 18% over time, reaching 3.91 million in 2017. The average age-standardized yearly death rate (ASMR) for chronic respiratory diseases decreased by 2.41% from 1990 to 2017. In 2017, COPD accounted for 81.7% of all deaths related to chronic respiratory diseases, which represents a 23% increase from 1990 (4). The incidence of asthma has tripled in the last three decades, with the highest rate found in highly developed countries (2). In Iran, Sharifi et al. conducted a cohort study spanning five distinct geographical regions (north, south, west, and east of Iran). The findings disclosed an overall estimated prevalence of COPD at 4.9%. Region-specific prevalence rates were identified as 2.8% in Mashhad, 3.7% in Mazandaran, 8.8% in Ahvaz, 4.1% in Tehran, and 13.9% in Kerman (5). Additionally, the prevalence of asthma in Iran was reported as 8.9% (6). The number of deaths attributed to asthma and COPD in Iran in 2015 was reported to be 6,686 and 8,832, respectively (7).

Asthma and COPD can be detected and distinguished using lung function tests, including post-bronchodilator spirometry, and bronchodilator reversibility testing. Nevertheless, differentiation of chronic asthma with airway alteration from COPD might be challenging. Respiratory functional investigation may include vital capacity (VC), forced expiratory volume in one second (FEV1), and forced vital capacity (FVC). Since airway resistance increases with the severity of the airflow limitation, FEV1 is hypothesized to be able to assess COPD severity. Airflow obstruction is defined as FEV1 below 80% of the predicted value and FEV1:FVC ratio of less than 70% of the predicted value (8). Asthma might be present in more than 40% of patients with COPD (9). Asthma itself has been considered a risk factor for COPD (9). COPD progression and comorbidities increase in patients with consequent asthma (overlap syndrome) (9).

Inherent factors play a role in the development of asthma and COPD in connection with environmental factors. Many environmental factors contribute to asthma and COPD, and some only contribute to asthma or COPD alone. The environmental factors involved in the pathology of asthma and COPD are (10) indoor and outdoor air pollution (for example, exposure to biomass fuel), job-related dangers, infections (10, 11), reduced physical activity, increased psycho-emotional stress (12), low socioeconomic status (13), and unhealthy diet (10, 14). Although previous studies have indicated a correlation between lifestyle behaviors and COPD and asthma, no study has yet evaluated the interactions between modifiable risk factors, including air pollution and lifestyle, and their impact on the risk of developing COPD and asthma. Therefore, this study aims to identify the prevalence of asthma and COPD and to investigate the interaction between modifiable risk factors and COPD and asthma in a cohort study.

Materials and Methods
Study population
This proposed cohort study will be incorporated into the ongoing PERSIAN Cohort study in the Mashhad University of Medical Sciences (POCM) study. The proposal for this study was approved by the Ethics Committee of the Mashhad University of Medical Sciences (Code No: IR.MUMS.MEDICAL.REC.1402.267). The study is based on cohort data, and no new measurements will be collected.

Mashhad, the second-largest city in Iran with a population exceeding 3 million, serves as the initial site within the metropolitan area, showcasing notable distinctions in terms of pathogenic and health determinants. These determinants include migration rates, air pollution, lifestyle diversity, cultural and economic factors; education, and entertainment facilities. As the study aimed to identify the prevalence of asthma and COPD in the POCM population, all participants who were enrolled in the POCM till the initiation of the study will be included taking into account the inclusion and exclusion criteria based on universal sampling. The required data will be obtained from the available POCM data, which includes a total of 12,000 participants. The average age of personnel at the start of the cohort was 39.4±8.9 years, with 44.4% being male.

The inclusion criteria for this study will be being between the ages of 30 and 70 at the time of enrollment, being of Iranian descent, having resided in Mashhad for at least 9 months per year, and not having any plans to relocate within the next 2 years. Informed consent was obtained from the participants prior to their participation in POCM and as this study will be conducted on the recorded data, no informed consent will be obtained from the participants (15).

All assessments and recorded variables in the POCM are presented in Figure 1 and Figure 2, respectively. The questionnaires in this study include demographic parameters, socioeconomic status, lifestyle, sleep and circadian rhythm, and physical activity. The medical questionnaire includes personal and family medical history, and past and current substance abuse (such as smoking, alcohol, and drug use).
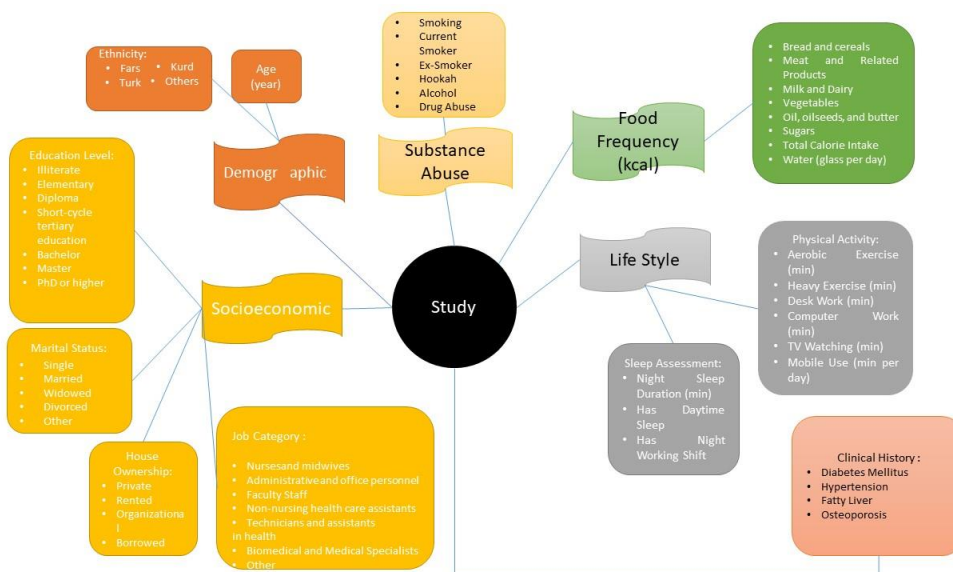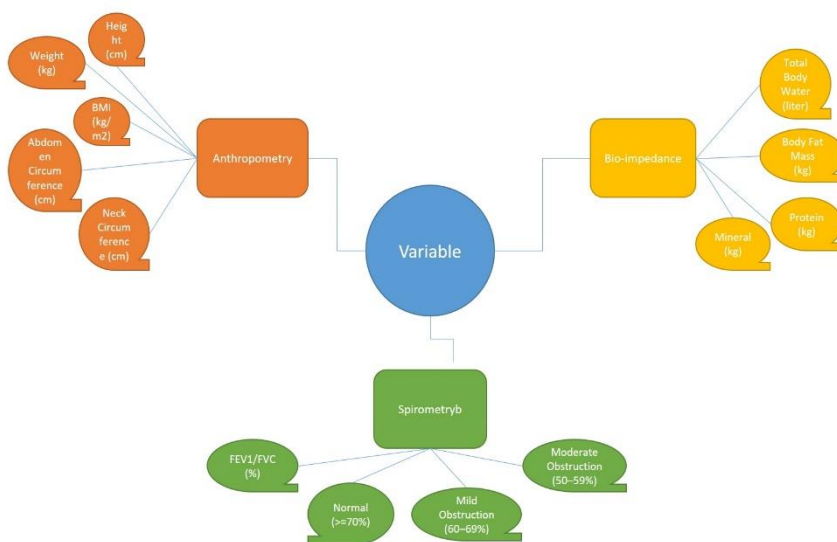
Figure 1. The POCM data collection items

Figure 2. The variables used in the study based on the POCM assessments

Dietary intake information spanning one year will be gathered utilizing the Willett format of the Food Frequency Questionnaire (FFQ). Additionally, data on food preparation and preservation techniques will be collected.

The assessment of depression, anxiety, and stress levels will be conducted through the utilization of the short-form version of the Depression Anxiety and Stress Scale (DASS-21), comprising 21 items (16). The validity of the Persian translation of the questionnaire has been previously examined and endorsed (17).

The Pittsburgh Sleep Quality Index (PSQI) is a self-report questionnaire comprising 19 items, designed to evaluate subjective sleep quality during the preceding month. These 19 items are categorized into seven domains, each assessing distinct aspects of sleep. The aggregate score across these domains classifies respondents as either "good" or "poor" sleepers (18). Farrahi Moghaddam et al. in Iran have verified the validity and reliability of this questionnaire (19). The short form of the International Physical Activity Questionnaire (IPAQ), comprising seven questions (20), has had its validity and reliability affirmed by Baghiani Moghadam et al. in Iran(٢١). Bioelectrical impedance assessment is conducted using the Inbody 770 (Inbody Company, Seoul, South Korea). The measurements of body composition encompass intracellular and extracellular water, total body water, skeletal muscle mass, visceral fat level and area, bone mineral content, body cell mass, basal metabolic rate, whole and segmental phase angle, waist-to-hip ratio, degree of obesity, and weight control indices (15).

To differentiate between asthma and COPD and evaluate the participants' FVC using a spirometer (MIR, Rome, Italy). This spirometer has been validated for research purposes, ensuring its reliability. According to the American Thoracic Society/European Respiratory Society (ATS/ERS) standards, FVC is measured following a specific protocol. 1) maximal inhalation, 2) a forceful exhalation, and 3) continued exhalation until the end of the test (15).

In this study, a personal geographic database will be created to store all geo code data files. The living addresses of chronic respiratory patients will be geocoded. The geo codes will be categorized within the geographic database. Due to patient privacy concerns, the personal data of the patients were accidentally exposed in a breach of 500 records (22).

Study Procedure
This study will evaluate the nutrient intakes of the participants of the POCM over the past year, using FFQ. Additionally, the diagnosis and severity of COPD and asthma will be assessed based on spirometry results. Sleep and mental status, as well as any underlying diseases, will also be recorded using the available data at the time of participation in the POCM. The study will evaluate the relationship between study outcomes and exposure to different dietary patterns in the past year.

Primary Objective
This study aims to comprehensively examine chronic pulmonary diseases in the POCM participants. Objectives include assessing disease prevalence and severity, identifying dietary patterns, understanding the relationship between dietary patterns and the disease, exploring the impact of sleep quality, and evaluating the relationship between physical activity and disease severity.

Secondary Objectives
1) To identify individual, behavioral, and environmental factors and other neighborhood characteristics in the POCM participants
2) To examine the spatial variability of chronic respiratory diseases burden in the POCM participants
3) To evaluate the relationship between depression and anxiety and chronic pulmonary diseases and their severity in the POCM participants.

Funding
As this study will be conducted on the recorded data of the POCM, no funding was granted to this study.

Statistical Analysis
The analysis will incorporate spatial analyses and multivariate regression analyses to examine the relative impact of autonomous hazard variables on chronic pulmonary diseases. Spatial analysis is a form of geographic analysis that seeks to elucidate patterns in human behavior and its spatial manifestation through the application of mathematics and geometry, particularly focusing on locational analysis. Statistical investigation will incorporate exploratory, descriptive, spatial examination,

and multivariate relapse investigation. The spatial examination will include mapping persons and aggregate results at the neighborhood level. To test for spatial autocorrelation within the result measures, Moran's I (worldwide autocorrelation) and the neighborhood marker of Spatial Autocorrelation (LISA) tests will be used. The latter test allows for the decomposition of the worldwide pointer into the commitment of each person's perception. Spatial relapse models will be assessed employing a range of natural, social, financial, behavioral, and well-being indicators (23).

Results

Drawing from the findings of prior studies, there is a hypothesis positing a connection between air pollution and the onset of COPD (24). Moreover, diet and nutrition are speculated to emerge as potential risk factors for both asthma and COPD. Specific dietary habits, such as the intake of refined grains, cured and red meats, desserts, sweets, French fries, and high-fat dairy products, may be pinpointed as risk factors for asthma and COPD (25).

Discussion

The outcomes of this study will contribute to enhancing our comprehension of the impact of non-medical determinants of health on chronic pulmonary diseases, particularly in the realms of health behaviors, living conditions, personal resources, and environmental factors affecting COPD and asthma. These findings can be used for the implementation of community interventions, policy formulation, and the development of public health strategies aimed at reducing chronic pulmonary diseases by improving living conditions and built environments.

In the study titled "Prevalence, Awareness, and Associated Factors of Airflow Obstruction in Russia: The Ural Eye and Medical Study in 2019" conducted by Bikbov et al., the objective was to evaluate the prevalence of airflow obstruction and asthma among individuals aged 40 years and above in a Russian population. The findings indicated a prevalence of 6.8% for airflow obstruction and 2.6% for asthma. Smoking was identified as the predominant risk factor for chronic pulmonary diseases (26).

In the study titled "Patterns of Medical Care Utilization According to Environmental Factors in Asthma and Chronic Obstructive Pulmonary Disease" conducted by Jo et al., the researchers explored the utilization patterns of medical care in individuals with asthma or COPD during the year 2020, with a specific focus on meteorological factors and air pollution. The results revealed that meteorological factors and air pollutants were associated with an increased utilization of medical care among patients with asthma and COPD, particularly among the elderly population. While the overall impact was more pronounced for COPD, the influence on older individuals was greater for asthma. Additionally, the alterations in medical care utilization patterns due to environmental factors varied by gender (27).

The study conducted by Wen et al., entitled "Associations of Adherence to the Dietary Approaches to Stop Hypertension (DASH) Diet and the Mediterranean Diet with Chronic Obstructive Pulmonary Disease among US Adults in 2023," aimed to investigate the correlation between the risk of COPD and adherence to DASH and Mediterranean diets in American adults. The study revealed that a higher adherence score to the Dietary Approaches to Stop Hypertension (DASH) diet was linked to enhanced COPD prevalence, improved lung function, and a reduction in respiratory symptoms (28).

In the 2023 study conducted by Peftoulidou et al., titled "Physical Activity and Quality of Life in Children with Well-Controlled Asthma," the researchers sought to investigate the relationship between lung function, physical activity, and quality of life in children with well-controlled asthma. The findings indicated that a low level of physical activity exhibited a negative correlation with the quality of life among children with well-controlled asthma (29).

Possible limitations of this study will be related to the sources of bias in cohort studies, namely selection bias, information bias, and confusion bias. In order to reduce the risk of these sources of bias the following strategies were implemented in this study. The universal sampling design of this study will eliminate selection bias. As this study will be a retrospective cohort study, there is a possibility of information bias, which is referred to missing data in follow ups. In order to decrease the risk of information bias, participants with missing data will be contacted and the missing data will be obtained from the participants. However, some data including body composition and laboratory tests may not be retrieved for the

past; therefore, there is still the possibility of losing data in this study. Confusion bias might be present in case of the existence of patterns that might mislead the researchers about casualty. This type of bias is mainly seen in terms of age and gender as cohort studies do not randomly include participants of all age groups or equal number of genders. This study will also be at risk for confusion bias. However, the researchers will try to evaluate the relationships using the highest number of possible confounding variables.

Author's Contributions

RR, FDD and AJE designed this study. FDD, AJE and SB conducted the library search, wrote the manuscript, and drafted and edited the manuscript. All authors have read and approved the final manuscript.

Acknowledgements

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