processes

MDPI

Article

Comparison Process of Blood Heavy Metals Absorption Linked to Measured Air Quality Data in Areas with High and Low Environmental Impact

Nicoletta Lotrecchiano [1,2], Luigi Montano [3,4,*], Ian Marc Bonapace [5], Tenore Giancarlo [6], Paolo Trucillo [7,8] and Daniele Sofia [1,2,8,*]

1 DIIN-Department of Industrial Engineering, University of Salerno, Via Giovanni Paolo II, 132, 84084 Fisciano, Italy; nlotrecchiano@unisa.it
2 Research Department, Sense Square Srl, 84084 Salerno, Italy
3 Andrology Unit and Service of Lifestyle Medicine in UroAndrology, Local Health Authority (ASL) Salerno, Coordination Unit of the Network for Environmental and Reproductive Health (EcoFoodFertility Project), Oliveto Citra Hospital, 84020 Oliveto Citra, Italy
4 Ph.D. Program in Evolutionary Biology and Ecology, Department of Biology, University of Rome Tor Vergata, 00133 Rome, Italy
5 Department of Biotechnology and Life Sciences, University of Insubria, 21100 Varese, Italy; ian.bonapace@uninsubria.it
6 NutraPharmaLabs, Department of Pharmacy, University of Naples Federico II, Via Domenico Montesano 49, 80131 Naples, Italy; giancarlo.tenore@unina.it
7 Department of Chemical, Material and Industrial Production Engineering, University of Naples Federico II, Piazzale V. Tecchio, 80, 80125 Naples, Italy; paolo.trucillo@unina.it
8 IODO Srl, Corso Vittorio Emanuele, 143, 84123 Salerno, Italy
* Correspondence: l.montano@aslsalerno.it (L.M.); dsofia@unisa.it (D.S.)

Citation: Lotrecchiano, N.; Montano, L.; Bonapace, I.M.; Giancarlo, T.; Trucillo, P.; Sofia, D. Comparison Process of Blood Heavy Metals Absorption Linked to Measured Air Quality Data in Areas with High and Low Environmental Impact. *Processes* **2022**, *10*, 1409. https://doi.org/10.3390/pr10071409

Academic Editor: Olivier Sire

Received: 28 June 2022
Accepted: 18 July 2022
Published: 19 July 2022

Abstract: Air pollution is a problem shared by the entire world population, and researchers have highlighted its adverse effects on human health in recent years. The object of this paper was the relationship between the pollutants' concentrations measured in the air and the quantity of pollutant itself inhaled by the human body. The area chosen for the study has a high environmental impact given the significant presence on the territory of polluting activities. The Acerra area (HI) has a waste-to-energy plant and numerous industries to which polluting emissions are attributed. This area has always been the subject of study as the numbers of cancer patients are high. A survey on male patients to evaluate the heavy metals concentrations in the blood was conducted in the two areas and then linked to its values aero-dispersed. Using the air quality data measured by the monitoring networks in two zones, one with high environmental impact (HI) and one with low environmental impact (LI), the chronicle daily intake (CDI) of pollutants inhaled by a single person was calculated. The pollutants considered in this study are PM10 and four heavy metals (As, Cd, Ni, Pb) constituting the typical particulates of the areas concerned. The CDI values calculated for the two zones are significantly higher in the HI zone following the seasonal pollution trend.

Keywords: PM10; chronicle daily intake; pollution absorption; pollution damage; heavy metals; ecofoodfertility; land of fires

1. Introduction

The containment of pollution and its harmful effects on human health is an emergence of public health worldwide. The World Health Organization (WHO) estimates that about a quarter of the diseases occurring today are caused by prolonged exposure to environmental risks/pollutants [1]. In particular, air pollution is among the top ten global health risk factors that can lead to premature mortality [2]. Epidemiological cohort studies, mainly conducted in the United States and Europe, have shown that long-term exposure to PM2.5 (particles with an aerodynamic diameter less than 2.5 µm) is associated with increased mortality from respiratory diseases, cardiovascular and lung cancer [2–7]. For this reason, in environmental epidemiology, there has been a progressive increase in the development and application of human biomonitoring as a tool for individual exposure assessment and susceptibility and the association between pollutants and early damage. The search for biological indicators in tissues or body fluids has proven reliable for assessing exposure based on environmental measures. It represents a fundamental approach to the characterization and management of health risks. Risk assessment is better defined by direct measurement of biomarkers of exposure and effect in body tissues and fluids versus extrapolation of pollutant concentration data in soil, air, and water, reflecting actual individual exposure to specific pollutants. The direct measure of exposure and the effect of biomarkers in tissues and body fluids is much more relevant to the risk assessment than the extrapolation from the concentration of pollutants in soil, air, and water, reflecting the real individual exposure to that particular pollutant.

Air quality analysis is essential to determine the pollutants' concentration and the impact on the surrounding environment [8]. The effects of airborne pollutants purged into the atmosphere over years of human activities are evident on land, water, food, and human health [9]. According to the literature and the most capable worldwide monitoring systems, the major pollutants present in the atmosphere are gas and particulate matter (PM). NO_x, SO_x, O_3, H_2S, and volatile organic compounds (VOCs) are the most detected gases. Atmospheric particulate matter is a set of solid and liquid particles with various physical, chemical, geometric, and morphological characteristics [10]. It is considered a good indicator of air quality [11]. The sources can be natural (soil erosion, marine spray, volcanoes, forest fires, pollen dispersion, etc.) or anthropogenic (industries, heating, vehicular traffic, and combustion processes). They are generally classified according to their size: particles with a diameter less than 10 μm are identified with the abbreviation of PM10, those with a diameter less than 2.5 μm as PM2.5, and those with a diameter less than 1 μm as PM1. In particular, PM10 (thoracic fraction) can pass through the nose and reach the throat and trachea. Smaller particles such as PM2.5 represent the inhalable fraction and can penetrate even deeper into the lungs, while particles with a smaller diameter can reach the pulmonary alveoli. Particulate matter, considered a good indicator of air quality [11], is made up of a set of solid particles of different nature, chemical composition, and size; it varies from city to city according to the degree of development of the urban center and the presence of industries, fuels used and type of domestic heating. The atmospheric particulate remains in the air from 5 to 16 h [12] and can be transported long distances. Atmospheric phenomena such as wind and rain can help dilute and reduce PM concentration in the air. Particulates emitted into the atmosphere directly from the source refers to the primary type, while the chemical–physical transformations of other substances are the secondary type. The major components of atmospheric particulate matter are sulfate, nitrate, ammonia, sodium chloride, carbon, and mineral powders. Numerous chemical substances, such as polycyclic aromatic hydrocarbons (PAHs) and metals (such as lead, nickel, cadmium, arsenic, vanadium, and chromium), can adhere to the surface of fine dust causing effects on the health of the exposed population. PM causes several health effects, including many respiratory-related ailments [13,14]. The International Agency for Research on Cancer (IARC) has classified air pollution in Group 1, which is characterized by carcinogenic substances for humans. The World Health Organization has defined guidelines to establish concentration limits to control airborne pollutants. Each country has implemented these guidelines with national directives: in Italy, the pollutants' concentrations are regulated by Legislative Decree 155/2010. This decree limits all pollutants' annual, daily, and hourly concentrations. Among the heavy metals included in the legislation, we find arsenic (As), cadmium (Cd), nickel (Ni), and lead (Pb), and their annual limits are 6 ng/m^3, 5 ng/m^3, 20 ng/m^3, 0.5 $\mu g/m^3$, respectively. The toxicity of these metals on soil, water, and human health are well known and extensively studied in the scientific literature [15].

Airborne heavy metals can enter the body through the skin, by inhalation, or ingestion of contaminated water or food. Toxicity derives from the replacement of elements ordinarily present in the body (blood, urine, and hair) with heavy metals and the alteration of the normal functions of the various organs. In most cases, people are not exposed to quantities of heavy metals that would trigger symptoms or require a test. Most chronic or acute exposures have an occupational origin, particularly in the case of manufacturing industries that use metals or produce batteries containing cadmium, lead, and mercury, or pesticides, containing arsenic or may originate in places with high levels of environmental pollution [16]. Cd is very mobile in the soil and is absorbed by microorganisms that absorb organic matter from the soil. It has been suggested that exposure to Cd doses has adverse effects on both human male and female reproduction and affects pregnancy or its outcome. Exposure to Cd affects human male reproductive organs/system and deteriorates spermatogenesis and semen quality, especially sperm motility and hormonal synthesis/release [17]. The Pb accumulation can negatively affect the soil pH and absorption capacity [18]. Heavy metals can also affect the human reproductive system: cadmium and lead act on the reproductive system, damaging it and limiting its correct functionality [19]. Cadmium and lead are present, albeit in minimal quantities, in all foodstuffs that are ingested and contribute to increasing the organism's toxicity. Therefore, these heavy metals are introduced into the human body by inhalation due to the fraction present in the atmosphere and by ingestion due to their presence in food, thus increasing the risk associated with them [17]. For example, high levels of cadmium can adversely affect kidney functions, causing decompensation due to its malfunction [20]. Arsenic negatively affects the digestive, urinary, cardiovascular, and DNA methylation systems [21]. Generally, the need for nickel is completely satisfied by the diet, but an excess can accumulate in the liver, kidneys, bones, and aorta. Excessive nickel intake has also been associated with an increased carcinogenic risk, such as lung and prostate cancers, heart attack, and stroke [22].

To verify the effects of environmental pollution on human health, it is necessary to have detailed information on the concentrations of the major airborne pollutants. National monitoring networks are available to measure the pollutants' concentrations in the air. Given their characteristics, the technologies implemented by these entities have a low spatial and temporal resolution. Recently, sensors for low-cost air quality monitoring based on IoT (Internet of Things) technology have been developed. This has allowed the implementation of air quality monitoring networks with high spatial and temporal resolution [23] that enable the detection of particulate matter of different sizes (PM10, PM2.5) and the measurement of the concentration of gases in the atmosphere (SO_2, NO_2, CO, O_3, VOC), reliably protecting data integrity [24]. The new type of intelligent measuring device could be easily installed in many parts of the city following an optimization in the choice of places [25]. The available air quality data are the basis for developing mathematical models for data spatialization [26] and forecasting [27]. Furthermore, dispersion models support experimental measures to define the behavior of pollutants in the atmosphere and verify their long-term effects in case of accidental occurrence [28]. Monitoring the number of dispersed pollutants and the implementation of long-term strategies to favor their reduction is necessary to safeguard the health [29–31] of resident populations and travelers [32]. Outdoor air quality can be reflected inside buildings, highlighting the importance of monitoring pollution levels to implement filtering and ventilation systems. This is especially important for home settings or other locations frequented by vulnerable individuals, for example, schools and elderly care centers [33–35]. Comparing the data from environmental pollution and exposure to chemical compounds with the actual contamination values found in the organism can verify their consistency and deterministic association. This will also help to translate the degree of exposure from the environment to the organism as a fundamental step in understanding the environment/health relationship. Measuring these substances and the resulting biological effect and establishing a close dose–effect relationship between them represents the right path to sharpen biological risk assessment.

The Environmental Protection Agency defines exposure as the contact of an organism (humans in the case of health risk assessment) with a chemical or physical agent [36]. Exposure involves any interaction, internal (e.g., respiratory tract) or external (e.g., skin) of the human body, with a contaminant present in the atmosphere. This phenomenon requires that, at the same time, there is the presence of a human subject and high levels of pollutants in a particular time and space [37]. It is quantitatively expressed by the duration of the contact and the relevant pollutant concentration and can be assessed using air quality data provided by air monitoring devices [38]. As defined by Asante and Duah, chronic daily intake (CDI) measures long-term (chronic) exposures. It is based on the number of events assumed to occur within an assumed lifetime for potential receptors. The intake value defines the amount of a chemical absorbed during the exposure. In contrast, the absorbed chemical quantity into the bloodstream during exposure is represented by the dose and is calculated by considering physiological parameters. In general, the physiological parameters are not readily available. Intake and dose are considered the same (i.e., a 100 percent bloodstream absorption from contact is assumed) [39]. In this perspective, also considering the study participants' characteristics, the CDI was calculated for each metal compared with the blood levels. In this work, air quality data measured by the regional monitoring network were used to calculate the absorption of inhaled pollutants in areas with high and low environmental impact in the Campania region (Southern Italy). The so-called "Land of Fires" in the northern part of the Naples metropolitan area is characterized by a multiplicity of pollution sources (illegal disposal of urban, toxic, and industrial wastes, dumping practices, traffic, and intensive agriculture). It is considered an area of high environmental impact. In comparison, the area with low environmental impact is Oliveto Citra in the Province of Salerno [40]. Several serious concerns for general health, including reproductive ones, in "Land of Fires" were reported. Bio-monitoring studies indicated that trace toxics elements (e.g., Cr, Cd, Ni, Pb, Al) feature prominently in this area [41,42], including dioxins [43]. In response to such serious concerns, the EcoFoodFertility initiative [44] has been launched to better understand the environmental impact of toxicants on healthy humans [42,45]. It is a multicenter, multidisciplinary research connecting human lifestyle and dietary habits to the environmental consequences of exposure to toxicants. In the frame of this project, the present paper aims to link the heavy metals in human blood compared with the pollutant concentrations that are aero-dispersed. The measured PM10 and heavy metals concentration was used to calculate the chronicle daily intake (CDI) over a year. Using the average population characteristics, the CDI equation parameters were set. The reference year for the measurements was 2016. The calculated CDI values for PM10 and the heavy metals were compared considering the different impact areas (HI and LI).

2. Materials and Methods

2.1. Participants

The biomonitoring study was carried out in accordance with the Code of Ethics of the World Medical Association [46], approved by the Ethical Committee of the Local Health Authority Campania Sud-Salerno (Committee code 43/2015/06). The recruitment of all participants within the fertile age (20–40 years old) across the two cities of the Campania Region (Acerra in the Province of Naples and Oliveto Citra in the Province of Salerno, as explained in Section 2.3, are representative of high and low environmental impact areas) was conducted during 2016. Enrolment criteria were as follows: residence for at least 10 years in the study area, no known chronic diseases (diabetes or other systemic diseases), no varicocele, no prostatitis, and other factors that could affect semen quality (such as fever, medications, exposure to X rays, etc.), no reported history of drug abuse and no known occupational exposures to toxic chemicals. The sample's representativeness was defined in relation to the numerous biomonitoring in these two areas, which have led to the carrying out of various studies [47–51]. Data were collected by questionnaire and physical examination, including the urogenital evaluation (testis volume and transrectal prostate evaluation). Informed consent was obtained from all males before sample collection. The mean age of participants from the low impact area was 30 years, and the Body mass index (BMI) was 24.6, while for the participants living in the high impact area, the age and the BMI values were 28 and 25, respectively. Upon enrolment, a code number (1, 2, 3 . . . n) was assigned to each volunteer by the recruiting andrologist (the recruiter). Each code number was uploaded into a computer database along with personal and clinical information (e.g., age, BMI, area of residence). The examining andrologist (the evaluator, different from the recruiter) performed semen quality evaluation, only having access to the code number assigned to each sample. The participants' characteristics are reported in Table 1.

Table 1. Participants' average characteristics.

	LI Area	HI Area
Number of male participants	35	40
Age, years	30	28
Weight, kg	78	77
Height, m	1.77	1.76
BMI	24.6	25

2.2. Heavy Metals Procedure to Assess the Blood Concentration

Blood samples were collected from each subject by veni-puncture. Aliquots (500 µL) of whole blood or semen contained in metal-free, no EDTA-containing tubes were placed onto a ceramic evaporating dish and heated at 90 °C for 1 hr. After cooling, 1 mL HNO_3 68% (Sigma Aldrich—Darmstadt, Germany) and 250 µL $HClO_4$ (Sigma Aldrich, Darmstadt, Germany) were added, and the mixture was heated at 150 °C until carbonization. Samples were placed in a muffle oven at 550 °C for 5 hrs, and the resulting ashes were dissolved in 10 mL 1% HNO_3. The elemental analyses of whole blood of trace elements were carried out by Inductively Coupled Plasma-Optical Emission Spectrometer (ICP-OES) by an iCAP™ 7000 Series ICP-OES (Thermo Fisher Scientific, Waltham, MA, USA). To prevent interference with calibration solutions, a matrix modifier was added to 100 µg/L yttrium solution (Merck KGaA, Darmstadt, Germany). Elemental contents were calculated using standard curves, and the final concentrations were expressed as mg/L. A stock solution (ICP multi-element standard solution Certipur®, 1000 mg/L, Merck KGaA, Darmstadt, Germany) was used to prepare the standard solutions. The limits of detection (LOD) and quantification (LOQ) were calculated as the blank signal plus three or ten times its standard deviation, respectively [42].

2.3. Air Quality

The areas considered in this study are two southern Italian cities of middle to small dimensions, which can be regarded as high and low impact areas. The High Environmental Impact area (HI) is Acerra, in the Metropolitan City of Naples, Italy, where a waste treatment plant has burnt 600,000 tons yearly since 2009. The study by Senior and Mazza underlined that cancer-related deaths in that area are much higher than the Italian average [52]. Moreover, the city is densely populated and is surrounded by a fast road that is highly trafficked. As a reference for the Low Environmental Impact area (LI), the city of Oliveto Citra (in the Southeast of the Salerno province, Italy) was chosen (Figure 1). The city, located in an area of relatively low human density, is characterized by a small industrial area. Due to the peculiarity of the areas investigated, the particulate matter PM10 (aero-dispersed particles with diameter < 10 µm) concentration was considered for analysis in 2016. The average PM10 particulate concentration data for 2016 were taken from the daily validated database of the Regional Environmental Protection Agency for the Campania Region (ARPAC). In the HI area, the ARPAC regional air quality monitoring network consisted of 3 measuring devices: Acerra Scuola (AS), Acerra Capasso (AC), and Acerra Industriale, classified as suburban, industrial, and urban traffic stations. The average of the three measuring devices was considered for the comparison with the LI area. In the LI area, there is no ARPAC air quality monitoring station. However, due to the similarity of both the orographic and the urban and extra-urban context, the population density, and the number of industrial activities, the nearby ARPAC monitoring station (OL) located in Battipaglia (province of Salerno) was considered. It can therefore be assumed that the

PM10 concentrations detected in Battipaglia are similar to those recorded in Oliveto Citra. To calculate the concentrations of heavy metals, the percentage compositions with respect to PM10 measured by ARPAC for the reference year (2016) were used. The concentrations obtained are reported in the Section 3.2 for each metal for the HI and LI zones.

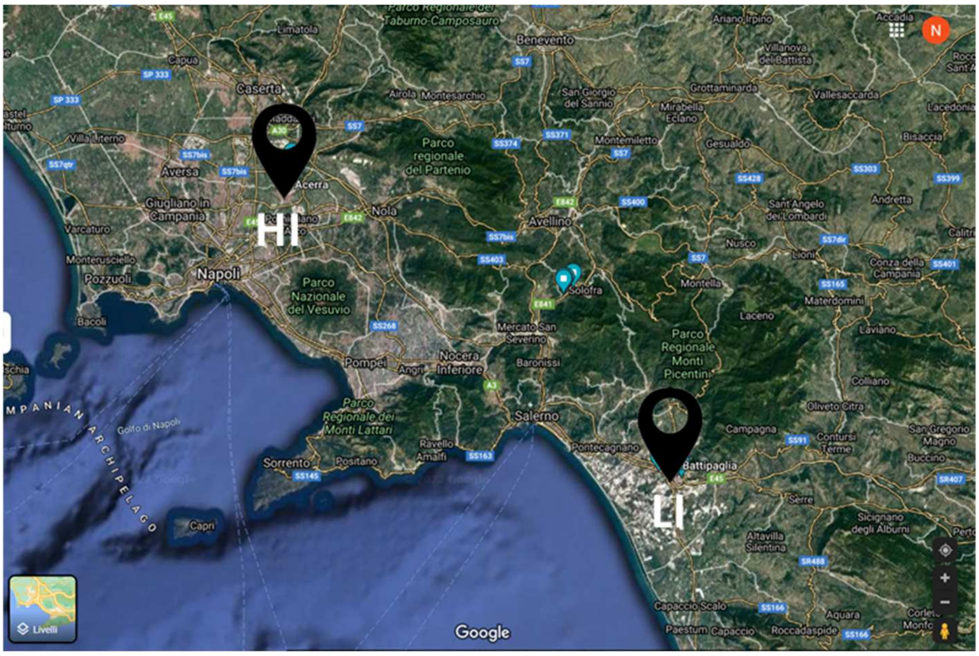

Figure 1. Localization of the high and low environmental impact areas, Acerra (HI) and Battipaglia (LI).

The measurement devices installed by ARPAC consist of buildings of approximately 6 m^2 which contain all the instruments suitable for controlling the parameters relating to air quality in accordance with the regulatory provisions of Legislative Decree 155/2010. The particulate matter measurement method is defined by the UNI EN 12341: 2014 standard "Ambient air-Reference gravimetric method for determining the mass concentration of suspended particulate PM10 or PM2.5". The measuring principle is gravimetry or absorption by β radiation. The concentration values used in this study are obtained gravimetrically. The reference method for the determination of PM10 particulate material is based on the collection of the PM10 fraction on a special filter and subsequent determination of its mass by gravimetric method in the laboratory after the conditioning filter has been carried out under controlled temperature conditions (20 °C ± 1 °C) and humidity (50 ± 5%). The same is carried out for PM2.5. In addition to the reference, there are equivalent methods for measuring PM10 (for example, automatic instrumentation that exploits the principle of absorption of β radiation by the sampled dust).

2.4. Pollutant Adsorption

To compare the air quality pollution with human health, the pollutant adsorption has been evaluated by computing the chronicle daily intake (CDI, [μg/kg]). This calculation has been performed according to Equation (1), developed by US EPA [53], and considers both the particle-bunds metals and the inhalation rate effects. The equation is reported as follows:

$$CDI = (C_i \times IR \times ET \times EF \times ED)/(BW \times AT) \quad (1)$$

where:

C_i is the contaminant concentration measured, [μg/m^3];
IR is the inhalation rate [m^3/h];

BW is the body weight [kg];
ET is the exposure time [h/day];
EF is the exposure frequency [days/year];
ED is the exposure duration [years]
AT is the averaging time [days].

Considering the population characteristics of the whole population tested, reference values for the inhalation rate for adult males (workers) were adopted according to ICRP and set at 1.5 m^3/h [54]. Likewise, the measured PM10 values were adopted for Ci. The exposure time (ET) and the exposure frequency (EF) were set equal to 24 h/day and 260 days/year, respectively. The exposure duration (ED) was considered equal to 24 years based on the US EPA [55]. Body weight (BW) was calculated as the average of the population tested, equal to 77 kg. Moreover, according to the US EPA [56], the averaging time (AT) was considered equal to 8760 days for adults for non-carcinogens, while for carcinogens, it was considered equal to 25,550 days. The CDI was calculated to assess the monthly people's exposure to account for the pollutant amount retained until the test. The contaminant concentration used to evaluate the adsorption was the PM10, while the metals (As, Cd, Ni, and Pb) that are part of PM10 were defined by the legislative decree 55/2010. Since the metal measurements in PM10 are not directly available from the 2016 ARPAC data, their corresponding presence in PM10 was assessed using the measurements available for 2019. This implies the assumption that the considered metals fraction in PM10 has been unchanged over the years.

3. Results and Discussion

3.1. Heavy Metals Blood Concentrations

The blood heavy metals average concentrations are reported in Figure 2. As explained in Section 2.2, the measurements refer to 2016, and the metals values reported in Figure 2 are the average in the period considered. The metal concentrations are higher in the patients belonging to the HI area. The average metals concentration has been calculated considering the whole patient set and adjusted for the age, BMI and attitude to smoking. The corresponding average value and the 95% confidence interval (CI) are reported in Table 2.

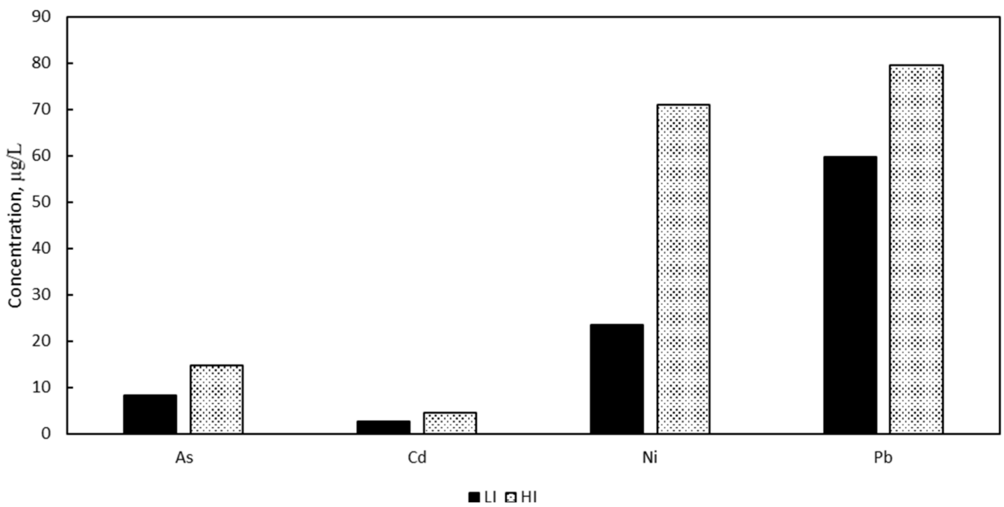

Figure 2. Heavy metals average concentrations measured in the patient blood of the LI and HI area, considering age, BMI, and attitude to smoking.

Table 2. Heavy metals metrics.

	Average Concentration, μg/L		95% CI	
	LI Area	HI Area	LI Area	HI Area
Arsenic	8	15	6–12	9–23
Cadmiums	2.6	4.5	1.4–5.1	2.1–9.4
Nickel	23.5	71	8–68.4	26.1–193
Lead	59.7	79.6	39.3–90.7	46.6–135.9

The reference limit values for the heavy metals have been obtained from the ISTITSAN Report [57]. According to the reference values, all the investigated heavy metals for the HI area exceeded the maximum reference concentration. In particular, nickel was 32% higher than the threshold, cadmium was 1.27%, and arsenic and lead were 1% below the threshold. The Ni and Cd average values also exceeded the maximum reference concentration in the LI area.

3.2. Air Quality

Analyzing the air quality data during 2016, there is a difference in the PM10 annual average between the HI and LI areas by 33% (Table 3). Figures 3 and 4 show PM10 and PM2.5 daily average concentrations in HI and LI areas. These values are often above the law limit of 50 μg/m^3 for PM10 and above 25 for PM2.5 μg/m^3 compared to the LI area. Compared to the LI, the HI area had higher exceedances over the law limit for both PM10 and PM2.5 observed over the years.

Table 3. PM10 and PM2.5 air quality indexes for HI and LI areas during 2016.

2016		Station			
		HI Area			LI Area
		AS	AC	AI	OL
PM10	Annual average, μg/m^3	39.4	42.5	33.6	25.7
	Standard deviation, μg/m^3	26.6	24.1	20.6	13.6
	Minimum, μg/m^3	1.8	5	2.8	3.2
	Maximum, μg/m^3	159.2	150.3	139.6	83.5
PM2.5	Annual average, μg/m^3	18.0	—	17.8	18.8
	Standard deviation, μg/m^3	25.2	—	18.7	10.5
	Minimum, μg/m^3	1.8	—	0.4	0.9
	Maximum, μg/m^3	104.5	—	84.5	45.5

As shown in Figure 3, the PM10 concentrations measured in the HI area exceed the law limit 66 times, but only 17 times in the LI area. In both areas the PM10 concentrations are high during the winter period due to the usage of domestic heating. Moreover, as previously said, the HI impact area is characterized by a high industrial development; therefore, the difference in PM10 levels between the two areas could be attributed to it. Figures 3 and 4 show low PM10 and PM2.5 concentration values during the summer due to reduced use of domestic heating systems. The pollution levels of the two areas are different, with the LI area levels being lower than those of the HI area. The minimum pollution level is reached in August for the HI area and October for the LI area. Given the seasonality of pollution, it is generally lower during the summer period, but considering that the LI area is located 10 km from the coastal area and is crossed by a busy highway, the pollution levels in summer are higher.

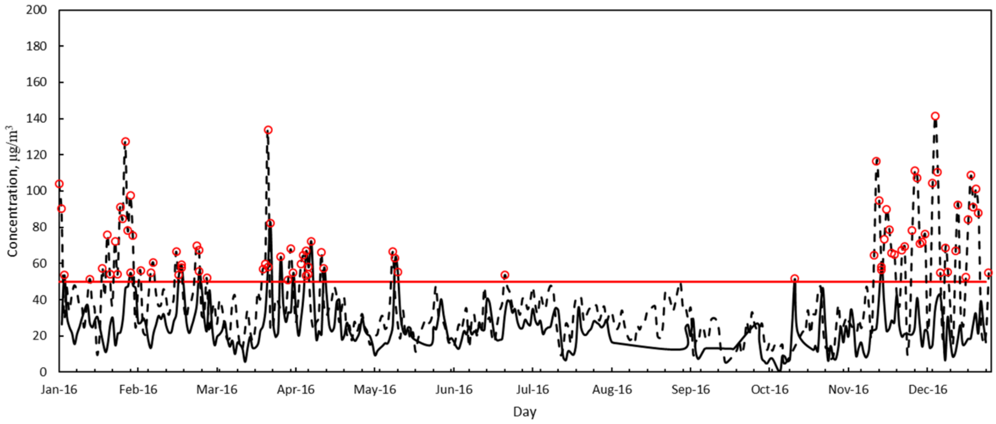

Figure 3. PM10 daily average concentrations measured in the HI (dashed black line) and LI (solid black line) area during 2016 from the ARPAC network. Exceedance from the law limit according to the D.Lgs. 55/2010 (solid red line) is represented by red dots.

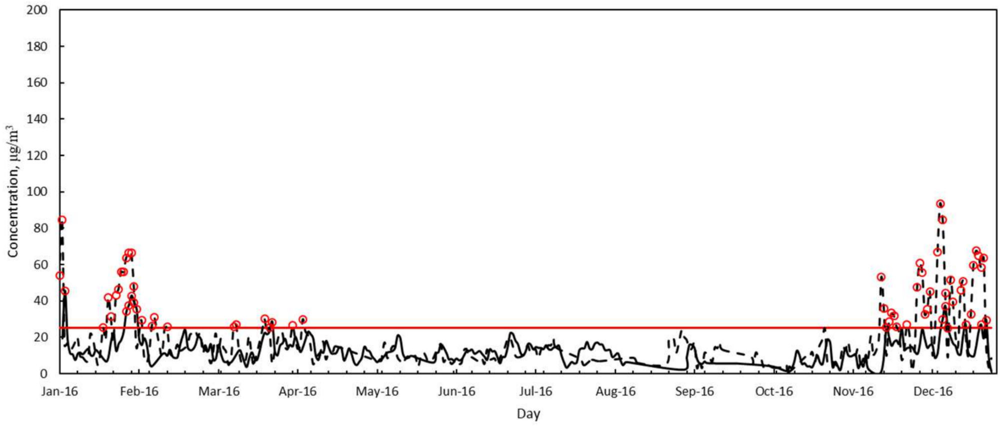

Figure 4. PM2.5 daily average concentrations measured in the HI (dashed black line) and LI (solid black line) area during 2016 from the ARPAC network. Exceedance from the law limit according to the D.Lgs. 55/2010 (solid red line) is represented by red dots.

The metals concentration values obtained using the percentages shown in Table 4 are shown in Figures 5–8. Considering the metals percentages found in PM10, a first difference is noted between the two areas. The metals values in the HI zone are higher than in the LI zone. Consequently, Figures 5–8 show higher metals concentrations for the HI zone than the L1 zone.

Table 4. PM10 metal concentration for HI and LI area during 2016.

		HI Area	**LI Area**
As	Annual average/± StandDev, μg/m^3	0.6 ± 0.4	0.4 ± 0.2
	% in PM10	1.7	1.5
Cd	Annual average/± StandDev, μg/m^3	0.5 ± 0.3	0.3 ± 0.2
	% in PM10	14	13
Ni	Annual average/± StandDev, μg/m^3	5.1 ± 3.2	3.0 ± 2.1
	% in PM10	14	12
Pb	Annual average/± StandDev, μg/m^3	0.08 ± 0.00	0.1 ± 0.003
	% in PM10	0.25	0.25

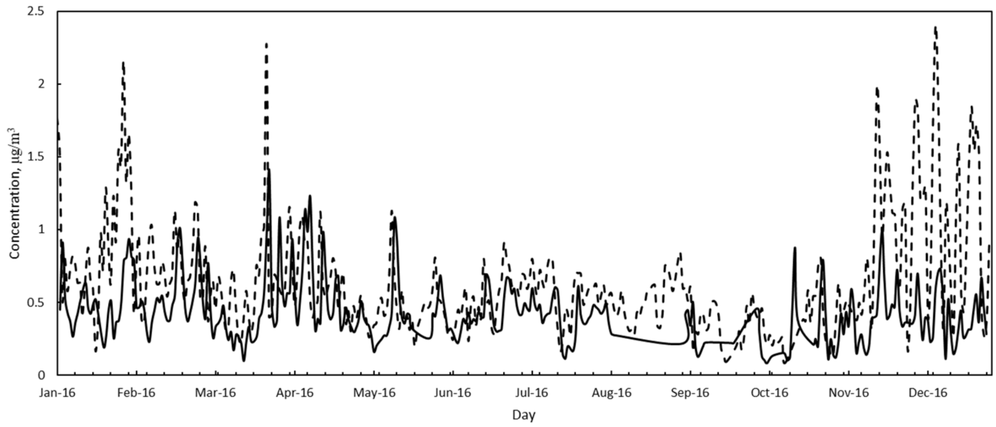

Figure 5. Arsenic daily average concentrations measured in the HI (dashed black line) and LI (solid black line) area during 2016 from the ARPAC network.

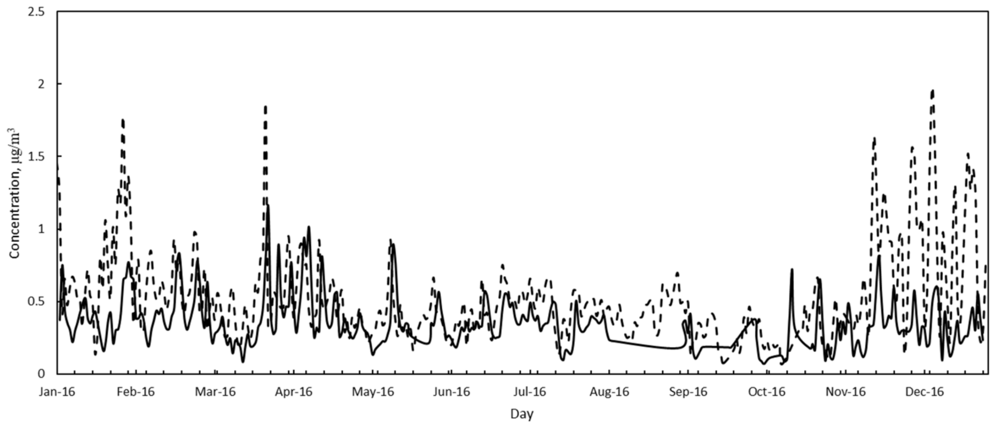

Figure 6. Cadmium daily average concentrations measured in the HI (dashed black line) and LI (solid black line) area during 2016 from the ARPAC network.

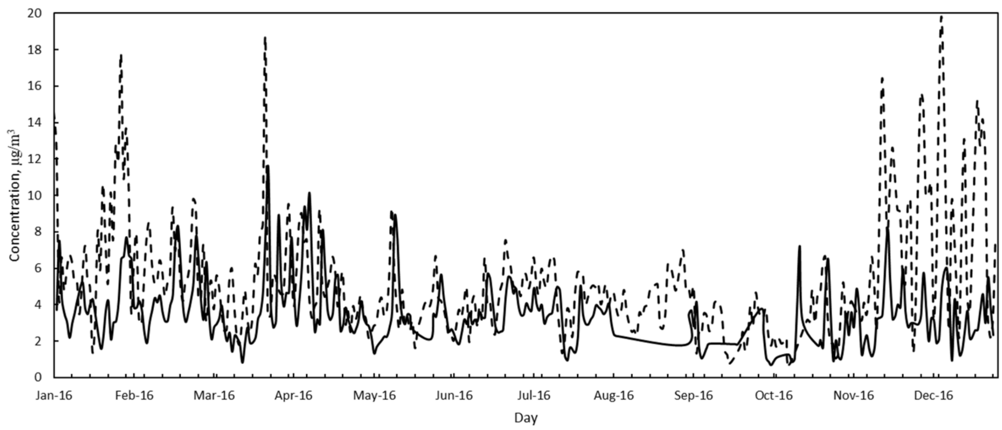

Figure 7. Nickel daily average concentrations measured in the HI (dashed black line) and LI (solid black line) area during 2016 from the ARPAC network.

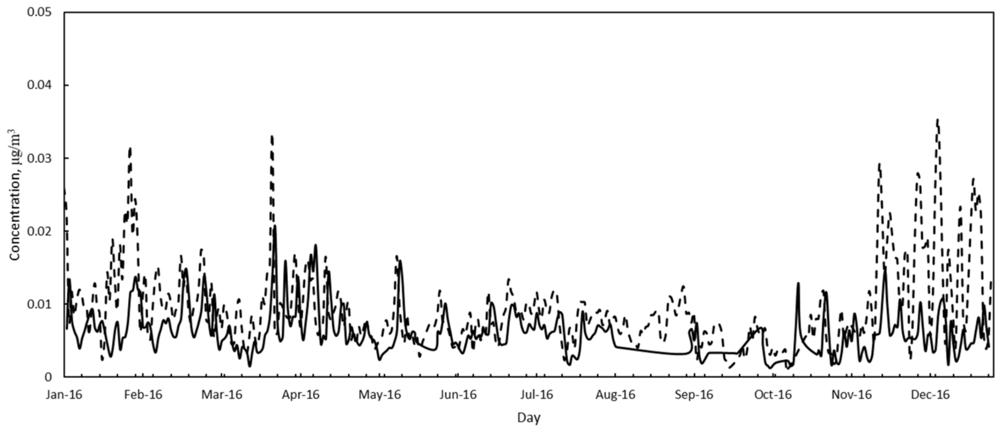

Figure 8. Lead daily average concentrations measured in the HI (dashed black line) and LI (solid black line) area during 2016 from the ARPAC network.

The difference between metals in the winter months (Sept-Dec) corresponds to the increase in domestic heating use. However, the HI area has values in metals higher than those measured in LI, which remain low and constant for most of the year. The difference between the values measured in the two zones is, therefore, attributable to a source of additive pollution with respect to the basic pollution from heating and the problem also encountered in LI.

3.3. Pollutants Adsorption

The CDI was calculated monthly (values are reported in Table 5) for 2016, using Equation (1). Figure 9 shows that the absorption levels in the HI zone are, on average, 74% higher than in the LI zone. Furthermore, absorption is greater in the winter when the concentrations of pollutants are notoriously higher. The minimum absorption occurs in the HI zone in October (linked with the minimum PM10 levels described in Figure 3). This stems from the high amount of rainfall recorded in October, which significantly reduced the measured pollution levels (as reported in the ARPAC reports).

Table 5. Chronicle Daily Intake Expressed in μg/(kg*day).

	Arsenic (As)		Cadmium (Cd)		Nickel (Ni)		Lead (Pb)	
	LI Area	**HI Area**	**LI Area**	**HI Area**	**LI Area**	**HI Area**	**LI Area**	**HI Area**
January	1.58	3.24	1.30	2.67	13.02	26.70	0.02	0.05
February	1.77	2.43	1.46	2.01	14.61	20.05	0.03	0.04
March	1.48	2.15	1.22	1.77	12.18	17.67	0.02	0.03
April	1.89	2.19	1.56	1.81	15.56	18.06	0.03	0.03
May	1.19	1.66	0.98	1.37	9.80	13.65	0.02	0.02
June	1.45	1.70	1.19	1.40	11.91	14.00	0.02	0.03
July	1.41	2.04	1.16	1.68	11.64	16.83	0.02	0.03
August	0.26	1.80	0.21	1.49	2.15	14.85	0.00	0.03
September	0.36	1.20	0.29	0.99	2.94	9.86	0.01	0.02
October	0.74	1.00	0.61	0.82	6.07	8.23	0.01	0.01
November	1.20	2.59	0.99	2.13	9.89	21.32	0.02	0.04
December	1.33	3.97	1.10	3.27	10.98	32.69	0.02	0.06

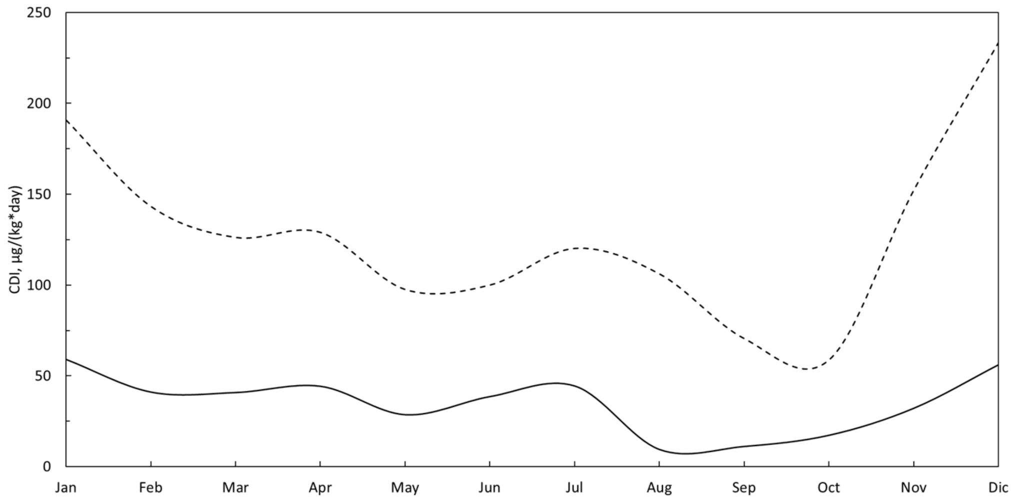

Figure 9. PM10 CDI for the HI (solid black line) and LI (dashed black line) area for every month in 2016.

The CDI calculated for the metals considered (As, Cd, Ni, Pb) are reported in Figures 10–13, respectively. The curves representing the HI and LI areas show a higher percentage average difference for all the metals. In detail, for all the metals considered, the difference between the HI and LI areas is around 40–50%.

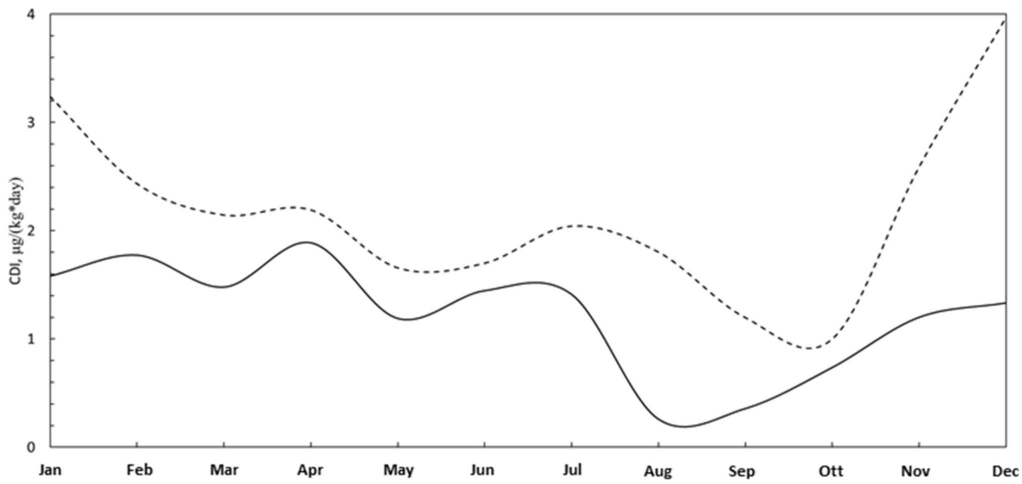

Figure 10. Arsenic (As) CDI for the HI (solid black line) and LI (dashed black line) area for every month in 2016.

The lead CDI values were below the oral reference dose (RfD) for lead (0.00014 mg/kg·day) for all the months in both areas. CDI values of cadmium were above the oral reference dose (RfD) (0.001 mg/kg·day) during 10 months in the HI area, achieving a maximum in December of 3.27 µg/(kg·day). In contrast, the values for the LI area are above the reference dose for 7 months. The HI area is highly industrialized, so the environmental contamination from industrial cadmium and human exposure has increased [58]. Considering the CDI values for Nickel, they are below the reference dose (RfD) (0.02 mg/kg·day) for all months and above the reference dose during the winter period (January, February, November, and December). The CDI values for arsenic exceed the oral reference dose (Rfd) (0.003 mg/kg·day) for all the months considered in the LI and HI area. The oral reference dose (RfD) is assumed as the threshold value (obtained from US EPA) [55]. The metal values were in line with those found in men exposed to road dust and high pollutants levels [59,60]. The test of the CDI average values calculated for each metal and the *p*-value obtained by the Poisson correlation were significantly different from zero. This highlights that the two distributions come from different populations. The CDI values for each metal indicate a proportionality between them and the measured pollutant concentrations. Above all, this proportionality is expected, considering the pollution seasonality and its variability during the year. When pollution levels are low, exposure is reduced, and consequently, the amount of pollutants inhaled by the human body decreases [61]. The high heavy metals concentration values measured in the HI area are probably linked to the heavy metals aero-dispersed. The causes of the high pollution levels are found in the characteristics of the areas considered. Industrialization, urbanization, traffic levels, and domestic heating technology predominantly affect the pollutants emissions. The population considered is also essential for the definition of pollutants absorption: age, attitudes to smoking, and the amount of time spent in the open air are further factors that massively influence the CDI value. A drastic decrease in pollution levels would be desirable to reduce the pollutants absorption by inhalation, which would significantly reduce the CDI values. Knowledge of the pollutants' impact on human health is a fundamental tool for the conscious management of the environment. The high values of heavy metals found in the bloodstream of the patients examined must alarm the institutions to apply policies that significantly reduce the concentrations of these metals. It is certain that installing air quality measurement systems closer to the population with a greater space–time resolution would lead to a more detailed and real-time analysis of pollution levels.

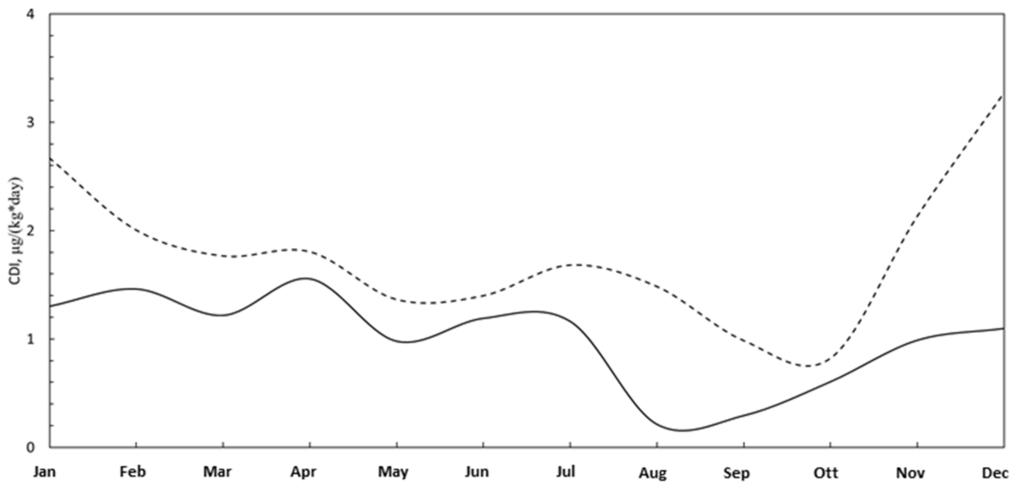

Figure 11. Cadmium (Cd) CDI for the HI (solid grey line) and LI (dashed grey line) area for every month in 2016.

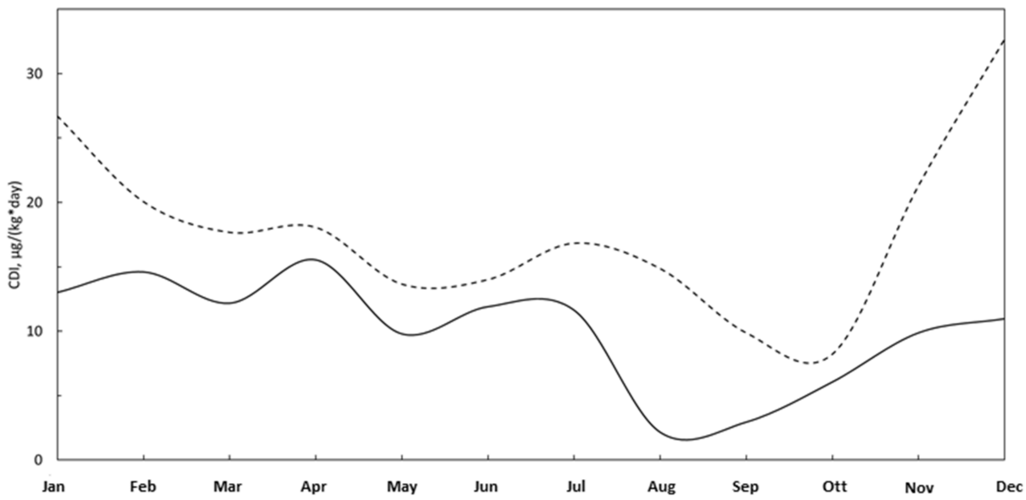

Figure 12. Nickel (Ni) CDI for the HI (solid black line) and LI (dashed black line) area for every month in 2016.

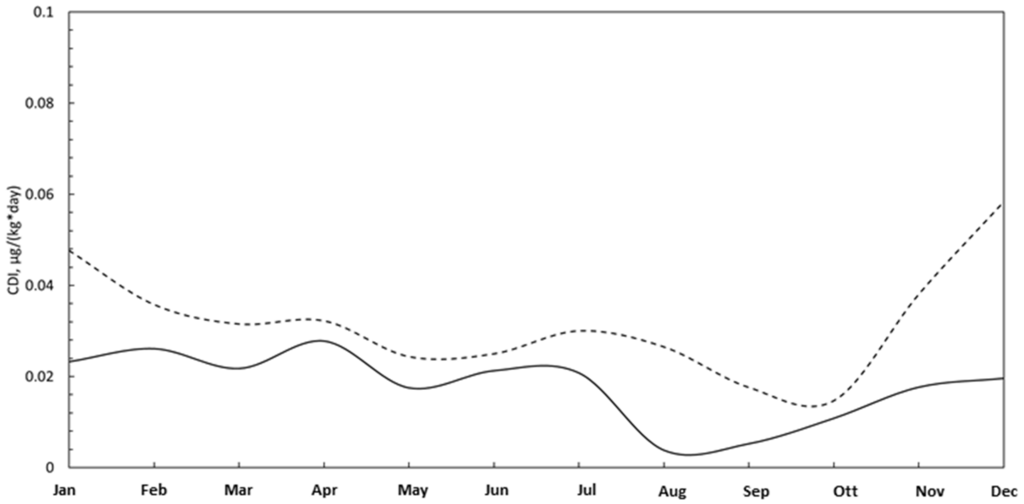

Figure 13. Lead (Pb) CDI for the HI (solid black line) and LI (dashed black line) area for every month in 2016.

4. Conclusions

A survey of 75 male patients was conducted in high and low environmental impact areas in 2016. The heavy metals blood concentrations measured in this study were higher in the high impact area than in the low impact area. Starting from the air quality data was calculated the impact of the heavy metals aero-dispersed on human health. The pollution expressed as PM10 concentration is higher in the HI area than in the LI area. In the area with high environmental impact, there is a variation in the concentration of PM10 during the year, which on average reaches a minimum in the July–November period. The potential pollutant adsorption in the HI area is 72% higher than in the LI area. The metals considered (As, Cd, Ni, Pb) are part of the PM10 measured and are higher in the HI area, meaning that people living in the HI area are more exposed to the pollutant adsorption. Further development of this work includes implementing an air quality monitoring network in the LI area to obtain more detailed information on the air characteristics. The results of this study can be supported by the measurement of metal concentrations in the human body. The next step of the study will be the urine analysis of the subjects belonging to the two investigated areas to verify the effective human absorption of pollutants. Furthermore, it will be interesting to investigate whether the absorption is also linked to PM2.5, which largely constitutes the airborne particulate.

Author Contributions: Conceptualization, N.L., P.T. and D.S.; methodology, N.L., D.S.; software, N.L., D.S.; validation, N.L., P.T. and D.S.; formal analysis, N.L., P.T. and D.S.; data curation, N.L., I.M.B. and T.G., writing—original draft preparation, N.L., D.S.; writing—review and editing, N.L., P.T., D.S., T.G., I.M.B. and L.M.; supervision, I.M.B. and T.G., project administration, D.S. and L.M. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data are available at https://www.arpacampania.it/aria (accessed on 11 January 2021).

Acknowledgments: This paper was performed in the frame of the EcoFoodFertility project.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. European Environment Agency (EEA). *Healthy Environment, Healthy Lives: How the Environment Influences Health and Well-Being in Europe*; Publications Office: Luxembourg, 2020. [CrossRef]
2. Lim, S.S.; Vos, T.; Flaxman, A.D.; Danaei, G.; Shibuya, K.; Adair-Rohani, H.; Amann, M.; Anderson, H.R.; Andrews, K.G.; Aryee, M.; et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet* **2012**, *380*, 2224–2260. [CrossRef]
3. Cohen, A.J.; Anderson, H.R.; Ostro, B.; Pandey, K.V.; Krzyzanowski, M.; Künzli, N.; Gutschmidt, K.; Pope, A.; Romieu, I.; Samet, J.M.; et al. The Global Burden of Disease due to Outdoor Air Pollution. *J. Toxicol. Environ. Health A* **2005**, *68*, 1301–1307. [CrossRef] [PubMed]
4. Ezzati, M.; Lopez, A.D.; Rodgers, A.; Vander Hoorn, S.; Murray, C.J. Selected major risk factors and global and regional burden of disease. *Lancet* **2002**, *360*, 1347–1360. [CrossRef]
5. Krewski, D.; Jerrett, M.; Burnett, R.T.; Ma, R.; Hughes, E.; Shi, Y.; Turner, M.C.; Pope, C.A., 3rd; Thurston, G.; Calle, E.E.; et al. Extended Follow-Up and Spatial Analysis of the American Cancer Society Study Linking Particulate Air Pollution and Mortality. *Res. Rep. Health Eff. Inst.* **2009**, *140*, 5–114; discussion 115.
6. Pope, C.A.; Ezzati, M.; Dockery, D.W. Fine-Particulate Air Pollution and Life Expectancy in the United States. *N. Engl. J. Med.* **2009**, *360*, 376–386. [CrossRef]
7. Laden, F.; Schwartz, J.; Speizer, F.; Dockery, D. Reduction in Fine Particulate Air Pollution and Mortality: Extended Follow-up of the Harvard Six Cities Study. *Am. J. Respir. Crit. Care Med.* **2006**, *173*, 667–672. [CrossRef]
8. Kim, D.; Chen, Z.; Zhou, L.-F.; Huang, S.-X. Air pollutants and early origins of respiratory diseases. *Spec. Issue Air Pollut. Chronic Respir. Dis.* **2018**, *4*, 75–94. [CrossRef]
9. Mitova, M.I.; Cluse, C.; Goujon-Ginglinger, C.G.; Kleinhans, S.; Rotach, M.; Tharin, M. Human chemical signature: Investigation on the influence of human presence and selected activities on concentrations of airborne constituents. *Environ. Pollut.* **2020**, *257*, 113518. [CrossRef]
10. Cambra-López, M.; Aarnink, A.J.A.; Zhao, Y.; Calvet, S.; Torres, A.G. Airborne particulate matter from livestock production systems: A review of an air pollution problem. *Environ. Pollut.* **2010**, *158*, 1–17. [CrossRef]
11. Hsu, A.; Reuben, A.; Shindell, D.; de Sherbinin, A.; Levy, M. Toward the next generation of air quality monitoring indicators. *Atmos. Environ.* **2013**, *80*, 561–570. [CrossRef]
12. Whelpdale, D.M. Particulate residence times. *Water. Air. Soil Pollut.* **1974**, *3*, 293–300. [CrossRef]
13. Anderson, J.O.; Thundiyil, J.G.; Stolbach, A. Clearing the Air: A Review of the Effects of Particulate Matter Air Pollution on Human Health. *J. Med. Toxicol.* **2012**, *8*, 166–175. [CrossRef]
14. Kim, K.-H.; Kabir, E.; Kabir, S. A review on the human health impact of airborne particulate matter. *Environ. Int.* **2015**, *74*, 136–143. [CrossRef]
15. Hussain, S.; Rengel, Z.; Qaswar, M.; Amir, M.; Zafar-ul-Hye, M. Arsenic and Heavy Metal (Cadmium, Lead, Mercury and Nickel) Contamination in Plant-Based Foods. In *Plant and Human Health, Volume 2: Phytochemistry and Molecular Aspects*; Ozturk, M., Hakeem, K.R., Eds.; Springer International Publishing: Cham, Switzerland, 2019; pp. 447–490. [CrossRef]
16. Sun, Z.; Zhu, D. Exposure to outdoor air pollution and its human health outcomes: A scoping review. *PLoS ONE* **2019**, *14*, e0216550. [CrossRef]
17. Satarug, S.; Gobe, G.C.; Vesey, D.A.; Phelps, K.R. Cadmium and lead exposure, nephrotoxicity, and mortality. *Toxics* **2020**, *8*, 86. [CrossRef]

18. Alengebawy, A.; Abdelkhalek, S.T.; Qureshi, S.R.; Wang, M.-Q. Heavy metals and pesticides toxicity in agricultural soil and plants: Ecological risks and human health implications. *Toxics* **2021**, *9*, 42. [CrossRef]
19. Massányi, P.; Massányi, M.; Madeddu, R.; Stawarz, R.; Lukáč, N. Effects of cadmium, lead, and mercury on the structure and function of reproductive organs. *Toxics* **2020**, *8*, 94. [CrossRef]
20. Satarug, S. Dietary cadmium intake and its effects on kidneys. *Toxics* **2018**, *6*, 15. [CrossRef]
21. Sijko, M.; Kozłowska, L. Influence of dietary compounds on arsenic metabolism and toxicity. Part i—Animal model studies. *Toxics* **2021**, *9*, 258. [CrossRef]
22. Silvera, S.A.N.; Rohan, T.E. Trace elements and cancer risk: A review of the epidemiologic evidence. *Cancer Causes Control.* **2007**, *18*, 7–27. [CrossRef]
23. Sofia, D.; Giuliano, A.; Gioiella, F. Air quality monitoring network for tracking pollutants: The case study of salerno city center. *Chem. Eng. Trans.* **2018**, *68*, 67–72. [CrossRef]
24. Sofia, D.; Lotrecchiano, N.; Trucillo, P.; Giuliano, A.; Terrone, L. Novel air pollution measurement system based on ethereum blockchain. *J. Sens. Actuator Netw.* **2020**, *9*, 49. [CrossRef]
25. Sofia, D.; Lotrecchiano, N.; Giuliano, A.; Barletta, D.; Poletto, M. Optimization of number and location of sampling points of an air quality monitoring network in an urban contest. *Chem. Eng. Trans.* **2019**, *74*, 277–282. [CrossRef]
26. Lotrecchiano, N.; Sofia, D.; Giuliano, A.; Barletta, D.; Poletto, M. Spatial Interpolation Techniques For innovative Air Quality Monitoring Systems. *Chem. Eng. Trans.* **2021**, *86*, 391–396. [CrossRef]
27. Lotrecchiano, N.; Gioiella, F.; Giuliano, A.; Sofia, D. Forecasting Model Validation of Particulate Air Pollution by Low Cost Sensors Data. *J. Model. Optim.* **2019**, *11*, 63–68. [CrossRef]
28. Lotrecchiano, N.; Sofia, D.; Giuliano, A.; Barletta, D.; Poletto, M. Pollution dispersion from a fire using a Gaussian plume model. *Int. J. Saf. Secur. Eng.* **2020**, *10*, 431–439. [CrossRef]
29. Sofia, D.; Gioiella, F.; Lotrecchiano, N.; Giuliano, A. Mitigation strategies for reducing air pollution. *Environ. Sci. Pollut. Res.* **2020**, *27*, 19226–19235. [CrossRef] [PubMed]
30. Sofia, D.; Gioiella, F.; Lotrecchiano, N.; Giuliano, A. Cost-benefit analysis to support decarbonization scenario for 2030: A case study in Italy. *Energy Policy* **2020**, *137*, 111137. [CrossRef]
31. Kunugi, Y.; Arimura, T.H.; Iwata, K.; Komatsu, E.; Hirayama, Y. Cost-efficient strategy for reducing PM 2.5 levels in the Tokyo metropolitan area: An integrated approach with air quality and economic model. *PLoS ONE* **2018**, *13*, e0207623. [CrossRef] [PubMed]
32. Singh, V.; Meena, K.K.; Agarwal, A. Travellers' exposure to air pollution: A systematic review and future directions. *Urban Clim.* **2021**, *38*, 100901. [CrossRef]
33. Hormigos-Jimenez, S.; Padilla-Marcos, M.Á.; Meiss, A.; Gonzalez-Lezcano, R.A.; Feijó-Muñoz, J. Assessment of the ventilation efficiency in the breathing zone during sleep through computational fluid dynamics techniques. *J. Build. Phys.* **2019**, *42*, 458–483. [CrossRef]
34. Becerra, J.A.; Lizana, J.; Gil, M.; Barrios-Padura, A.; Blondeau, P.; Chacartegui, R. Identification of potential indoor air pollutants in schools. *J. Clean. Prod.* **2020**, *242*, 118420. [CrossRef]
35. Mendes, A.; Bonassi, S.; Aguiar, L.; Pereira, C.; Neves, P.; Silva, S.; Teixeira, J.P. Indoor air quality and thermal comfort in elderly care centers. *Urban Clim.* **2015**, *14*, 486–501. [CrossRef]
36. Environmental Protection Agency (EPA). *Proposed Guidelines for Exposure-Related Measurements*; Federal Register: Washington, DC, USA, 1988.
37. Ott, W.R. Total human exposure. *Environ. Sci. Technol.* **1985**, *19*, 880–885. [CrossRef]
38. Sexton, K.; Barry Ryan, P. Assessment of Humen Exposure to Air Pollution: Methods, Measurements, and Models. In *Air Pollution, the Automobile, and Public Health*; Health Effects Institute, National Academy Press: Washington, DC, USA, 1988.
39. Asante-Duah, K. Exposure Assessment: Analysis of Human Intake of Chemicals. In *Public Health Risk Assessment for Human Exposure to Chemicals*; Asante-Duah, K., Ed.; Springer: Dordrecht, The Netherlands, 2017; pp. 189–229. [CrossRef]
40. Triassi, M.; Alfano, R.; Illario, M.; Nardone, A.; Caporale, O.; Montuori, P. Environmental Pollution from Illegal Waste Disposal and Health Effects: A Review on the "Triangle of Death". *Int. J. Environ. Res. Public. Health* **2015**, *12*, 1216–1236. [CrossRef] [PubMed]
41. Maisto, G.; Baldantoni, D.; De Marco, A.; Alfani, A.; Virzo De Santo, A. Biomonitoring of trace element air contamination at sites in Campania (Southern Italy). *J. Trace Elem. Med. Biol.* **2003**, *7* (Suppl. 1), 51–55.
42. Posters. *Andrology* **2014**, *2*, 45–117. [CrossRef]
43. Pacini, N.; Abate, V.; Brambilla, G.; De Felip, E.; De Filippis, S.P.; De Luca, S.; di Domenico, A.; D'Orsi, A.; Forte, T.; Fulgenzi, A.R.; et al. Polychlorinated dibenzodioxins, dibenzofurans, and biphenyls in fresh water fish from Campania Region, southern Italy. *Chemosphere* **2013**, *90*, 80–88. [CrossRef]
44. EcoFoodFertility project. Available online: http://www.ecofoodfertility.it/the-project.html. (accessed on 18 January 2021).
45. Montano, L.; Iannuzzi, L.; Rubes, J.; Avolio, C.; Pistos, C.; Gatti, A.; Raimondo, S.; Notari, T. EcoFoodFertility—Environmental and food impact assessment on male reproductive function. *Andrology* **2014**, *2* (Suppl. 2), 69.
46. World Medical Association. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. *JAMA* **2013**, *310*, 2191–2194. [CrossRef]

47. Vecoli, C.; Montano, L.; Borghini, A.; Notari, T.; Guglielmino, A.; Mercuri, A.; Turchi, S.; Andreassi, M.G. Effects of Highly Polluted Environment on Sperm Telomere Length: A Pilot Study. *Int. J. Mol. Sci.* **2017**, *18*, 1703. [CrossRef]
48. Montano, L.; Ceretti, E.; Donato, F.; Bergamo, P.; Zani, C.; Viola, G.; Notari, T.; Pappalardo, S.; Zani, D.; Ubaldi, S.; et al. Effects of a Lifestyle Change Intervention on Semen Quality in Healthy Young Men Living in Highly Polluted Areas in Italy: The FASt Randomized Controlled Trial. *Eur. Urol. Focus* **2022**, *8*, 351–359. [CrossRef]
49. Lettieri, G.; D'Agostino, G.; Mele, E.; Cardito, C.; Esposito, R.; Cimmino, A.; Giarra, A.; Trifuoggi, M.; Raimondo, S.; Notari, T.; et al. Discovery of the Involvement in DNA Oxidative Damage of Human Sperm Nuclear Basic Proteins of Healthy Young Men Living in Polluted Areas. *Int. J. Mol. Sci.* **2020**, *21*, 4198. [CrossRef]
50. Bosco, L.; Notari, T.; Ruvolo, G.; Roccheri, M.C.; Martino, C.; Chiappetta, R.; Carone, D.; Lo Bosco, G.; Carrillo, L.; Raimondo, S.; et al. Sperm DNA fragmentation: An early and reliable marker of air pollution. *Environ. Toxicol. Pharmacol.* **2018**, *58*, 243–249. [CrossRef]
51. Longo, V.; Forleo, A.; Ferramosca, A.; Notari, T.; Pappalardo, S.; Siciliano, P.; Capone, S.; Montano, L. Blood, urine and semen Volatile Organic Compound (VOC) pattern analysis for assessing health environmental impact in highly polluted areas in Italy. *Environ. Pollut.* **2021**, *286*, 117410. [CrossRef]
52. Senior, K.; Mazza, A. Italian "Triangle of death" linked to waste crisis. *Lancet Oncol.* **2004**, *5*, 525–527. [CrossRef]
53. US Environmental Protecgtion Agency (EPA). Users' Guide and Background Technical Document for USEPA Region 9—Preliminary Remediation Goals (PRG) Table. 2013. Available online: https://semspub.epa.gov/work/02/103453.pdf (accessed on 30 April 2021).
54. I International Commission on Radiological Protection (ICRP). Human Respiratory Tract Model for Radiological Protection. A report of a Task Group of the International Commission on Radiological Protection. *Ann. ICRP* **2002**, *32*, 307–309.
55. US Environmental Protecgtion Agency (EPA). *Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A)*; Environmental Protection Agency: Washington, DC, USA, 1989.
56. US Environmental Protecgtion Agency (EPA). *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment)*; Environmental Protection Agency: Washington, DC, USA, 2003.
57. Alimonti, A.; Bocca, B.; Mattei, D.; Pino, A. Biomonitoraggio della popolazione italiana per l'esposizione ai metalli: Valori di riferimento 1990–2009. *Rapp. Istisan-Ist. Super. Di Sanità* **2010**, *10*, 58.
58. Elinder, C.G.; Järup, L. Cadmium Exposure and Health Risks: Recent Findings. *Ambio* **1996**, *25*, 370–373.
59. Baralić, K.; Javorac, D.; Marić, D.; Đukić-Ćosić, D.; Bulat, Z.; Antonijević Miljaković, E.; Anđelković, M.; Antonijević, B.; Aschner, M.; Buha Djordjevic, A. Benchmark dose approach in investigating the relationship between blood metal levels and reproductive hormones: Data set from human study. *Environ. Int.* **2022**, *165*, 107313. [CrossRef]
60. Magnano, G.C.; Marussi, G.; Pavoni, E.; Adami, G.; Larese Filon, F.; Crosera, M. Percutaneous metals absorption following exposure to road dust powder. *Environ. Pollut.* **2022**, *292*, 118353. [CrossRef] [PubMed]
61. Chen, Y.; Luo, X.-S.; Zhao, Z.; Chen, Q.; Wu, D.; Sun, X.; Wu, L.; Jin, L. Summer–winter differences of PM2.5 toxicity to human alveolar epithelial cells (A549) and the roles of transition metals. *Ecotoxicol. Environ. Saf.* **2018**, *165*, 505–509. [CrossRef] [PubMed]