

Associations between sampling characteristics, nutritional supplemental taking and the SARS-CoV-2 infection onset in a cohort of Italian nurses

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Ethical approval and consent to participate: ethical concerns of the study were stated within the presentation of the questionnaire. Participation in the present study, being free and voluntary, was considered an expression of consent. It was emphasized that participation was voluntary and those interested in participating were presented with the opportunity to express informed consent and the confidentiality and anonymous nature of the information was guaranteed according to the Declaration of Helsinki principles. The present study was approved by the Ethical Committee of the General Hospital Policlinic, Bari, Italy with approve number: 6667/2020.

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ABSTRACT

The aim of the present study was to analyze any relations existed between sampling characteristics and the onset of the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) infection, also by considering the number of times that it occurred in a cohort of Italian nurses interviewed. Additionally, by considering the nutritional supplemental taking, this research wanted to assess any differences both in the onset and in the number of times in which the infection occurred among participants. An observational cohort study was carried out thorough all Italian nurses by advertising the questionnaire through some professional Internet pages. Work typology ($P=0.021$), coronavirus disease 2019 (COVID-19) ward ($P=0.002$) and regular meal assumption ($P=0.019$) significantly associated to the onset of the SARS-CoV-2 infection. Most of nurses who contracted the SARS-CoV-2 infection worked during the night shift (53.7%), 44.3% worked in a no-COVID-19 ward and 53% declared to have a regular meals' assumption. Ward typology significantly associated to the times of the SARS-CoV-2 onset ($P=0.003$), as most of nurses who contracted almost one time the SARS-CoV-2 infection were employed in a no-COVID-19 ward (55.5%) and 54.1% of them declared to have a regular meals' assumption. The onset of the SARS-CoV-2 infection seemed to be more present in the most part of the sample collects. The present study could be considered as pilot in this sense and also more studies will be performed in order to better relate the function of supplemental food intakes with a better functioning of the immune system.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic is defined as a worldwide health emergency, becoming in Wuhan, China, and rapidly spreading to all around the world. Due to the high number of cases worldwide both for infections and deaths,¹ most countries have engaged non-pharmacological preventive initiatives, such as adopting public health approaches by decreasing the transmission of the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) infection. However, many individuals implemented additional preventive protection measures thanks to the assumption of dietary and nutraceuticals intakes, which

are might due to beneficial effects.² Additionally, healthcare workers, especially nurses who represented a fundamental role in the healthcare organizations face up to the COVID-19 pandemic since they are directly involved in the treatment and care of patients.³⁻⁵ Nurses experience heavy and prolonged psychological pressure since they are particularly exposed to the caring of the SARS-CoV-2 infection, and they become devastated by fear and anxiety for the security of their families and their patients and also of their own health, since also nurses could be suffered from comorbidities of cardiovascular or pulmonary diseases.^{6,7} Working conditions during the COVID-19 have dramatically adapted, since nurses experience endless and excessive working shifts and workloads, including the night shift and distress due to ward typology, like COVID-19 or no COVID-19 wards assignments.^{8,9} Additionally, eating habits and its relating flexibility to eat seemed to be linked with the nursing shifting profession, also with the years of work experience and consequentially with age, also with ward assignment, too.¹⁰ In fact, nurses who were employed during the night shift, mostly for more years, ate more an irregular diet rich in saturated and high-caloric fats, complex sugars, mostly during the night shift, which contributed to arise their body's weights.

Nutritional intakes and immune system

A successful strategy to decrease the risk of viral infections is to manage the actions of the inflammation intermediaries through adaptable risk determinants such as diet, exercise, and healthful lifestyle habits.¹¹ Engaging a persistent dietary model is the successful strategy to improve human health. On the other hand, an unhealthy lifestyle, such as unhealthy diet assumption and unsatisfactory physical activity regimen is related to a high level in oxidative stress, by improving non-communicable diseases.^{12,13} Several studies¹⁴ explained how high body mass index or excessive adiposity might involve complications during the COVID-19 infection.¹⁵ This might be caused by the presence of different pulmonary diseases in overweight and obese populations compared to healthy weight subjects.¹⁶ Additionally, obese subjects might be considered at risk of contracting the COVID-19 disease and associated severe consequences, due to the presence both of cardiovascular and pulmonary comorbidities.¹⁷ Therefore, a balanced and adequate diet could represent an essential point in preventing and treating the COVID-19 disease.¹⁸⁻²⁰ The World Health Organization (WHO) recommended increasing in fresh vegetables, fruits, and unprocessed foods assumptions and also an adequate water consumption (8-10 cups), by decreasing the consumption of saturated fat, trans fat, salt, and sugar, and eating outside the home.²¹ Furthermore, the WHO suggested no smoking, to perform regular physical activity, to sleep

sufficiently.²² In this perspective, micronutrients are dietary elements that may provide to a healthy immune system.^{23,24}

Important micronutrients like vitamins A, D, E, C, B6, B12, and folate and fewer quantities of microelements such as iron, zinc, and selenium, present in different fresh animal, and vegetables food, may help the body's capability to contrast infections.^{25,26} Since health and survival are directly influenced by the functioning of the immune system, like a rapid innate immune response provide phagocytes and, at the same time, an adaptive immune response more specifically recognizes the invading pathogen. Basically, these immune responses are regulated by T cells, which identify the antigens and are categorized as cytotoxic T cells. Cytotoxic T cells suppress contaminated, injured cells and the T helper cells Th1 and Th2. These cells are implicated in antiviral, cellular, humoral and antiparasitic immune action responses. A powerful immune system guarantees host defense and unbiased nutrition increases the immune system to bring an adequate defense against infectious vehicles. Childs *et al.*¹³ recognized the important role of the immune system as well as the defense processes regarded in safeguarding the body from assaulting agents, specifically with an accurate healthy nutrition. Thevarajan *et al.*²⁷ demonstrated the pathophysiology of the immune response to Covid-19, such as the increasing concentrations in follicular helper T cells, antibody-secreting cells, activated CD4 β and CD8 β T cells, and immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies. Other studies have identified integrative supplements in vitamin C^{28,29} as a strategic approach to fight respiratory infections among older patients. Grant *et al.*³⁰ demonstrated that doses of vitamin D3 more than 10,000 IU/d may have a curative effect in the treatment of COVID-19 patients. Additionally, omega-3 polyunsaturated fatty acids (n-3 PUFA)³¹ has identified as a protective element for the COVID-19 infection. Other studies suggested that nutraceuticals containing phycocyanobilin, n-acetylcysteine, glucosamine, selenium, or phase 2 inductive nutraceuticals, such as ferulic acid, lipoic acid, or sulforaphane could prevent or modulate RNA virus infections via amplification of the signaling activity of mitochondrial antiviral-signaling protein and activation of Toll-like receptor 7.^{2,32} Phase 2 inductive molecules adopted in the production of nutraceuticals are recognized to activate nuclear factor erythroid 2-related factor 2 (Nrf2), which regulates antioxidant enzymes necessary to several antioxidant enzymes activations, such as gamma-glutamylcysteine synthetase.

Consequentially, micronutrient deficiencies, such as zinc, selenium, and vitamin D, frequently present in old age groups, suggesting the age-related diseases, such as: hypertension, coronary heart disease and diabetes,³³⁻³⁵ which might evolve in the metabolic syn-

drome condition,³⁶ recognized by low-grade inflammation.^{37,38} Pre-infectious signs of inflammation, such as elevated values for C-reactive protein (CRP), represent a common aggravating factor in COVID-19.¹¹

Aim

The aim of the present study was to analyze any relations existed between sampling characteristics and the onset of the SARS-CoV-2 infection, also by considering the number of times that it occurred in a cohort of Italian nurses interviewed. Additionally, by considering the nutritional supplemental taking, this research wanted to assess any differences both in the onset and in the number of times in which the infection occurred among participants, too.

Materials and Methods

Study design

An observational cohort study was carried out thorough all the Italian territory from November 2020 and a re-call was performed until August 2022.

Enrollment

All Italian nurses who were employed as nurse both in private and public healthcare facilities were potentially reachable to participate to the present study. The questionnaire was publicized through some professional Internet pages, like Facebook and Instagram. Participation was voluntary and no form of personal restitution of the results obtained was involved.

The questionnaire

The questionnaire collected several socio-demographic characteristics relating to the reference sample, such as: i) sex, as female and male; ii) age, divided into different groups, such as: until 30 years, 31-40 years, 41-50 years, 51-60 years and over 61 years; iii) years of work experience as nurse, divided into groups, as: until 10 years, 11-20 years, 21-30 years, over 31 years; iv) work typology, if the interviewer worked only during the daily hours or also during the night shift; v) ward typology, such as COVID-19 or no COVID-19; vi) if the participant suffered from a pulmonary disease or not; vii) if the participant suffered from a cardiovascular disease or not; viii) if the participant, during the COVID-19 pandemic, contracted the SARS-CoV-2 infection or not; ix) the number of times which the interviewer contracted the SARS-CoV-2 infection, such as: none, one time or two and more times; x) if the interviewer regularly assumed almost three meals par day; xi) if the participant assumed supplemental taking among those proposed, like: vitamin C, vitamin D, zinc, nutraceu-

tical substances, omega fats (type 3: DHA, EPA; type 6: ω -3 PUFA) or preparations of polyphenols.

Ethical concerns

In the first part of the questionnaire, there was a clear explanation of the study, including its aim. All participants who did not give their consent were not enrolled in the study. The present study was approved by the Ethical Committee of Polyclinic in Bari, Italy, with id number 6667/2020.

Data analysis

All data were collected in an Excel data sheet and then processed thanks to the Statistical Package for the Social Sciences, version 20. All sampling characteristics were explained as frequencies and percentages, by dealing with categorical variables. Linear regression was assessed to explore what were the potential factors that contributed to the SARS-CoV-2 onset and also the number of times in which the onset occurred, too. Finally, chi-square tests were performed to assess any differences in supplemental taking in nurses who contracted the SARS-CoV-2 infection and also by considering the number of times in which the onset occurred. All P-values <0.05 were considered as statistically significant.

Results

296 Italian nurses were enrolled in this study. All sampling characteristics were reported in Table 1.

By considering how sampling characteristics influenced the onset of the SARS-CoV-2 infection, Table 2 reported that work typology (P=0.021) ward COVID-19 (P=0.002) and regular meal assumption (P=0.019) seemed to be significantly associated to the onset of the SARS-CoV-2 infection.

As reporting in Tables 3 and 4, most of interviewers who contracted the SARS-CoV-2 infection worked during the night shift (53.7%), 44.3% worked in a no-COVID-19 ward and 53% declared to have a regular meals' assumption.

Additionally, ward typology was significantly associated to the times of the SARS-CoV-2 onset (P=0.003) and Table 5 shows how this statistically significant trend was explained, as most of nurses who contracted almost one time the SARS-CoV-2 infection were employed in a no-COVID-19 ward (55.5%) and 54.1% of them declared to have a regular meals' assumption.

Table 6 shows which supplemental taking nurses assumed: the onset of the SARS-CoV-2 infection seemed to be more present in the most part of the sample collect, however, there were nurses who regularly summed supplemental takings, who did not contract the infection.

Finally, Table 7 shows that the most part of nurses who took supplements contracted the infection only one time ($P < 0.001$).

Discussion and Conclusions

The aim of the present study was to analyze any relations existed between sampling characteristics and the onset of the SARS-CoV-2 infection, also by considering the number of times that it occurred in a cohort of Italian nurses interviewed. Additionally, by considering the nutritional supplemental intake, this research wanted to assess any differences both in the onset and in the number of times in which the infection occurred among participants, too.

It might be considered that in the literature very few evidence focused on the nutritional aspect of nurses in the COVID-19 era, therefore, the present study could be considered as pilot in this sense.

By taking into account how sampling characteristics influenced the onset of the SARS-CoV-2 infection, data reported that work typology ($P = 0.021$), ward typology ($P = 0.002$) and regular meal assumption ($P = 0.019$) significantly influenced to the onset of the SARS-CoV-2 infection, specifically, most of the interviewers who contracted the SARS-CoV-2 infection were employed during the night shift (53.7%), in a no COVID-19 ward (44.3%) and assumed regular meals (53%).

Our data agreed with the current literature, since most of viral infections, including influenza, are noticeably associated to circadian rhythms, and night shift workers who often interrupt their circadian rhythms, so their seemed to be at a more considerable risk of COVID-19 infection.³⁹ In a current study, it was explained how the clock genes might induce the seasonal modification, identifying a positive association between COVID-19 and androgen sensitivity.^{40,41} Androgen sensitivity is moderated by the seasonal showing of specific genes and proteins.⁴¹ Clock genes modulate a set of predictively reactions to modifications in the

Table 1. Sampling characteristics (N=296).

Variables	N (%)
Gender	
Female	184 (62.2)
Male	112 (37.8)
Age	
Until 30 years	83 (28)
31-40 years	84 (28.4)
41-50 years	64 (21.6)
51-60 years	61 (20.6)
Over 61 years	4 (1.4)
Work experience	
0-10 years	135 (45.6)
11-20 years	69 (23.3)
21-30 years	48 (16.2)
Over 31 years	44 (14.9)
Work typology	
Daily	70 (23.6)
Daily and night	226 (76.4)
Ward typology	
COVID-19	120 (40.5)
No COVID-19	176 (59.5)
Existence of pulmonary diseases	
Yes	23 (7.8)
No	273 (92.2)
Existence of cardio circulatory diseases	
Yes	29 (9.8)
No	267 (90.2)
Onset SARS-CoV-2 infection	
Yes	201 (67.9)
No	95 (32.1)
Times of onset SARS-CoV-2 infection	
None	8 (2.7)
1 time	156 (52.7)
2 or more times	45 (15.2)
Not answered	87 (29.4)
Regularity in meals assumptions per day	
Yes	219 (74)
No	77 (26)
Taking supplements	
Vitamin C	85 (28.7)
Vitamin D	70 (23.6)
Zinc	7 (2.4)
Nutraceutical substances	13 (4.4)
Omega fats (type 3: DHA, EPA; type 6: ω -3 PUFA)	17 (5.7)
Preparations of polyphenols	0 (0)
Not answered	104 (35.1)

Table 2. How sampling characteristics influenced the onset of SARS-CoV-2 infection.

Variables	Non-standardized coefficients		Standardized coefficients Beta	t	P-value	CI 95% per B	
	B	SE				Minimum	Maximum
Gender	0.016	0.056	0.016	0.279	0.780	-0.095	0.126
Age	0.024	0.046	0.058	0.512	0.609	-0.067	0.115
Work experience	0.028	0.048	0.066	0.584	0.560	-0.066	0.122
Work typology	-0.149	0.064	-0.135	-2.328	0.021*	-0.274	-0.023
Ward assigned	-0.176	0.055	-0.185	-3.186	0.002*	-0.285	-0.067
Existence of pulmonary diseases	-0.106	0.101	-0.061	-1.050	0.295	-0.306	0.093
Existence of cardio circulatory diseases	0.010	0.091	0.006	0.110	0.912	-0.169	0.189
Regular meals assumption	0.143	0.061	0.135	2.360	0.019*	0.024	0.263

* $P < 0.05$ is statistically significant.

Table 3. How varied significant associations between the groups considered.

Variables/SARS-CoV-2 infection onset	Yes N (%)	No N (%)
Work typology		
Daily	42 (14.2)	28 (9.5)
Daily and night	159 (53.7)	67 (22.6)
Ward typology		
COVID-19	70 (23.6)	50 (16.9)
No COVID-19	131 (44.3)	45 (15.2)
Regularity in meals assumptions par day		
Yes	157(53)	62 (20.9)
No	44 (14.9)	33 (11.1)

Table 4. How sampling characteristics influenced the times of SARS-CoV-2 infection.

Variables	Non-standardized coefficients		Standardized coefficients Beta	t	P-value	CI 95% per B	
	B	SE				Minimum	Maximum
Gender	0.105	0.066	0.107	1.590	0.113	-0.025	0.234
Age	-0.048	0.053	-0.114	-0.901	0.369	-0.152	0.057
Work experience	0.044	0.055	0.102	0.805	0.422	-0.064	0.153
Work typology	0.003	0.079	0.002	0.035	0.972	-0.152	0.158
Ward assigned	-0.197	0.065	-0.202	-3.016	0.003*	-0.326	-0.068
Existence of pulmonary diseases	0.131	0.128	0.067	1.025	0.307	-0.121	0.384
Existence of cardio circulatory diseases	-0.024	0.102	-0.016	-0.237	0.813	-0.225	0.176
Regular meals assumption	-0.363	0.073	-0.329	-5.007	>0.001*	-0.506	-0.220

*P<0.05 is statistically significant.

Table 5. How varied significant associations between the groups considered.

Variables/SARS-CoV-2 infection times	None N (%)	One time N (%)	Two or more times N (%)
Ward typology			
COVID-19	8 (3.8)	40 (19.1)	30 (14.4)
No COVID-19	0 (0)	116 (55.5)	15 (7.2)
Regularity in meals assumptions par day			
Yes	2 (1)	113 (54.1)	44 (21.1)
No	6 (2.9)	43 (20.6)	1 (05)

context in which are mentioned to as circadian rhythms. Circadian rhythms are modulated by an inside time-keeping system, which keep also external stimuli like light or heat. Alterations in the internal molecular clocks have been associated to the risk of several disorders.⁴² In this scenario, other evidence suggested that night shift work might be linked to cancer and other chronic disorders.⁴³ Specifically, night shift work has been correlated to risks of metabolic syndrome, obesity, and diabetes, as well as breast cancer and prostate cancer, too,⁴⁴⁻⁴⁷ and, at the same time, disruptions in sleep might negatively influence the immune system functioning, by increasing susceptibility to infec-

tion.^{39,48-52} However, other studies suggested the same trend also before the COVID-19 pandemic,⁵³⁻⁵⁵ by showing the importance also of the work typology, which was highlighted also in the present study, too.

Literature evidenced how, both the adaptive (or acquired) immune system and innate immune system were influenced to circadian rhythm disorders, by variations in circulating cytokines regulation, depressed proliferative responses of immune cells, and altered and desynchronized immune cell counts.⁵⁶⁻⁵⁹ Additionally, poorer sleep quality and reduced rest's hours also suggested reduced health and security measures, by increasing infection vulnerability.^{53,54}

Table 6. Differences in supplements taking among nurses who suffered from the SARS-CoV-2 infection.

Onset SARS-CoV-2 infection	Vitamin C n (%)	Vitamin D N (%)	Zinc N (%)	Nutraceutical substances N (%)	Omega fats N (%)	Not answered N (%)	P-value
Yes	63 (21.3)	50 (16.9)	0 (0)	6 (2)	3 (1)	79 (26.7)	<0.001*
No	22 (7.4)	20 (6.8)	7 (2.4)	7 (2.4)	14 (4.7)	25 (8.4)	

*P<0.05 is statistically significant.

Table 7. Differences in supplements taking by considering the times of SARS-CoV-2 infection.

Onset SARS-CoV-2 infection	Vitamin C n (%)	Vitamin D N (%)	Zinc N (%)	Nutraceutical substances N (%)	Omega fats N (%)	Not answered N (%)	P-value
None	0 (0)	1 (0.5)	0 (0)	6 (2.9)	0 (0)	1 (0.5)	<0.001*
1 time	48 (23)	38 (18.2)	0 (0)	6 (2.9)	3 (1.4)	61 (21.2)	
2 or more times	15 (7.2)	12 (5.7)	0 (0)	0 (0)	0 (0)	18 (8.6)	

*P<0.05 is statistically significant.

The present data showed that the onset of the SARS-CoV-2 infection seemed to be more present in the most part of the sample collected; however, there were nurses who regularly assumed supplemental takings, who did not contract the infection (2.9%).

The most part of nurses who assumed nutritional supplements contracted the infection only one time (P<0.001), particularly, most of them assumed vitamin C supplement (23%) and vitamin D (18.2%).

In this aspect, also Cena *et al.*⁶⁰ highlighted that to improve the efficiency of the immune system, it would be enhancing particular foods in the dietary habit as great availabilities of antioxidants, such as fresh fruit and vegetables, soy, nuts,⁶¹ and omega-3 fatty acids all constituting low in saturated fats and trans fats.⁶² Furthermore, moderate and healthy diet was recommended for obese/overweight individuals and diabetic patients.⁶³ Dietary conditions were considered as an important factor that might mitigate the outcome of COVID-19 patients.^{4,64-66} Recent studies suggested an exhaustive list of nutritional supplemental intakes that seemed to have a mitigation effect among COVID-19 patients and a preventive function, too.^{9,31}

Numerous elements, such as vitamins A, B6, B12, C, D, E, and folate, and minerals, like zinc, iron, selenium, magnesium, and copper, also different substances such as essential fatty acids, linoleic acids, essential amino acids, could ameliorate the immune response.⁶⁷ In agreement with the present study, three recent reviews have analyzed how sufficient nutritional intake, associated with different functional foods, improved the immune system functioning.⁶⁸⁻⁷⁰ Particularly, vitamin C⁷¹⁻⁷⁵ and vitamin D seemed to prevent and/or treat COVID-19 diseases.

Also, zinc could prevent the COVID-19 infection,

by developing a functioning maintenance of the immune system.⁷⁶ In this context, it was accounted that 16% of all deep respiratory infections worldwide⁷⁷ were associated to a zinc-related deficiency, too.^{78,79} Finally, the role of probiotics in preventing viral respiratory infections has also been recently considered, by suggesting their assumptions, balancing the inflammatory response.⁸⁰

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