



## SPECIAL ARTICLE COVID-19

# The Pattern of Anosmia in Non-hospitalized Patients in the COVID-19 Pandemic: A Cross-sectional Study\*

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## Abstract

**Introduction** It is now evident that the loss of smell and/or taste may be consistent accompanying symptoms of the SARS-CoV-2 infection.

**Objective** To estimate the social behavior of recent anosmic non-hospitalized patients in the COVID-19 pandemic and to try to obtain the natural pattern in society in a cross-sectional study.

**Methods** A cross-sectional study conducted on 4,860 patients with anosmia complaints during the COVID-19 pandemic. Patients who needed a consultation for an anosmia complaint confirmed that they had completed the survey regarding age, gender, history of general diseases, history of nasal disease, associated COVID-19 symptoms, smoking, blood group, and risk factors.

**Results** A total of 4,860 patients with a mean age of  $34.26 \pm 11.91$  years completed the study. There was a predominance of female patients: 3,150 (58.9%). Most patients (4,083 patients; 83%) developed sudden anosmia. In 85% (4131 patients) of the patients, a previous history of contact with anosmic patients was present. The most prevalent blood group was O (39%). In total, 67.4% of the patients underwent medical treatment. A history of unusual influenza attacks in December 2020 was reported by 27% (1312 patients) of the patients.

**Conclusion** Despite large diversity of behaviors among anosmic patients in the COVID-19 pandemic, we can observe a great similarity in the pattern of anosmia in non-hospitalized patients, especially in the way it spreads, the predisposing factors, and the individual recovery.

## Keywords

- ▶ anosmia
- ▶ COVID-19
- ▶ non-hospitalized patients
- ▶ pandemic

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## Introduction

The coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a global pandemic that started in China in December 2019.<sup>1</sup>

The most frequently reported COVID-19 symptoms are fever, cough, and shortness of breath, myalgia, arthralgia, headache, diarrhea, rhinorrhea, and sore throat.<sup>2</sup> Sudden loss of smell and taste have been recently recognized as important symptoms of COVID-19.<sup>3</sup>

Olfactory dysfunction has been reported in up to 85.6% of COVID-19 patients.<sup>4</sup> In total, 40% of the cases of anosmia occur in postviral infections, mainly by rhinovirus, parainfluenza virus, Epstein-Barr virus, and coronavirus.<sup>5</sup> Olfactory dysfunction in these cases is caused by inflammation and edema of the nasal mucosa, and is usually associated with rhinorrhea. Anosmia in COVID-19 patients is unique, as it is not associated with rhinorrhea or other nasal symptoms.<sup>4</sup>

The SARS-CoV-2 may also have neuroinvasive and neurotropic activities, making it able to cause neuronal impairment, as has been shown in other human respiratory coronaviruses.<sup>6</sup> The olfactory neural system can regenerate throughout life; this may explain why recovery of olfaction is common.<sup>7</sup> In a large study,<sup>4</sup> the recovery of smell was shown to take an average of  $7.1 \pm 3.1$  days.

The early recovery of olfactory dysfunction in most patients suggests that direct viral infection and destruction of olfactory neurons is unlikely.<sup>8</sup> Moreover, the olfactory bulb was normal on the magnetic resonance imaging (MRI) scan of a confirmed COVID-19 patient with anosmia.<sup>9</sup>

The aim of the present cross-sectional study is to estimate the social behavior of recent anosmic non-hospitalized patients in the COVID-19 pandemic and to try to obtain the natural pattern in society.

## Patient and Methods

The present is a cross-sectional study conducted on 4,860 patients with anosmia complaints during the COVID-19 pandemic. The study was conducted in the second half of May 2020, and was approved by the editorial boards of Kafrelsheikh and Tanta Universities, Egypt. The study included 4,860 adults (aged  $\geq 18$  years) seeking medical advice due to olfactory dysfunction, such as anosmia or hyposmia, with recent-onset within the previous two months. All patients started with a telemedicine consultation and free communications via the electronic survey sheet on the official public page of the ear, nose and throat (ENT) clinic. The survey to assess the olfactory dysfunction and associated symptoms was conducted anonymously and without any reward offered for its completion. The patients who needed a consultation for olfactory dysfunction confirmed that they had completed the survey and reported also sharing it with some family members, friends, and colleagues who were similarly afflicted.

We excluded anosmic patients with history of anosmia for more than three months and any duplication of e-mail reports.

The data taken from the sample history included age, gender, history of general diseases, history of nasal disease, other associated COVID-19 symptoms, smoking, blood group, and risk factors.

The survey was taken by the patients over the course of 10 days in the second half of May 2020. After this period, we received a total of 4,860 email replies, and the database was checked to exclude any duplications.

The collected data were entered into Microsoft Excel (Microsoft Corp., Redmond, WA, US) spreadsheets. Means standard deviations were calculated in the data analysis, the qualitative data were expressed as frequencies (numbers and percentages) through the Chi-squared test, and multivariate logistic regression was used to adjust the confounding factors using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY, US) software, version 26.0. The following levels of significance were adopted:  $p > 0.05$ : not significant;  $p < 0.05^*$ : significant; and  $p < 0.001^{**}$ : highly significant.

## Results

A total of 4,860 patients (3,150 females [64.8%] and 1,710 males [35.2%]) completed the study; their mean age was of  $34.26 \pm 11.91$  years, and 72.1% of them were aged under 40 years ( $\rightarrow$  Fig. 1). Overall, 18.7% of the patients were smokers; 16% were health workers; and 37% (1,798 patients) had a history of contact with COVID-19-positive patients in the previous week.

Most patients (4,083; 83%) developed sudden anosmia, while some patients (822; 17%) developed gradual loss of smell; 85% of the sample had a previous history of contact with anosmic patients. Besides, 41.1% of the patients could identify the source of the infection, and 83.1% reported a history of contact with anosmic patients.

The majority of the patients with anosmia 86% (4,180 patients) isolated themselves at home for 14 days. In total, 1,701 (35%) patients were tested for confirmation of COVID-19 infection through polymerase chain reaction (PCR), with 1,264 (74.3%) patients testing positive, and 437 (25.7%) testing negative. Overall, 3,159 (65%) patients were not tested ( $\rightarrow$  Fig. 2).

Regarding the recovery of the sudden olfactory dysfunction, 1,701 (35%) patients reported full recovery, 2,022

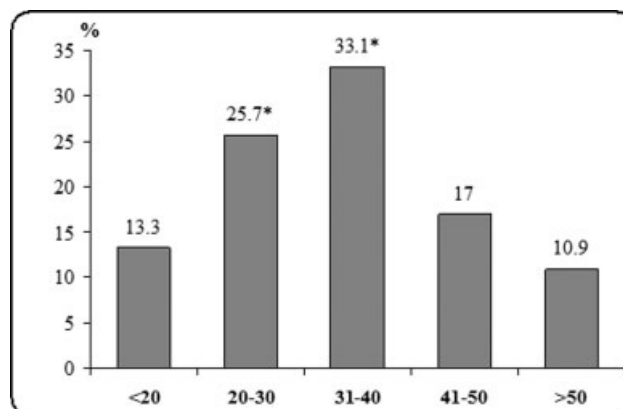
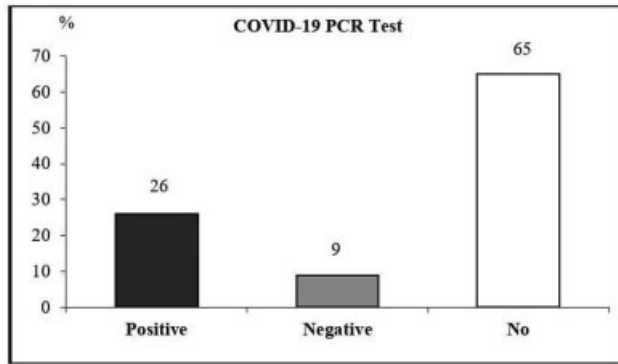
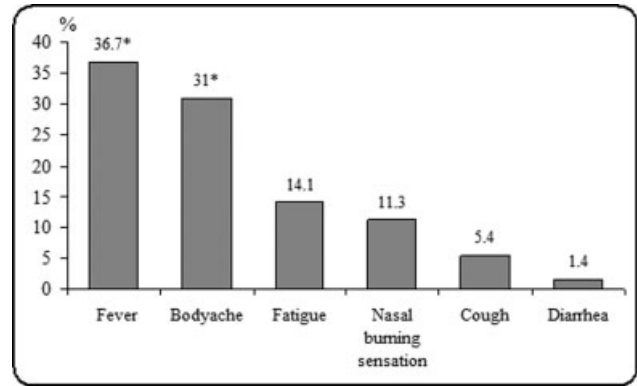


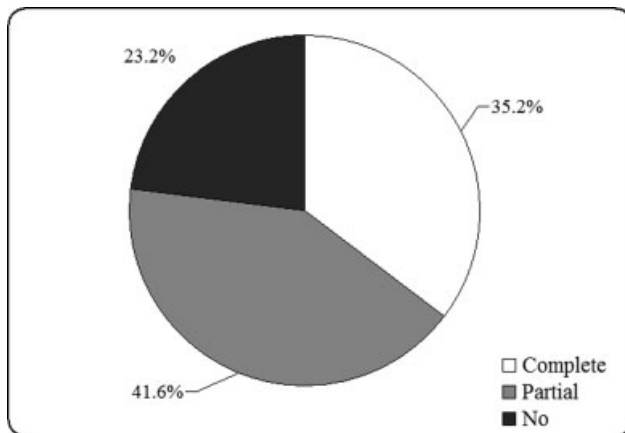
Fig. 1 Age distribution of the participants of the study.



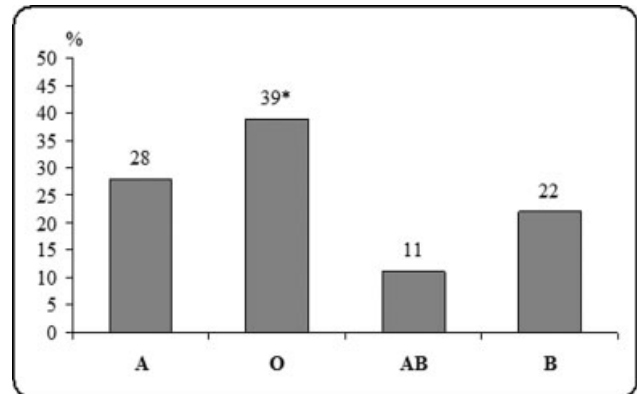
**Fig. 2** Polymerase chain reaction (PCR) test for COVID-19 of the participants.



**Fig. 4** Incidence of associated manifestations among anosmic patients.



**Fig. 3** Pattern of recovery of the patients.



**Fig. 5** Distribution of ABO blood groups in the study.

(41.6%) patients reported partial recovery within one month of the loss of olfaction, and 23.2% (1,128 patients) reported no recovery, as shown in ►Figure 3).

Other investigations regarding COVID-19 were performed, such as a complete blood work and computed tomography (CT) of the chest, but only for 1,591 (32.7%) patients. Loss of smell was accompanied by non-specific inflammatory symptoms, such as low fever (36.7%), generalized body ache (31%), malaise or fatigue (15%), cough (12%), and diarrhea (1.4%). Nasal symptoms, such as nasal obstruction, sneezing, coryza, purulent rhinorrhea, nasal pruritus, and/or nasal burning, were reported by 11% (535 patients) of the patients (►Fig. 4).

Some patients reported comorbidities, such as diabetes mellitus (DM; 16%), hypertension (8%), or associated allergic rhinitis (25%), sinusitis (16%), asthma (17%), and cardiac disease (9%).

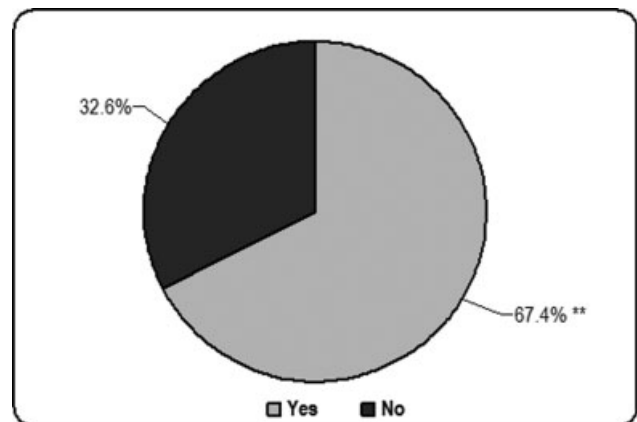
Concerning the blood groups of the anosmic patients, the most prevalent blood group was O (39%), followed by A (28%), B (22%), and AB (11%) (►Fig. 5).

In total, 67.4% of patients received medical treatment in the form of nasal saline irrigation and nasal steroid spray (►Fig. 6), and a history of unusual influenza attacks in December 2020 was reported by 27% (1,312 patients) of the patients.

## Discussion

It is now evident that loss of smell and/or taste may be consistent accompanying symptoms of the SARS-CoV-2 infection. Most observations suggest transient anosmia with recovery after days to weeks, but it remains unclear in how many cases these symptoms would be permanent.<sup>10</sup>

The exact pathogenesis of this olfactory condition in such patients is still ambiguous. However, SARS-CoV-2 seems to target non-neural cell types in the peripheral olfactory



**Fig. 6** Percentage of patients who received medical treatment for anosmia.

system rather than directly targeting the olfactory neurons, and this seems to be enough to cause an impairment in the function of the olfactory neurons, altering the transduction of odor, which takes place on their cilia.<sup>11</sup>

We strongly believe that the short-term anosmia linked to COVID-19 reported in the literature is based on the hypothesis that SARS-CoV2 dramatically affects the olfactory epithelium, which can quickly renew and recover following the period of viral clearance.<sup>12</sup>

The current study was completed by 4,860 patients with a mean age of  $34.26 \pm 11.91$  years; 65% (3,159 patients) of their sample was aged  $> 40$  years. Similarly, in a multicentric study on COVID-19 patients performed by Lechien et al.,<sup>4</sup> 357 patients were recruited, with mean age of 37 years and female predominance (63.1%). We attribute this female predominance regarding olfactory complaints to the fact that females have a greater concern for their health, as well as to the decreased ability of men to perceive olfactory disorders.

Moreover, Guan et al.<sup>13</sup> analyzed data from 1,590 laboratory-confirmed hospitalized patients with a mean age was 48.9 years, and 686 (42.7%) them were female. We hypothesize that the middle-aged group (30 to 50 years) are more vulnerable during this pandemic, as they tend to indulge more in outdoor activities with required life demands than other age groups.

In the current study, loss of smell was accompanied by non-specific inflammatory symptoms such as low fever (36.7%), generalized body ache (31%), malaise or fatigue (15%), cough (12%), and diarrhea (1.4% [68 patients]). Nasal symptoms (nasal obstruction, sneezing, coryza, purulent rhinorrhea, nasal pruritus, and/or nasal burning) were reported by 11% of the patients. Likewise, a Brazilian study<sup>14</sup> reported sudden anosmia in 83.3% of the patients, with other nasal symptoms, such as "rhinorrhea, purities" in 43.9%, fever in 49%, and myalgia and fatigue in 28% of the affected patients.

Moreover, Beltrán-Corbellini et al.<sup>15</sup> reported acute onset of olfactory disorder in 71% of their patients, with only 12.9% of concomitant nasal manifestations reported. In the detailed study by Lechien et al.,<sup>4</sup> 48% of the cohort reported fever, 59% reported myalgia, and nasal obstruction and rhinorrhea occurred in 32% and 37% of their patients respectively.

In the present study, the patients reported comorbidities such as DM (16%), hypertension (8%) or associated allergic rhinitis (25%), sinusitis (16%), asthma (17%), and cardiac disease (9%). Concerning the blood groups of the anosmic patients, the most prevalent blood group was O (39% [1,895 patients]), followed by A (28% [1,361 patients]), B (22% [1,069 patients]), and AB (11% [535 patients]).

In a detailed study<sup>16</sup> performed in China to correlate the ABO blood group and the COVID-19 infection, the results showed that blood group A was associated with a higher risk of acquiring COVID-19 compared with non-A blood groups. In contrast, blood group O was associated with a lower risk of acquiring the infection compared with non-O blood groups, and even samples collected from dead patients showed the same results.

Given the similarity of the nucleic acid sequence and the binding similarity of the receptor angiotensin-converting enzyme 2 (ACE2) between SARS-CoV and SARS-CoV-2-11, the

lower susceptibility of blood group O and higher susceptibility of blood group A to acquire COVID-19 could be linked to the presence of natural anti-blood group antibodies, particularly anti-A antibody, in the blood.<sup>17</sup>

This speculation requires direct studies in order to be proven. And further studies are necessary to elucidate the other possible mechanisms underlying the differences in susceptibility for COVID-19 regarding the ABO blood group.<sup>17</sup>

## Conclusion

Despite the great diversity in behavior among anosmic patients in the COVID-19 pandemic, we can observe a great similarity in the pattern of anosmia in non-hospitalized patients, especially in the way it spreads, the predisposing factors, and individual recovery.

### Ethical Approval

All procedures involving human participants in the present study were performed in accordance with the ethical standards of the institutional research editorial boards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

### Consent

Formal consent was provided by the patients to share and publish their data in the present research.

### Availability of Data and Materials

The datasets used and/or analyzed in the current study are available from the corresponding author on reasonable request.

### Authors Contributions

H.E: methodology, idea formulation and reference collection; M.A: data collection, revision; A.A: data collection; M.D: final revision; A.N: data collection and revision; S.Z: review, writing and editing of the final draft.

### Conflict of Interests

The authors have no conflict of interests to declare.

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