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Enzymatic Activity and Oxidant Stress in Pleural Fluid and PM2.5 in Patients from the Metropolitan Area of the Valley Of Mexico

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Abstract - Pleural fluid plays a crucial role in maintaining pulmonary health. Diseases like pneumonia, congestive heart failure, and cancer can lead to pleural effusion, where excessive fluid accumulates. This fluid, normally devoid of severe inflammation or infection, can become complicated in such cases. Epidemiological studies have consistently linked airborne particulate matter (PM), particularly PM2.5, to increased morbidity and mortality due to its ability to induce oxidative stress and inflammation upon inhalation. In this study, we evaluated the enzymatic activity and oxidative stress in pleural fluid and their relationship with exposure to particulate matter in patients with respiratory diseases from the Metropolitan area of the Valley of Mexico. The study was conducted in a third-level hospital specialized in respiratory diseases and focused on adults residing in the metropolitan area who required hospitalization due to respiratory conditions, including lung cancer, that required thoracocentesis. Air quality data from nearby monitors were used to assess PM2.5 exposure.
The results revealed a negative linear relationship between methylglyoxal and PM2.5 exposure before four days of the hospital admission, while gamma-glutamyl transpeptidase and arginase exhibited non-linear relationships, decreasing at low PM2.5 concentrations and increasing at high concentrations. Myeloperoxidase and catalase activity increased three and five days before the hospital admission, and malondialdehyde levels rose consistently with PM2.5 concentrations. These findings support the notion that increased exposure to particulate matter correlates with heightened toxicological effects, likely due to the initiation of oxidoreductive reactions in the respiratory tract, leading to inflammation and oxidative stress.

***Keywords*:** PM2.5, air pollution, pleural fluid, enzymatic activity, oxidative stress

1. Introduction

Pleural fluid mainly originates from the pleural capillaries of the parietal pleura, lymphatic vessels, intrathoracic blood vessels, lung space, and peritoneal cavity. Among its constituent substances are alpha-amylase, glucose, cholesterol, creatinine, bilirubin, hyaluronic acid, enzymes such as lysozyme, lactate dehydrogenase, and triglycerides [1]. When a disease such as pneumonia and congestive heart failure develops, pleural fluid accumulates excessively, and pleural effusion (PD) may occur. Uncomplicated pleural effusion is free of severe inflammation or infection, while complicated PD involves significant inflammation or infection. PD may contain proteins that originate from plasma filtrate released during inflammation, mainly in cancer [1]. There are specific criteria, such as biochemical parameters, for classifying and diagnosing the cause of pleural effusions. In toxicological and occupational studies, pleural fluid effusion is used to evaluate the condition of the lung microenvironment [2,3]; In a population-based case-control study, a greater risk of developing lung cancer was identified in patients who presented high concentrations of particulate matter (PM2.5) in pleural fluid.[4]. It is well known that an association has been demonstrated between airborne pollutants, especially PM2.5, and an increased risk of morbidity and mortality [5]. The processes by which PM2.5 produces these adverse effects are still unclear; however, they

could derive from oxidoreductive reactions that increase the inflammatory process and oxidative stress. In Mexico, air pollution, mainly associated with PM2.5 particulate matter, represents one of the most pressing challenges in terms of air quality; as urbanization and industrialization continue to expand, concentrations of pollutants, especially PM2.5, have reached worrying levels in numerous cities in the country, especially in metropolitan areas such as Mexico City and the Valley of Mexico (ZMVM). In 2023, 88 (24.1%) days were considered as clean air, 96.1% of the days exceeded the permissible values (41 μg/m^3) of PM2.5 in the ZMVM, according to the data reported for the total of the criteria pollutants evaluated [7]. For this reason, this study aimed to evaluate the relationship between markers of enzymatic activity and oxidative stress in pleural fluid of patients with respiratory disease and its relationship with particulate matter exposure in the Metropolitan Area of the Valley of Mexico.

2. Metodology

This study was carried out at the Instituto Nacional de Enfermedades Respiratorias Ismael Cosío Villegas, a third-level hospital whose scope of competence is the entire national territory. For this study, only adults residing in the Metropolitan Zone of the Valley of Mexico (ZMVM) were included, who required hospitalization for different conditions, including lung cancer, and who also required thoracocentesis. Each patient was georeferenced to locate his home and be able to assign the air quality monitor closest to the home from the Air Quality Monitoring System of Valley of Mexico (RAMA). In this way, the exposure to PM2.5 for each participant was estimated as the concentration corresponding to the 24-hour average from the assigned monitor and reflecting the exposure from one to 6 days before hospitalization. Pleural fluid (PF) samples were obtained and centrifuged at 1500 rpm for 5 min. The aqueous phase was transferred to 1.5 mL Eppendorf tubes for handling and frozen at -70°C until analysis of the following biological markers was performed: methylglyoxal (MGO), advanced oxidation proteins products (AOPPs), malondialdehyde (MDA). Total glutathione S transferase (GST), arginase (ARG). gamma-glutamyl transpeptidase (GGT), myeloperoxidase (MPO) and catalase (CAT) activity were also measured.

Statistical analysis was performed by summarizing the information using central tendency and dispersion measures and classifying patient's characteristics by diagnosis. Linear regression models were performed to evaluate the relationship between markers of enzyme activity and oxidative stress in the pleural fluid with the PM2.5 concentration 24 hours before the day of the hospital admission and up to 6 days before.

2. Results and Discussion

During the days evaluated, particulate matter concentrations varied from 3 to 55 ug/m^3. Regarding the relationship between exposure to particulate matter and each parameter, a decrease in MGO per unit increase in PM2.5 was found 4 days before the hospital admission, a non-linear relationship between GGT and PM2.5 exposure and ARG and PM2.5 5 days before the hospital admission, these non-linear relationships showed a decrease in activity at low concentrations and an increase at high concentrations of PM2.5 (>11 ug/m3) of each GGT and ARG, respectively. An increase in MPO and CAT activity was found on days 4 and 6 before the hospital admission, and an increase in MDA was consistent with a higher PM2.5 concentration from day one to day 4 before the hospital admission. (Table 1).

Table 1: Relationship between enzyme activity and oxidative stress in pleural fluid and PM2.5.

Parameter	$PM_{2.5}$	□ (coefficient)	(IC)95%		p-value
			Min	Max	
Methylglyoxal, mM (MGO)	Lag 5	-0.0228	-0.0418	-0.0038	0.02
Total Glutathione S transferase activity, nmol/min/mg protein (GST)	Lag 6	-0.0050	-0.0244	0.0144	0.605
Advanced Oxidation Protein Product, mM/mg of protein (AOPPs)	Lag 5	-0.0128	-0.0539	0.0283	0.534

Gamma Glutamyl transpeptidase activity, U/mg of protein (GGT)	Lag 4	0.0169	-0.0102	0.0439	0.217
All	Lag 5	0.0308	-0.0010	0.0627	0.058
At PM2.5<11ug/m3	Lag 5	-0.4888	-1.0197	0.0421	0.066
At PM2.5>11ug/m3	Lag 5	0.0616	0.0270	0.0961	0.001
	Nonlinear (Quadratic equation Lag 5)	-0.1815	0.3248	0.3825	0.014
		0-005	0.0084	0.0017	0.004
Arginase activity, mg of Urea/mg of total protein (ARG)	Lag 6	0.0393	0.0097	0.0689	0.01
	Lag 5	0.0093	-0.0027	0.0213	0.127
	Nonlinear (Quadratic equation Lag 5)	-0.1736	-0.3047	-0.0425	0.01
		0.0051	0.0020	0.0081	0.002
	Nonlinear (Quadratic equation Lag 6)	-0.0791	-0.1556	-0.0027	0.043
		0.0020	0.0002	0.0038	0.034
Myeloperoxidase activity, in arbitrary U/mg of protein (MPO)	Lag 4	0.0194	-0.0031	0.0420	0.089
Catalase activity, U/mg protein (CAT)	Lag 6	0.0507	0.0093	0.0921	0.019
Malondialdehyde, mM (MDA)	Lag 1	0.0178	-0.0014	0.0370	0.069
	Lag 2	0.0132	-0.0042	0.0306	0.135
	Lag 3	0.0152	-0.0037	0.0340	0.113
	Lag 4	0.0131	-0.0022	0.0283	0.092
	Lag 5	0.0210	0.0023	0.0397	0.028
	Lag 6	0.0097	-0.0058	0.0252	0.216

4. Conclusion

Despite the cross-sectional limitation of the study, our results coincide with the hypothesis that the greater the exposure to particulate matter, the greater the toxicological effect, since when it enters either in the form of heavy metals, black carbon or another. The respiratory tract may be involved in oxidoreductive reactions that increase the inflammatory process and oxidative stress, thus causing greater damage.

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