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Covid-19 and vit-d: Disease mortality negatively correlates with sunlight exposure

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ABSTRACT

The novel COVID-19 disease is a contagious acute respiratory infectious disease whose causative agent has been demonstrated to be a new virus of the coronavirus family, SARS-CoV-2. Alike with other coronaviruses, some studies show a COVID-19 neurotropism, inducing de-myelination lesions as encountered in Guillain-Barré syndrome.

In particular, an Italian report concluded that there is a significant vitamin D deficiency in COVID-19 infected patients.

In the current study, we applied a Pearson correlation test to public health as well as weather data, in order to assess the linear relationship between COVID-19 mortality rate and the sunlight exposure. For instance in continental metropolitan France, average annual sunlight hours are significantly (for a p-value of 1.532×10^{-32}) correlated to the COVID-19 mortality rate, with a Pearson coefficient of -0.636.

This correlation hints at a protective effect of sunlight exposure against COVID-19 mortality. This paper is proposed to foster academic discussion and its hypotheses and conclusions need to be confirmed by further research.

La nouvelle infection au COVID-19 est une maladie respiratoire infectieuse sévère dont l'agent causal a été identifié comme un nouveau virus de la famille des coronavirus, SARS-CoV-2. Comme les autres coronavirus, des études montrent un neurotropisme du COVID-19, induisant des lésions démyélinisantes comme dans le syndrome de Guillain-Barré.

Plus particulièrement, une note italienne conclue qu'il y a un déficit significatif en vitamine D chez les patients infectés par le COVID-19.

Dans cette étude, nous avons utilisé un test de corrélation de Pearson sur des données de santé publique et météorologiques, dans le but de statuer sur une possible relation entre l'ensoleillement et la mortalité induite par le COVID-19. Pa exemple dans la France métropolitaine continentale, la moyenne des heures d'ensoleillement est significativement (pour une p-value de 1.532×10^{-32}) corrélée au taux de mortalité due au COVID-19, avec un coefficient de Pearson de -0.636.

Cette corrélation établit un effet protecteur de l'ensoleillement contre la mortalité due au COVID-19. Ce manuscrit est proposé uniquement pour une discussion académique et les hypothèses et ses conclusions doivent être confirmées par d'autres recherches.

Mots-clés: COVID-19; Coronavirus; France; Corrélation; Vitamine D; Photothérapie; UV.

1. Introduction

The novel coronavirus pneumonia (COVID-19) is a contagious acute respiratory infectious disease whose causative agent has been demonstrated to be a new virus of the coronavirus family, SARS-CoV-2. This illness was first evinced in December 2019 in the Seafood Market of Wuhan, Hubei Province, in southern China (Wang et al., 2020; Huang et al., 2020). Patients with the coronavirus pneumonia typically exhibit a fever, with temperature above 38° © and other symptoms such as dry cough, fatigue, dyspnea, difficulty breathing, and diarrhea (Chang et al., 2020; Guan et al., 2020; Wang et al., 2020; Diao et al., 2020). Furthermore, this

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diseases has a relatively high transmission rate as compared to other upper respiratory illnesses. As a result of this and other factors such as international travel and trade, the initial epidemic has turned into a pandemic in March 2020, with hundreds thousands of individuals confirmed to be infected worldwide – and most likely millions of unreported cases (Diao et al., 2020).

Similar to other coronaviruses-caused illnesses (Talbot and Jouvenne, 1992), COVID-19 infection has shown some amount of neurotropism (Poyiadji et al., 2020; Zhao et al., 2020; Mao et al., 2020), with lesions not unlike those of the Guillain-Barré demyelination (Zhao et al., 2020) or hemorrhagic necrotizing encephalopathy (Poyiadji et al., 2020; Mao et al., 2020). Meanwhile, it has long been noted that in the case of Guillain-Barré syndrome, vitamin D deficiency, in relation with high latitude climates, is both a causal and a risk factor (Tsujino et al., 2019; Elf et al., 2014). Furthermore, a recent Italian note has demonstrated a significant vitamin D deficiency in a cohort of COVID-19 infected elderly women (Isaia and Medico, 2020).

Therefore, it is important to assess the effect of vitamin D blood levels on COVID-19 infection rate and disease course, as it may offer preventative and/or curative options in the context of the ongoing pandemic.

Specifically in the context of continental metropolitan France, the correlation between sunlight exposure and SARS-CoV-2 infection will be studied in this article, by using an adjusted Pearson test applied to public health and weather data (Santé Publique France 2020; Météo France 2020; INSEE. Insee 2020).

2. Methods

2.1. Study and participants

We conducted a descriptive observational cross-sectional study in order to define a hypothetical relationship between sunlight exposure and SARS-CoV-2 infection. The source and targeted populations are the whole humanity in view of the ongoing COVID-19 pandemic. The eligible population is constituted by the residents of metropolitan continental France.

The study was conducted by a consortium of two data analysts, a MD-PhD specialized in radiology, and a medical student in clinical years. NexGen Analytics had no role in making the decision to submit manuscript to the publication, nor did it receive any fee or compensation in the context of this work. The first author vouches for the data and analyses, as well as for the fidelity of this report to the study protocol.

2.2. Enrollment

We gathered COVID-19-related data from various public health and social sources (Santé Publique France, 2020; INSEE. Insee, 2020). A parallel multiple group analysis was performed. We excluded the population from the non-metropolitan jurisdictions of France(Guyane, Mayotte, Martinique, Reunion, Guadeloupe, etc.), due to (1) the fact that their climates vastly differ from that of metropolitan France, and (2) the substantially lower access to healthcare in these areas. Moreover, albeit part of metropolitan France, the island of Corsica was excluded from this study because of poorer access to healthcare there than on the continent.

2.2. Outcome measures

We chose to use COVID-19 mortality rate as the primary variable to evaluate the role of SARS-CoV-2 infection in our hypothetical correlation. Sunlight exposure was evaluated by using the average annual hours of sunshine exposure, as reported by that country's national weather service ("Météo France") (Météo France, 2020). Our null hypothesis (H_0) was the non-correlation between average sunlight hours at the locality (X) and COVID-19 mortality rate (Y).

In order to assess the potential effect of confounding factors, we also considered (1) demographic variables (sex ratio, age, life expectancy, birth rate, death rate measured by 12/31/2019); (2) economic status (taxable income as reported assessed by 12/31/2017); (3) comorbidities (current smoking status, and prevalence of diabetes, Chronic Obstructive Pulmonary Disease, chronic renal failure prevalence, and obesity, as measured respectively by 01/21/2019, 12/31/2016, 12/31/2014, 12/31/2017, 12/31/2012); (4) healthcare access variables (availability of facilities for the elderly, physician per capita, hospital beds per capita as measured by 12/31/2017). The availability of facilities for the elderly was assessed by combining the number of beds at long-term care nursring homes with that of residences for independent seniors, and assisted care at home for people aged 75 years or more. The number of hospital beds per capita accounted for medical and surgical beds, both at public and private hospitals.

Finally, in order to further sustain our analysis, we also considered the confirmed COVID-19 infection cases as well as the number of verified recovered COVID-19 patients.

2.3. Statistical analysis

We began by computing several descriptive statistics for each variable: arithmetic mean, sample variance, standard deviation and the corresponding confidence intervals (justified by having Shapiro-Wilk tested each of these variables). Obviously unrelated to COVID-19 mortality, the 2019 birth and death rates were kept off the analysis. Furthermore, age was also eliminated from this analysis as the national statistics in this regard are provided in the form of age classes not directly usable in the context of Pearson correlation analysis. All other variables were treated using the Pearson correlation test, and the corresponding p-value are reported here in order to assess the statistical significance of these correlations.

3. Results

3.1. Populations

The included population gathers all 67,063,703 residents of France born before 01/01/20 (INSEE. Insee, 2020). After applying the aforementioned exclusion criteria, the cardinality of our studied sample set was of 64,553,275 individuals residing in continental metropolitan France. COVID-19 infection parameters (infection rate, healed rate, mortality rate) were calculated using data reported data as of 04/25/2020 (Santé Publique France, 2020).

This population was subsequently partitioned by region of residence (NB: "region" is the largest sub-national jurisdiction of France), as summarized in Table 1. We note that none of the resulting subgroups was found to exhibit values significantly outside of their respective confidence intervals, per a MANOVA-Wilk test performed at the 5% significance level (Table 2).

3.2. Outcomes

The primary outcome of this analysis was the Pearson coefficient between sunlight exposure and COVID-19 mortality rate, for which we found a value of -0.6368. With a corresponding p-value 1.532×10^{-32}, this allows us to reject the null hypothesis H_0 (Table 3). In other words, we surmise that sunlight exposure may have a protective effect against COVID-19 mortality, with a p-value of 1.532×10^{-32}.

Table 1
Data for each continental metropolitan region of France.

Regional code	84	27	53	24	44	32	11	28	75	76	52	93	
Inhabitants (N)	8032,377	2783,039	3340,379	2559,073	5511,747	5962,662	12,278,210	3303,500	5999,982	5924,858	3801,797	5055,651	
Sex ratio	0.946	0.946	0.942	0.938	0.949	0.942	0.931	0.934	0.927	0.934	0.946	0.916	
Male (%)	48.6	48.6	48.5	48.4	48.7	48.5	48,2	48,3	48,1	48,3	48,6	47,8	
Female (%)	51.4	51.4	51,5	51,6	51,3	51,5	51.8	51.7	51.9	51.7	51.4	52.2	
Age	0–24y (%)	29.8	27.6	28.4	28.2	28.5	31.6	32.0	28.9	26.7	27.8	29.9	27.4
	25–59y (%)	43.9	41.9	42.1	42.1	44.0	43.8	47.5	42.2	42.2	42.7	42.6	42.8
	>60y (%)	26.3	30.5	29.5	29.7	27.5	24.6	20.5	28.9	31.1	29.5	27.5	29.8
Life expectancy	83.3	82	82	82.3	81.9	80.7	83.8	81.7	82.7	82.9	83	82.9	
Male	80.5	78.9	78.7	79.3	79.0	77.5	81.4	78.3	79.7	80.1	79.8	80.0	
Female	85.9	85.0	85.2	85.2	84.6	83.8	86.1	84.9	85.5	85.5	86.0	85.6	
Birth rate (‰)	11.2	9.4	9.4	10.1	10.0	11.3	14.1	10.2	9.0	9.8	10.4	11.1	
Death rate (‰)	8.7	10.9	10.6	10.6	9.7	9.3	6.1	10.4	10.9	10.1	9.2	10.2	
Taxable income rate (%)	52.7	50.6	49.5	51.1	49.8	45.7	63.9	49.2	48.5	46.6	49.2	51.7	
Prevalence of comor-bidities	Active smoker	26.2	28.6	26.5	28	30.1	30.5	21.3	25.6	28.1	28.6	23	32.2
	Diabetes	4.7	5.06	3.31	5.13	5.59	6.16	5.4	4.79	4.48	4.56	4.04	4.96
	COPD	28.2	27.3	34.5	24	36.7	37.7	25.8	27.5	26.5	29.3	25	27.3
	CKD	0.94	0.83	0.8	0.98	1	1.07	1.2	0.92	0.84	0.94	0.9	1.01
	BMI > 30	13.4	15.1	12	16.9	17.8	20.7	14.4	17	14.8	13.2	11.8	12.1
Health-care	Senior assisted living beds (‰)	148	154	156	150	147	160	140	170	150	132	180	120
	Physicians (‱)	340	297	321	265	321	302	396	288	337	356	289	408
	Short-term hospital beds	30,458	11,464	12,905	9.692	22.728	23.963	44.672	12.763	23.603	21.714	12.864	21.885
	Hospital beds density (‱)	379	412	386	379	412	402	364	386	393	366	338	433
Sunlight exposure (accumulated, hours)	2003	2092.5	1850	2130.7	2084	1702.4	1984.6	1854.9	2150.7	2462.1	2091.2	2550.9	
Infection	Confirmed cases	9067	4378	1362	2519	14,539	7650	34,460	2022	2752	3292	2245	5790
	Infection rate (%)	0.113	0.157	0.041	0.098	0.264	0.128	0.281	0.061	0.,046	0.056	0.059	0.115
	Recovered cases	4671	2237	772	1069	7274	3685	15,899	984	1284	2015	1121	3376
	Recovery rate (%)	51.6	51.1	56.7	42.4	50.1	48.1	46.1	48.6	46.6	61.2	49.9	58.3
	Deceased cases	1226	797	203	355	2737	1291	5578	319	294	362	314	631
	Mortality rate (%)	13.5	18.2	14.9	14.1	18.8	16.9	16.2	15.8	10.7	11	14	10.9

Table 2
Statistical parameters of continental metropolitan French population.

Parameter	Sum	Average	Variance	SD	CI 95 %	
Inhabitants (nb.)	64,553,275					
Sex ratio		0.938	9.354×10^{-5}	9.671×10^{-3}	0,933	0,994
Male (%)		48.4	0.067	0.259	48.236	48.723
Female (%)		51.6	0.067	0.259	51.436	51.923
Age						
0–24y (%)		28.9	2.691	1.64	27.858	29.714
25–59y (%)		43.2	2.439	1.562	42.208	43.994
>60y (%)		27.9	8.952	2.992	25.999	28.999
Life expectancy		82.4	0.697	0.835	81.87	82.981
Male		79.4	1.093	1.046	78.736	80.05
Female		85.3	0.424	0.651	84.886	85.813
Birth rate (‰)		10.5	1.829	1.352	9.641	11.239
Death rate (‰)		9.7	1.797	1.34	8.848	10.435
Taxable income rate (%)		50.7	21.164	4.6	47.777	52.063
Health status						
Current smokers prevalence		27.4	9.612	3.1	25.43	28.519
Diabetic prevalence		4.8	0.543	0.737	4.332	5.345
COPD prevalence		29.2	21.019	4.585	26.287	30.561
Chronic kidney failure prevalence		0.9	0.013	0.114	0.828	1.115
Obesity prevalence		14.9	7.432	2.726	13.168	15.949
Healthcare access						
Senior assisted living rate (‰)		150.6	253.174	15.911	140.49	153.134
Density of physicians (‱)		326.7	1894.242	43.523	299.047	330.892
Places in short hospitalization service	248,711					
Hospitalization bed density (‰ES)		387.5	647.727	25.45	371.329	390.705
Sunlight exposure (accumulated, hours)		2079.75	57,890.461	204.604	1943.615	2088.526
Infection						
Confirmed cases	84,286					
Infection rate (%)		0.11825	0.007	0.081	0.065	0.299
Recovered cases	8047					
Recovery rate (%)		50.892	29.415	5.424	47.446	52.372
Deceased cases	14,107					
Mortality rate (%)		14.583	7.605	2.758	12.831	15.638

Table 3
Pearson test between each variable and mortality rate.

	Pearson coefficient	Student	P-value
Sex ratio			
Male	0.663	7115.601	7.396×10^{-33}
Female	−0.663		
Age			
0–24y	**NOT**		
25–59y	**USED**		
$>$60y			
Life expectancy	−0.485	4456.166	7.971×10^{-31}
Male	−0.425	3773.210	4.207×10^{-30}
Female	−0.524	4940.527	2.841×10^{-31}
Birth rate			
Death rate			
Taxable income rate	0.154	1252.252	2.595×10^{-25}
Health status			
Current smokers prevalence	−0.112	905.562	6.636×10^{-24}
Diabetic prevalence	0.439	3925.652	2.831×10^{-30}
COPD prevalence	0.444	3981.265	2.46×10^{-30}
Chronic kidney failure prevalence	0.194	1588.880	2.4×10^{-26}
Obesity prevalence	0.562	5459.060	1.047×10^{-31}
Healthcare access			
Senior assisted living rate	0.403	3537.921	8.00×10^{-30}
Density of physicians	−0.403	3537.921	8.00×10^{-30}
Short-term hospital beds	−0.035	281.380	7.905×10^{-19}
Hospital beds	−0.15	1218.967	3.398×10^{-25}
Sunlight exposure	−0.6368	6615.680	1.532×10^{-32}
COVID-19 infection			
Confirmed cases			
Infection rate	0.618	6315.775	2.437×10^{-32}
Healed cases			
Recovery rate	−0.373	3229.973	1.991×10^{-29}
Deceased cases			
Mortality rate	**REFERENCE VARIABLE**		

The secondary outcomes showed other variables significantly correlated with COVID-19 mortality:

1. positively-correlated variables indicating a potential risk factor: being male (p-value: 7.396×10^{-33}); higher rate of senior assisted living beds (p-value: 7.913×10^{-30}); taxable income (p-value: 2.595×10^{-25});
2. negatively-correlated variables indicative a potential protective effect: life expectancy (p-value: 7.951×10^{-31}), current smoking status (p-value: 6.636×10^{-24}), physician density (p-value: 7.921×10^{-30}); hospital bed density (p-value: 3.398×10^{-25}).

4. Discussion

We have shown via Pearson correlation that sunlight exposure is significantly correlated (p-value: 1.532×10^{-32}) COVID-19 mortality rate in continental metropolitan France (Table 3), which is the main outcome of this study.

Besides, we acknowledge an interesting secondary finding: namely, the protective effect of life expectancy (Pearson r: 0.512; p-value: 7.951×10^{-31}) and discuss it further as it appears counter-intuitive, as older age is already been broadly documented as being associated with worse COVID-19 outcomes. However, we also note that in our sample life expectancy is strongly positively correlated with sunlight exposure (Pearson r: 1.628×10^{-3}; p-value: 3.88×10^{-31}), which indicates that life expectancy is a mere surrogate of sunlight exposure in this data set, and can therefore be safely explained out of this analysis.

This study is of course limited by two important factors: (1) lack of measurement time; (2) lack of direct vitamin D measurements; (3) confounding variables. First, the brief duration (2 months) across which measurements were taken did not allow us to well understand the time-evolution of the evinced correlations, a crucial point indeed in the context of a pandemic. Secondly, our data set did not include a variable measuring actual plasma vitamin D levels in the studied population, for which we used sunlight exposure as an imperfect surrogate. Last but not least, we are also concerned by the influence of other co-factors well-known to be associated with poor prognosis in Intensive Care Unit population infected by COVID-19, such as high BMI or diabetes (Table 3), and possibly other unknown population confounding variables.

Nevertheless, our regression, linked with the hypothesized physiopathological mechanism (Isaia and Medico, 2020), suggests a first order effect at least. We thus contend that the findings presented in our analysis should be taken into account, in order to envision possibly effective yet inexpensive diagnostic and therapeutic options against the novel COVID-19.

Our conclusions could easily be tested and further assessed by screening the prevalence of COVID-19 infected among vitamin D deficient patients. In addition, in vitro cell studies and animal models could be of interest to test our statistical correlation and the physiopathological hypothesis.

Declaration of Competing Interest

None

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None

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