New Onset of Smell and Taste Loss Are Common Findings Also in Patients With Symptomatic COVID-19 After Complete Vaccination

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The aim of this study is to investigate the clinical profile of patients who developed coronavirus disease 2019 (COVID-19) after full vaccination. Demographic, epidemiological and clinical data were collected through medical records and online patient-reported outcome questionnaire from patients who developed symptomatic SARS-CoV-2 infection, confirmed by nasopharyngeal swab, at least 2 weeks after completion of vaccination. A total of 153 subjects were included. The most frequent symptoms were: asthenia (82.4%), chemosensory dysfunction (63.4%), headache (59.5%), runny nose (58.2%), muscle pain (54.9%), loss of appetite (54.3%), and nasal obstruction (51.6%). Particularly, 62.3% and 53.6% of subjects reported olfactory and gustatory dysfunction, respectively. Symptom severity was mild or moderate in almost all cases. Chemosensory dysfunctions have been observed to be a frequent symptom even in subjects who contracted the infection after full vaccination. For this reason, the sudden loss of smell and taste could continue to represent a useful and specific diagnostic marker to raise the suspicion of COVID-19 even in vaccinated subjects. In the future, it will be necessary to establish what the recovery rate is in these patients.

Key Words: COVID-19, anosmia, ageusia, olfactory dysfunction, gustatory dysfunction, vaccination.
Level of Evidence: 4

INTRODUCTION

Vaccines are the main weapon to protect population from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Vaccine safety has been widely demonstrated as well as their effectiveness in preventing the onset of severe coronavirus disease 2019 (COVID-19).[1] The effectiveness in preventing symptomatic COVID-19 is instead variable between 73% and 91% in patients with complete vaccination and for the currently known variants.[2,3] Furthermore, vaccines have been shown to be effective in reducing the duration of symptoms and accelerating viral clearance.[2] To the best of our knowledge there are no studies reporting the clinical pattern of COVID-19 after complete vaccination. The knowledge of these clinical pictures is important for posing the diagnostic suspicion of infection and because probably (and hopefully) these forms of vaccine-mitigated COVID-19 will be the ones that will remain after the immunization of the population.

MATERIALS AND METHODS

An online questionnaire was released in August and September 2021[4] across Europe. The survey was aimed exclusively at subjects who had had symptomatic COVID-19, confirmed by nasopharyngeal swab, at least 2 weeks after completion of vaccination. Compliance with the inclusion criteria was assessed with specific questions and subjects who did not meet them were excluded. The presence and severity of symptoms was investigated using the COVID-19 symptom index.[5] The study was approved by the ethics committee of the University of Cagliari (PG/2021/7118).

RESULTS

Of the 176 responses collected, 23 were excluded as the subjects did not have a confirmed diagnosis so that 153 responses were considered in the analysis (99 females, 54 males, mean age 41.3 years). The anti-SARS-CoV-2

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TABLE 1.
COVID-19 Symptom Index Results.

	No Problem	Mild Problem	Moderate Problem	Severe Problem	Very Severe Problem
I had fever (>38°C)	88 (57.5%)	40 (26.1%)	19 (12.4%)	6 (3.9%)	0 (0%)
I was tired	27 (17.6%)	57 (37.2%)	57 (37.2%)	6 (3.9%)	6 (3.9%)
I had cough	85 (55.6%)	53 (34.6%)	15 (9.8%)	0 (0%)	0 (0%)
I had chest pain	130 (85%)	20 (13.1%)	3 (2%)	0 (0%)	0 (0%)
I had low/no appetite	70 (45.7%)	52 (34%)	25 (16.3%)	6 (3.9%)	0 (0%)
I had joint pain	78 (51%)	55 (36%)	12 (7.8%)	6 (3.9%)	2 (1.3%)
I had muscle pain	69 (45.1%)	55 (36%)	23 (15%)	6 (3.9%)	0 (0%)
I had headache	62 (40.5%)	49 (32%)	33 (21.6%)	6 (3.9%)	3 (2%)
I had diarrhea	136 (88.9%)	10 (6.5%)	2 (1.3%)	2 (1.3%)	3 (2%)
I had abdominal pain	145 (94.8%)	3 (2%)	2 (1.3%)	3 (2%)	0 (0%)
I had nausea or vomiting	139 (91%)	8 (5.2%)	6 (3.9%)	0 (0%)	0 (0%)
I had conjunctivitis	144 (94.1%)	6 (3.9%)	3 (2%)	0 (0%)	0 (0%)
I had urticarias	145 (94.8%)	6 (3.9%)	2 (1.3%)	0 (0%)	0 (0%)
I had breathing difficulties	132 (86.3%)	18 (11.8%)	3 (2%)	0 (0%)	0 (0%)
I had sticky throat mucus	109 (71.2%)	27 (17.6%)	14 (9.1%)	3 (2%)	0 (0%)
I had nasal obstruction	74 (48.4%)	34 (22.2%)	31 (20.3%)	14 (9.1%)	0 (0%)
I had runny nose	64 (41.8%)	54 (35.3%)	25 (16.3%)	10 (6.5%)	0 (0%)
I had nasal burning	76 (49.7%)	55 (36%)	22 (14.4%)	0 (0%)	0 (0%)
I had throat pain	116 (75.8%)	35 (22.9%)	2 (1.3%)	0 (0%)	0 (0%)
I had ear pain or pressure	123 (80.4%)	23 (15%)	7 (4.6%)	0 (0%)	0 (0%)
I had face pain or pressure	122 (79.7%)	26 (17%)	2 (1.3%)	0 (0%)	3 (2%)
I had difficulties to swallow	128 (83.7%)	20 (13.1%)	5 (3.3%)	0 (0%)	0 (0%)
I had hoarseness/voice difficulties	113 (73.9%)	28 (18.3%)	12 (7.8%)	0 (0%)	0 (0%)
I had tongue burning	136 (88.9%)	15 (9.8%)	2 (1.3%)	0 (0%)	0 (0%)

	Unchanged	Partially Loss	Completely Loss
During COVID-19 my smell was	58 (37.9%)	32 (20.9%)	63 (41.2%)

	Unchanged	Reduced, Loss, or Modified
During COVID-19 my taste was	71 (46.4%)	82 (53.6%)

vaccination was performed with Pfizer/BioNTech (106 cases), AstraZeneca (32 cases), Moderna (12 cases), or Johnson & Johnson (three cases) vaccines.

Table 1 shows the symptoms reported by the subjects. The most frequent were: asthenia (82.4%), chemosensory dysfunctions (CDs) (63.4%), and headache (59.5%). Particularly, 62.3% and 53.6% of subjects reported olfactory and gustatory dysfunction, respectively. Symptom severity was mild or moderate in almost all cases. There were no significant differences in the prevalence of CD between patients who received viral vector or mRNA vaccine.

DISCUSSION

As social distancing measures relax, vaccine-mitigated forms of COVID-19 are likely to become increasingly frequent or even endemic. It is therefore important to know their clinical pictures to predict their social and health impact. In the present series, the prevalence of severe respiratory symptoms such as dyspnea was very low (13.8%) and in any case mild (11.8%) or moderate (2%). The frequency and severity of symptoms is comparable to that reported by other authors in patients with second episodes of COVID-19[6] while no data on infected subjects after complete vaccination are reported in the literature.

In the present study, CD were observed to be a frequent symptom in COVID-19 after full vaccination with similar prevalence to that reported in the past in unvaccinated patients.[7–9] For this reason, the sudden loss of smell and taste could continue to represent a useful and specific diagnostic marker to raise the suspicion of COVID-19 even in vaccinated subjects. In the future, it will be necessary to establish what the recovery rate is in these patients. Residual CD are in fact turning out to be one of the most frequent symptoms of long-COVID-19, with persistent anosmia rates beyond 6 months varying between 1% and 11%.[10–15] If this prevalence were so high even in vaccinated subjects, we could still have a high number of subjects who will require assistance for such disabling disorders. The risk factors and causes of persistence of CD in some patients have not yet been identified.[16–20] Early studies found no significant correlation between serum immunoglobulin levels and duration of olfactory

disfunction.[21,22] The correlation is instead significant with nasal immunoglobulin.[22] Interestingly, it seems that patients with severe COVID-19 had higher serum antibody levels while nasal antibodies were higher in milder disease.[23] The effects of vaccination on the nasal immune response are yet to be verified and could represent a determining factor on the duration of CD in vaccinated patients.

This study has several limitations: First, it is based on self-reported olfactory and gustatory loss which may underestimate the true prevalence of CD. Second, the survey was aimed only at symptomatic subjects, a comparison with asymptomatic should performed in the future. Third, while immunization can also result in smell loss, an analysis of the differences between nonimmunized and immunized subjects that become infected could not be performed. The role of immunization should be investigated in the future. Fourth, although the delta variant was predominant at the time of the survey, we have no information regarding the virus strain that infected the patients. It is possible that this factor influenced the results of the study and the viral strain will need to be taken into account in future studies.

CONCLUSIONS

Based on the results of this survey, the sudden loss of smell and taste could continue to represent a useful and specific diagnostic marker to raise the suspicion of COVID-19 even in vaccinated subjects.

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