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PhD THESIS

AIRBORNE PARTICULATE MATTER AND CARDIO-PULMONARY RISK

– A B S T R A C T –

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STUDY 1: AIR POLLUTION EXPOSURE—THE (IN)VISIBLE RISK FACTOR FOR RESPIRATORY DISEASES.

CONTEXT

Air pollution represents one of the biggest risk factors for human health. It is an invisible killer that hides around us, influencing both young and old generations. According to the World Health Organization (WHO), each year, 7 million people die due to air pollution. The most affected pathologies are chronic obstructive pulmonary disease, lung cancer, and respiratory infections, including pneumonia, stroke, and heart disease. Nine out of 10 individuals breathe air with polluted compounds, which penetrate deep into the lung tissue, and furthermore in the cardiovascular system. The most exposed individuals are elderly persons, infants, pregnant women, and persons with comorbidities. An estimated 43% of lung diseases and 24% of strokes are attributed to air pollution. We performed an electronic search on PubMed for literature published in the last 5 years, with the last search date on February 15, 2020.

SUMMARY OF FINDINGS

Across the globe, the repercussions of air pollution on human health are garnering heightened attention, given its standing as one of the most formidable threats to global well-being. Astonishingly, a staggering nine out of 10 individuals are exposed to air adulterated with harmful compounds that adversely affect lung tissues. The relationship between air pollution and its health impacts is intricate and multifaceted, and the scientific community continually uncovers new insights and updates on this nexus.

Our comprehensive review was aimed at encapsulating the significance of primary air pollutants and their consequential effects on major respiratory diseases. These maladies encompass chronic obstructive pulmonary disease, asthma, lung cancer, idiopathic pulmonary fibrosis, respiratory infections, bronchiectasis, and tuberculosis. Among the most detrimental air pollutants are sulfur dioxide, nitrogen dioxide, carbon monoxide, volatile organic compounds, ozone, particulate matter, and the smoke emanating from biomass. Our exploration pivoted predominantly on respiratory diseases because of the evident escalation in their incidence attributed to air pollution. The accumulating evidence underscores the undeniable fact that these air contaminants are exacerbating respiratory health issues on a global scale.

In light of these revelations, there is a palpable urgency to bolster and refine policy initiatives addressing air quality. This call to action is not limited to high-income nations alone; it is equally crucial for low-income countries where the ramifications of poor air quality can be even more pronounced due to limited resources and infrastructure. Mitigating the immediate and long-term consequences of air pollution is paramount for safeguarding global public health. As such, continuous efforts must be made to curate and implement stringent air quality standards worldwide.

Table 2. Risk factor analysis for gestational hypertension – adapted from [240].

Authors	Disease	Air pollutant association	Ethnicity/nationality
Liang et al. (2019)	COPD	PM2.5	China
Huang et al. (2019)	COPD	PM2.5	Taiwan
Havet et al. (2019)	Asthma	PM10, O3	France
Cadelis et al. (2014)	Asthma	PM10, PM2.5–10	Caribbean
Akpinar-Elci et al. (2015)	Asthma	PM10, PM2.5–10	Caribbean
Guarnieri and Balmes (2014)	Asthma	PM2.5, PM 10	Meta-analyses
Xing et al. (2019)	Lung cancer	PM2.5, PM10, O3	China
Hamra et al. (2014)	Lung cancer	PM2.5	Meta-analyses
Gharibvand et al. (2017)	Lung cancer	PM2.5	USA, Canada
Wang et al. (2019a)	Lung cancer	PM2.5	China
Winterbottom et al. (2018)	IPF	PM10	USA
Johannson et al. (2018)	IPF	NO2, PM2.5, PM10	USA
Johannson et al. (2014)	IPF	O3, NO2	South Korea
Nsoh et al. (2019)	Respiratory infections	PM2.5	Cameroon
Z. Zhang et al. (2019)	Respiratory infections	PM2.5, PM2.5–PM10	China
Zheng et al. (2017)	Respiratory infections	PM10, NO2, SO2	China
Goeminne et al. (2018)	Bronchiectasis	PM10, NO2	UK
Garcia-Olivé et al. (2018)	Bronchiectasis	SO2	Spain
Popovic et al. (2019)	Tuberculosis	PM2.5	Asia, Europe, North America
Zhu et al. (2018)	Tuberculosis	PM10, NO2, SO2	China
Lai et al. (2016)	Tuberculosis	PM2.5	Taiwan
Jassal et al. (2012)	Tuberculosis	PM2.5	USA
Li et al. (2019)	Tuberculosis	PM2.5	China
Yao et al. (2019)	Tuberculosis	PM2.5, PM10, O3, CO	China

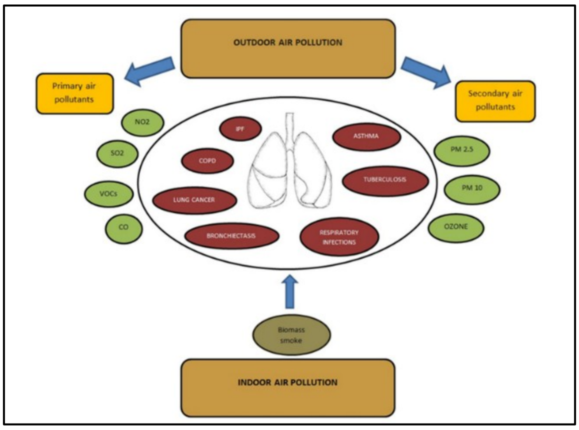

Figure 1 – Presentation of air pollutants and their effects on respiratory health.

CONCLUSIONS

Today, although we know the impact of pollution on the respiratory system, we have tried to describe up-to-date information on how pollution affects the respiratory system and the pathologies associated with it. This depends on the type of pollutant, its concentration in the environment, and its size. Air pollution potentiates the increase in respiratory pathology. It is important to constantly measure the quality of the air, both in developed and less-developed countries to ensure continued improvement. The characteristics of this review refer in particular to the lung diseases caused by air pollutants. The lung is one of the main human organs that have direct contact with the air and is able to filter inhalable pollutants. Lung damage by any other pathology corroborated with inhalable pollutants can later affect other organs and the whole body. For this reason, we considered it of major importance to classify the air pollutants and to present how each pollutant influences lung pathologies and can later affect the whole body.

STUDY 2: A PROSPECTIVE ANALYSIS OF VITAMIN D LEVELS IN PREGNANT WOMEN DIAGNOSED WITH GESTATIONAL HYPERTENSION AFTER SARS-COV-2 INFECTION.

CONTEXT

The composition of air is diversified, and air pollutants can cause negative effects on the respiratory system. Ambient particulate matter (PM) has a complex composition, being divided due to its size: PM 2.5 represents particles with dimensions smaller than 2.5 µm, being more present in gaseous substances, and which are more susceptible to cause respiratory symptoms, while PM 10 has dimensions greater than 10 µm, and thus is found more in dust and has a probability of remaining in the upper respiratory tract. In a meta-analysis conducted by Li et al., it was observed that for a 10 µg/m3 increase in PM 2.5, the number of hospitalizations of COPD patients increased by 3.1%.

Patients exposed to high concentrations of PM 2.5 were associated with the development of COPD, and their short-term exposure to high concentrations was corroborated with an increase in the number of exacerbations and hospitalizations. At the same time, PM 1.0 is not sufficiently studied in the literature. The size of the particles is inversely proportional to the damage they cause to the lungs. The smaller their size, the more harmful they can be to the respiratory system and especially to the lungs. In the United States, there have been several requests for PM 1.0 to be considered a standard environmental risk factor. There were several concerns about whether this is a different risk factor compared to PM 2.5 and whether it could provide additional information on its role and health impairment. Several studies have shown that the origin of PM 1.0 is the same as that of PM 2.5.

The aim of this study was to assess whether frequently exacerbating patients compared to infrequently exacerbating patients live in residences with higher values of air pollution. The reason we chose this comparison is that these patients have a faster decrease in lung function with each exacerbation, generating a very high consumption of financial resources and an increased risk of developing subsequent depression.

RESULTS

In our study comprising 79 individuals diagnosed with COPD, almost half (39 participants) reported experiencing frequent exacerbations. The average age of the participants was 65.49 years, with the majority being male and hailing from urban regions. Notably, there was no significant discrepancy when comparing participants with frequent exacerbations to those with infrequent ones based on general characteristics or the type of cooking source they utilized. However, a clear distinction was observed in relation to the energy type chosen for heating homes, with this difference being statistically significant.

Our analysis of the living conditions indicated varying temperature, humidity, and atmospheric pressure levels within the homes of participants. Specifically, patients with frequent exacerbations had slightly higher average indoor temperatures, albeit this was not statistically significant. Conversely, their homes had marginally lower levels of atmospheric pressure and humidity, though these differences were also deemed non-significant. Diving deeper into air quality parameters, we assessed the average values of PM 1.0, PM 2.5, and PM 10 during the study. While the group with frequent exacerbations consistently had higher values for these pollutants, a significant disparity was solely observed for PM 1.0 levels. By employing logistic regression, we discerned that with each incremental increase in average PM values, the risk of frequent exacerbations rose modestly.

Our subsequent exploration involved establishing potential predictive markers of frequent exacerbations in COPD patients based on particulate matter (PM) levels. The Receiver Operating Characteristic (ROC) curves created for average PM values rendered Areas Under the Curves (AUCs) of 0.673, 0.654, and 0.622 for PM 1.0, PM 2.5, and PM 10, respectively. A subsequent univariate regression analysis highlighted that patients with PM values exceeding established cutoffs in their homes were considerably more susceptible to frequent exacerbations. After making adjustments for variables like age, gender, smoking habits, and comorbidities, the analysis indicated that those exposed to higher PM 2.5 and PM 10 levels in their homes were significantly more likely to report frequent exacerbations.

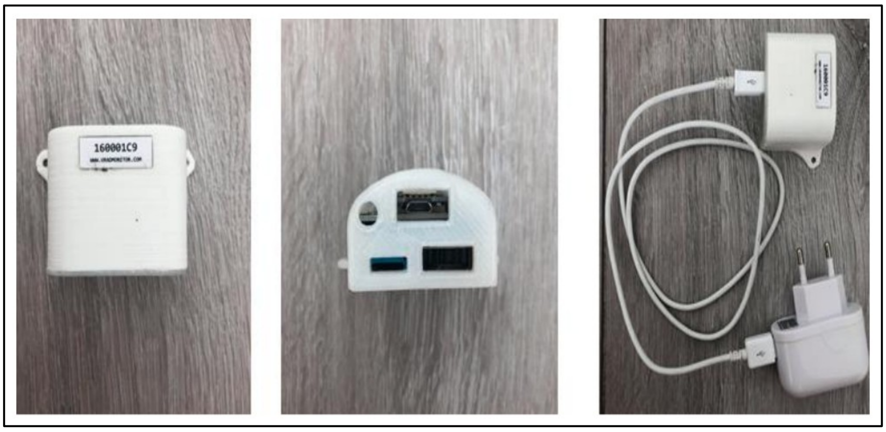

Figure 2 – uRADMonitor SMOGGIE-PM.

CONCLUSIONS

Our research offers illuminating insights into the living conditions of patients diagnosed with COPD, particularly concerning the prevalence of specific micro-particles in their homes. In our cohort of 79 patients, it was evident that those who frequently experienced exacerbations were residing in homes with significantly elevated levels of PM 1.0, PM 2.5, and PM 10 when juxtaposed against their counterparts with infrequent exacerbations. Significantly, to our knowledge, this pioneering study stands as the first of its kind in Romania. What sets this research apart from others is the meticulous approach of monitoring and quantifying microparticles directly within the patients' homes, as opposed to solely evaluating the broader outdoor environment.

While our findings shed light on the probable correlations between indoor air pollution and the frequency of COPD exacerbations, it underscores the overarching need for further exploration in this realm. Managing COPD and enhancing the quality of life of affected individuals demands a deeper comprehension of the myriad factors influencing their health. Thus, subsequent studies are imperative to rigorously assess and quantify the ramifications of air pollution on such susceptible populations. Only through a comprehensive understanding can we pave the way for effective interventions and solutions tailored for these vulnerable patients.

STUDY 3: AIRBORNE PARTICULATE MATTER SIZE AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATIONS: A PROSPECTIVE, RISK-FACTOR ANALYSIS COMPARING GLOBAL INITIATIVE FOR OBSTRUCTIVE LUNG DISEASE 3 AND 4 CATEGORIES.

CONTEXT

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) stratifies COPD patients into four distinct categories, GOLD 1 through GOLD 4, based on the intensity of their airflow limitation determined by spirometry. GOLD 3 and GOLD 4 represent the more severe stages of COPD, marked by a significant reduction in the forced expiratory volume in one second (FEV1). Such classification aids in devising specific interventions and management techniques, especially targeting the frequent exacerbations typical of these advanced COPD stages. Crucial tools, like the COPD Assessment Test (CAT) and the Modified British Medical Research Council (mMRC) dyspnea scale, are indispensable for comprehending exacerbation patterns within these categories. While CAT gauges the overall health status of COPD patients, the mMRC dyspnea scale assesses the severity and frequency of breathlessness they experience.

Air pollution, especially from particulates like PM 1.0, PM 2.5, and PM 10, significantly impacts COPD patients. These particles, mainly arising from combustion processes like vehicle emissions and industrial activities, vary in their ability to infiltrate the respiratory system. The geographical positioning of individuals, particularly their closeness to high-traffic and industrial zones, has been linked with the severity of COPD exacerbations. While extensive research exists on air pollution's effects on respiratory health, a more specific analysis exploring the interplay between airborne particle size and COPD exacerbations, particularly within GOLD 3 and GOLD 4 stages, is lacking. This study aims to bridge this gap, hypothesizing a strong link between particle size and exacerbation frequency in advanced-stage COPD patients. It further surmises that living near main roads and industrial areas exacerbates the risk. By quantifying these relationships, this research seeks to pave the path for targeted interventions and a more profound understanding of managing COPD.

RESULTS

The current research observed a total of 79 patients, distinguishing them based on the GOLD 3 category (n = 47) and the GOLD 4 COPD severity (n = 32). The average age was marginally higher in the GOLD 3 group compared to the GOLD 4. However, no statistical significance was found regarding age difference or male population distribution between the two groups. Both groups also showed similar education levels and smoking status. When assessing daily activity, a greater percentage of GOLD 4 individuals were less active than those in the GOLD 3 category. Signs and symptoms like cough, phlegm production, and dyspnea were prevalent in both groups without any notable statistical differences. Nonetheless, significant disparities were found in BMI distributions and the occurrence of specific comorbidities between the categories.

Regarding living conditions, a significant number of GOLD 3 patients resided in urban areas compared to the GOLD 4 group. The GOLD 3 group, on average, had a considerably larger living area than the GOLD 4 group. The proximity of the residences to main roads also differed significantly; the GOLD 3 group lived considerably farther from main roads than the GOLD 4 group. Building heights remained consistent for both groups, while sources for cooking and heating showed a significant difference, especially concerning gas usage for heating.

Airborne particulate matter was also assessed, and there were marked differences in concentrations between the two groups. GOLD 4 individuals showed higher values in PM 1.0, PM 2.5, and PM 10 concentrations than the GOLD 3 group. However, environmental parameters like temperature, humidity, and atmospheric pressure measurements within the homes displayed no significant differences between the two groups. Analysis also indicated a higher percentage of GOLD 4 individuals experiencing frequent exacerbations and using oxygen supplementation, but these differences were not statistically significant.

The study's lung function examinations revealed pronounced differences in spirometry parameters between the two groups. GOLD 4 patients exhibited a significant decrease in various spirometry measures, indicating a marked decline in lung function compared to the GOLD 3 category. COPD assessment scores, like CAT scores and mMRC, were marginally higher in the GOLD 4 group, hinting at potentially worse quality of life and higher disability level, although these were not statistically significant. In other assessments, no significant disparities were observed in systolic and diastolic blood pressure, creatinine, and glucose levels between the groups. However, blood urea nitrogen (BUN) levels did present a notable difference.

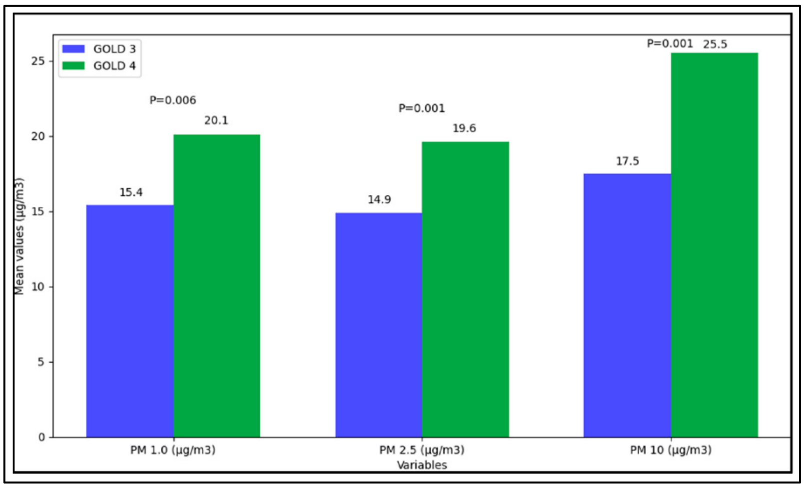

Figure 3 – Home air measurements stratified by COPD severity.

CONCLUSIONS

This study provides initial insights into factors that may influence the severity of COPD in patients classified as GOLD 3 and GOLD 4. Notably, we observed a potential connection between higher concentrations of PM and increased COPD severity in GOLD 4 individuals, hinting at an environmental link. Living closer to heavy traffic areas appeared to exacerbate symptoms, while larger living spaces seemed to offer some protection. However, it's crucial to approach these findings cautiously due to our limited sample size, emphasizing the need for more extensive studies with larger participant groups to confirm these preliminary observations. Further research in this area is necessary to establish more robust causal relationships and implications for clinical management and public health interventions.