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Meteorology

Influence of environmental variables on functional capacity in patients with lung disease

Influência de variáveis ambientais na capacidade funcional em pacientes com doença pulmonar

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ABSTRACT

Air pollution is related to negative impacts mainly on people with Chronic Respiratory Diseases (CRD), reflecting on respiratory health, reduced physical performance and so on. The objective was to investigate the influence of meteorological and air quality variables on the functional capacity of patients with CRD. This was a descriptive, retrospective and cross-sectional study of information collection in a database from 2016 to 2019. For the analysis of environmental variables, three different databases were used, one from the automatic air quality monitoring station in Novo Hamburgo, and the weather stations of Novo Hamburgo and Campo Bom (RS). The monitored data were: NO_2, CO, O_3, PM_{10}, $PM_{2,5}$, average temperature, minimum temperature, maximum temperature, precipitation, average wind speed and relative humidity. The sample consisted of 85 individuals from the Pulmonary Rehabilitation Program (PRP), where the variables spirometry and six-minute walk test (6MWT) were collected. It was observed that the higher the concentration of PM_{10} and the higher the minimum temperature, the lower the spirometric results. Furthermore, the greater the concentration of $PM_{2.5}$, the shorter the distance that the individual travels. A relationship was found between environmental data and functional tests, where individuals with CRD are more sensitive to high levels of air pollutants, as well as to lower temperatures.

Keywords: Air Pollution; Chronic obstructive pulmonary disease; Air quality; Walking test; Spirometry

RESUMO

A poluição do ar está relacionada a impactos negativos principalmente em pessoas com Doenças Respiratórias Crônicas (DRC), refletindo na saúde respiratória, redução do desempenho físico e etc. O objetivo foi investigar a influência de variáveis meteorológicas e de qualidade do ar na capacidade funcional de pacientes com DRC. Tratou-se de um estudo descritivo, retrospectivo e transversal de coleta de informações em banco de dados de 2016 a 2019. Para a análise das variáveis ambientais, foram utilizadas três bases de dados distintas, uma da estação de monitoramento automático da qualidade do ar em Novo Hamburgo, e as estações meteorológicas de Novo Hamburgo e Campo Bom (RS). Os dados monitorados foram: NO_2, CO, O_3, MP_{10}, $MP_{2,5}$, temperatura média, temperatura mínima, temperatura máxima, precipitação, velocidade média do vento e umidade relativa do ar. A amostra foi composta por 85 indivíduos do Programa de Reabilitação Pulmonar (PRP), onde foram coletadas as variáveis espirometria e teste de caminhada de seis minutos (TC6'). Observou-se que quanto maior a concentração de MP_{10} e maior a temperatura mínima, menores os resultados espirométricos. Além disso, quanto maior a concentração de $MP_{2,5}$, menor é a distância que o indivíduo percorreu. Foi encontrada uma relação entre dados ambientais e testes funcionais, onde indivíduos com DRC são mais sensíveis a níveis elevados de poluentes atmosféricos, bem como a temperaturas mais baixas.

Palavras-chave: Poluição do ar; Doença pulmonar obstrutiva crônica; Qualidade do ar; Teste de caminhada; Espirometria

1 INTRODUCTION

Air pollution easily found in large urban centers is responsible for 7 million premature deaths annually, contributing to the development of various diseases, including respiratory and cardiovascular diseases and infections (OPAS; OMS, 2018). Health and the environment have been objects of study due to their interrelationship, interdependence and direct or indirect influence on the quality of life of human beings. In general, the main pollutants that interfere with human health are: Particulate Matter (PM), Ozone (O_3), Nitrogen Dioxide (NO_2), Sulfur Dioxide (SO_2) and Carbon Monoxide (CO) (WHO, 2006). These pollutants are able to cause changes in exercise capacity, lung function, increase in morbidity and mortality, incidence and prevalence of Chronic Respiratory Disease (CRD), increase in respiratory symptoms and changes in physiological functions, accentuating in more sensitive individuals, such as individuals elderly, especially CRD patients (KÜNZLI *et al*., 2010; SINHARAY *et al*., 2018; VIEIRA *et al*., 2016).

Individuals with Chronic Obstructive Pulmonary Disease (COPD) are more vulnerable to increased levels of pollutants in the atmosphere, being affected even when the pollutants are within the limits established by legislation (GOLD, 2020; GREEN; SÁNCHEZ, 2013; MORAES *et al*., 2010). Exposure to these pollutants increases oxidative stress and inflammatory processes, providing an increase in respiratory symptoms, thus aggravating their disease (BROOK *et al*., 2010; WU *et al*., 2016).

Currently the disease is the fourth leading cause of death worldwide; more than 3 million people died of COPD in 2012. Its incidence in Brazil is high, its morbidity and mortality and complications are very representative and its incidence increases with the aging of the population and exposure to risk factors, becoming a challenge for public health (GOLD, 2020; MOREIRA *et al*., 2015).

In addition, air pollution causes effects on meteorological conditions, with the climate and its various weather conditions, such as variations in temperature, humidity, wind direction and precipitation, directly influenced by this pollution, which can generate aggravations of diseases, mainly respiratory, causing harmful effects to human health (NOBRE *et al*., 2010). Air quality and meteorological variables are closely linked to the walking ability of these individuals (BOS *et al*., 2013). High concentrations of $PM_{2.5}$ can reduce the exercise tolerance of exposed people, adding to this fact the increase in O_3 and CO that can increase respiratory symptoms (GILES; KOEHLE, 2014; VIEIRA *et al*., 2016). The aim of the study was to investigate the influence between meteorological variables and air quality on the functional capacity of patients with COPD.

2 METHODS

2.1 Study design, participants, and data collection

This was a historic cohort study cross-sectional, observational, descriptive study of all analyzed variables, retrospective, where all information were previously collected in different databases. The study area was the city of Novo Hamburgo, located in the state of Rio Grande do Sul, Brazil.

The sample was for convenience and consisted of 85 individuals of both sexes who were in the database of the Pulmonary Rehabilitation Program (PRP) at a university in Vale do Sinos from 2016 to 2019, who met the following inclusion criteria: have the complete clinical profile, which corresponds to the personal data of the participants, in addition to the clinical history of the disease, present spirometry and the six-minute walk test (6MWT). Exclusion criteria were patients who did not present some of the tests mentioned above, or who did not have the complete clinical profile.

2.2 Environmental data

For the collection of environmental data, the database previously generated by the Automatic Air Quality Monitoring Station in the city of Novo Hamburgo, from 2016 to 2019, was used. Measurements of concentrations of these pollutants were collected through daily averages, totaling 63 days analyzed. The station monitors the following pollutants: nitrogen dioxide (NO_2), carbon monoxide (CO), ozone (O_3), in addition to particulate matter concentrations less than 10μm (PM_{10}) and less than 2.5μm ($PM_{2.5}$).

The measurement method for NOx is based on the chemiluminescent energy emitted in the reaction between NO and O_3 in a vacuum chamber, generating NO_2 molecules, the light energy is converted into an electrical signal, which is subsequently quantified (LACAVA, 2003). CO collection was performed by an infrared correlation filter based on the absorption of infrared radiation, with a wavelength of 4.50 to 4.90 μm, this method differentiates the absorption of CO from other gases; the difference between these absorption signals is divided by the intensity of the radiation source in which the CO concentration is generated (LACAVA, 2003). As for the O_3 pollutant, the measurement principle is based on ultraviolet spectrophotometry at a wavelength of 254 nm, where its concentration is calculated from the absorption of ultraviolet radiation (LACAVA, 2003). For the PM collection, a dichotomous analyzer was used, which performs the inertial separation of the particles through the segregation of the sampling flow, dividing these particles into 900 L min-1 for fine particles and 100 L min-1 for coarse particles. The PM fragments were captured on Millipore 47 mm diameter and 0.5

μm porosity Fluorophore (PTFE) membrane filters; all were weighed previously. The PM analyzes were conducted at the Clean Technologies Center of a university in Vale do Sinos.

The evaluated parameters were compared with world legislation. For CO pollutant, the WHO legislation does not stipulate daily limits. For this reason, it was used the Institute of Energy and Environment (IEE) of 2012, in which several countries were identified that adopt daily standards, the most restrictive value being 8000 μg/m³ (8 mg/m³) in 24 hours. For the O_3 pollutant, the IEE (2012) was also used, with the maximum desirable value being 30 μg/m³ in 24 hours. For the NO_2 pollutant, the IEE (2012) standards were used, with the most restrictive value being 80μg/m³ in 24 hours. PM_{10} was compared with the legislation of the World Health Organization (WHO) of 2005, where the legislation foresees desirable values of up to 50μg/m³, as well as $PM_{2.5}$ with concentrations up to 25μg/m³ (IEMA, 2012; WHO, 2005).

To obtain the meteorological data, the database for the period from 2016 to 2019 was used, provided by the National Institute of Meteorology (INMET), through the meteorological station in Campo Bom/RS - A884, code OMM 86991 and data generated from the meteorological station located in a university in Vale do Sinos, of the Davis brand. The weather station has specific sensors to measure and record abiotic data, among others. Measurements are constantly taken and recorded; these results can be viewed through the station's console or by a station connection with a computer. The frequency of data generated is 24 hours, shown through a monthly table. The meteorological parameters evaluated in this study were: average temperature (°C), minimum temperature (°C), maximum temperature (°C), precipitation (mm), average wind speed (Km/h) and relative air humidity (%), totaling 85 days of collections.

2.3 Six-minute walk test

The 6MWT was performed according to the guidelines of the American Thoracic Society (ATS, 2002). The 6MWT data collection was from a database from the Pulmonary Rehabilitation Project (PRP) of a university in Vale do Sinos, from 2016 to 2019, totaling 85 tests. The 6MWT is a submaximal test used to assess the cardiorespiratory and metabolic endurance of various pathologies, including COPD. It was held at the university, outdoors, in a 30-metre, flat corridor, with distances previously marked every three meters and the beginning and end of the route. The variables analyzed in the 6MWT were the date, the distance covered during the course, Heart Rate (HR), Peripheral Oxygen Saturation (SpO_2), subjective feeling of shortness of breath and Subjective Perception of Exertion (SPE) assessed using the scale modified from BORG. To calculate the predicted distance covered according to age and gender, the reference equation by Iwama *et al*., (2009) was used (ATS, 2002; IWAMA *et al*., 2009).

2.4 Pulmonary function test

The collection of pulmonary function test variables was performed from the university's PRP database. The variables analyzed were the Forced Vital Capacity (FVC), the Forced Expiratory Volume in the first second (FEV_1) and the relationship between these two parameters (FEV_1/FVC), also called the Tiffeneau index (GOLD, 2020; PEREIRA, 2002). The test was performed according to the Guidelines for Pulmonary Function Testing (PEREIRA, 2002).

2.5 Ethical aspects

The project entitled “Validation of an assessment and rehabilitation protocol for patients with COPD” was approved by the Research Ethics Committee number CAAE 50281115.4.0000.5348, in which it is recommended, in the use of data collection, the total commitment of the researcher to maintain the integrity of the participants.

2.6 Statistical analysis

To assess the relationship between environmental data and functional tests, data were initially collected in separate databases, organized and tabulated in Microsoft Excel® version 365 ProPlus software spreadsheets. After this step, descriptive statistics were used through absolute (n) and relative (%) frequencies; data were expressed as median and interquartile range. To perform the inferential statistics, the database was exported to the Statistical Package for Social Sciences (SPSS) version 25.0 software. To test the assumption of normality of the variables involved in the study, the Kolmogorov-Smirnov test was applied; the variables did not show normal distribution. Thus, non-parametric tests were applied, accepting a significance level of $p \leq 0.05$, with a 95% confidence interval. To assess the association of environmental data with functional variables, the linear regression test was used, with the stepwise selection method.

3 RESULTS AND DISCUSSION

3.1 Patient characteristics

Eighty-five patients participated in this study, 55.3% male and 44.7% female. Data were expressed as median and interquartile range; the median age was 65 (60.50-70.00) years. The predominant clinical diagnosis was COPD in 76.47% of the sample, followed by asthma and pulmonary fibrosis with 4.70% each; sarcoidosis with 1.17% and 12.94% had no medical diagnosis. Regarding lung function, the median of the Tiffeneau Index (FEV1/FVC) 55 (38.00-74.50) % was found, which associated with the FEV1% 44 (30.50-63.00) % characterized the sample as severe COPD according to the GOLD 2020 guidelines (Table 1).

Table 1 – Characterization of participants and daily average environmental variables

Variable	**Minimum**	**Maximum**	**Average**	**Median**	**Standard deviation**	**Interquartile range (25-75)**
Age (years)	28	86	64,32	65	9,54	60,50-70,00
Stature (m)	1	2	1,64	1,65	0,09	1,56-1,72
Weight (kg)	45	118	71,76	69	15,36	62,25-81,00
BMI	18	42	26,55	25,96	5,10	22,49-30,42
FVC (l)	1,04	4,88	2,63	2,67	0,82	1,93-3,16
FVC (%)	4,60	127	72,74	70	24,03	55,0-88,50
FEV_1 (l)	0,57	4,07	1,45	1,26	0,71	0,87-1,90
FEV_1 (%)	2	120	48,55	44	24,20	30,50-63,00
FEV_1/FVC	26	90	55,80	55	18,85	38,00-74,50
Travelled distance (m)	100	686	413,55	407,50	98,99	347-479
HR basal (bpm)	50	123	83	82,00	15	73-93
HR post test (bpm)	54	149	95	93,00	18	81-108
SpO_2 basal (%)	86	100	96	97,00	3	94-98
SpO_2 post test (%)	81	100	95	96,00	4	93-98
Dyspnea basal	0	3	1	1	1	0,5-2,0
Dyspnea post teste	0	7	3	3	2	1,25-4,0
SPE basal	0	4	1	1	1	0,25-3,0
SPE post test	0	7	3	3	2	1,0-4,0
EDT (m)	482,16	632,27	537,73	547,36	34,63	504,31-565,82
EDT (%)	19,90	129,50	76,70	76,19	16,60	65,13-86,97
NO_2 (µg/m³)	0,00	317,58	27,42	24,26	51,60	0,00-36,06
CO (ppm)	0,02	11,25	0,56	0,32	1,42	0,15-0,55
CO (µg/m³)	0,00	12895,50	514,36	366,72	1548,97	171,90-630,30
O_3 (µg/m³)	13,69	72,40	41,49	42,26	17,09	27,34-55,04
PM_{10} (µg/m³)	8,17	188,60	56,76	44,60	41,49	25,47-70,52
$PM_{2.5}$ (µg/m³)	4,86	65,91	18,24	13,55	14,51	8,78-21,91
Average Temperature (ºC)	8,30	26,40	19,98	20,98	4,23	17,61-22,95
Maximum Temperature (ºC)	10,80	35,40	25,82	26,40	5,47	23,15-29,80
Minimum Temperature (ºC)	6,20	23,00	15,60	16,00	4,38	12,55-18,95
Precipitation (mm)	0,00	79,90	5,43	0,00	13,22	0,00-3,30
AWS (km/h)	0,50	13,80	4,06	3,67	2,52	2,70-4,75
Relative humidity (%)	60,20	91,90	75,81	75,10	7,93	69,90-81,75

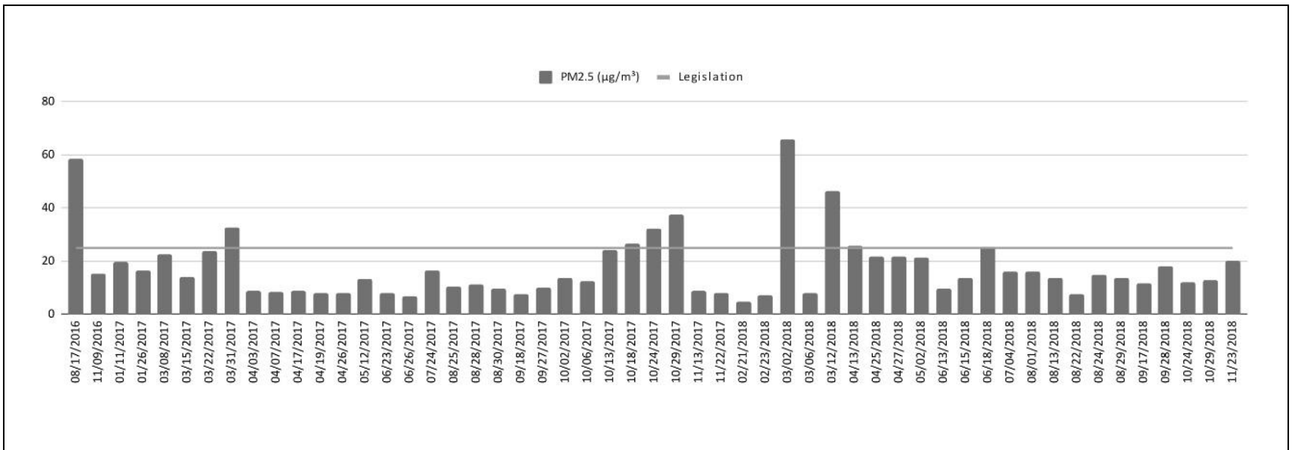
Source: Author's (2021)
Subtitle: BMI: Body Mass Index. FVC: Forced Vital Capacity. FEV_1: Forced Expiratory Volume in the first second. FEV_1/FVC: Tiffeneau Index. HR: Heart Rate. SpO_2: Peripheral Oxygen Saturation. SPE: Subjective Perception of Exertion. EDT: Estimated Distance Traveled. NO_2: nitrogen dioxide. CO: carbon monoxide. O_3: ozone. PM_{10}: Particulate Matter of a diameter of less than 10µm. $PM_{2.5}$: Particulate Matter of a diameter of less than 2.5µm. AWS: Average Wind Speed
Note: For the assessment of Fatigue for Lower Limb and Dyspnea, the BORG Scale was used. Values in bold are above the limits established by the WHO (2005) and IEE (2012) legislation

The participants obtained an median of the distance covered in the 6MWT' of 407.50 (347.00-479.00) meters; as predicted distance covered considering age and gender, an median of 547.36 (504.31-565.82) meters was found, reaching 76.19 (65.13-86.97) % of the expected; the median baseline HR, that is, before the physical test was 82 (73-93) bpm and after the test it was 93 (81-108) bpm; the median baseline peripheral oxygen saturation was 97 (94-98) % and post-test 96 (93-98) %; the subjective sensation of shortness of breath as well as SPE was measured by the modified BORG scale where initial dyspnea of 1 (0.5-2) very mild was referred to, and final dyspnea of 3 (1.25-4.0) moderate , as well as for SPE, initially obtained 1 (0.25-3) very mild and 3 (1-4) moderate at the end of the test. These results can be seen in Table 1.

3.2 Environmental and abiotic data

Several pollutants were evaluated, and their values can be seen in Table 2 below. It can be seen that in 9 days the levels of $PM_{2.5}$ exceeded the values established by the WHO, remaining above 25μg/m³ (Graph 1).

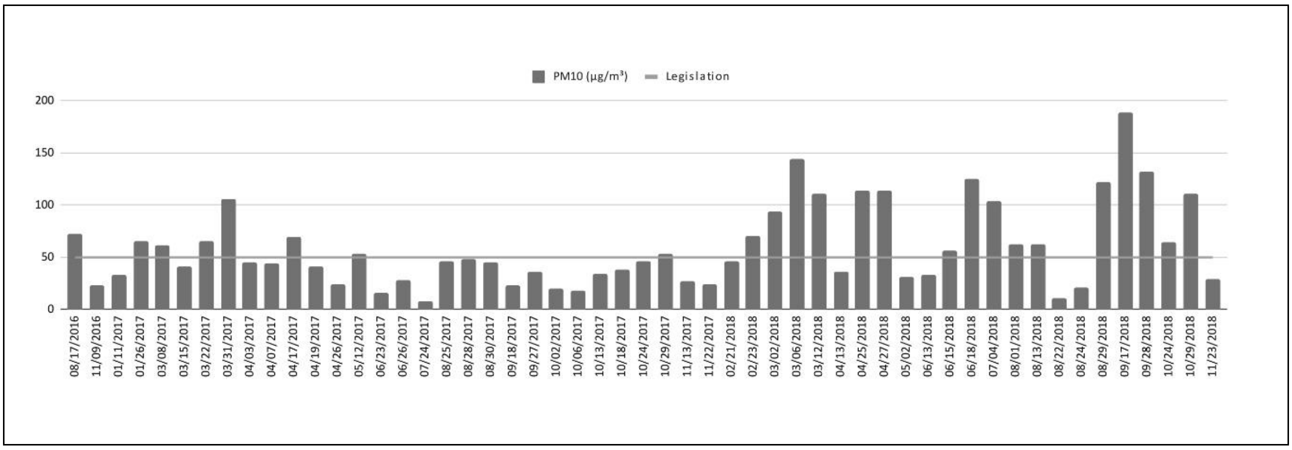
Graph 1 – Concentrations of $PM_{2.5}$ (μg/m³)



Source: Author's (2021)

The pollutant PM_{10} exceeded the limits established in 24 days analyzed, remaining above 50μg/m³ (Graph 2).

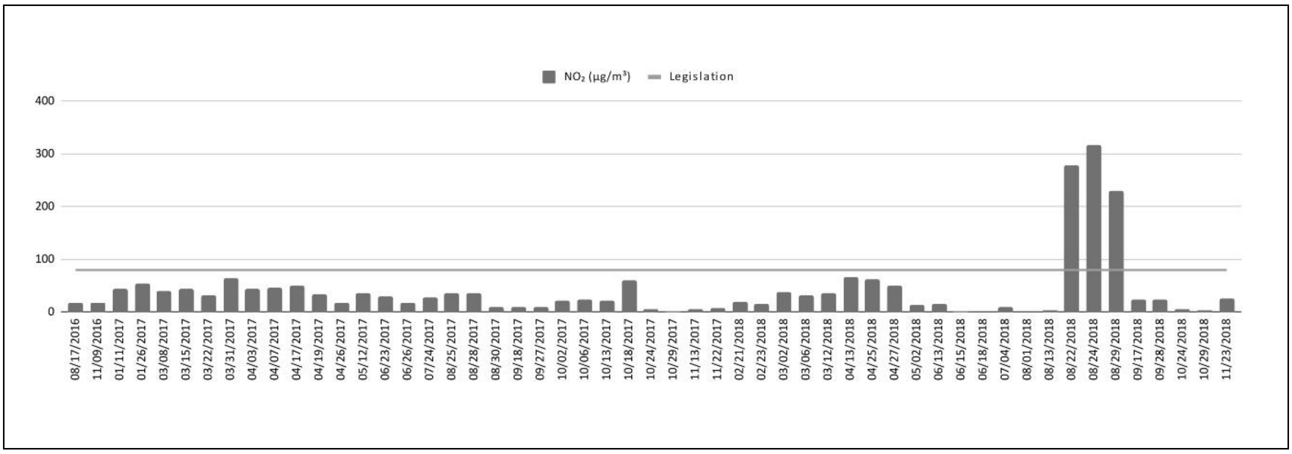
Graph 2 – Concentrations of PM_{10} (μg/m³)



Source: Author's (2021)

The NO_2 pollutant exceeded the limit of 80μg/m³ in 24 hours in three days analyzed (Graph 3).

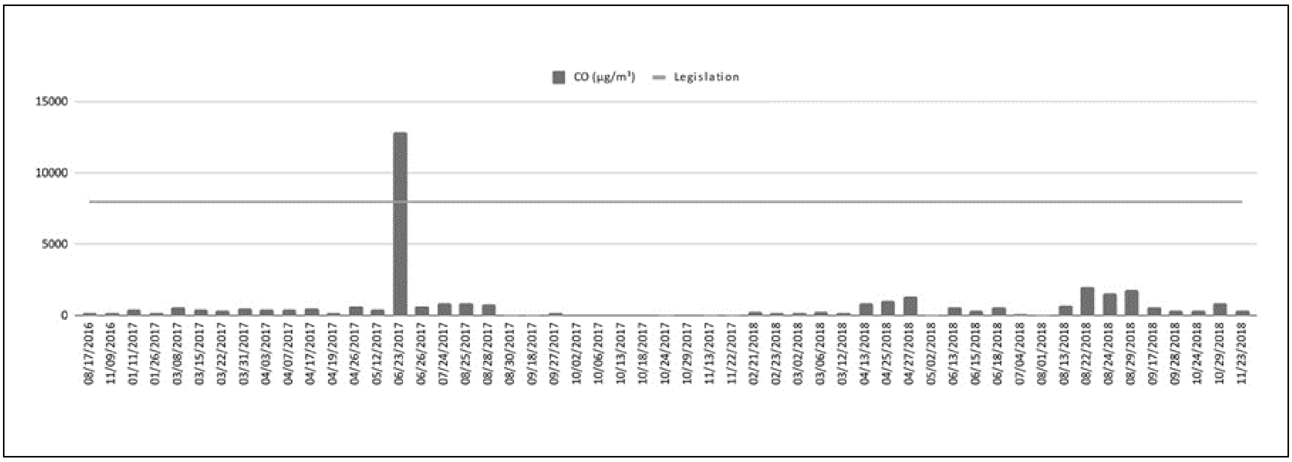
Graph 3 – NO_2 concentrations (μg/m³)



Source: Author's (2021)

It was found that CO exceeded the levels established by legislation of 8000 μg/m³ (8 mg/m³) in 24 hours only once (Graph 4).

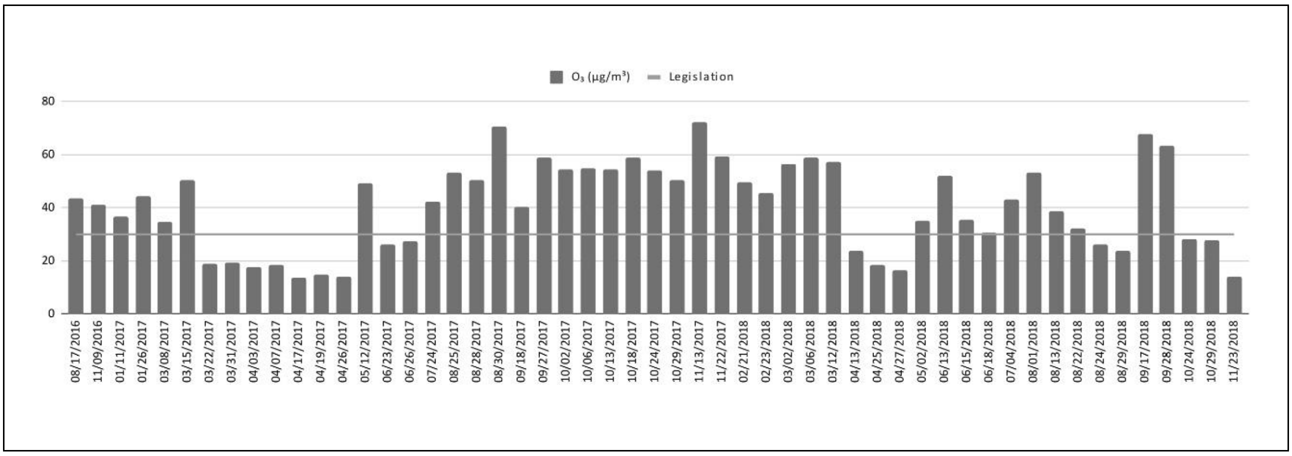
Graph 4 – CO concentrations (μg/m³)



Source: Author's (2021)

O_3 levels exceeded 36 times the established limits, with the maximum desirable value being 30 μg/m³ in 24 hours (Graph 5).

Graph 5 – O_3 concentrations (μg/m³)



Source: Author's (2021)

Another aspect evaluated in this study were the meteorological variables, in which their values can be observed in Table 1.

The linear regression analysis showed a relationship between the spirometry variables and the minimum temperature ($p=0.001$) and the concentration of PM_{10} ($p<0.000$), with the coefficient of the variable being negative, suggesting that the higher the concentration of PM_{10} and minimum temperature, the lower the spirometry results. A relationship was found between the difference in baseline and final HR with the distance covered as a percentage of the 6MWT ($p=0.045$), with the variable coefficient being positive, suggesting that the greater the distance, the greater the HR variation, and with the difference of basal and final SpO_2 with the pollutant PM_{10} ($p=0.018$), this coefficient being negative, indicating that the higher the concentration of PM_{10}, the smaller the difference in SpO_2. There was a relationship between the pollutant $PM_{2.5}$ with the distance covered during the 6MWT ($p=0.024$), with the coefficient of the variable being negative, indicating that the higher the concentration of $PM_{2.5}$, the less distance the individual will travel during the test. The other variables did not show statistical differences.

Chart 1 - Result of Linear Regression with respective coefficients

Dependent Variable	Constant	Non-Standardized Coefficients		Standardized Coefficients	t	Sig.
		B	standard error	Beta		
FEV_1/FVC	Minimum temperature	-1,510	0,443	-0,351	-3,411	0,001
	PM_{10}	-0,202	0,054	-0,430	-3,723	0,000
FEV_1	Minimum temperature	-0,045	0,017	-0,274	-2,595	0,011
	PM_{10}	-0,008	,002	-0,442	-3,852	0,000
Estimated Distance Traveled. (%)	Difference of baseline and post-test HR	0,003	0,001	0,221	2,035	0,045
Difference of basal and post-test SpO_2	PM_{10}	-0,025	0,010	-0,302	-2,432	0,018
Travelled distance in 6MWT	$PM_{2.5}$	-1,965	0,850	-0,284	-2,311	0,024

Source: Author's (2021)
Subtitle: FEV_1: Forced Expiratory Volume in the first second. FEV_1/FVC: Tiffeneau Index. HR: Heart Rate. SpO_2: Peripheral Oxygen Saturation. 6MWT: Six-Minute Walk Test. PM_{10}: Particulate Matter of a diameter of less than 10μm. $PM_{2.5}$: Particulate Matter of a diameter of less than 2.5μm. AWS:

From the data above it can be identified that some pollutants exceeded the values provided for by legislation in up to 31 days analyzed. This scenario of increased concentrations of $PM_{2.5}$ and PM_{10} can contribute to the increase in respiratory symptoms, leading to an increase in the number of hospitalizations, in addition to a reduction in cardiorespiratory resistance in exposed individuals (LEE; REZAEI; JEONG, 2018; LEELASITTIKUL, 2017; NASCIMENTO *et al*., 2016). Lung function decreased as PM_{10}, and minimum temperature increased. These findings are compatible with results found in a study carried out in London, where they evaluated the cardiorespiratory effects of short-term exposure to air pollution during a 2-hour walk in an environment with higher levels of pollutants and another with lower levels of pollution (SINHARAY *et al*., 2018). A reduction in FEV_1 and FVC was observed 3h after walking. This reduction was significantly associated with the increase in $PM_{2.5}$, ultrafine particles and NO_2. A reduction in FVC was also significantly associated with increased PM_{10} concentrations, in addition to these individuals having small airway obstruction associated with these pollutants (SINHARAY *et al*., 2018). These findings reaffirm that patients with CRD are much more sensitive to air pollution, in terms of effects pulmonary and cardiovascular conditions, which can generate changes in pulmonary function and arterial stiffness (SINHARAY *et al*., 2018), in line with the results obtained in this study, demonstrating an association between pulmonary function variables and the pollutant PM_{10}.

An association between temperature and air pollution with cardiorespiratory morbidity and mortality can be observed in Brazil, this association being high due to the impact of high concentrations of PM_{10} at low temperatures for cardiovascular mortality, and at high temperatures for respiratory mortality, considering levels of pollution around 60μg/m^3, a value very close to the average of PM_{10} found in this study of 56.75μg/m^3 (PINHEIRO *et al*., 2014). In addition, climate variables can interfere with air pollution (CAMILLO; SOUZA; RAMSER, 2020). Higher temperatures are associated with lower FEV1 values, and their effects are similar to those of atmospheric pollution (COLLACO *et al*., 2018). Extremes of temperature, whether hot or cold, are associated with morbidity and mortality in people with COPD; the interactive effect between air pollution and high temperatures has been shown to be even more harmful (HANSEL; MCCORMACK; KIM, 2016; PINHEIRO *et al*., 2014).

A relationship was found between the basal/final SpO_2 difference and PM_{10} levels; the higher the pollutant concentration, the smaller the SpO_2 difference. The literature demonstrates that there is a reduction in SpO_2 and pulmonary diffusion capacity after physical exercise due to PM_{10}, increasing systemic inflammation in individuals with COPD (LEE *et al*., 2016). Studies show that short-term exposure to air pollution can reduce SpO_2 in minutes and its effects can last for hours (XIA *et al*., 2020). However, it is noteworthy that the ability to walk can reduce SpO_2 due to the patients' underlying disease.

The distance covered in the 6MWT and the $PM_{2.5}$ levels showed a relationship, with the distance being shorter when the pollutant levels were higher. This exposure to atmospheric pollutants (PM_{10} and NO_2) reduces the functional capacity of elderly people (ZWART *et al*., 2018). In Thailand, meteorological variables such as fog can increase the obstructive risk and decrease the resistance in the 6MWT, in addition to the pollutants being able to influence the function pulmonary (LEE; REZAEI; JEONG, 2018). High concentrations of $PM_{2.5}$ reduce exercise tolerance in exposed individuals, in addition to reducing the O_2 pulse and VO_2 by up to 30% in cardiac patients (VIEIRA *et al*., 2016). In addition, exposure to PM_{10} causes physiological changes such as increased Blood Pressure (BP) and Heart Rate (HR). These changes are caused due to imbalances in the Autonomic Nervous System (ANS) generated from this exposure, which can lead the individual to suffer acute cardiovascular events (BROOK *et al*., 2014).

4 CONCLUSION

This study demonstrated that the concentrations of $PM_{2.5}$, PM_{10}, NO_2, O_3 and CO were above the limits established by the WHO and more restrictive world legislation. Therefore, it is possible to cause negative effects to the health of this more sensitive population.

It was possible to verify that there is a relationship between the environmental data and the functional tests of spirometry and 6MWT, where higher temperatures and the presence of PM_{10} reduce pulmonary function, as well as high levels of PM_{10} reduce the difference in SpO_2 before and after the 6MWT. In addition, the individual had a reduced functional performance in the presence of $PM_{2.5}$, thus altering his ability to walk. This data confirms that these individuals are more sensitive to changes in the concentration of pollutants, which, added to the increase in temperature, generate significant impacts on respiratory health and functional capacity. These negative impacts may reflect an increase in the use of healthcare and public health-related costs. Human health and environmental health becomes an inseparable union.

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