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onset in a cohort of Italian nurses

Elsa Vitale[1*], Rocco Mea[2]

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Elsa Vitale[1]*, Rocco Mea[2]

Running head: SARS-CoV-2 infection among Italian nurses

Affiliations

1. Centre of Mental Health Modugno, Local Healthcare Company Bari, Italy

2. San Carlo Hospital, Potenza, Italy

*Corresponding author:

Elsa Vitale, Centre of Mental Health Modugno, Local Healthcare Company Bari, Italy,

via X marzo, 43, 70026 Modugno, Bari

E-mail: vitaleelsa@libero.it

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ETHICAL STATEMENT

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.

Authors' contribution

E.V.: conceived and planned the study, elaborated and interpreted data and wrote the manuscript. R.M.: collected data

All the authors read and approved the final version of the manuscript.

Abstract

Background: 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 which the infection occurred among participants

Method: An observational cohort study was carried out thorough all Italian nurses by advertising the questionnaire through some professional internet pages.

Results: Work typology (p=0.021), ward Covid-19 (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 collect.

Conclusion: 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.

Keywords: Infection; Nurse; Nutrition; Onset; SARS-CoV-2; Supplemental taking.

Introduction

The Covid-19 pandemic is defined as a worldwide health emergency, becoming in Wuhan, China, and rapidly spreading to all around the world (Ayer & Celep, 2022; Musulin et al., 2021). Due to the high number of cases worldwide both for infections and deaths (WHO, 2021), most countries have engaged non-pharmacological preventive initiatives, such as adopting public health approaches by decreasing the transmission of the 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 (Lordan et al., 2021). 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 (Hu et al., 2020; Liu et al., 2020; Zhan et al., 2020). 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 (Vitale et al., 2021; Joo & Liu, 2021). 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 (Vitale et al., 2021; Vitale et al., 2021). 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 (Vitale et al., 2022). 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 (Zheng et al., 2020). 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 regimens is related to a high level in oxidative stress, by improving non-communicable diseases (NCDs) (Wu, 2020; Childs et al., 2019). Several studies (WHO, 2020) explained how high body mass index (BMI) or excessive adiposity might involve complications during the Covid-19 infection (Fiori et al., 2020). This might be caused by the presence of different pulmonary diseases in overweight and obese populations compared to healthy weight subjects (Costa et al., 2008). 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 (Wu & McGoogan, 2020). Therefore, a balanced and adequate diet could represent an essential point in preventing and treating the Covid-19 disease (Macit, 2020; Lange, 2021; BourBour et al., 2020). 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 (WHO, 2021). Furthermore, the WHO suggested not to smoke, to perform regular physical activity, to sleep sufficiently (FAO, 2020). In this perspective, micronutrients are dietary elements that may provide to a healthy immune system (Gupta et al., 2019; Messina et al., 2020).

Important micronutrients like vitamins A, D, E, C, B6, B12, and folate and less 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 (Elmadfa & Meyer, 2019; Romagnani, 2000). 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 (Romagnani, 2000). 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. (2019) 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. (2020) demonstrated the pathophysiology of the immune response to Covid-19, such as the increasing concentrations in follicular helper T cells, antibody-secreting cells, activated CD4þ and CD8þ T cells, and immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies. Other studies have identified integrative supplements in vitamin C (Hemila & Chalker, 2013; Ran et al., 2018) as a strategic approach to fight respiratory infections among older patients. Grant et al. (2020) 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) (Zhang & Liu, 2020) has identified as a protective element for the Covid-19 infection. Other studies suggested that nutraceuticals containing phycocyanobilin, Nacetylcysteine, 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 (MAVS) protein and activation of Toll-like receptor 7 (Lordan et al., 2020; McCarty & DiNicolantonio, 2020). 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 (Bjørklund et al., 2020; Farrokhian et al., 2016; Holmberg et al., 2017), which might evolve in the metabolic syndrome condition (Grundy, 2006), recognized by low-grade inflammation (12, Sanada, 2018; Vitale et al., 2022). Pre-infectious signs of inflammation, such as elevated values for CRP (C-reactive protein), represent a common aggravating factor in COVID-19 (Zheng et al., 2020).

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 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:

- sex, as female and male;
- age, divided into different groups, such as: until 30 years, 31-40 years, 41-50 years, 51-60 years and over 61 years;
- years of work experience as nurse, divided into groups, as: until 10 years, 11-20 years, 21-30 years, over 31 years;
- work typology, if the interviewer worked only during the daily hours or also during the night shift;

- ward typology, such as Covid-19 or no Covid-19;

- if the participant suffered from a pulmonary disease or not;

- if the participant suffered from a cardiovascular disease or not;

- if the participant, during the Covid-19 pandemic, contracted the SARS-CoV-2 infection or not;

- the number of times which the interviewer contracted the Sars-CoV-2 infection, such as: none, one time or two and more times;

- if the interviewer regularly assumed almost three meals par day;

- if the participant assumed supplemental taking among those proposed, like: vitamin C, vitamin D, zinc, nutraceutical 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 (SPSS), version 20. All sampling characteristics were explained as frequencies and percentages, by dealing with categorical variables. Linear regression was assessed to explore what were potential factors which contributed to the SARS-CoV-2 onset and also the number of times 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 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 the Table 1.

Table 1. Sampling characteristics (n=296)

Variables	n(%)
Sex	
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 par 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)

By taking into account 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.

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

Variables	Non-standardized coefficients		Standardized coefficients	t	p-value	C.I. 95% per B	
	B	SE	Beta			Minimum	Maximum
Sex	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 statistical significant.

As reporting in the Table 3, 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.

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)

Additionally, ward typology was significantly associated to the times of the SARS-CoV-2 onset (p=0.003) and Table 5 showed 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 4. How sampling characteristics influenced the times of SARS-CoV-2 infection.

	Non-standardized coefficients		**Standardized coefficients**	t	p-value	**C.I. 95% per B**	
Variables	B	SE	Beta			Minimum	Maximum
Sex	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 statistical 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 No Covid-19	8(3.8) 0(0)	40(19.1) 116(55.5)	30(14.4) 15(7.2)
Regularity in meals assumptions par day Yes No	2(1) 6(2.9)	113(54.1) 43(20.6)	44(21.1) 1(05)

Table 6 showed 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.

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

Onset SARS-CoV-2 infection	Vitamin C	Vitamin D	Zinc	Nutraceutical substances	Omega fats	Not answered	p-value

	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	
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 statistical significant.

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

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

Onset SARS-CoV-2 infection	Vitamin C	Vitamin D	Zinc	Nutraceutical substances	Omega fats	Not answered	p-value
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	
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 statistical significant.

Discussion

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 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 were in agreement 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 (Lim et al., 2020). 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 (Wambier et al., 2020; Goren et al., 2020). Androgen sensitivity is moderated by the seasonal showing of specific genes and proteins (Goren et al., 2020). Clock genes modulate a set of predictively reactions to modifications in the context 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 (Andreani et al., 2015). In this scenario, other evidence suggested that night shift work might be linked to cancer and other chronic disorders (Hansen, 2017). Specifically, night shift work has been correlated to risks of metabolic syndrome, obesity, and diabetes, as well as breast cancer and prostate cancer, too (Barul et al., 2019; D'Ettorre et al., 2019; Shan et al., 2018; Liu et al., 2018), and, at the same time, disruptions in sleep might negatively influence the immune system functioning, by increasing susceptibility to infection (Almeida & Malheiro, 2016; Mohren et al., 2002; Prather & Carroll, 2021; Belingheri et al., 2021; Lim et al., 2020; Silva et al., 2021). However, other studies suggested the same trend also before the Covid-19 pandemic (Fatima et al., 2021; Maidstone et al., 2021; Rowlands et al., 2021), 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 (Cermakian et al., 2022; Cuesta et al., 2016; Liu et al., 2021; Loef et al., 2019a). Additionally, poorer

sleep quality and reduced rest's hours also suggested reduced health and security measures, by increasing infection vulnerability (Fatima et al., 2021; Maidstone et al., 2021).

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. (2020) 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 (Yahfoufi et al., 2018), and omega-3 fatty acids all constituting low in saturated fats and trans fats (Seidelmann et al., 2018). Furthermore, moderate and healthy diet was recommended for obese/overweight individuals and diabetic patients (Petrilli et al., 2020). Dietary conditions were considered as an important factor that might mitigate the outcome of Covid-19 patients (Laviano et al., 2020; Correia, 2020; Liu et al., 2020; Budhwar et al., 2020). Recent studies suggested an exhaustive list of nutritional supplemental intakes which seemed to have a mitigation effect among Covid-19 patients and a preventive function, too (Zhang & Liu, 2020; Vitale et al., 2021).

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 (López-Varela et al., 2002). 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 (Gombart et al., 2020; Valenzano et al., 2020; Moscatelli et al., 2020). Particularly, vitamin C (Simonson, 2020; Chen et al., 2020; Feyaerts & Luyten, 2020; Cheng, 2020; Hiedra et al., 2020) 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 (Wessels et al., 2017). In this context, it was accounted that 16% of all deep respiratory infections worldwide (WHO, 2003) were associated to a zinc-related

deficiency, too (Wessels et al., 2020; Mayor-Ibarguren et al., 2020). Finally, the role of probiotics in preventing viral respiratory infections has also been recently considered, by suggesting their assumptions, balancing the inflammatory response (Infusino et al., 2020).

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