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Effects of PM_{10} and Weather on Respiratory and Cardiovascular Diseases in the Ciuc Basin (Romanian Carpathians)

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Abstract: This study presents the PM_{10} concentration, respiratory and cardiovascular disease hospital admissions evolution in the Ciuc basin for a period of 9 years (2008–2016), taking into consideration different meteorological conditions: boundary layer, lifting condensation level, temperature-humidity index, and wind chill equivalent chart index. The PM_{10} and hospital admissions evolution showed a very fluctuated hourly, weekly, monthly, yearly tendency. The PM_{10} concentration in winter (34.72 $\mu g/m^3$) was 82% higher than the multiannual average (19.00 $\mu g/m^3$), and almost three times higher than in summer (11.71 $\mu g/m^3$). During the winter, PM_{10} concentration increased by an average of 9.36 $\mu g/m^3$ due to the increased household heating. Climatological parameters have a demonstrable effect on the PM_{10} concentration variation. Children, the elderly and men are more sensitive to air pollution, the calculated relative risk for men was (*RR* = 1.45), and for women (*RR* = 1.37), respectively. A moderate correlation (0.51) was found between PM_{10} and pneumonia (P), while a relatively weak correlation (0.39) was demonstrated in the case of PM_{10} and upper respiratory tract infections (URTI). Furthermore, except thermal humidity index (THI), strong negative correlations were observed between the multiannual monthly mean PM_{10} and the meteorological data. The PM_{10} followed a moderate negative correlation with the boundary layer (−0.61). In the case of URTI and P, the highest number of hospital admissions occurred with a 5 to 7-day lag, while the 10 $\mu g/m^3$ PM_{10} increase resulted in a 2.04% and 8.28% morbidity increase. For lung cancer (LC) and cardiovascular diseases (AMI, IHD, CCP), a maximum delay of 5–6 months was found. Three-month delay and an average growth of 1.51% was observed in the case of chronic obstructive pulmonary disease (COPD). Overall, these findings revealed that PM_{10} was and it is responsible for one-third of the diseases.

Keywords: PM_{10}; health impact; specific atmospheric conditions; Carpathian Mountains

1. Introduction

Ambient air pollution plays an important role in a broad spectrum of health disorders, emerging as a leading worldwide environmental health problem. The World Health Organi-

zation estimates that 22% of global death and disability can be attributed to environmental factors [1].

Epidemiological studies revealed worsening life quality and health symptoms, such as deterioration of lung function due to elevated particle pollution levels resulting in an increased use of medication [2–5]. Short-term symptoms from exposure to air pollution include itchy eyes, nose and throat, wheezing, coughing, shortness of breath, chest pain, headaches, nausea, as well as respiratory infections [6]. Long-term exposure to high concentrations of PM_{10} (particulate matter with a diameter of 10 μm or less) can result in several health impacts and premature death like lung cancer, cardiovascular disease, chronic respiratory illness, and allergies [7,8]. PM_{10} can reach the trachea bronchial and alveolar regions of the respiratory tract, having a greater impact on human health. Noteworthy, specific groups, people with cardiovascular risk factors or pre-existing cardiovascular disease (CVD) are more vulnerable to the aforesaid harmful effects.

There is an increasing body of evidence showing air pollution as a critical risk factor for cardio-respiratory morbidity and mortality. Numerous studies have shown that there is a strong association between exposure to particulate matter and the increased risk of cardiovascular and respiratory disease [9–16]. In 2004, the American Heart Association (AHA) published a scientific statement regarding air pollution and cardiovascular disease, concluding that particulate matter is a large contributor to cardiovascular morbidity and mortality [12]. In 2010, the abovementioned statement was updated, providing a comprehensive review of new evidence linking exposure to PM with cardiovascular disease [12].

Existing statistics are based on large cohort studies conducted mostly in North America and Western Europe, with less information available from Eastern Europe [17–24]. According to air monitoring databases [25], people living in Eastern Europe are generally subjected to higher levels of PM_{10} than those in Western Europe. The PM_{10} exposure on human health shows variability, so the data cannot be extrapolated to other regions and populations, for the reason that various specific factors such as demographic and genetic factors, may affect the impact of PM_{10} on human health.

It has been shown that air particulates with a diameter of less than 10 μm (PM_{10}) can reach the trachea bronchial and alveolar regions of the respiratory tract, having a substantial impact on human health [26]. Particulate matter is often divided into two main groups based on characteristics, sources, and potential health effects: fine particles, $PM_{2.5}$ (with a diameter between 0.1 and 2.5 μm) and coarse particles, $PM_{10\text{-}2.5}$ (having a diameter between 2.5–10 μm).

In Romania, only a few studies have been published in terms of respiratory health effects of PM_{10} [27]. There is an unmet need for studies addressing the burden of pollution-attributable cardio-respiratory diseases in our country.

The purpose of this study is twofold: firstly, to analyze the temporal distribution of ambient particulate matter (PM_{10}) in the Ciuc basin over a period of 9 years (2008–2016), and secondly, to assess the short- and long-term effects on respiratory and cardiovascular morbidity taking into account the meteorological conditions.

2. Materials and Methods

2.1. Studied Region

The Ciuc basin is located in the middle of the Eastern Carpathians, at an altitude of 650 m, with a population of ~150,000 (Figure 1). Due to its enclosed character, the Ciuc basin is known for its specific microclimatic and meteorological conditions, with long episodes of static stability and thermal inversion periods, hence favoring the accumulation of pollutants.

2.2. Air Pollution, Medical and Meteorological Data

The PM_{10} concentration data were obtained from the HR01 regional monitoring station located near the municipality of Miercurea Ciuc, the "Cold Pole" of Romania [28,29], at 46.33° N, 25.81° E, at an elevation of 697 m a.s.l. PM_{10} data were sampled with an

automated analyzer type LSPM10; for further analysis, the daily gravimetric and hourly values ($\mu g/m^3$) were used.

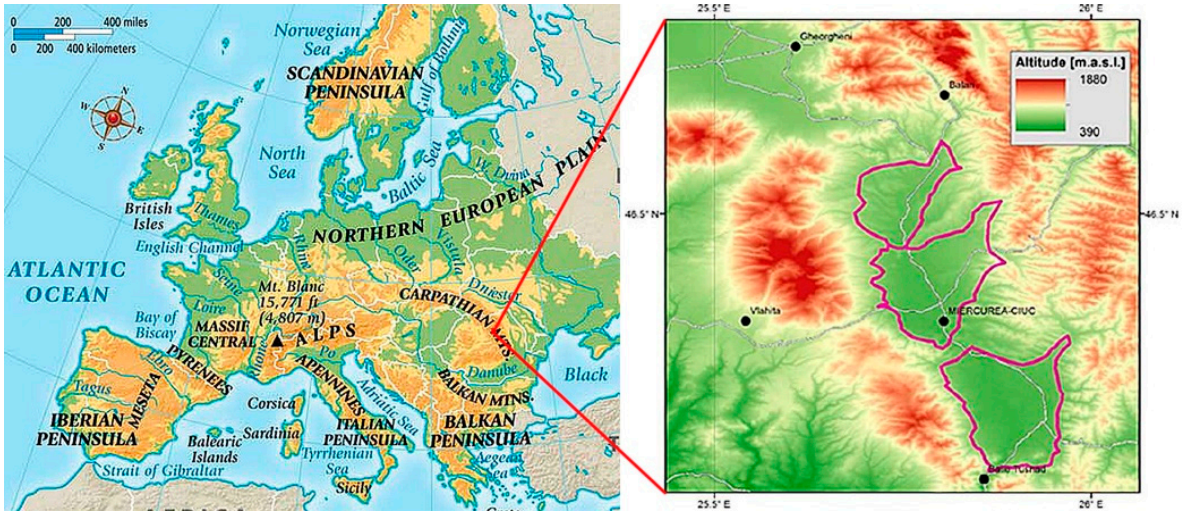

Figure 1. Sampling site location. The main parts of the Ciuc basin are marked with red lines.

The daily respiratory and cardiovascular hospital admission data from 1 January 2008 to 31 December 2016 (3288 days) were obtained from the Regional Emergency Hospital of Miercurea Ciuc, which is the single regional hospital in the studied region. During the studied period, 18,286 hospital admissions were registered [27]. The selection was made according to the International Classification of Disease, 10th Revision (ICD-10) by the World Health Organization. Seven different types of diseases were studied: lung cancer -LC (ICD-10 code C33–C34); acute myocardial infarction -AMI (ICD-10 code I21); ischemic heart diseases-IHD (ICD-10 code I20-I25 except I21); chronic cardiopulmonary disease-CCP (ICD-10 code I27.9); upper respiratory tract infections-URTI (ICD-10 code J00-J06); pneumonia-P (ICD-10 code J12–J18); chronic obstructive pulmonary diseases-COPD (ICD-10 code J44). Hospital admissions were examined based on sex and age groups [0–5], (5–14], (14–40], (40–60] and 60+ years, respectively. The number of patients coming from outside the basin was negligible.

Climatological parameters such as daily temperature, precipitation amount and the relative humidity index were provided by the National Meteorological Administration (Meteo Romania). Regarding the lifting condensation level (LCL) it was calculated according to Equation (1):

$$LCL = 20 + \frac{T}{5}(100 - RH) \quad (1)$$

where: *LCL*—lifting condensation level, *T*—air temperature (°C), *RH*—relative humidity (%).

Furthermore, the temperature-humidity index (THI) and the wind chill equivalent chart index (WCT) were also calculated, LCL and THI, being strongly related to the PM_{10} concentration evolution, while WCT is a dimensionless human comfort index. Lastly, the daily value of the boundary layer was extracted from ERA5 reanalysis using the mean value of all the pixels covering the Ciuc basin region [30,31].

2.3. Statistical Analysis

In order to determine the monthly, seasonal and yearly PM_{10} concentrations, the daily gravimetric measurements were used, while the diurnal and weekly variations were estimated by using the hourly PM_{10} concentrations. The relationship between the daily hospital admissions, meteorological conditions, and PM_{10} concentration, was determined using different statistical indices: mean, standard deviation, coefficient of variation, minimum, median, maximum, 25th and 75th percentile values, and confidence interval. To

assess the impact of PM_{10} contribution to respiratory and cardiovascular morbidity, different methods were used, such as the Pearson correlation, the Fourier transform, the Aunan's calculation procedures, relative risk, as well as the morbidity increase caused by a 10 $\mu g/m^3$ rise in PM_{10}. The Pearson correlation coefficient was considered statistically significant (p-level < 0.05), if the r value was greater than 0.203 or below -0.203.

On the other hand, the PM_{10} values resulted during the household heating with wood (HPM_{10}) were estimated using Equation (2), hence the residential heating contribution to outdoor PM_{10} was determined by considering the average winter and summer concentrations as well as the average boundary layer (BL) height ratio:

$$HPM_{10} = C_{PM10w} - \left(\frac{BLs}{BLw} \times C_{PM10s}\right) \quad (2)$$

where: HPM_{10}—the average PM_{10} increase during winter caused by heating ($\mu g/m^3$), C_{PM10w}—the average PM_{10} in winter period ($\mu g/m^3$), C_{PM10s}—the average PM_{10} in summer period ($\mu g/m^3$), BLs—the average boundary layer in summer (m), BLw—the average boundary layer in winter (m).

In order to estimate the health effects of cold and heat extremes, according to Dobrinescu et al. [32], five discomfort classes can be established: severe danger from cold (WCT ≤ -35 °C), extremely cold (-35 °C > W ≤ -20 °C), uncomfortably cold (-20 °C > THI $\leq$ 0 °C), uncomfortably hot (66 $\leq$ THI < 80), severe danger from heat THI $\geq$ 80, respectively:

$$THI = (1.8T_A + 32) - \left(0.55 - \frac{0.55RH}{100}\right)(1.8T_A - 26) \quad (3)$$

where: T_A is the air temperature (°C) measured at a standard level (2 m).

The critical threshold above which the human body feels strong discomfort is 80 units. THI is expressed in dimensionless form.

In the winter season, the severe danger from cold, extremely cold and uncomfortably cold was estimated, using WCT:

$$WCT = 13.12 + 0.6215T_A - 11037FF_{10}^{0.16} + 0.3965T_AFF_{10}^{0.16} \quad (4)$$

where: FF_{10} is the wind speed (km/h) measured at 10 m a.g.l.

Usually, WCT only expresses a human sensation and it is linked to the way the human skin perceives the temperature on a calm day.

Regarding the PM_{10} concentration data, four classes were established: low < 25 $\mu g/m^3$, moderate between 25 $\mu g/m^3$ and 37.5 $\mu g/m^3$, high ranging from 37.5 $\mu g/m^3$ to 50 $\mu g/m^3$, and very high concentrations > 50 $\mu g/m^3$, respectively.

Since there is a latency period between exposure and appearance of disease the Fourier transform method was used to decipher the relation. The Fourier transform is a mathematical technique that transforms a signal from the time domain to the frequency domain, showing that any wave form can be rewritten as the sum of sinusoidal functions [33], the method has been applied to the air pollution, medical and meteorological time series as well. The Fourier transform gives us a point of view in order to better understand the association between exposure to PM_{10} and the influence of climate on hospital admissions.

It is formed by a set $W_n(t) = e^{int}, n = 0.1 \ldots$ orthogonal functions, of period 2π:

$$F_{(\omega)} = \int_{-\infty}^{\infty} f(t)e^{-i\omega t}\partial t \quad (5)$$

$$\omega = 2\pi f \quad (6)$$

where: $|f(\omega)|$ is the amplitude of each component ω of the signal [34].

To assess the total damage of PM_{10} to human health in the Ciuc basin Aunan's calculations procedures were used, briefly, the annual number of symptom-days was calculated from the daily mean PM_{10} concentration variation [35].

The odds ratio (OR) was estimated from the regression coefficient β and the increase of concentration level from baseline to C_i:

$$OR_i = e^{\beta * \Delta Ci} \tag{7}$$

$$P^{ab\,s} = (OR - 1) \times 100 \tag{8}$$

The hypothetical zero-concentration prevalence is given by:

$$p_0 = \frac{p^{abs}\,(C_i)}{OR_i - OR_i \times\ p^{abs}\,(C_i) + p^{abs}\,(C_i)} \tag{9}$$

The health effects of exposure-response functions generally are derived from the relation between daily mean concentrations, C_i, and the daily prevalence of the effects, $p(C_i)$:

$$S_{sum} = \sum_{i=1}^{365} (p(C_i)\ \times N = \sum_{i=1}^{365} p_0 \times\ exp(\beta \times\ C_i)N \tag{10}$$

According to the literature the annual number of symptom days (S_{sum}) in a population (N) ideally can be estimated by calculating the daily number of affected persons in the respective population and sum over the year (Equation (10)).

Starting from daily hospital admission and PM_{10} concentration databases, we analyzed the evolution of respiratory diseases from a 1 to 10 days delay. In the case of CVD, a time delay of 1 to 10 months was used. As boundary condition was set, that only positive values will be followed, in the case of PM_{10} only the changes larger than 5 $\mu g/m^3$ were evaluated, and the baseline was set to 10 $\mu g/m^3$. The two variables had to meet the set conditions at the same time: if $\Delta PM_{10} > 5$ $\mu g/m^3$ and Morbidity > 0. In addition, we considered the percentage increase of cases concerning the PM_{10} change of 10 $\mu g/m^3$, comparing the average increase to the number of days tested. To determine the time delay, the day/month corresponding to the maximum value obtained with the time difference tested was taken.

3. Results

The results show that the multiannual PM_{10} concentration is 19.00 $\mu g/m^3$ and on an average day 6 respiratory and cardiovascular diseases have been recorded (Table 1). The coefficient of variation (CV) for PM_{10} and WCT was 0.61, and 0.93, respectively. The lowest coefficient variation was found in the case of P and COPD with a value of 0.37.

3.1. Ambient PM_{10} Trend

Multiannual average concentrations of PM_{10} were used to detect hourly, daily, and weekly changes. The hourly mean concentration of PM_{10} ranged between 17.0 and 30.1 $\mu g/m^3$. Daily PM_{10} values show the bimodal daily pattern, the first peak is in the morning correlated to the rush hours of road traffic (8–11 a.m.) and the second peak occurs at midnight (Figure 2).

The lowest concentration values were found on Sundays (20.8 $\mu g/m^3$) and Mondays (19.8 $\mu g/m^3$), known as the "holiday and after holiday effect", because of lower emissions from vehicle traffic and other sources [36]. At the beginning of the week, the daily PM_{10} concentrations are starting to increase, and reach the maximum on Wednesdays 25.9 $\mu g/m^3$ and Thursdays 25.5 $\mu g/m^3$. The monthly PM_{10} concentrations show significant fluctuations over the year (Figure 3). The lowest PM_{10} value was measured in June: 10.36 $\mu g/m^3$, when the boundary layer level is three-time higher than in winter.

Table 1. Summary statistics of daily hospital admission numbers, meteorological conditions and PM_{10} concentration. –LC: lung cancer; AMI: acute myocardial infarction; IHD: ischemic heart diseases; CCP: chronic cardiopulmonary disease; URTI: upper respiratory tract infections; P: pneumonia; COPD: chronic obstructive pulmonary diseases; GT: global trends; Prec.: precipitation; LCL: lifting condensation level; BL: boundary layer; THI: thermal humidity index; WCT: wind chill equivalent chart index.

Types of Diseases	Mean + SD	CV	Min	P(25)	P(50)	P(75)	Max	CI95−	CI95+
LC	0.48 ± 0.34	0.70	0.03	0.21	0.39	0.68	1.39	0.42	0.54
AMI	0.13 ± 0.08	0.62	0.00	0.07	0.13	0.19	0.35	0.12	0.15
IHD	0.38 ± 0.33	0.88	0.00	0.13	0.23	0.55	1.35	0.31	0.44
CCP	0.39 ± 0.26	0.66	0.00	0.17	0.39	0.55	1.32	0.34	0.44
URTI	0.77 ± 0.45	0.58	0.10	0.45	0.69	1.03	2.39	0.69	0.86
P	2.71 ± 1.13	0.37	1.13	1.90	2.57	3.45	5.82	2.52	2.90
COPD	0.70 ± 0.26	0.37	0.19	0.51	0.68	0.84	1.65	0.66	0.75
GT	5.57 ± 1.65	0.30	2.74	4.30	5.41	6.32	11.82	5.26	5.88
Meteo. conditions									
Prec **	49.31 ± 34.41	0.70	0.20	24.05	38.50	70.63	177.30	42.82	55.80
LCL *	462.23 ± 208.50	0.45	1.43	289.59	497.90	600.38	1000.63	422.91	501.56
BL *	428.87 ±156.49	0.36	135.78	278.89	467.57	549.40	748.20	399.35	458.38
THI *	32.33 ± 11.53	0.36	−2.80	25.83	35.13	40.25	54.17	30.16	34.51
WCT *	4.95 ± 4.63	0.93	−7.41	2.04	5.34	7.90	15.32	4.08	5.82
PM_{10}	19.00 ± 11.59	0.61	4.39	11.61	14.51	21.50	57.71	16.82	21.19

* monthly average values ** monthly summaries values.

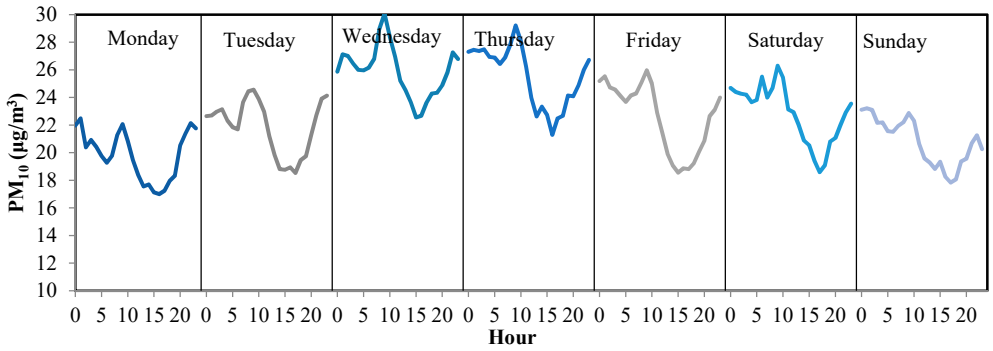

Figure 2. Weekly evolution of hourly PM_{10} concentration (multiannual means).

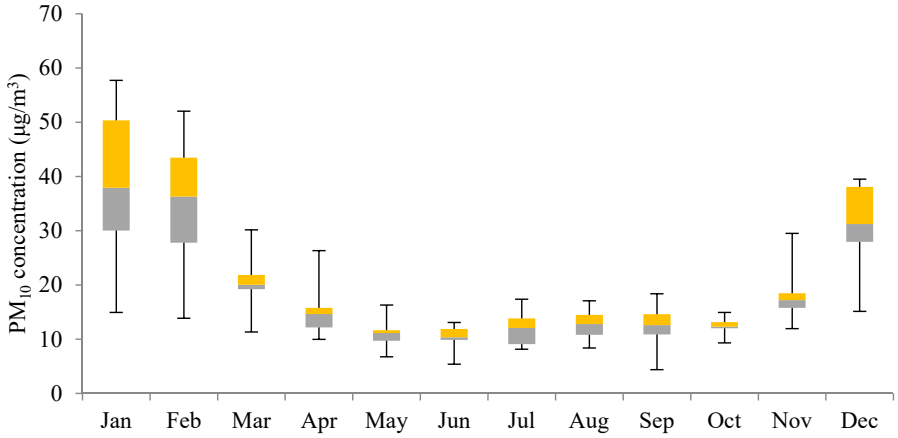

Figure 3. Box-plot analysis of monthly PM_{10} concentrations (multiannual means). The lower (grey) and upper (yellow) limits represent the first (25P) and third (75P) quartiles, and the ends of the whiskers represent the minimum and the maximum values.

Annual evolution shows that in the first three studied years (2008–2010) a constant increase was detected, with an average of 10.08%. The PM_{10} concentration was higher than the annual WHO Air Quality admissible level (20 μg/m^3) in 2009 (22.39 μg/m^3), and in 2010 (23.00 μg/m^3), respectively. This rise was followed by a longer fluctuating period (2011–2015) with an average decrease of 3.23%, and a significant 30.56% drop in the year of 2016, when was recorded the minimum concentration level (13.08 μg/m^3) (Figure 4a). This decreasing trend could be explained by the implementation of environmental regulations imposed by the EU.

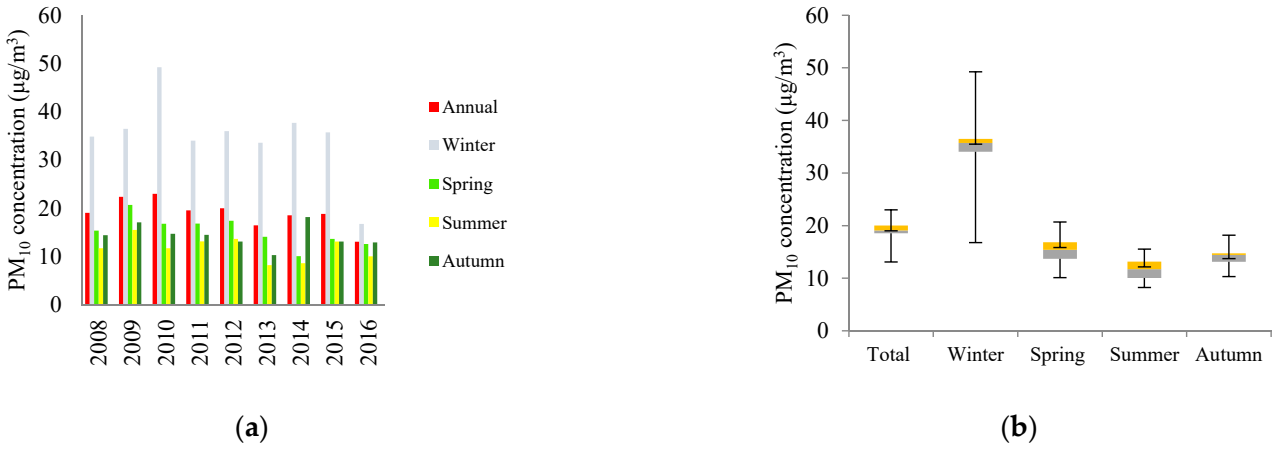

Figure 4. Annual (**a**) and seasonal (**b**) mean PM_{10} concentration. 4.b Box-plot analysis of seasonal PM_{10} concentrations The lower (grey) and upper (yellow) limits represent the first (25P) and third (75P) quartiles, and the ends of the whiskers represent the minimum and the maximum values.

The average seasonal PM_{10} concentration varies considerably throughout the year (Figure 4b); in winter (34.72 μg/m^3), they are 82% higher than the multiannual average (19.00 μg/m^3), and almost three times higher than in summer (11.71 μg/m^3). The highest seasonal concentration was measured during the winter of 2009–2010 (47.62 μg/m^3), close to the WHO's daily acceptable limit of 50 μg/m^3 [37].

According to the calculations, the increased PM_{10} concentration depends on the high changes in the winter and summer boundary layer and from the increased emission from heating in the winter period. During the winter, PM_{10} concentration increased by an average of 9.36 μg/m^3 due to the heating season.

According to the PM_{10} classification (low, moderate, high and very high concentration), the PM_{10} concentration was higher than 50 μg/m^3 in 177 cases; 88% of them were in winter, 8.5% occurred in spring, and 2.8% in autumn (Figure 5). The number of days with very high pollution and high pollution were $_{3.81}$5.42%$_{7.01}$ and $_{3.71}$4.43%$_{5.16}$ of the total, respectively.

Thus, taking into consideration the annual PM_{10} evolution categories the number of exceedances represents 5.42%, on the other hand, significant changes were observed between seasons. The highest 18.95% was found in winter, due to the main reasons stated out earlier, while in autumn and spring the value was only 1.81% and 0.61%, respectively, meanwhile, there were no exceedances during summer.

3.2. Relationship between PM_{10} Concentration and Meteorological Variables

Climatological parameters have a demonstrable effect on the PM_{10} concentration variation. Except for THI, the multiannual monthly mean of PM_{10} and the meteorological data show strong negative correlations (Figure 6).

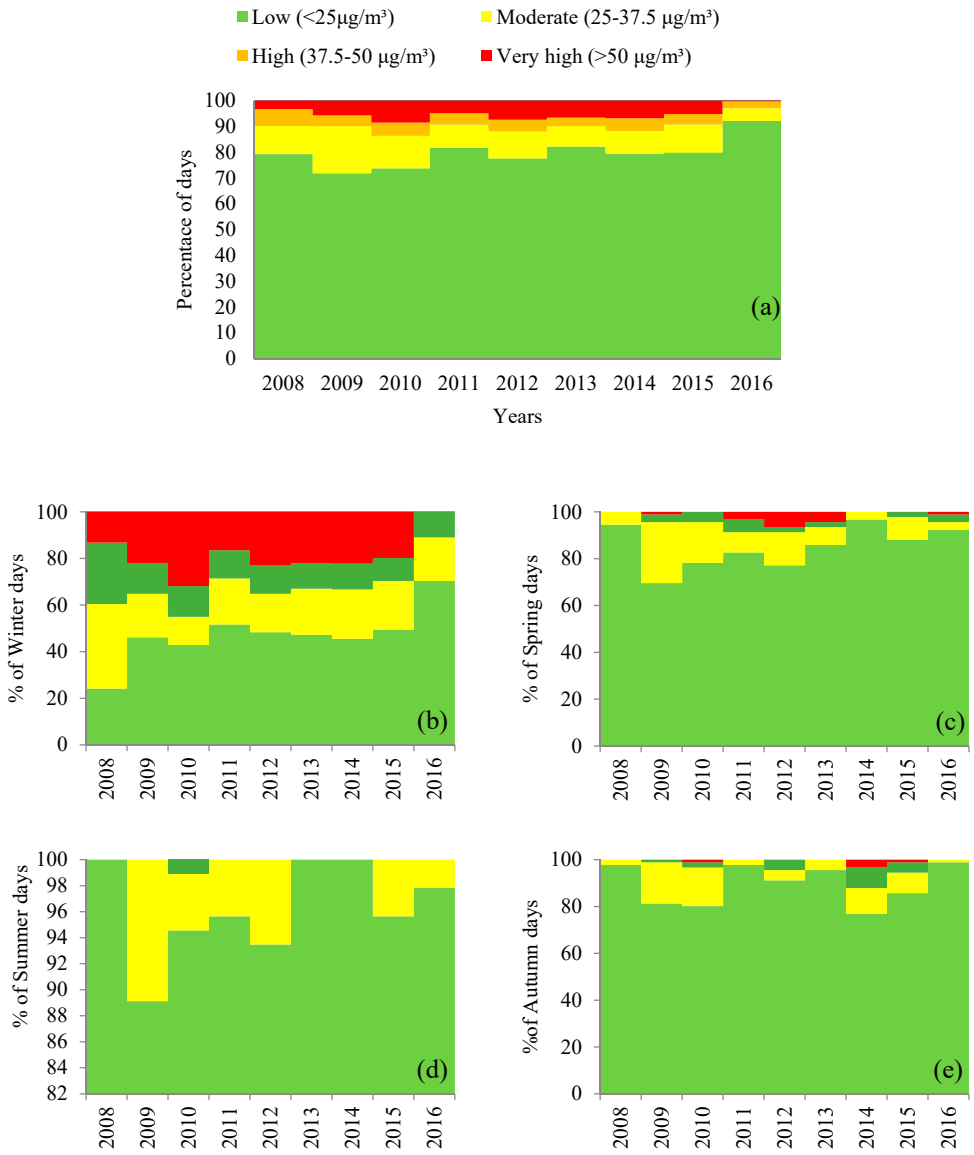

Figure 5. Annual and seasonal PM_{10} categories evolution during the studied period ((**a**)—total days, (**b**)—winter days, (**c**)—spring days, (**d**)—summer days, (**e**)—autumn days).

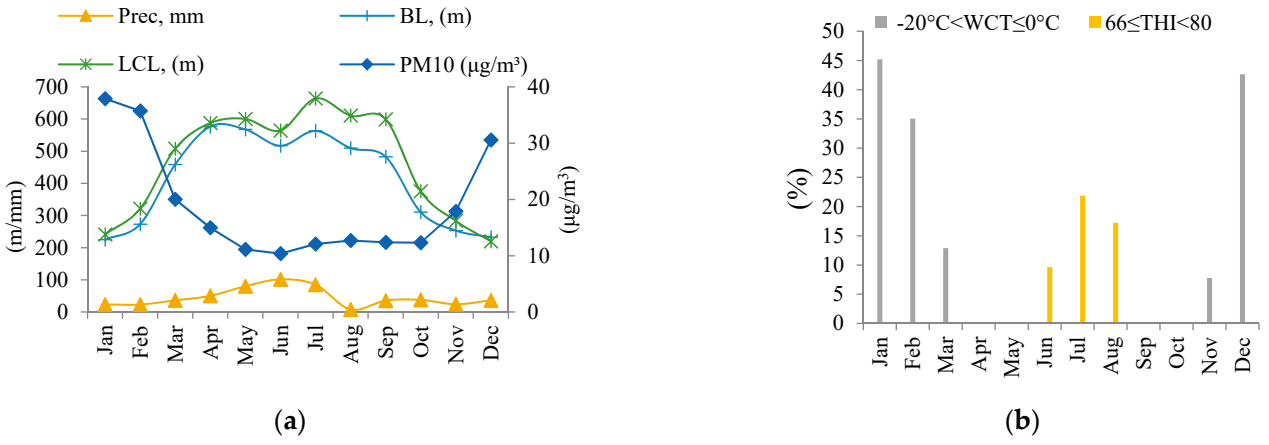

Figure 6. Monthly PM_{10} concentrations and meteorological parameters: (**a**): Prec., BL, LCL, (**b**): WCT, THI.

Two classes of human discomfort were detected (Figure 6b): uncomfortably cold and uncomfortably hot. Uncomfortably cold represented 40.96% of the total winter days, 3.22% resulting from the spring days, and 2.59% from the autumn days, while uncomfortably hot occurred during the summer, exhibiting 16.23% of the total summer days, respectively. For the entire studied period, 28.59% of the total days were uncomfortable. Precipitation has a positive effect, by reducing through wet scavenging the PM_{10} concentration. This effect is more significant during summer, when the quantity of precipitation is the highest (avg. 81.44 mm). The monthly PM_{10} evaluation shows a reverse trend with the boundary layer and lifting condensation level. There are two categories of accumulation conditions if the values of boundary layer and air pressure are high, strong anticyclonic systems are formed, leading to the Brunt Vaisala effect that often produces thermal inversions, favoring pollutant accumulation. The second accumulation condition occurs when the cloud base is low and the relative humidity is high, leading to fog formation.

3.3. Hospital Admission Evaluation

Admissions in Ciuc Emergency Hospital due to respiratory and cardiovascular causes were analyzed in detail. The incidence of the disease was examined in five different age groups: [0–5], (5–14], (14–40], (40–60], 60+. In 2010, 2012 and 2014, the number of days with high and very high pollution was higher in comparison with other years, resulting in the surge of hospital admissions. Diseases were found to be most common in the elderly age group 60+ representing 41.3%. The second large number of patients were children; below 5 years old, with 28.9% followed by the patients between (40–60], accounting for up to 20.4%. A lower rate was found in the case of children (5–14] years with 3.4% and young people (14–40] years with 6.0%, respectively. Furthermore, hospital admissions also show a weekly, and monthly cycle. The maximum hospital admission is on Monday and Friday and the minimum on Sunday. The average number of monthly hospital admissions shows a maximum in March (n = 230) and a minimum in August (n = 122). Most hospital admissions were for P in the children's age group [0–5] years with 19.5% and in the case of elderly people 60+ years with 14.9% proportion (Figure 7).

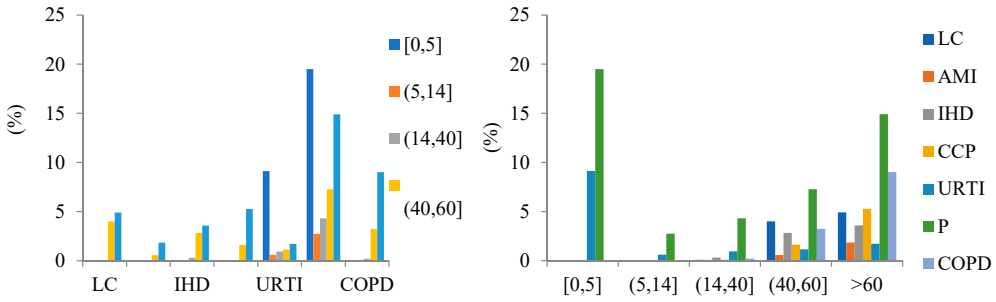

Figure 7. Diseases occurrence in different age groups.

In addition, the URTI was also common with 13.55%, in this case, the most affected age category was children [0–5] with a weight of 9.12%. The next most frequent disease was COPD with 12.5%, followed by LC 9.01%, CCP 6.99, IHD 6.73%, and AMI 2.5%, respectively.

3.4. Fourier Transformation

The PM_{10} concentration and climatological data (LCL, BL, THI, WCT) impact on the seven different types of diseases, during all seasons, and based on the five age group category was calculated (Table 2). From the total 459 Fourier transform significant correlation was found, using Pearson's correlation coefficient approach, in the case of 255, representing 55.56%. After the transformation, the Pearson correlation was applied to ten samples, knowing that in that case if n is between 0.01 and 0.02 the correlation should be 0.745.

Table 2. Significant Pearson correlation coefficients between PM_{10}, climatological data, and disease occurrence after the Fourier transforms.

PM_{10}																				
Age Categories	**[0–5]**				**(5–14]**				**(14–40]**				**(40–60]**				**>60**			
	W	**Sp**	**Su**	**A**	**W**	**Sp**	**Su**	**A**	**W**	**Sp**	**Su**	**A**	**W**	**Sp**	**Su**	**A**	**W**	**Sp**	**Su**	**A**
1. LC													*	*	*	*	*	*	*	*
2. AMI													*		*		*	*	*	*
3. IHD													*	*	*	*		*	*	*
4.CCP													*	*	*	*		*	*	*
5. URTI	*	*		*					*			*		*		*	*	*		*
6. P	*	*	*		*	*	*		*	*	*		*	*	*		*	*	*	
7. COPD													*	*	*	*	*	*	*	*
BL																				
Age categories	[0–5]				(5–14]				(14–40]				(40–60]				>60			
	W	Sp	Su	A	W	Sp	Su	A	W	Sp	Su	A	W	Sp	Su	A	W	Sp	Su	A
1. LC														*	*		*	*	*	*
2. AMI													*	*	*		*	*	*	*
3. IHD															*	*		*	*	*
4.CCP													*	*	*	*		*	*	
5. URTI	*	*	*	*							*			*		*		*		*
6. P	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
7. COPD													*	*	*	*	*	*	*	*
WCT																				
Age categories	[0–5]				(5–14]				(14–40]				(40–60]				>60			
	W	Sp	Su	A	W	Sp	Su	A	W	Sp	Su	A	W	Sp	Su	A	W	Sp	Su	A
1. LC													*		*				*	*
2. AMI															*				*	*
3. IHD									*											*
4.CCP																			*	
5. URTI	*				*											*				
6. P									*		*		*		*	*	*			*
7. COPD															*	*				*

(Where: W = winter, Sp = spring, Su = summer, A = autumn,). *- climatological effects; gray background: PM_{10} effects.

Predominantly the PM_{10} effects were accountable in all age groups in case of URTI and Pneumonia, and all types of diseases occurred at ages higher than 40 years old. The PM_{10} effects were linked with the WCT and BL, marked with gray backgrounds, based on the numerous assimilations identified during analysis (Table 2). Examining the overlap between the PM_{10} and studied meteorological parameters, it was observed that on average 68.9% had the same effect. The highest association was between the PM_{10}-BL with 86.9% similarity. A significant effect was found in the case of WCT's which was reflected in increased IHD in the winter period. The results showed that the climatological parameters (BL, WCT) had additional effects on morbidity, which are marked with red dots (Table 2). On the other hand, BL had additional effects on P and URTI diseases in autumn for all age categories. In winter the WCT shows a strong positive correlation.

3.5. Gender Distribution of Morbidity and Relative Risk Calculation

A significant gender difference was found between men and women. According to the statistics, 60.7% of the total number of hospitalized patients were men (Figure 8). With the exception of IHD, where men showed significantly higher susceptibility.

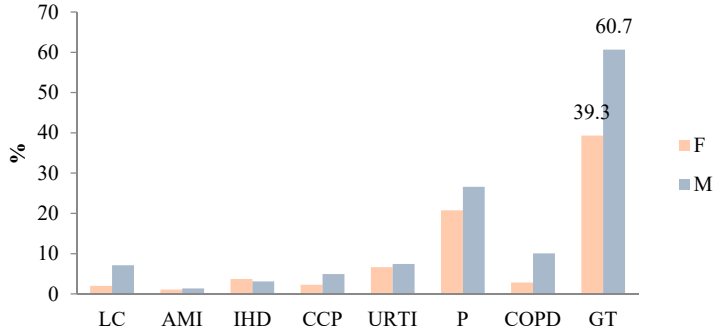

Figure 8. Disease frequency in different age categories and gender distribution.

The relative risk is the ratio of the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group.

$$RR = \frac{EER}{CER} = \frac{A/(A+B)}{C/(C+D)} \quad (11)$$

where: *EER* is the experimental event rate and *CER* is the control event rate.

The PM_{10} concentration level in summer was the lowest (10 $\mu g/m^3$), hence August was selected as a control month. The lowest PM_{10} concentration and morbidity rate was taken as a reference value.

Relative risk calculation was carried out in different age and gender groups. There was substantial variation in risk between male and female and different age categories. The mean value of *RR* was 1.37 for women and 1.45 for men. The most significant effect was seen in the case of PM_{10} and P and URTI (Figure 9).

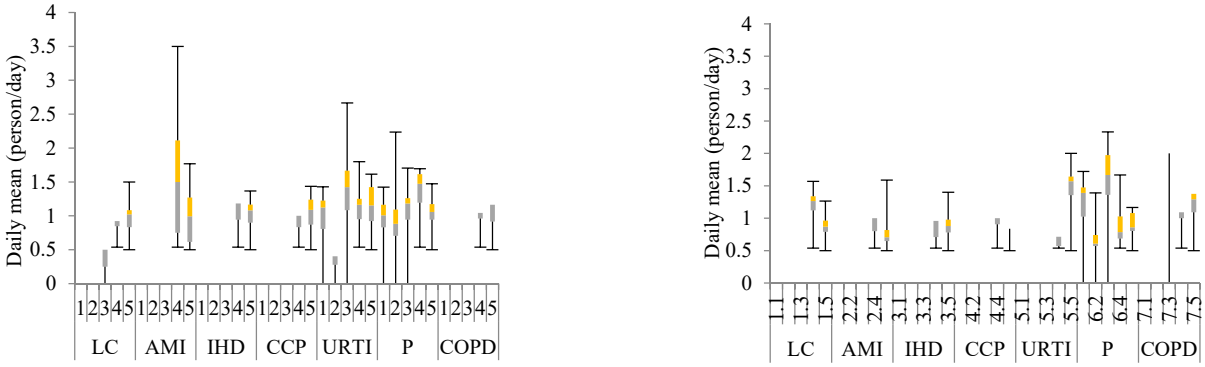

Figure 9. Box-plot analysis of relative risk evaluation in different gender groups: (**a**) men; (**b**)-women. The lower (grey) and upper (yellow) limits represent the first (25P) and third (75P) quartiles, and the ends of the whiskers represent the minimum and the maximum values.

3.6. Correlation Analysis

The Pearson correlation coefficient was used to determine the correlation between the multiannual monthly PM_{10} concentration and morbidity. Except the AMI for each disease, the Person correlation coefficient was significant: URTI (0.61), P (0.68), IHD (0.56), LC (0.53), CCP (−0.44), and COPD (0.47), respectively. The median multiannual monthly PM_{10} concentration is marked with the blue line, and the other hand the morbidity monthly evaluation is marked with the green line (Figure 10).

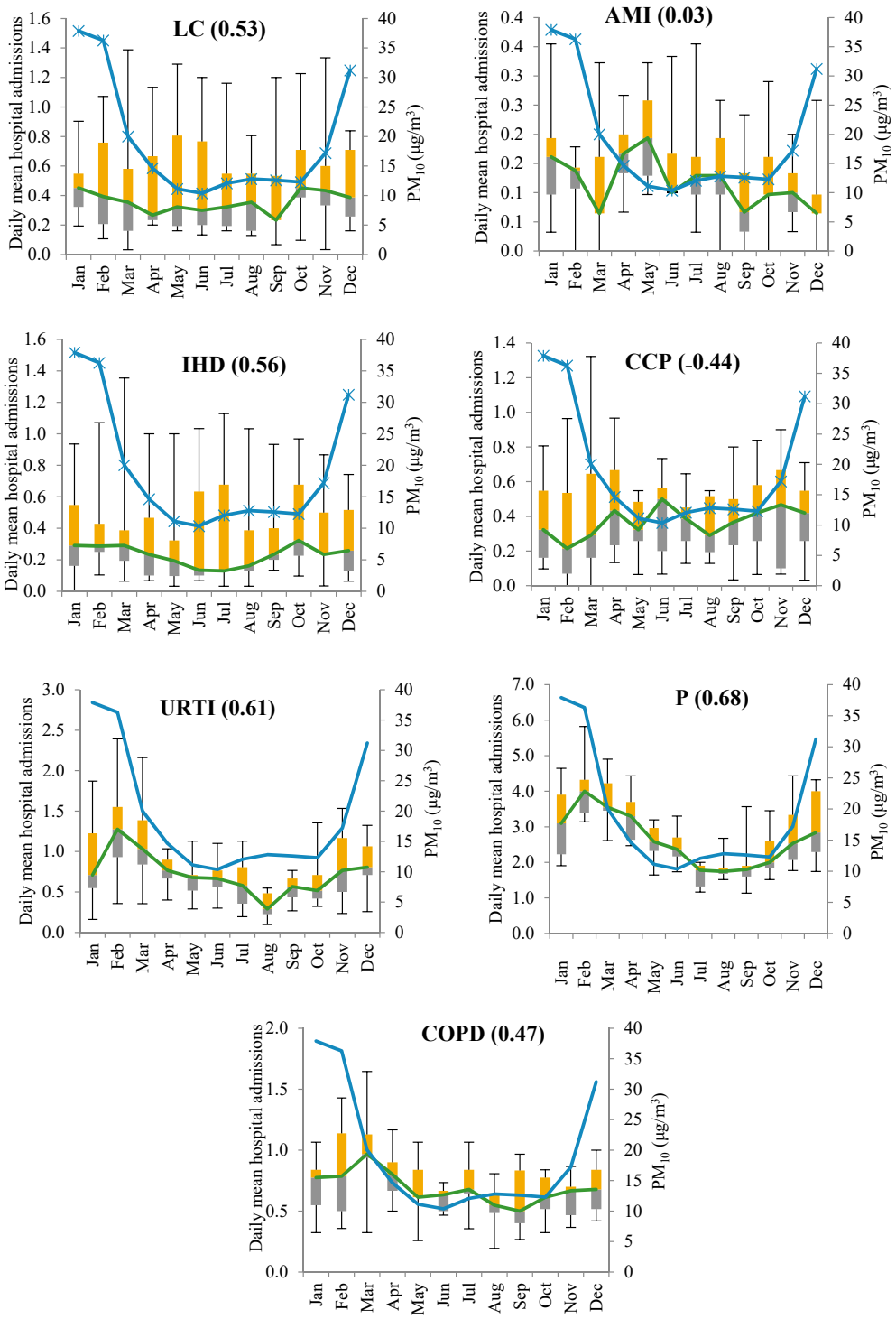

Figure 10. Box-plot analysis of daily mean hospital admissions. The lower (grey) and upper (yellow) limits represent the first (25P) and third (75P) quartiles, and the ends of the whiskers represent the minimum and the maximum values.

The Pearson correlation between monthly means of PM_{10}, hospital admissions and meteorological parameters over the entire period 2008–2016 has been studied. Pearson's correlation in many cases shows a significant correlation (r = ±0.23) (Figure 11). A moderate correlation was found between PM_{10} and P (0.51) and URTI (0.39), respectively. Furthermore, the PM_{10} followed a moderate negative correlation with the boundary layer (−0.61). As the THI index shows in summer has an additional effect on disease evolution, hence

moderate correlation was found between the LC (0.63), IHD (0.52), CCP (0.45), and a weak correlation with the COPS (0.31). In winter the WCT showed moderate correlation with the LC (0.54), IHD (0.48), and CCP (0.41).

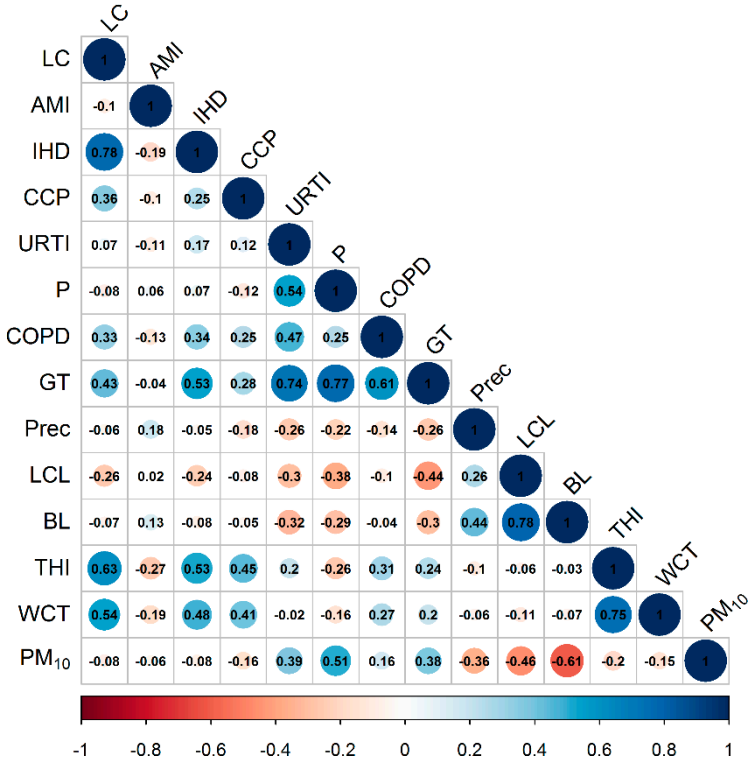

Figure 11. Pearson's rank correlation coefficients between PM_{10}, health effect and meteorological data.

3.7. Morbidity Increase Due to a 10 µg/m³ Rise in PM_{10}

The daily morbidity increase associated with a 10 µg/m³ change in PM_{10} was calculated (Equation (12)).

$$\%\ Morbidityinc_{10\mu g/m3} = \frac{1}{n} * \sum_{1}^{n} \left(\frac{10 * \%\ Morbidityincrease_{1-n}}{\Delta C_{PM10}} \right) \quad (12)$$

where: $\%\ Morbidityinc_{10\mu g/m3}$ —10 µg/m³ PM_{10} disease caused by average growth; $\%Morbidityincrease(1-n)$—individual current disease growth in percent; ΔC_{PM10}—PM_{10} concentration change compared to the previous one (1–10 days); n—the number of days tested.

The most significant increase caused by 10 µg/m³ increase in PM_{10} concentration was found for P, with ${}_{6.84}8.28\%_{8.95}$ after five days (Figure 12).

In the case of URTI and P, the highest number of hospital admissions occurred between the 5th to 7th day, while the 10 µg/m³ PM_{10} increase resulted in a 2.04% and 8.28% morbidity increase. For lung cancer (LC) and CVD (AMI, IHD, CCD), a maximum delay of 5–6 months was found. Except for AMI (<0.1%), an increase of 0.5% was found. Three months of time offset was observed in the case of COPD, identifying an average of 1.51% growth.

3.8. Theoretical Calculation of Hospital Admissions

The ratio between the theoretical and practical disease evaluation was analyzed (Figure 13). The PM_{10} contribution to the hospital admissions on average was 0.34 from

the total number of hospitalizations. The minimum value of 0.27 was obtained in 2012 for AMI while the highest PM_{10} contribution was observed in 2011—0.49 in the case of IHD.

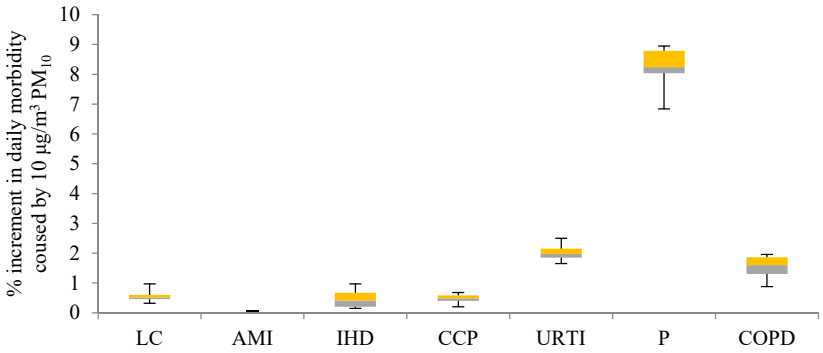

Figure 12. Box-plot analysis of percent increase of hospitalizations for each 10 $\mu g/m^3$ increment of PM_{10}.The lower (grey) and upper (yellow) limits represent the first (25P) and third (75P) quartiles, and the ends of the whiskers represent the minimum and the maximum values.

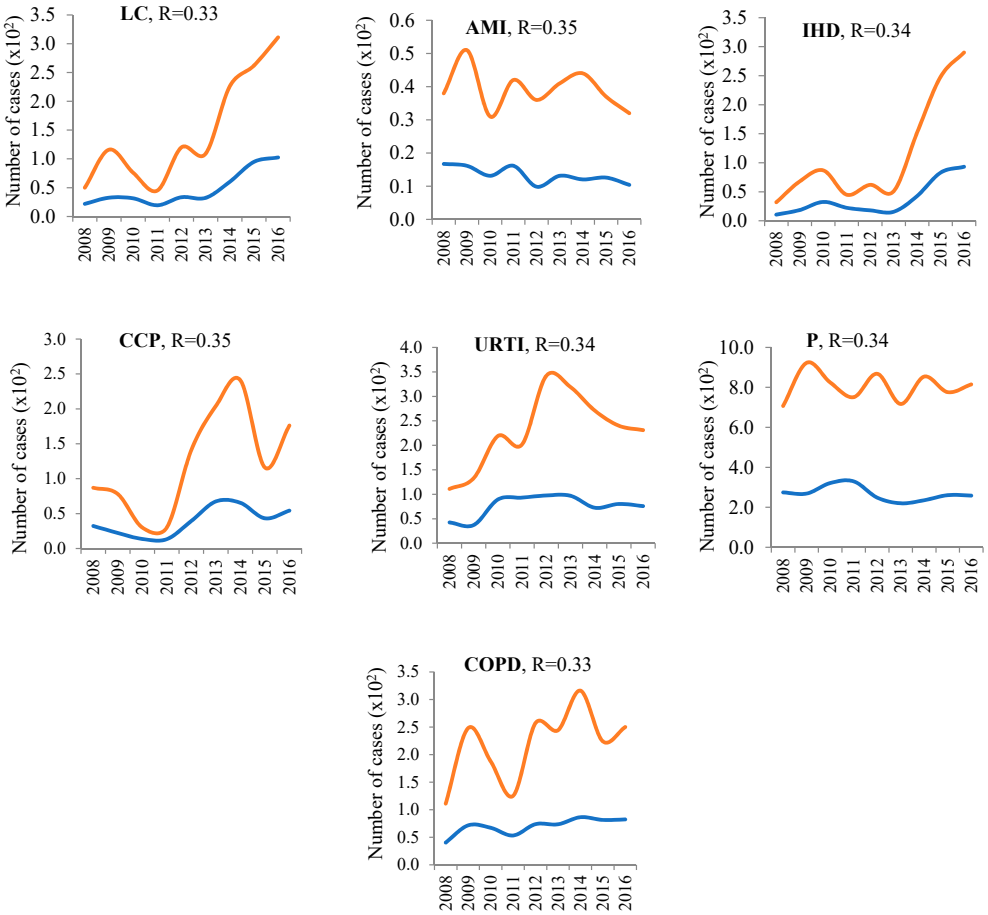

Figure 13. Health endpoint attributable to short- and long-term exposure to PM_{10}.

The orange line represents the total number of cases per year and the blue one marks the PM_{10} contribution to the disease morbidity. In the studied region, ambient PM_{10} concentration had a yearly contribution of $_{500}$,552,$_{603}$ cases to the total morbidity. Taken into consideration the different types of disease frequency the contribution ratio is between 0.88–17.11% (Figure 14).

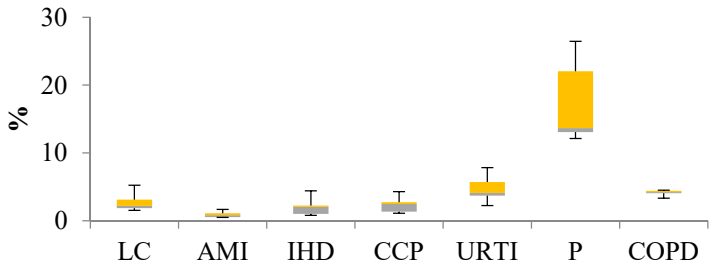

Figure 14. Box-plot analysis of PM_{10} contribution to the annual mean disease frequency. The lower (grey) and upper (yellow) limits represent the first (25P) and third (75P) quartiles, and the ends of the whiskers represent the minimum and the maximum values.

The annual mean disease evaluation caused by the PM_{10} is $_{1.85}2.71\%_{3.58}$ for LC, $_{1.21}2.11\%_{3.02}$ for AMI and IHD, $_{1.62}2.29\%_{2.96}$ CCP. URTI represented by $_{3.68}4.72\%_{5.76}$ P and COPD were the most frequent, with $_{13.46}17.13\%_{20.8}$ and $_{3.99}4.21\%_{4.42}$, respectively.

4. Discussion

The study provides comprehensive information on the combined effect of PM_{10} and climate parameters on human health. Our results are consistent with previous studies showing an increased number of hospital admissions due to cardio-respiratory diseases after increased $PM_{10\text{-}2.5}$ particulate concentration [38–41]. A meta-analysis of 23 mortality and 10 hospital admissions studies confirmed increased morbidity and mortality as a result of higher short-term $PM_{10\text{-}2.5}$ concentrations, with more robust correlations for respiratory than cardiovascular endpoints [42].

Symptom exacerbations and disease progression are prompted by particle-triggered molecular and cellular mechanisms. Locally, PM_{10} deposited in the respiratory tract elicit inflammation by causing oxidative stress, with bronchial hyperactivity, increased sputum production, and injury of the alveolar cells, including alveolar macrophages [43]. These processes lead to impaired lung function and weakened the local immune system, resulting in an increased risk of respiratory disorders following pollutant exposure. Moreover, PM_{10} air pollution exerts deleterious effects on vascular endothelium, sympathetic nervous system, and systemic inflammation, causing increased cardiovascular morbidity and mortality, primarily of ischemic nature [44–46]. Noteworthy, specific groups (e.g., people with cardiovascular risk factors or pre-existing cardiovascular disease) are more vulnerable to the aforesaid harmful effects.

On the other hand, significant differences existed frequently in PM_{10} concentrations between the weekends and weekdays. Daily mean PM_{10} concentration on weekdays 23.1 $\mu g/m^3$ was significantly higher than those on weekends 21.8 $\mu g/m^3$. According to the results, diurnal variations and weekly cycles are a function of emission sources, and meteorological parameters [47,48]. During winter, there are several influencing factors responsible for the higher PM_{10} concentration, like thermal inversion, increased PM_{10} emissions due to indoor heating, and stable atmospheric conditions. The uneven distribution of precipitation reduces the efficiency of the washout mechanism by wet scavenging [49] and the unfavorable topography conditions of the closed basin. As for summer, the evapotranspiration plays an important role in the mixing of air mass by wet convection.

The highest correlation between the PM_{10} and diseases was found in the case of P (0.51), followed by URTI (0.39). The same finding shows that besides PM_{10} the meteorological parameters also have an important contribution to the disease occurrence [50]. Winter cold stress is associated with an increase in influenza and respiratory infections that may affect cardiovascular disease. In addition, THI plays an important role in disease frequency, except for the URTI disease. Furthermore, WCT has a big contribution to the LC, IHD, CCP, COPD. The time delay between the dose-response is closely related to certain AMI subtypes and individual characteristics [51]. Studies assessing hospital admissions due to

COPD indicated that coarse PM has a stronger or as strong short-term effect as fine PM, stating that $PM_{10-2.5}$ are also capable to activate severe adverse reactions enough to require hospitalization [52].

On the other hand, meteorological parameters might have an important impact on PM_{10} concentration; a negative significant correlation between the PM_{10} and boundary layer (−0.605), lifting condensation level (−0.46) and precipitation (−0.36) was observed. The PM_{10} accumulation and this reverse ratio can be explained in light of clouds low position and the presence of frequent fog phenomena which are very common in the Ciuc basin [53].

Song et al. [54] conducted a systematic review and meta-analysis in China, United States, and Europe, in order to assess the consequence of a 10 $\mu g/m^3$ increase in PM_{10} concentration on COPD in the aforementioned countries. Their findings showed a similar intensification of hospital admission number which increased by 1% in China and Europe, and by 2% in the United States, respectively [54]. Despite the significance of the ambient PM_{10} effect in the Ciuc basin, there is little information available in the literature on temporal trend and long-term health effects of PM_{10} in this area. The high air pollution level during the cold season in the Ciuc basin is likely the result of wood-burning, specific topographical and meteorological conditions.

Particle pollution has been linked to a higher risk of exacerbations and respiratory symptoms in subjects with pre-existing lung maladies, compared to the healthy ones.

In concordance with our results, the findings from the European Study of Cohorts for Air Pollution Effects (ESCAPE) revealed a significant association for PM_{10} concentration and the risk for LC (HR 1.22 [95% CI 1.03–1.45] per 10 $\mu g/m^3$). The meta-analysis included 312,944 subjects from 17 cohort studies and 9 European countries, counting 2095 incident lung cancer cases diagnosed during a mean follow-up of 12.8 years. The results were confirmed by further studies, which also indicated that the relationship appeared to be more manifest among men [7].

Studies assessing hospital admissions due to COPD indicated that coarse PM had a stronger or as strong short-term effect as fine PM, which supports that $PM_{10-2.5}$ are also capable to activate severe adverse reactions enough to require hospitalization [52]. After the increased particulate contamination, epidemiological studies have shown deterioration in symptoms and quality of life, increased use of medication and deterioration in lung function [2–5]. Moreover, in a recent meta-analysis of 85 studies from 12 low- and middle-income countries (mostly East Asia and the Pacific), short-term PM_{10} exposure was proved to have stronger associations with COPD morbidity [14].

In recent years, solid evidences were also gathered in relation to air pollution and the cardiovascular system. In line with prior studies conducted in different geographical locations, our findings revealed positive associations between ambient $PM_{10-2.5}$ and hospital admissions for several cardiovascular maladies (i.e., AMI, IHD, and CCP). For example, studies conducted in Western Europe and North America, including the ESCAPE pooled study, detected augmented number of ischemic cardiac events due to higher PM_{10} exposure, indicating increased risk for each 10 $\mu g/m^3$ increase in PM_{10} concentration [55–58]. Similarly, Feng et.al. reported a significant fluctuation in emergency department admissions for selective cardiovascular diseases (including IHD) in Beijing, China, following short-term PM_{10} exposure [59]. As for CCP, to the best of our knowledge, there are no existing studies that specifically addressed the PM-related disease load. According to our observations, in the Ciuc basin, we found a linear relationship between PM_{10} level and hospitalization frequency. This could be explained by the detrimental effect of PM on the right ventricular function. Indeed, the analysis of cardiac magnetic resonance images from 1490 participants from the Multi-Ethnic Study of Atherosclerosis evidenced robust correlation between long-term $PM_{10-2.5}$concentrations and right ventricular mass in specific subpopulations (i.e., individuals with emphysema and current smokers) [42].

In our study, subjects $\geq$ 60 years old (41.3%) and males (60.7%) were the most susceptible to respiratory illnesses owing to the increased level of $PM_{10-2.5}$. These findings

are consistent with literature data and offer a broader view of the demographic-specific associations between air pollution, respiratory and cardiovascular diseases. Indeed, a recent study conducted on a large sample size of 56,221 cardiovascular and 92,464 respiratory emergency admissions in 10 general hospitals from Beijing, reported that males and people aged $\geq$ 65 years were more vulnerable to air pollution [59]. The relationship between pollution exposure and increased morbidity and mortality in the elderly is well-recognized [60,61]. Due to co-morbidities, reduced lung function and weaker immune systems, in case of elder people are prone to exacerbations of chronic diseases (such as COPD) or to respiratory tract infections (particularly pneumonia) [62]. Existing evidence acknowledges gender as a modifier of air pollution effects on human health, but the current findings are inconsistent regarding which gender is more vulnerable. As for male gender, available data indicates that men who smoke respond more intensely to ambient pollution [59]. There is a number of possible explanations for why men are more susceptible to develop pollution-related conditions. Several gendered behaviors (such as alcohol consumption and smoking) have been linked to increased susceptibility to adverse immune-related health effects, including respiratory infections [63]. Gender differences in terms of work-related exposure may also be responsible, men generally spending significantly more time outdoors than women (16.1 h/week versus 9.2 h/week) [64]. Last but not least, sex-linked physiological dissimilarities (e.g., hormonal status, lung maturation and size, airway and vascular responsiveness) are also considered as key factors [63,65].

Our data revealed that children under the age of 5 were more affected by air pollution, with increased hospitalizations for P and URTI. Previous studies have established that outdoor pollution amplifies the burden of severe acute respiratory infections, with increased hospital admissions and mortality, particularly in young children (under 5 years old) [66–68].

Furthermore, the association between exposure to PM and childhood P has been confirmed by data from 10 European birth cohorts within the ESCAPE Project [69]. The main reasons why children face greater risks from air pollution have been comprehensively discussed in previous papers [70,71]. First, their lungs, as well as their immune system, are still developing, hence the susceptibility to inflammation is higher. Secondly, they usually breathe faster than adults, inhaling more pollutants relative to their body size. Thirdly, they spend more time out and are more active outdoors than adults, which also result in higher doses of inhaled pollutant.

Epidemiological evidence suggests that the affinity to disease occurrence increases with age and it is higher after 40 years [72]. The prevalence of the disease is highly dependent on age since the human organism is more sensitive to increased PM_{10} concentration in early childhood and elderly age. In the case of the young generation, the weaker developing immune system is responsible for the frequent illness [73].

5. Study Limitations

Our study was subject to some limitations. First, our survey did not comprise information on documented potential confounders such as occupational/educational/marital status, body mass index, smoking, and alcohol consumption. Second, we were not able to discriminate re-admission frequencies. It is possible for a few patients to have been re-hospitalized within the analyzed timeframe, resulting in underestimation of PM_{10}-related risk variance.

6. Conclusions

We analyzed the influence of meteorological data and PM_{10} concentration, on health in the Ciuc basin, Romania, from 2008 to 2016. Our results indicate that increasing PM_{10}-concentration is associated with increased hospital admissions for cardio-respiratory diseases. In general, the highest PM_{10} concentration was observed in winter, especially in January, due to the high atmospheric stability in winter period, thermal inversions, the higher atmospheric pressure and the increased emission from the biomass burning. The

damaging effects of air pollution can occur from 5–7 days in the case of respiratory diseases and to 3–6 months for pulmonary and cardiovascular diseases. Children under 5 years, men and the elderly up to 60 years are the most likely to suffer from respiratory disease than other age groups, due to air pollution. According to the calculation, one-third of the affected people could be attributed to PM_{10}. The short-term exposure to outdoor air pollutant PM_{10} was positively associated with respiratory admissions. Regarding the long-term exposure, it can be concluded that PM_{10} had negative effect on cardiovascular disease, however, there was a significant delay in dose-response. Furthermore, the PM_{10} and the climate indexes (WCT, THI) have an important role in the increase of disease frequency.

The present study contributed to the limited information about the effects of air pollution in Romania/Eastern Europe and emphasizes the need for additional research on this topic.

Particulate matter (PM) air pollution is an important and modifiable risk factor for adverse health outcomes including cardiovascular disease. Reduction in air pollution exposures is essential to attaining global targets, such as the American Heart Association and World Heart Federation goal of reducing premature CVD mortality by 25% by 2025 [74].

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