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Original investigations/commentaries

Air pollutants and SARS-CoV-2 in 33 European countries

Rosalba Lembo[1], *Giovanni Landoni*[1,2], *Lorenzo Cianfanelli*[1], *Antonio Frontera*[1]

[1]IRCCS San Raffaele Scientific Institute, via Olgettina 60, Milan, Italy

[2]Vita-Salute San Raffaele University, Milan, Italy

Abstract. *Background and aim:* A potential correlation between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and air pollution has been suggested in some nationwide studies. It is not clear whether air pollution contributes to the spread of SARS-CoV-2 and related coronavirus disease 2019 (COVID-19) and to increase mortality. *Methods:* Data on COVID-19 incidence, mortality rate, air pollution, and greenhouse gas element of 33 European countries were extracted from public available databases and analysed with Pearson correlation analysis for the overall population and normalizing for the population over 65 years. *Results:* Air pollutant agents such as particulate matter <10µm (PM_{10}), particulate matter <2.5µm ($PM_{2.5}$), ammonia (NH_3), sulphur dioxide (SO_2), non-methane volatile organic compounds (NMVOCs), nitrogen dioxide (NO_2) and greenhouse gas elements recorded showed a remarkable correlation with cumulative positive number of SARS-CoV-2 cases and with cumulative number of COVID-19 deaths. $PM_{2.5}$ ($r = 0.68$, p-value = 0.0001 for cumulative positive cases; $r = 0.73$, p-value <0.0001 for cumulative deaths) and nitrogen oxides ($r = 0.85$, p-value <0.0001 for cumulative positive cases; $r = 0.70$, p-value 0.0001 for cumulative deaths) were among the pollutant agents with the strongest correlation for both positive cases and deaths. *Conclusions:* High levels of pollution in European countries should be considered a potential risk for severe COVID-19 and SARS-CoV-2-related death. (www.actabiomedica.it)

Key words: Air pollution; Atmosphere pollution; greenhouse gas emissions; ARDS; SARS-CoV-2; COVID-19

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is characterized in its severe forms by severe acute respiratory distress syndrome. The first outbreak was identified in Wuhan, China in December 2019. On March 11th 2020 World Health Organization (WHO) recognized the pandemic (1) when coronavirus disease 2019 (COVID-19) affected almost 120,000 people and spread over 110 countries (2).

One of most unknown characteristics of this pandemic is why some countries (e.g. Iran, Italy, Belgium, the Netherlands, United Kingdom and the United States of America) were among the hardest hit when compared to others. Several factors have been called into question as climate (3), population density (4), genetic of population (5) and spike protein mutation (6) which may cause an aggressive variant of the SARS-CoV-2 virus.

Air pollution has been correlated with SARS-CoV-2 outbreaks (7-9); and the persistence and the high contagion rate of some areas might be justified by certain orographic characteristics which, mixed with weather condition of poor rain fall, and absence of wind, may create a hood of air pollutants (10). Air pollution may favor the spread of the infection, increasing the number of contagion and the mortality rate. A possible explanation relies on the over expression of angiotensin-converting enzyme 2 (ACE-2) receptors at alveolar level in patients chronically exposed to air pollutants (11). ACE-2 are known to be SARS-CoV-2 entry site in the cells (12), and increased expression may cause increased patient susceptibility. Furthermore, nitrogen dioxide (NO_2), whose concentration in polluted areas is exceedingly high, has been called as potential booster for the higher mortality encountered in certain areas of the world (11). However, previous publications focused on Italy and data concerning other European countries are scarce. The aim of this research was to correlate SARS-CoV-2 outbreaks with air pollution in the entire Europe.

Methods And Materials

Number of SARS-CoV-2 positive and COVID-19 deaths per country were manually exported from the World Health Organization web site for the Situation Report number 118 (13).

Data of six air pollution agents (particulate matter < 10 μm - PM_{10}, particulate matter < 2.5 μm - $PM_{2.5}$, ammonia - NH_3, sulphur dioxide - SO_2, non-methane volatile organic compounds - NMVOCs and nitrogen dioxide - NO_2) were extracted from the EUROSTAT website (14) with the last available data corresponding to 2017 and selected as "Total sectors of emissions for the national territory". Another extraction was performed for Greenhouse gas emissions, listed as single elements from EUROSTAT based on European Environment Agency (EEA) information (15): Carbon dioxide; Methane; Nitrous oxide; Hydrofluorocarbones; Perfluorocarbones; Sulphur hexafluoride; were collected Data were selected from labeling as "All sectors and indirect carbon dioxide (CO_2) (excluding LULUCF and memo items, including international aviation)". Last year of available data was 2017.

The rate of elderly (>65 years old) people in each European country except Liechtenstein was obtained from EUROSTAT and United Nations (16).

The European Countries included in the analysis are (in alphabetic order): Austria, Belgium. Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, and the United Kingdom. Twenty countries listed in WHO as European regions were excluded from analysis for missing data on EUROSTAT website: Albania, Andorra, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Holy See, Israel, Kazakhstan, Kyrgyzstan, Monaco, Montenegro, North Macedonia, Republic of Moldova, Russian Federation, San Marino, Serbia, Ukraine and Uzbekistan.

Statistical Analysis. In order to investigate the potential relationship between air pollution agents, greenhouse gas emissions, SARS-CoV-2 positive cases and COVID-19 deaths in all analysed countries, Pearson correlation analysis was applied for the overall population, normalizing for the population over 65 years. Normalization for age was calculated as total number of cases (SARS-CoV-2 positive cases or COVID-19 deaths, respectively) divided by population aged >65 years multiplied by 1000. To control type I error rate due to multiple comparisons, Bonferroni correction was used and the adjusted level of significance was $p < 0.05$ after this correction. All statistical analyses were performed using the STATA 16 software with a threshold of significance, $p = 0.05$.

Results

A total of 1,480,130 SARS-CoV-2 positive cases were collected from 33 European countries from 11th February to 17th May 2020, in a time span of almost 14 weeks. **Table 1** shows European countries demographic characteristics, number of SARS-CoV-2 positive cases and number of COVID-19 deaths.

The highest number of positive cases was collected from United Kingdom (n = 240,165), followed by Spain (n = 230,698) and by Italy (n = 224,760) as shown in **Table 1**. However, if we consider cases normalized for population aged over 65 years old we had Luxemburg (0.62), Iceland (0.50) and Spain (0.49) as the most hit countries in terms of SARS-CoV-2 positive cases.

Mortality was extremely variable among countries (**Table 1**). On 17th May 2020 the highest number of deaths was reached by United Kingdom (n = 34,466), followed by Italy (n = 31,763) and France (n = 27,578). However, after normalization according to population over 65 years old, the countries burdened by the highest number of deaths were Belgium (0.20) followed by Spain (0.15) and United Kingdom (0.14).

Table 1. Number of SARS-CoV-2 positive cases, number of COVID-19 deaths to SARS-CoV-2 infection, and demographic characteristics of 33 European Countries.

Country	Cumulative cases	Cumulative deaths	Population 2020	Population over 65	Normalized cumulative cases for population over 65 x 1000	Normalized cumulative deaths for population over 65 x 1000
Liechtenstein	83	1	38019	—	0.218312	—
Malta	546	6	497724	184862	0.109699	0.003246
Cyprus	914	17	885907	282148	0.103171	0.006025
Luxemburg	3930	104	625669	177043	0.628128	0.058743
Iceland	1802	10	358568	101378	0.502555	0.009864
Estonia	1770	63	1326601	524106	0.133424	0.012021
Slovenia	1465	103	2083676	825641	0.070308	0.012475
Latvia	997	19	1905482	778054	0.052323	0.002442
Lithuania	1534	55	2759230	1104620	0.055595	0.004979
Croatia	2224	95	4054406	1677011	0.054854	0.005665
Switzerland	30489	1601	8607483	3159444	0.354215	0.050674
Slovakia	1493	28	5455848	1745346	0.027365	0.001604
Bulgaria	2211	108	6943254	2983134	0.031844	0.00362
Ireland	24048	1533	4943466	1378240	0.48646	0.111229
Denmark	10858	543	5839809	2269841	0.185931	0.023922
Hungary	3509	451	9739030	3778432	0.03603	0.011936
Sweden	29677	3674	10348449	4067422	0.286777	0.090328
Finland	6286	297	5528576	2407589	0.1137	0.012336
Austria	16140	628	8908676	3335343	0.181172	0.018829
Portugal	28810	1203	10261867	4478286	0.280748	0.026863
Norway	8197	232	5369143	1835668	0.152669	0.012639
Czech Republic	8455	296	10674178	4171430	0.07921	0.007096
Belgium	54989	9005	11487179	4334844	0.478699	0.207735
Romania	16704	1081	19282488	7185749	0.086628	0.015044
Greece	2819	162	10691204	4699906	0.026368	0.003447
Netherlands	43870	5670	17342709	6623729	0.252959	0.085601
Italy	224760	31763	60233172	27541264	0.37315	0.115329
Spain	230698	27563	47054924	18190878	0.490274	0.151521
Turkey	148067	4096	83429615	7280089	0.177475	0.056263
Poland	18257	915	37968244	13402471	0.048085	0.006827
France	140008	27578	67204763	26813142	0.208331	0.102853
United Kingdom	240165	34466	67086777	24500348	0.357992	0.140676
Germany	174355	7914	83159604	35797688	0.209663	0.022108

Further details are given in **Tables 2** which shows environmental levels of air pollutants and in **Table 3** which shows greenhouse gas emissions across different European countries.

Air pollutant agents recorded across European countries in 2017 were put in correlation with both SARS-CoV-2 cumulative positive number of cases and cumulative number of COVID-19 deaths in **Table 4**.

Table 2. Environmental levels of air pollutants in European Countries ordered by levels of Nitrogen Oxydes pollution. All units of measurement are tonne*

Country	Ammonia	Nitrogen oxides	Non-methane volatile organic compounds	Particulates <10µm	Particulates <2.5µm	Sulphur oxides
Liechtenstein	213	492	241	39	34	16
Malta	1113	5343	2815	378	238	151
Cyprus	6488	14543	12321	2054	1290	16391
Luxemburg	5805	18314	12101	2005	1345	1011
Iceland	5280	22555	5628	1682	1284	49735
Estonia	10255	33200	22245	13911	9222	38653
Slovenia	18634	34711	29808	12986	11480	4878
Latvia	16519	37421	38100	25009	17973	3996
Lithuania	29547	53437	45727	14196	9081	13177
Croatia	37642	54852	63241	25378	16726	12557
Switzerland	55155	61149	78369	14922	6547	5424
Slovakia	26545	65665	89478	22587	18068	27037
Bulgaria	49440	102813	77232	47030	31967	103071
Ireland	118496	110307	113349	27281	11970	13221
Denmark	76333	111954	102258	31058	20061	10254
Hungary	87700	119283	141520	68866	47988	27722
Sweden	53336	124025	146939	40302	20098	17566
Finland	31083	129850	88323	29179	17800	35020
Austria	69095	144712	120189	27942	15613	12809
Portugal	57606	159009	167536	72805	51268	47520
Norway	33420	162730	152534	36860	27907	14925
Czechia	67003	163205	207340	51280	39940	109962
Belgium	66749	176273	109104	33408	23088	37573
Romania	164336	231717	240088	143200	111925	106932
Greece	55209	249536	148098	56505	25814	105844
Netherlands	132119	251905	252074	26928	14004	26898
Italy	384192	709070	935000	195690	164677	115171
Spain	518192	738890	617768	172098	105098	220443
Turkey	739704	784697	1098974	764935	16761	2350019
Poland	307522	803661	690737	246310	147281	582656
France	606358	807225	611960	254230	164487	143782
United Kingdom	283147	893108	809420	170786	106814	172877
Germany	673251	1187502	1068758	205986	99056	315477

* 1 tonne (metric) = 1 megagram (Mg) = 106 g

Table 3. Greenhouse gas emissions across different European countries. All units of measurement are thousand tonnes*

Country	Carbon dioxide	Hydrofluoro carbones	Methane	Nitrogen trifluoride	Nitrous oxide	Nitrous oxide (CO2 equivalent)	Perfluoro carbones	Sulphur hexafluoride
Liechtenstein	155.99	10.69	0.72	—	0.03	9.74	0.02	0.05
Malta	2036.24	310.93	7.5	—	0.16	46.97	0	0.99
Cyprus	8536.82	249.56	34.57	—	1.01	301.38	.	0.17
Luxemburg	10925.92	71.64	23.75	—	1.12	332.68	.	9.41
Iceland	4761.21	204.91	23.25	—	0.98	293.36	68.04	2.31
Estonia	18833.81	236.24	42.84	—	3.08	917.22	.	2.44
Slovenia	14333.1	357.48	84.07	—	2.36	702.27	17.45	15.81
Latvia	7680.07	234.92	72.19	—	6.8	2025.81	.	10.32
Lithuania	13724.6	711.26	130.3	0.01	10.19	3036.69	.	7.73
Croatia	19165.83	488.71	164.33	.	5.72	1703.32	.	6.39
Switzerland	43568.89	1511.7	194.17	0.54	8.18	2437.27	30.76	196.55
Slovakia	36198.66	739.06	184.05	.	6.47	1928.21	8.62	7.08
Bulgaria	48114	1817.89	271.39	.	17.96	5351.35	0.02	17.51
Ireland	41764.18	1143.3	561.39	1.26	22.74	6775.51	47.2	39.22
Denmark	37981.3	405.43	275.39	.	18.39	5479.42	1.09	75.45
Hungary	50341.26	1801.17	301.55	.	15.75	4692.68	1.06	113.8
Sweden	44803.23	1138.31	180.75	.	16.47	4907.42	36.58	47.09
Finland	46855.43	1278.58	184.25	.	15.79	4705.6	5.84	50.23
Austria	72225.23	1724.77	263.91	12.01	11.82	3523.79	44.09	399.03
Portugal	58683.66	3257.1	379.17	.	10.55	3144.33	16.87	25.25
Norway	45371.18	1402.75	200.95	.	8.09	2410.05	130.96	58.83
Czechia	107389.4	3640.8	540.44	2.75	19.62	5846.77	1.37	74.31
Belgium	102366.5	2805.39	318.95	0.63	20.06	5976.58	167.66	92.03
Romania	76003.92	2177.68	1149.05	.	26.32	7843.88	5.56	54.19
Greece	78279.35	6179.32	396.62	.	14.7	4379.65	125.79	5.01
Netherlands	176945.7	1826.38	721.31	.	29.6	8821.28	77.03	126.38
Italy	360157.6	15294.12	1754.17	23.5	60	17879.24	1313.68	417.49
Spain	291353.4	6309.32	1600.64	.	61.79	18414.7	127.77	225.6
Turkey	436344.4	8048.73	2167.81	.	129.62	38626.84	73.11	73.12
Poland	339052.7	6893.27	1976.53	.	69.95	20844.98	11.92	82.43
France	363707.1	18711.33	2250.3	7.64	141.39	42133.27	707.68	460.21
United Kingdom	419518.5	14085.33	2058.36	0.53	65.3	19460.12	371.47	525.41
Germany	827082.5	11010.81	2209.96	.	127.31	37939.49	90.12	3834.33

Greenhouse gas emission - European countries ranked for Nitrogen oxides
* 1 tonne (metric) = 1 megagram (Mg) = 10^6 g.

Table 4. Air pollutant agents recorded across European countries in correlation with both cumulative SARS-CoV-2 positive cases and cumulative COVID-19 deaths.

	Cumulative SARS-CoV-2 **positive cases**		**Cumulative** COVID-19 **deaths**	
	Pearson's correlation	**P value**	**Pearson's correlation**	**P value**
Air pollution agents				
Ammonia, t	0.81	<0.0001	0.62	0.0013
Nitrogen Oxides, t	0.85	<0.0001	0.70	0.0001
Non-methane volatile organic compounds, t	0.86	<0.0001	0.64	0.0002
Particulates <10 μm, t	0.58	0.0035	0.35	0.44
Particulates <2,5 μm, t	0.68	0.0001	0.73	<0.0001
Sulphur Oxides, t	0.35	0.42	0.07	0.99
Greenhouse gas emissions				
Carbon dioxide, *§*	0.81	<0.0001	0.60	<0.0001
Hydrofluorocarbones, *§*	0.83	<0.0001	0.83	<0.0001
Methane, *§*	0.83	<0.00001	0.70	<0.0001
Nitrogen trifluoride, *§***	0.46	0.99	0.44	0.99
Nitrogen oxide, *§*	0.75	<0.0001	0.59	0.0026
Perfluorocarbones, *§* *	0.64	0.0030	0.77	<0.0001
Sulphur hexafluoride, *§* *	0.46	0.067	0.23	0.99

** data available for 9 countries * data available for 27 countries
t: 1 tonne (metric) = 1 megagram (Mg) = 106 g; § thousand tonnes

A significant association was found to be present as high levels of ammonia, nitrogen oxides, non-methane volatile compounds, particulate matter <10 micrometers, and particulate matter <2.5 micrometers were linked to high number of positive cases of SARS-CoV-2 infection. Similarly, high environmental levels of ammonia, nitrogen oxides, non-methane volatile compounds and particulate matter <2.5 micrometers were also associated with high number of deaths for COVID-19.

$PM_{2,5}$ (r = 0.68 with p-value = 0.0001 for cumulative positive cases; r = 0.73 with p-value <0.0001 for cumulative deaths) and nitrogen oxides (r = 0.85 with p-value <0.0001 for cumulative positive cases; r = 0.70 with p-value 0.0001 for cumulative deaths) were the pollutant agents with the strongest correlation for both SARS-CoV-2 positive cases and COVID-19 deaths (see **Table 1**). Specifically, **Figure 1** shows the linear correlation between $PM_{2.5}$ levels and normalized cumulative deaths for population over 65 years old per 1000, across European countries visually describing how countries with the highest levels of $PM_{2.5}$ (such as Spain, United Kingdom, France and Italy) are the one with the highest number of victims, circles were sized for population number.

Discussion

The main finding of this research study is that both particulates and greenhouse gases high levels are associated with SARS-CoV-2 and that $PM_{2.5}$ and nitrogen oxides are among the pollutant agents with the strongest correlation for both SARS-CoV-2 positive cases and COVID-19 deaths. Environmental factors, such as urban air pollution, may play an important role in increasing susceptibility to severe outcomes of COVID-19.

Air pollution is responsible for almost 7 million deaths per year in the world (17). Particularly, the air pollution in urban area is a true cocktail of PM represented by gases, semi-volatile liquids, and particles. Our data suggest a strong link between certain air pollutants and high mortality reached in some countries. During the 2003 outbreak of SARS in China studies

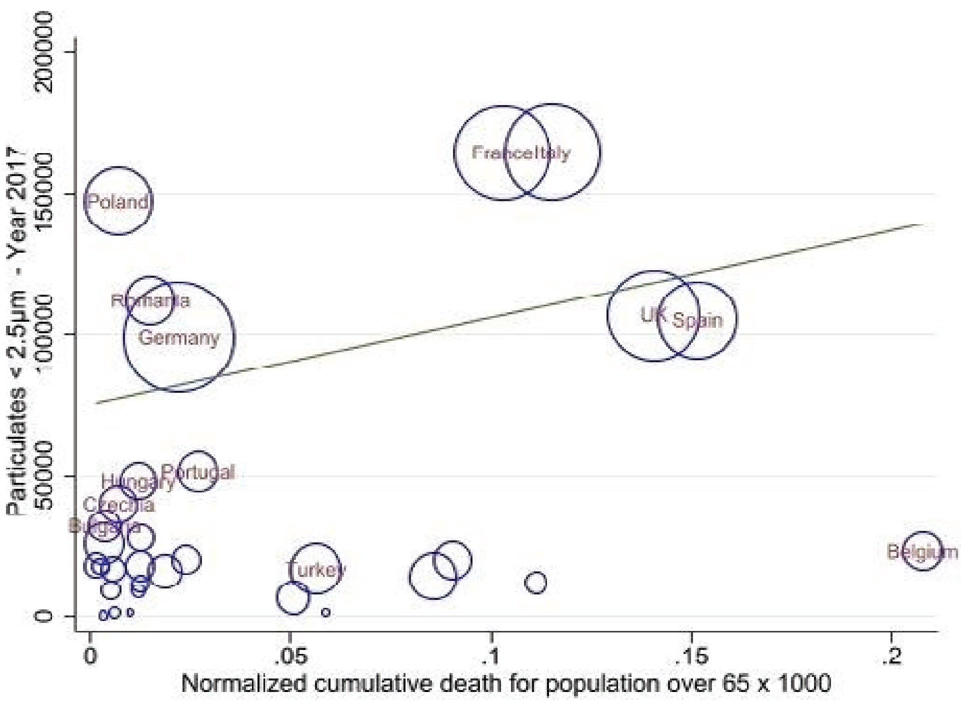

Figure 1. Correlation between particulates<2.5µm emission and normalized cumulative COVID-19 deaths for population over 65 years per 1000 – Circles sized for population.

have found higher mortality rates in urban regions with severe air pollution compared to low pollution areas, although these results were not adjusted for important confounders, such as age, sex and comorbidities (18).

Exposure to air pollutants is known to have detrimental effects on patients' health, being associated with higher incidence of respiratory diseases, cardiovascular diseases and number of deaths.[19] Possible explanations linking pollution to increased susceptibility to lung infections are local inflammation, decrease muco-ciliary clearance and exacerbation of underlying asthma and chronic obstructive pulmonary disease (20-22). Moreover, areas with elevated concentration of pollutants are the ones with the highest population density where disease transmission is favoured (23). It is therefore likely that a combination of the aforementioned factors may favour the establishment of overt COVID-19 infection and may promote different illness severity in different patients, eventually leading to the higher rate of mortality recorded in most polluted areas.

Our group has recently published the "double hit" hypothesis where we suggested that chronic exposure to $PM_{2.5}$ may cause over expression of angiotensin-converting enzyme (ACE-2) receptors (11). This may explain why children are preserved from SARS-CoV-2 infection. Furthermore, the double hit hypothesis is based on the enhancement caused by NO_2. This gaseous pollutant may be responsible for the high mortality in some countries where levels are high. Although the number of studies on this issue are still scarce, most results indicate that chronic exposure to air pollutants may leads to more severe and lethal forms of this disease and complicates recovery of COVID-19 patients.[24]

We acknowledge that the latest available data about air pollution agents and green gas house elements publicly available is dated 2017.

Conclusions

After normalizing mortality data for population over 65 years old, air pollutants were associated to high SARS-CoV-2 infection and COVID-19 deaths.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership,

equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Correspondence
Professor Giovanni Landoni, MD
Associate Professor of Anesthesiology
Vita-Salute San Raffaele University
Department of Anesthesia and Intensive Care
IRCCS San Raffaele Scientific Institute
Via Olgettina, 60 – 20132, Milan, Italy
Tel. +39 02 2643 6158
Fax. +39 02 2643 6152
Email: landoni.giovanni@hsr.it
Twitter: @giovannilandoni - @SRAnesthesiaICU