ORIGINAL ARTICLE

OLFACTORY/GUSTATORY DYSFUNCTIONS IN COVID-19 IN NORTH AFRICA

DYSFONCTIONNEMENTS OLFACTIF ET GUSTATIF DANS LE COVID-19 EN AFRIQUE DU NORD

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ABSTRACT

Aim: To determine the prevalence of olfactory dysfunction (OD) and gustatory dysfunction (GD) among patients with SARS-CoV2 infection, and to identify their predictive factors that may be associated with these conditions.
Methods: This was an analytical cross-sectional study. All Tunisian adult patients (aged 18 years and above) who tested positive for SARS-CoV2 between March 2020 and February 2022 were included. The Data were collected over the course of was one month (February 2022). Patients completed an online questionnaire created using Google Forms, which requested information on age, sex, the onset and duration of OD and GD, comorbidities, otorhinolaryngological and general symptoms,
Results: Our study involved a total of 1911 participants with OD and GD being present in 55.1% and 50.0% of cases respectively. The mean age of patients was 37.25 ±9.18 years. The major part of patients were female (n=1510; 80% vs n=377; 20%) with a sex ratio of 0.25. Other associated symptoms that were commonly reported included headache (71.6%), body aches (62.7%), arthralgia (58.2%), fever (51.7%), sore throat (49.4%) and myalgia (41.8%). The results of the multivariate analysis indicated that not having received the vaccination prior to infection and having GD were the predictive factors associated with OD. The multivariate study demonstrated that predictive factors of GD were dysthyroidism, lack of vaccination prior to infection, nausea and arthralgia.
Conclusion: The most common clinical signs were OD and OG, which were among frequently accompanied by headache and body aches. Individuals of female gender and those under 35 years of age were observed to be at a higher risk of developing OD and OG. Furthermore, a notable correlation between the two conditions and those who had not received the vaccination.
Keywords: Olfaction, Smell, taste, Risk factors, COVID-19

RÉSUMÉ

But: Déterminer la prévalence du dysfonctionnement olfactif (DO) et du dysfonctionnement gustatif (DG) chez les patients infectés par le COVID-19 et leurs facteurs prédictifs.
Méthodes: Il s'agissait d'une étude analytique transversale. Tous les patients tunisiens adultes (≥18 ans) testés positifs au COVID-19 de mars 2020 à février 2022 ont été inclus. La collecte des données s'est déroulée sur un mois (février 2022). Les patients ont rempli un questionnaire en ligne (Google Forms) comprenant l'âge, le sexe, les comorbidités, les symptômes généraux et ORL, l'apparition et la durée du DO et DG.
Résultats: Notre étude a porté sur un total de 1911 participants et les prévalences DO et DG étaient respectivement de 55,1 % et 50,0 %. L'âge moyen était de 37,25 ± 9,18 ans. La plupart des patients étaient des femmes (n = 1 510 ; 80 %) avec un sex-ratio de 0,25. Les autres symptômes associés étaient principalement des céphalées (71,6 %), des courbatures (62,7 %), des arthralgies (58,2 %), de la fièvre (51,7 %), odynophagie (49,4 %) et des myalgies (41,8 %). L'analyse multivariée a montré que la non vaccination avant l'infection et la DG étaient les facteurs prédictifs du DO. Pour le dysfonctionnement gustatif, l'analyse multivariée a montré que la dysthyroïdie, les patients non vaccinés avant l'infection, les nausées et les arthralgies étaient les facteurs prédictifs.
Conclusion: DO et DG figuraient parmi les signes cliniques les plus fréquents avec céphalées et courbatures. La vaccination partielle ou complète avant l'infection était un facteur de protection de l'DO et de l'DG.
Mots clés: Olfaction, Odeur, Goût, Facteurs de risque, COVID-19

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INTRODUCTION:

The 2019 novel coronavirus (2019 nCoV) was subsequently designated Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2), which was transmitted in Wuhan, China in December 2019 [1]. Then, the Coronavirus Disease 2019 (COVID-19), has proliferated exponentially across the world, leading the World Health Organization (WHO) to formally recognize it as a pandemic disease on March 11, 2020 [2]. The disease was most commonly described by the presence of the most characteristic symptoms namely cough, fever, and shortness of breath. However, it is acknowledged that there is considerable heterogeneity in the severity of disease presentation, with symptoms ranging from asymptomatic to severe acute respiratory distress syndrome and death. It can cause otorhinolaryngological manifestations [3]. OD and GD may be significant symptoms of coronavirus and useful predictors of asymptomatic COVID-19 carriers. OD may occur at any stage of the infection, but is typically observed at the onset of symptoms in patients with COVID-19 disease course [4].

Many studies have demonstrated an important prevalence of OD and GD among COVID-19 patients [5]. This study aims to determine the prevalence of OD and GD among patients with coronavirus infection, and to identify predictive factors associated with these symptoms.

MATERIALS AND METHODS:

Study design

The study was a cross-sectional analytic study conducted among Tunisian individuals infected with the virus between March 2020 and February 2022.

Study population

The study population comprised individuals of Tunisian nationality who had contracted the virus at least once and who consented be in the study. The requisite sample size was determined using the following formula: n=[(Zα/2)2 ×p x (1-p)]/i2. The prevalence of long COVID-19 ranges from 5% to 50% [6]but whether breakthrough SARS-CoV-2 infection (BTI. In order to maximize the sample size [6]but whether breakthrough SARS-CoV-2 infection (BTI, a long COVID-19 proportion (p) of 50% was selected, with a precision (i) of 5%, a risk error (α) of 5%, and a 30% loss due to ineligibility (non-Tunisian residents, individuals under the age of 18, etc.) taken into account. Consequently, a minimum sample size of 501 participants was required. The study excluded individuals under 18 years old, Tunisian nationals residing abroad, non-Tunisian residents in Tunisia, and those who had been infected within the past two months allowing for a two-month period for the manifestation of long COVID symptoms.

Data collection

The data collected via online French and Arabic language self-administered questionnaire developed with Google Forms. In order to capitalize on the extensive usage of Facebook in Tunisia [7], the questionnaire was disseminated via social media (specifically Facebook), as well as through television channels and radio for a duration of one month (February 2022). To encourage participation, regular reminders were provided on a weekly basis. Participants were asked about their history, socio-demographic characteristics, the number of times they had been infected with COVID-19, vaccination status prior to infection, the type of vaccine they had received, the clinical signs, management, and the symptoms they had experienced following infection.

Data analysis

The data was entered and analysed using the Statistical Package for Social Sciences (SPSS) version 21.0. In order to ascertain the normality of the distribution of the quantitative variable, the Kolmogorov-Smirnov was employed. Accordingly, the data were presented as means ± standard deviations when the distribution was normal and compared using the Student's t-test. When the distribution was not normal, the data were presented as medians and compared using the Mann-Whitney U-test. Categorical variables were described by percentages and compared by the Chi-square test when the conditions of validity allowed it (theoretical numbers per cell are ≥ 5). Otherwise, Fisher's exact test was used. A 5% margin of error was retained for the analysis of the results. Univariate analyses were conducted to investigate the associations between OD and GD and their predictive factors. Studied factors were as follow: sex, age (> or < 35 years according to literature) ,tobacco, alcohol,respiratory history, hypertension, diabete, dysthyroidism, alergy, vaccination,fever,headache, sore throat, body aches , nausea, vomit, diarrhea, runny nose, arthralgia, myalgia and dyspnea. Binary stepwise logistic regression was used in the multivariate analyses to identify explanatory factors for OD and GD. All variables with a p-value of 20% or less in the univariate analysis were introduced into this multivariate analysis. The significance threshold was set at 5% and the strength of association was estimated by calculating the Odds Ratio (OR) and its 95% confidence interval.

RESULTS:

Descriptive study:

A total of 1916 participants in the study. Following the exclusion of subjects under the age of 18 (n=5), the total number of participants retained was 1911. Following the exclusion of non-Tunisian participants (n=5) and Tunisian individuals residing in other countries (n=19), the final sample size was 1887.

The mean age of individuals was 37.25 ±9.18 years. The majority of patients were female (n=1510; 80% vs n=377; 20%) with a sex-ratio H/F of 0.25. The majority of respondents were from the governorates of Tunis (19.1%), Sousse (16.5%), Ariana (10.5%), Ben Arous (8.5%), Sfax (6.1%) and Monastir (5.6%). Of the participants, 446 were health professionals representing 23.6% of the total sample. Almost a quarter of the participants (22,5%, n=424) had at least

one comorbidity. The most prevalent comorbidities were respiratory diseases (6%), arterial hypertension (5.4%), diabetes (4%), thyroid disease (5.7%), cardiac diseases (1.1%) and immunodepression (1.4%). The prevalence of smoking was 18.2%, while the prevalence of alcohol consumption was 11.6%. The prevalence of overweight was 38.1% and obesity 18.8% in the population under study. The majority of cases involved a single infection (69.5%), two infections (25.6%), three times (4.1%), four times (0.6%) and five times in 0.2% of cases. The majority of cases were symptomatic (95%).

The most frequently observed clinical signs were OD and GD, with a prevalence of 55.1% and 50.0% respectively. The remaining symptoms were headache (71.6%), body aches (62.7%), arthralgia (58.2%), fever (51.7%), sore throat (49.4%), and myalgia (41.8%).

Isolated taste and smell disorders were identified in 1.1% of cases (n=21). The median duration of the isolated smell disorder is 5 days with extremes ranging from 3 to 30 days.

In the univariate analysis, OD was found to be significantly associated with female gender, age greater than 35 years, hypertension, lack of vaccination prior to infection, fever, headache, vomiting, diarrhea, arthralgia, dyspnea, fatigue, skin eruption, cough, GD and hospitalization in the intensive care unit (Table I).

Table I: Factors associated with olfactory and gustatory dysfunction: Univariate analysis

	Olfactory dysfunction		**p**	**OR [IC 95%]**	**Gustatory dysfunction**		**p**	**OR [IC 95%]**
	Yes	No			Yes	No		
Sex								
M	190 (50.4)	187 (49.6)			168 (44.6)	209 (55.4)		
F	850 (56.3)	660 (43.7)	0.040	1.26[1.01-1.58]	776 (51.4)	734 (48.6)	0.018	1.31 [1.04-1.65]
Age								
≤35	477 (57.7)	350 (42.3)			440 (53.2)	387 (46.8)		
>35	563 (53.1)	497 (46.9)	0.048	0.83[0.69-0.99]	504 (47.5)	556 (52.5)	0.015	0.79 [0.66-0.95]
Tabaco								
Yes	177 (51.5)	167 (48.5)			162 (47.1)	182 (52.9)		
No	863 (55.9)	680 (44.1)	0.131	-	782 (50.7)	761 (49.3)	0.229	-
Alcohol								
Yes	113 (51.6)	106 (48.4)			101 (46.1)	118 (53.9)		
No	927 (55.6)	741 (44.4)	0.266	-	843 (50.5)	825 (49.5)	0.219	-
Respiratory history								
Yes	71 (62.3)	43 (37.7)			64 (56.1)	50 (43.9)		
No	969 (54.7)	804 (45.3)	0.112	-	880 (49.6)	893 (50.4)	0.178	-
Hypertension								
Yes	66 (65.3)	35 (34.7)			61 (60.4)	40 (39.6)		
No	974 (54.5)	812 (45.5)	0.034	1.57[1.03-2.39]	883 (49.4)	903 (50.6)	0.032	1.56[1.03-2.34]
Diabetes								
Yes	35 (46.7)	40 (53.3)			32 (42.7)	43 (57.3)		
No	1005 (55.5)	807 (44.5)	0.133	-	912 (50.3)	900 (49.7)	0.193	-
Dysthyroid								
Yes	64 (59.3)	44 (40.7)			64 (59.3)	44 (40.7)		
No	976 (54.9)	803 (45.1)	0.372	-	880 (49.5)	899 (50.5)	0.048	1.48[1.00-2.20]
Allergy								
Yes	10 (66.7)	5 (33.3)			10 (66.7)	5 (33.3)		
No	1030 (55.0)	842 (45.0)	0.366	-	934 (49.9)	938 (50.1)	0.196	
Vaccinal Status before infection								
Not vaccinated	723 (70.3)	306 (29.7)			655 (63.7)	374 (36.3)		
Partial vaccinated	66 (46.8)	75 (53.2)			58 (41.1)	83 (58.9)		
Fully vaccinated	251 (35.0)	466 (65.0)	<10-3		231 (32.2)	486 (67.8)	<10-3	
Fever								
Yes	567 (58.2)	408 (41.8)			529 (54.3)	446 (45.7)		
No	473 (51.9)	439 (48.1)	0.006	1.29 [1.07-1.54]	415 (45.5)	497 (54.5)	<10-3	1.42[1.18-1.70]
Headache								
Yes	769 (56.9)	582 (43.1)			708 (52.4)	643 (47.6)		

No	271 (50.6)	265 (49.4)	0.012	1.29[1.05-1.57]	236 (44.0)	300 (56.0)	0.001	1.40[1.14-1.71]
Sore throat								
Yes	483 (51.8)	450 (48.2)			447 (47.9)	486 (52.1)		
No	557 (58.4)	397 (41.6)	0.004	0.76[0.63-0.91]	497 (52.1)	457 (47.9)	0.069	-
Body aches								
Yes	665 (56.2)	519 (43.8)			619 (52.3)	565 (47.7)		
No	375 (53.3)	332 (46.8)	0.233	-	325 (46.2)	378 (53.8)	0.011	1.27[1.05-1.53]
Chest pain								
Yes	347 (57.3)	259 (42.7)			325 (53.6)	281 (46.4)		
No	693 (54.1)	588 (45.9)	0.197	-	619 (48.3)	662 (51.7)	0.031	1.23[1.01-1.50]
Nausea								
Yes	273 (58.3)	195 (41.7)			262 (56.0)	206 (44.0)		
No	767 (54.1)	652 (45.9)	0.106	-	682 (48.1)	737 (51.9)	0.003	1.37[1.11-1.69]
Vomit								
Yes	175 (61.8)	108 (38.2)			162 (57.2)	121 (42.8)		
No	865 (53.9)	739 (46.1)	0.014	1.38[1.06-1.79]	782 (48.8)	822 (51.2)	0.008	1.40[1.09-1.81]
Diarrhea								
Yes	404 (64.4)	223 (35.6)			372 (59.3)	255 (40.7)		
No	636 (50.5)	624 (49.5)	<10-3	1.77[1.45-2.16]	572 (45.4)	688 (54.6)	<10-3	1.75[1.44-2.13]
Runny nose								
Yes	452 (54.5)	378 (45.5)			407 (49.0)	423 (51.0)		
No	588 (55.6)	469 (44.4)	0.612	-	537 (50.8)	520 (49.2)	0.446	-
Arthralgia								
Yes	631 (57.4)	468 (42.6)			592 (53.9)	507 (46.1)		
No	409 (51.9)	379 (48.1)	0.018	1.24[1.04-1.50]	352 (44.7)	436 (55.3)	<10-3	1.44[1.20-1.73]
Myalgia								
Yes	440 (55.8)	348 (44.2)			415 (52.7)	373 (47.3)		
No	600 (54.6)	499 (45.4)	0.593		529 (48.1)	570 (51.9)	0.052	-
Dyspnea								
Yes	234 (65.9)	121 (34.1)			218 (61.4)	137 (38.6)		
No	806 (52.6)	726 (47.4)	<10-3	1.74[1.36-2.21]	726 (47.4)	806 (52.6)	<10-3	1.76[1.39-2.23]
Fatigue								
Yes	819 (57.2)	613 (42.8)			756 (52.8)	676 (47.2)		
No	221 (48.6)	234 (51.4)	0.001	1.41[1.14-1.74]	188 (41.3)	267 (58.7)	<10-3	1.58[1.28-1.96]
Skin eruption								
Yes	59 (66.3)	30 (33.7)			59 (66.3)	30 (33.7)		
No	981 (54.6)	817 (45.4)	0.030	1.63[1.04-2.56]	885 (49.2)	913 (50.8)	0.002	2.02[1.29-3.17]
Cough								
Yes	30 (42.3)	41 (57.7)			26 (36.6)	45 (63.4)		
No	1010 (55.6)	806 (44.4)	0.026	0.58[0.36-0.94]	918 (50.6)	898 (49.4)	0.021	0.56[0.34-0.92]
Gustatory dysfunction								
Yes	892 (94.5)	52 (5.5)			-	-		
No	148 (15.7)	795 (84.3)	<10-3	92.14[66.23-128.18]	-	-	-	-
Treatment								
No treatment	94 (42.5)	127 (57.5)			85 (38.5)	136 (61.5)		
Treatment at home	881 (56.3)	684 (43.7)			799 (51.1)	766 (48.9)		
Hospitalizationin a medical ward	54 (63.5)	31 (36.5)			50 (58.8)	35 (41.2)		
Hospitalizationin an intensive care unit	11 (68.8)	5 (31.2)	<10-3		10 (62.5)	6 (37.5)	0.001	

In the multivariate analysis of OD, two variables were identified as significant: not having received the vaccine prior to infection and GD (Table II).

Table II: Factors associated with olfactory and gustatory dysfunction: Multivariate analysis

	Olfactory dysfunction		p	OR [CI 95%]
	Yes	No		
Vaccine before infection				
Not vaccinated	723 (70.3)	306 (29.7)	Reference	
Partial vaccinated	66 (46.8)	75 (53.2)	0.022	0.51[0.29-0.90]
Fully vaccinated	251 (35.0)	466 (65.0)	<10-3	0.31[0.22-0.43]
Gustatory dysfunction				
Yes	892 (94.5)	52 (5.5)	<10-3	82.98[59.29-116.15]
No	148 (15.7)	795 (84.3)		
	Gustatory dysfunction			
Dysthyroid				
Yes	64 (59.3)	44 (40.7)	0.042	2.00[1.02-3.90]
No	880 (49.5)	899 (50.5)		
Vaccine before infection				
Not vaccinated	655 (63.7)	374 (36.3)	Reference	
Partial vaccinated	58 (41.1)	83 (58.9)	0.183	-
Fully vaccinated	231 (32.2)	486 (67.8)	0.023	0.68[0.49-0.94]
Nausea				
Yes	262 (56.0)	206 (44.0)	0.033	1.48[1.03-2.14]
No	682 (48.1)	737 (51.9)		
Arthralgia				
Yes	592 (53.9)	507 (46.1)	0.006	1.53[1.13-2.09]
No	352 (44.7)	436 (55.3)		

With regard to outcome of GD, the following factors were identified as significant in the univariate analysis: female gender, age > 35, hypertension, thyroid disease, lack of vaccination prior to the infection, fever, headache, body aches, chest pain, nausea, vomiting, diarrhea, arthralgia, dyspnea, fatigue, skin eruption, cough and hospitalization in the intensive care unit (Table I). In the multivariate analysis of GD, dysthyroidism), lack of vaccination prior to infection, nausea and arthralgia were identified as significant factors (Table II).

DISCUSSION:

The global spread of the SARS-CoV2 virus, which causes the illness known as COVID-19, was rapid and accompanied with a range of common symptoms , including cough, fever and shortness of breath [8]. As the disease spread and became pandemic, an increasing number of symptoms were reported, including gastrointestinal involvement, neurological complications, neuropsychiatric and ENT symptoms [9,10]. The existence of OD and GD has been demonstrated in published studies[11,12]. Consequently, the aim of this study was to ascertain the prevalence of OD and GD in patients with coronavirus infection and identify predictive factors that contribute to the set of these conditions.

Our study indicated that patients with COVID- 19 infection may experience OD or GD as a symptom. The majority of published studies have confirmed the occurrence of symptoms of dysgeusia and anosmia in patients with COVID-19 infection [12–15].

The present study revealed that patients with COVID-19 infection had OD (55,1%) and GD (50%). Our prevalence of OD was in accordance with the findings of studies by Qiu et al. (47%) and Agyeman et al (41%) [16]. In the serie of Mutiawati, out of 32,142 COVID-19 patients from 107 studies, OD was reported in 12,038 patients with a prevalence of 38.2% (95% CI: 36.5%, 47.2%); whereas, GD was reported in 11,337 patients out of 30,901 COVID-19 patients from 101 studies, with prevalence of 36.6% (95% CI: 35.2%, 45.2%), worldwide. Furthermore, the prevalence of OD was 10.2-fold higher (OR: 10.21; 95% CI: 6.53, 15.96, $p < 0.001$) and that of GD was 8.6-fold higher (OR: 8.61; 95% CI: 5.26, 14.11, $p < 0.001$) in COVID-19 patients compared to those with other respiratory infections or COVID-19 like illness [17]. [17]. There was a significant association between GD and OD. OD was the only symptom in 1,1% of patients with SARS-CoV2 infection, in comparison with the study of Lechien which found OD was the only symptom in 11,8%, and Kaye also found a low percentage (27%) [18,19]. OD and GD were concomitant and constitued the only manifestation in 46,3% of cases. There was a divergence of opinion concerning the importance of the association between OD and GD. For example an Italian study of 59 hospitalized SARS-coV2 patients showed that 23.7% of cases suffered from OD, with the majority also reporting concomitant GD [3]. In comparison, a study led by Lechien reported a significantly higher percentage with 85.6% of patients indicating a subjective decrease in smell which is associated with the disease, that was correlated with GD. Of those reporting a decreased sense of smell, 79.6% reported an anosmia [18]. Another study by Yan et al described that of 59 patients complaining of flu-like symptoms and testing positive for SARS-coV2, 68% reported GD [20].

Mao et al. identified OD and GD as presenting symptoms of COVID-19. Mao et al. conducted a study on the neurological symptoms among 214 hospitalized patients in Wuhan, China. They observed that found 5.1% and 5.6% of their patients had hyposmia and hypogeusia, respectively. However, these findings were not statistically significant [21].

Nevertheless, the number of studies examining OD and GD as clinical manifestations of COVID-19 increased rapidly from the United States and Europe. In a series of 417 patients, Lechien et al. reported that 85.6% and 88% experienced OD and GD, respectively [18]. However, Kaye et al reported that 73% of patients had anosmia prior to COVID-19 confirmation, with this being the initial symptom of COVID-19 in 26.6% of the cases [19]. In a further study comprising 1480 patients, Yan et al. observed that OD and GD were present in 68% and 71% of those with infection, compared to 16% and 17% in those who had negative test. This finding establishes an important association between OD and GD with COVID-19 [20]. Kai Chua et al. found that 22.6% of patients, who were tested positively, experienced OD [22].

The present study revealed that OD was significantly more prevalent among females, and was also found to be significantly associated with hypertension. No significant association was observed between OD and nasal obstruction or rhinorrhea.

In ENT practice, sudden onset of OD can be attributed to nasal trauma and viral infection [23]. The OD is

explained by conductive loss secondary to mucosal oedema and rhinorrhea. It normalizes as the infection resolves, however, post-viral anosmia is an entity that lasts beyond the resolution of the disease [24]. A number of viral agents have been identified as potential causes of post-viral anosmia with the coronavirus [25]. While the occurrence of OD following COVID-19 infection may be attributed to the presence of other factors, the current outbreak of COVID-19 infection presents a unique set of characteristics. Notably, rhinorrhea or nasal obstruction were not found to be associated with OD among COVID-19 like in our cohort. In contrast to previous observations in other settings [18,26]. Secondly, it is notable that OD is the only presenting manifestation in patients with COVID 19 infection. In the final analysis, the infected patients functioned as a silent vector, inadvertently disseminating the virus. Thirdly, OD in COVID-19 develops rapidly, although, post-viral anosmia becomes apparent as the infection progresses [27]. Another noteworthy observation is the rapid recovery of OD among patients with COVID-19 compared to the prolonged recovery period typically observed in post-viral anosmia [24]. The overall median recovery time in our study was 5 days when OD was the only presenting symptom and 7 days when it was associated with other symptoms. The majority of studies have reported that OD resolves within 14 days of symptom onset [5]. This is corroborated by the findings of Ramasamy, who observed a median duration of OD and GD to be 7 days, with 70.5% of patients exhibiting full recovery within 7 days of onset [24]. In their study, Levinson et al. reported a median duration of 7.6 days for OD and 7.1 days for GD [27]. Kaye et al found that patients infected with COVID-19 and OD experienced improvement of OD with a median duration of 7.2 days. The pathophysiology of OD in patients with COVID-19 remains incompletely understood. Despite the identification of COVID-19 in the rhinorrhea of individuals with OD, Suzuki et al. proposed that inflammation and nasal congestion may not be the only etiological factors in all cases, as some patients infected with COVID-19 had normal acoustic rhinometry results [19,25].

Netland et al found that the olfactory bulb is a target of the COVID-19 virus, as evidenced by the presence of the virus in this region following research on small animals [28,29].

In light of the magnetic resonance imaging (MRI) findings in cases infected with the virus and presenting with OD, a number of studies have postulated that, following initial replication in the nasal mucosa, the virus may disseminate from the olfactory epithelium to the olfactory bulb, and subsequently to the posterior gyrus rectus via the lateral olfactory tract [28]. A destruction of the cortical region of the brain suggestive of viral invasion in the posterior gyrus rectus, is related to olfaction, has been reported [28]. However, several limitations of many studies, in question must be acknowledged. Firstly, the sample size of the series was relatively small. Secondly, the majority of patients recovered from anosmia, which made it impossible to put attention on the possibility of the temporal evolution of the tract or olfactory bulb [18].

The currently available data indicates a female predominance amongst those SARS-cov 2 patients suffering from OD and GD [18,24,26,30,31]. Our study found females to be significantly associated with OD as well. Previous studies have indicated that this may be due to gender-based differences in questionnaire completion [18,26,30,31].

Furthermore, the female predilection can be attributed to the existence of disparities between genders in sexual dimorphisms and inflammatory cytokine production in the olfactory bulb [24]. In our study, older patients were more susceptible to get OD and GD, which was in accordance with the study by Marelene and in discordance with many studies where OD is more prevalent in younger age groups [16,24,26]. Additionally, younger patients are more susceptible to develop OD and GD. Our present serie also found that hypertension is significantly associated with OD, which is in accordance with the study by Huang reporting a significant association between hypertension, OD and GD [32].

A significant association was identified between OD and a number of symptoms, including dyspnea, fatigue, cough, digestive symptoms, headache, fever and odynophagia. These parameters were not significantly associated with the risk of OD and GD, which was in discordance with the majority of studies. The reasons for this discrepancy were not mentioned [2,8,24].

Respiratory allergy in particular was significantly associated with olfactory dysfunctions (multivariable OR 2.30, 95% CI 1.02-5.17). Significant inverse associations were observed for patients aged 60 years or more (multivariable OR 0.33, 95% CI 0.19-0.57) and hospitalization (multivariable OR 0.22, 95% CI 0.06-0.89). Considering gustatory dysfunctions, after allowance of other variables a significant direct association was found for respiratory allergies (OR 2.24, 95% CI 1.03-4.86), and an inverse association was found only for hospitalization (OR 0.21, 95% CI 0.06-0.76) [33].

Concerning our study, In the multivariate analysis of GD, dysthyroidism), lack of vaccination prior to infection, nausea and arthralgia were identified as significant factors, Concerning the OD, two variables were identified as significant: not having received the vaccine prior to infection and GD.

COVID-19 patients included in the current literature are heterogeneous with respect to recruitment, severity of disease, and symptoms experienced. Understandably, patients with the most severe disease (eg, patients in intensive care) are highly underrepresented in these initial studies. Moreover, there may be many other COVID-19 patient populations who are not yet captured and characterized due to limited testing. Finally, although OD appears to be highly predictive of COVID-19 during the COVID-19 pandemic, sensitivity and specificity are unknown, and it is unclear how predictive value will change as prevalence of COVID-19 decreases [30,31,32].

CONCLUSION

OD and OG were among the most frequent clinical signs with headache and body aches. Partial or full vaccinated before infection were protective factors of OD and OG.

Conflict of interest:

There are no conflict of interest.

Ethical considerations

The research adhered to the ethical guidelines outlined in the Declaration of Helsinki and received approval from the Ethical Committee of Farhat Hached University Hospital (Reference of opinion of the committee of medical ethics and research: CER:34-2022).

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