Acta Scientific MEDICAL SCIENCES (ISSN: 2582-0931)

Volume 6 Issue 4 April 2022

Research Article

New-onset Anosmia Among COVID-19 Suspected Patients in a Tertiary Care Hospital, Cairo, Egypt

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Received: February 17, 2022

Published: March 09, 2022

Abstract

Introduction: The pandemic caused by the SARS-CoV2 virus, which was first reported in Wuhan, China in late 2019 and quickly spread to 213 countries and territories. As we race to get a better understanding of its pathology and how to manage it, a few trends have been noticed. Among these is the anecdotal finding of patients reporting sudden loss of smell and taste as one of the preliminary, and sometimes only, symptom

Aim: This study aims to describe the characteristics of patients that present with new onset anosmia during the COVID-19 pandemic.

Methods: Sample will target patients that present to the Emergency COVID-19 clinic at Ahmed Maher Teaching Hospital. The study data will be collected by data collection forms filled out by the researchers. All patients presenting to the covid-19 Emergency clinic with new onset anosmia within a two-month period.

Results: Out of total 81 participants from whom data was collected, 15 cases had diminished sense of smell as preliminary symptom, and 6 cases had only that at time of swab., 38.5% of all positive patients had their olfactory function affected as preliminary symptom. Thus, we can say that almost one in three positive patients displays a diminished sense of smell as a preliminary symptom.

The mean duration of anosmia was 9.4 ± 10.4 days in cases with anosmia who were confirmed by PCR to be positive, as compared to 10.74 ± 9.39 in cases with anosmia who showed negative results; without significant difference (P = 0.660). Duration was < 7 days for 55% (11/20), 7-14 days for 20% (4/20), and > 14 days for 25% (5/20).

Conclusion: While anosmia has been proven to be an anecdotal finding in COVID-19 positive patients, the presence of new onset anosmia in patients during the COVID-19 era cannot be fully explained by the SARS- CoV-2 virus. However, as healthcare workers, wearing full PPE while dealing with anosmia patients is recommended, as anosmia could be a preliminary symptom and this could prevent infection.

Keywords: Anosmia; COVID-19; SARS-CoV2

Literature Review

The world is currently in the midst of a pandemic caused by the SARS-CoV2 virus, which was first reported in Wuhan, China in late 2019 and quickly spread to 213 countries and territories [1]. As we race to get a better understanding of its pathology and how to manage it, a few trends have been noticed. Among these is the anecdotal finding of patients reporting sudden loss of smell and taste as one of the preliminary, and sometimes only, symptom. In Germany it is

reported that more than 2 in 3 confirmed cases have anosmia. In South Korea, where testing has been more widespread, 30% of patients testing positive have had anosmia as their major presenting symptom in otherwise mild cases [2].

Prof C. Hopkins, as President of British Rhinological Society, published a letter describing "the loss of sense of smell as a marker of COVID-19 infection" and proposed that adults presenting with anosmia but no other symptoms should self-isolate for seven days [2]. This could potentially reduce the number of otherwise asymptomatic patients who unknowingly continue to spread the disease. This should also make ENT surgeons wary of any case that presents with new onset anosmia during this period and take proper precautions while dealing with suspected patients.

Infection with a virus from the coronavirus family can be mild, asymptomatic, or can lead to serious and life-threatening respiratory disease. In contrast to the first coronavirus pandemics in the 21st century (SARS-CoV (2003) and MERS-CoV (2012)), SARS-CoV-2 appears to be more infectious [3]. At the time writing this study (9/11/2020) Egypt alone has over 109 thousand confirmed cases (according to the daily updates by the Egyptian ministry of health), with almost 6400 COVID-19 related deaths [4]. According to the WHO, worldwide this number increases to about 49,578,590 confirmed cases, and 1,245,717 COVID-19 related deaths with new cases reported daily [5].

SARS-CoV-2 replicates massively in the oropharynx and hypopharynx area in affected patients, but is also found in the oral cavity and in the nose [6]. The virus spreads mainly by droplet infection, and the WHO recommends keeping a safety distance of at least 1 meter to avoid spray small liquid droplets from the nose or mouth of infected people which may contain virus. However, if the virus is aerosolized, for example by manipulation and, above all, invasive measures on the affected mucous membrane, there is a correspondingly higher level of infectivity and risk of infection [7].

A new study by researchers from the Massachusetts Institute of Technology (MIT) and Harvard University found thatSARS-CoV-2 uses two proteins that act as receptors to invade host cells and replicate. These proteins are angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2). Using that they were able to determine which cells the virus is more likely to attach to. The researchers found that in the nasal passages, "goblet secretory cells" — which produce mucus — express RNA that allows them to produce both ACE2 and TMPRSS2. In lung tissue, they settled on type II pneumocytes, which are the cells that line the alveoli (air sacs) and allow them to stay open. Finally, in the small intestine, the team closed in on absorptive enterocytes, which are the cells that ensure the absorption of key nutrients [8]. This could explain why patients usually have symptoms related to respiration and digestion.

A disturbance in olfactory function is a recurring symptom in COVID-19 patients, but a direct causality hasn't yet been established.

A study carried out by D. Brann., *et al*. using bulk gene sequencing demonstrated that mouse, non-human primate and human olfactory mucosa expresses two key genes involved in CoV-2 entry, ACE2 and TMPRSS2.This analysis revealed that ACE2 expression was absent from olfactory bulb neurons and instead was observed only in vascular cells, predominantly in pericytes, which are involved in blood pressure regulation, maintenance of the blood-brain barrier, and inflammatory responses, suggesting that olfactory bulb neurons are likely not a primary site of infection, but that vascular pericytes may be sensitive to CoV-2. Thus, primary infection of non- neuronal cell types — rather than sensory or bulb neurons — may be responsible for anosmia and related disturbances in odor perception in COVID-19 patients [9].

It has recently been suggested that nasal respiratory epithelium has higher expression of CoV-2 entry genes than the respiratory epithelium that lines the trachea or lungs, and it has been demonstrated through single cell RNA sequencing analysis that the highest expression of ACE2 and TMPRSS2 was in nasal goblet and ciliated cells, suggesting that these cell types may serve as a viral reservoir during CoV-2 infection [10,11].

Many viruses can cause anosmia, including those responsible for the common cold. These can account for up to 40% of anosmia cases [12]. The mechanism of smell disorder in post-viral anosmia is believed to be viral damage to the olfactory epithelium independent of nasal congestion [13]. In a recent case report by Eliezer., *et al*. [14] a patient with COVID-19 and complete olfactory loss had a bilateral obstructive inflammation of the olfactory clefts on imaging without other nasal obstruction or rhinorrhea, and no anomalies of the olfactory bulbs and tracts.

Another study carried out on Three hundred eighty-two subjects through 2 surveys responses, each one week apart, revealed that at the time of completing the first survey, 14.9% who reported smell and/or taste disturbance did not report any other symptom thought to be associated with COVID-19. In patients who reported other symptoms, 14.9% reported anosmia before their onset, 39.3% at the same time, and in 45.8% the onset of anosmia came after other symptoms. At the time of the second survey, of the 57 patients who presented with isolated anosmia, 44 had subsequently developed other symptoms associated with COVID-19 infection, leaving isolated loss of sense of smell or taste in only 3.4% of the cohort. Only 15 patients had been tested for COVID-19, but of those 80% tested positive for COVID-19 [12]. The same study revealed that overall recovery rate (regarding post-viral anosmia) after a three- week period was 71%.

In comparison to symptoms of MERS-CoV and SARS-CoV 2003 infections, clinical symptoms of COVID-19 are broader and more variable [15]. Differences in transmissibility and viral shedding suggest the *in vivo* replication sites and/or replication efficiency of SARS- CoV-2 differ significantly from SARS-CoV.

In addition to anosmia, a few other ENT manifestations have been associated with the SARS- CoV2 virus. A meta- analysis done of studies that included 1773 COVID-19 laboratory-confirmed positive patients revealed that rhinorrhea was reported in 38 patients (2.1%), nasal congestion was detected in 72 patients (4.1%), smell affection was documented in 107 patients (6%), nasal obstruction was manifested in 61 patients (3.4%), sore throat was reported in 200 patients (11.3%), pharyngeal erythema was documented in 98 patients (5.3%), tonsil enlargement was noticed in 23 patients (1.3%), headache was presented in 189 patients (10.7%), and URTI was reported in 33 patients (1.9%) There was no reported sneezing, epistaxis, post nasal discharge, facial edema or tenderness, diminution of hearing, vertigo, hoarseness, or stridor [16] (El- Anwar).

In Another study by Kaye., *et al*. report on 237 US patients with COVID-19 and anosmia, collated through an AAO-HNS resource, and state that loss of sense of smell was present before diagnosis in 73% of respondents, and was the initial symptom in 26.6% [17]. Interestingly, these early reports have suggested a predominance of olfactory dysfunction in younger, female patients; this is in contrast to the general population, where olfactory function has been found to be lower in males and older patients [17,18].

It has also been established that patients with comorbid conditions such as diabetes, hypertension, bronchial asthma, and COPD are at an increased risk of becoming infected with COVID-19 virus due to their weakened immunity. In addition, these at -risk groups tend to have higher mortality rates than those without comorbid conditions.

This study aims to describe the characteristics of patients that present with new onset anosmia during the COVID-19 pandemic. Some research has shown that anosmia is more common in female patients with mild symptoms, and sometimes presents as the only symptom, or as the preliminary symptom and is followed by other symptoms of COVID-19. To accomplish this, we will rely on self- reported anosmia - which has proven to have high specificity, but low sensitivity - [18] and a data collection form to gather information and determine whether these patients might possibly share other characteristics, including demographic information (age, occupation, marital status, etc.), other ENT conditions (sneezing, burning, nasal obstruction, postnasal discharge, previous operations or trauma), and other comorbid conditions. We will also follow up with these patients that presented with anosmia and assess how many of them test positive for COVID-19 by PCR swab.

Methodology

Study design

Descriptive study will be followed in this project to assess which patients are more likely to present with anosmia as a sign of COVID-19.

Study setting

This work is going to be carried out in "Ahmed Maher Teaching Hospital" (AMTH) in Cairo, Egypt. This is one of the biggest teaching hospitals in Cairo and provides service to hundreds of patients a day, with various internal and surgical departments. Since the start of the COVID-19 pandemic, and under orders from the ministry of health, the hospital has been turned into a quarantine facility dealing exclusively with COVID-19 patients.

Sample will target patients that present to the Emergency COVID-19 clinic at AMTH. The study data will be collected by data collection forms filled out by the researchers.

Subjects

Target population

All adult (over 18) patients attending Emergency COVID-19 clinic at AMTH complaining of anosmia.

Methods of sampling

Comprehensive sampling of all patients that present to the Emergency COVID-19 clinic for two months.

Sample size:

A comprehensive sample of patients presenting to the covid-19 Emergency clinic with new onset anosmia within a two-month period.

Methods used in data collection

Concurrent data collection for all patients presenting to the COVID-19 emergency clinic daily for two months.

Data collection

Data collection form filled out by the doctor taking the swab.

Data management

Descriptive statistics such as means and standard deviation for quantitative variables, and frequency and proportion for categorical variables were produced. Also, Analytic statistics used to get the statistical signiciance of a difference if exist (p value) using student t test for quantitiative variables and chi square test for categorical variables using SPSS version 23.

Results

This study focuses attention on patients with anosmia and its relation to COVID-19 in Egypt. Data was collected from a total of 81 cases with altered sense of smell and suspected to be infected with COVID-19. Nearly two thirds (65.4%) were females (N = 53) and 28 were males with average age 39.41 ± 14.04 years (Table 1).

The mean duration of anosmia was 9.4 ± 10.4 days in cases with anosmia who were confirmed by PCR to be positive, as compared to 10.74 ± 9.39 in cases with anosmia who showed negative results; without significant difference (P = 0.660). Duration was < 7 days for 55% (11/20), 7-14 days for 20% (4/20), and > 14 days for 25% (5/20).

As for the other ENT symptoms, dysgeusia was noticed in 61.5% of positive cases (n = 24). In addition, watery discharge was present in 30.8% of patients. Also, burning, sneezing as well as nasal obstruction was detected in 20.5% of cases (n = 8) for each symptom. Five patients had rhinorrhea (12.8%) and only 3 patients (7.7%) had itching.

As for other symptoms, eight symptoms were present in more than half of patients: fever (64.1%, n = 25), sore throat (53.8%, n = 21), fatigue (74.4%, n = 29), cough (64.1%, n = 25), headache (59%, n = 23), muscle ache (myalgia) (66.7%, n = 26), chest tightness (59%, n = 23), and diarrhea (61.5%, n = 24) (Table 1).

Out of total 81 cases from whom data was collected, 39 (48.14%) cases tested positive for COVID-19 by PCR. The majority of the positive cases were married 26(66.7%). More than half of the confirmed COVID-19 cases 20 (51.3%) were college graduates, 11(28.2%) had primary or secondary school education, 2(5.1%) were postgraduates, and 6(15.4%) were illiterate.

Participants were asked as part of the study to state their working status. In the present study we compared the working status for any one testing positive in the study, and the rate of infection appears to be higher among people who reported working, especially those who were employees (38.5%) as well as health-care workers, mainly nurses (15.4%).

Most positive cases in the study were overweight (46.2%). The most frequent comorbidities among positive cases were hypertension (15.4%, n = 6), Diabetes mellitus (12.8%, n = 5), Allergic rhinosinusitis (12.8%, n = 5), and asthma (7.7%, n = 3). Other comorbidities were less frequent.

Moreover, 9.9% of participant were smokers, 7.4% were ex-smokers, and 1.2% smokes water pipes. This study also detected those symptomatic individuals with blood types A were more likely to test positive for COVID-19, while those with blood type B were less likely to test positive.

Regarding the current situation, the source of infection appears mainly to be contact with infected patients. In the present study, about three-quarters of the participants who had been in contact with confirmed infected cases were also infected. In addition, 48.7% of infected cases had family members who were also infected.

Out of total 81 participants from whom data was collected, 15 cases had diminished sense of smell as preliminary symptom, and 6 cases had only that at time of swab. Therefore, 38.5% of all positive patients had their olfactory function affected as preliminary symptom. Thus, we can say that almost one in three positive patients displays a diminished sense of smell as a preliminary symptom. Furthermore, complete affection of sense of smell (anosmia) was detected in 43 (53.1%) of the total number of patients, and approximately half of cases who had anosmia (46.5%) were confirmed by PCR to be positive. Mild-moderate affection (hyposmia) was detected in 38 patients, with both negative and positive cases being represented almost equally; 45.2% and 48.7%, respectively. So, Based on these results, there seems to be no association between having anosmia and being positive for COVID-19.

	Cases N = 81	**COVID negative (N = 42)**	**COVID positive (N = 39)**	**P-Value**
Age (years)	39.41 ± 14.04	39.00 ± 14.72	39.85 ± 13.46	0.557
Male/Female Percentage of male (%)	28/53 34.6%	15/27 35.7%	13/26 33.3%	0.822
Marital status Single Married Divorced Widow	 19(23.5%) 58(71.6%) 1(1.2%) 3(3.7%)	 7(16.7%) 32(76.2%) 0(0%) 3(7.1%)	 12(30.8%) 26(66.7%) 1(2.6%) 0(0%)	0.093
Educational level College Illiterate Primary Secondary Postgraduate	 48(59.3%) 11(13.6%) 3(3.7%) 17(21%) 2(2.5%)	 48(59.3%) 11(13.6%) 3(3.7%) 17(21%) 2(2.5%)	 20(51.3%) 6(15.4%) 3(7.7%) 8(20.5%) 2(5.1%)	0.185
Occupation Student Housewife Private sector Employee Doctor Nurse Unemployed Dentist Sales Retired Accountant Cleaner	 2(2.5%) 14(17.3%) 12(14.8%) 30(37%) 4(4.9%) 10(12.3%) 4(4.9%) 1(1.2%) 1(1.2%) 1(1.2%) 1(1.2%) 1(1.2%)	 1(2.4%) 9(21.4%) 7(16.7%) 15(35.7%) 2(4.8%) 4(9.5%) 1(2.4%) 1(2.4%) 1(2.4%) 0(0%) 0(0%) 1(2.4%)	 1(2.6%) 5(12.8%) 5(12.8%) 15(38.5%) 2(5.1%) 6(15.4%) 3(7.7%) 0(0%) 0(0%) 1(2.6%) 1(2.6%) 0 (0%)	0.864
Body Mass index Underweight (<18kg/m^2) Normal (18-24.9 kg/m^2) Overweight (25-29.9 kg/m^2) Obese (30-34.9 kg/m^2) Severe obesity (35-39.9 kg/m^2)	 2(2.5%) 31(38.3%) 31(38.3%) 12(14.8%) 5(6.2%)	 1(2.4%) 17(40.5%) 13(31%) 8(19%) 3(7.1%)	 1(2.6%) 14(35.9%) 18(46.2%) 4(10.3%) 2(5.1%)	0.633

Smoking: No-smoker Smoker Ex-smoker Shisha	 66(81.5%) 8(9.9%) 6(7.4%) 1(1.2%)	 33(78.6%) 5(11.9%) 3(7.1%) 1(2.4%)	 33(84.6%) 3(7.7%) 3(7.7%) 0(0%)	0.907
Smoking index (Pack/day) 1/3 pack/day 1-3 pack/day ½ pack/day 1 pack/day	 1(1.2%) 2(2.5%) 1(1.2%) 3(3.7%)	 0(0%) 2(4.8%) 1(%) 2(4.8%)	 1(2.6%) 0(0%) 0(0%) 1(2.6%)	0.215
Blood group: Unknown A+ group B+ group AB+ group O+ group A-ve AB-ve O-ve	 32(39.5%) 14(17.3%) 6(7.4%) 7(8.6%) 16 (19.8%) 3(3.7%) 1(1.2%) 2(2.5%)	 16(38.1%) 6(14.3%) 4(9.5%) 3(7.1%) 8(19%) 3(7.1%) 0(0%) 2(4.8%)	 16 (41%) 8(20.5%) 2(5.1%) 4(10.3%) 8(20.5%) 0(0%) 1(2.6%) 0(%)	0.520
Comorbidities Diabetes Mellitus Hypertension Cardiovascular disease Asthma HCV Allergic rhinosinusitis Chronic chest infection Blood disorder Immune disorder Renal dialysis	 11(13.6%) 12(14.8%) 5(6.2%) 10(12.3%) 0 (0%) 13(16%) 1(1.2%) 0 (0%) 0 (0%) 1(1.2%)	 6(14.3%) 6(14.3%) 3(7.1%) 7(16.7%) 0(0%) 8(19%) 0(0%) 0 (0%) 0 (0%) 0(0%)	 5(12.8%) 6(15.4%) 2(5.1%) 3(7.7%) 0(0%) 5(12.8%) 1(2.6%) 0 (0%) 0 (0%) 1(2.6%)	 0.847 0.889 1.000 0.315 - 0.446 0.481 - - 0.481
Causes of disease Interaction with COVID +ve patients COVID +ve family history	 62(76.5%) 31(38.3%)	 32(76.2%) 12(28.6%)	 30(76.9%) 19(48.7%)	0.938 062
Diminished sense of smell as preliminary Symptom No Yes	 52 (64.2%) 29(35.8%)	 28 (66.7%) 14(33.3%)	 24 (61.5%) 15(38.5%)	0.631
Diminished sense of smell as only symptom at time of swab No Yes	 70(86.4%) 11(13.6%)	 37(88.1%) 5(11.9%)	 33(84.6%) 6(15.4%)	0.648
Presence of hyposmia No Yes	 43(53.1%) 38(46.9 %)	 23(54.8%) 19(45.2%)	 20(51.3%) 19(48.7%)	0.098

Presence of anosmia No Yes	 38(46.9%) 43(53.1)	 19(45.2%) 23(54.8%)	 19(48.7%) 20(51.3%)	 0.098
Duration of anosmia <7 days 7-14 days >14 days Mean ± SD	 19(44.2%) 14(32.6%) 10(23.3%) 10.12 ± 9.78	 8(34.8%) 10(43.5%) 5(21.7%) 10.74 ± 9.39	 11(55%) 4(20%) 5(25%) 9.40 ± 10.4	 0.286
ENT symptoms Dysgeusia Burning Nasal obstruction Sneezing Allergic rhinosinusitis Watery discharge History of nasal trauma Itching Previous nasal operation	 48 (59.3%) 21(25.9%) 18 (22.2%) 18 (22.2%) 6 (7.4%) 20(24.7%) 1(1.2%) 9(11.1%) 1(1.2%)	 24(57.1%) 13(31%) 10(23.8%) 10(23.8%) 1(2.4%) 8(19%) 1(2.4%) 6(14.3%) 1(2.4%)	 24(61.5%) 8(20.5%) 8(20.5%) 8(20.5%) 5(12.8%) 12(30.8%) 0(0%) 3(7.7%) 0(0%)	 0.687 0.284 0.721 0.721 0.101 0.222 1.000 0.485 1.000
Other symptoms Fever measured > 38 ◦ C Sore throat Dry cough Headaches Muscle ache Skin rash Chest tightness Diarrhea Fatigue	 54 (66.7%) 52 (64.2%) 56(69.1 %) 48 (59.3%) 58(71.6%) 1(1.2%) 52(64.2%) 49(60.5%) 56(69.1 %)	 29(69%) 31(73.8%) 31(73.8%) 25(59.5%) 32(76.2%) 1(2.4%) 29(69%) 25(59.5%) 27(64.3%)	 25(64.1%) 21(53.8%) 25(64.1%) 23(59%) 26(66.7%) 0(0%) 23(59%) 24(61.5%) 29(74.4%)	 0.637 0.061 0.345 1.000 0.342 1.000 0.345 0.853 0.327

Table 1

Discussion

Many healthcare workers have reported anosmia as a common finding in COVID-19 patients in the setting of this pandemic. For our research, we gathered information from patients that presented with signs and symptoms suggestive of COVID-19, who also had anosmia as one of the symptoms, over a two- month period. This study evaluates the frequency of new onset anosmia in patients suspected of being infected with COVID-19, and the social and demographic characteristic of these patients. 81 patients were included in this study, and while all of them had an altered sense of smell, 39 tested positive for COVID-19, while 42 tested negative. Out of the 81, 28 were males and 53 were female. Of the positive cases, 38.5% complained of an altered sense of smell as a preliminary symptom, and before the development of any other COVID-19 related symptoms. The average duration of anosmia in positive patients was 9.31 ± 8.89 days. For the purposes of this discussion, we will divide our findings into two main portions: firstly, concerning the demographics and characteristics of the participating subjects, and secondly concerning the clinical findings, with a special focus on changes in sense of smell.

Concerning the subjects' socio-demographic characteristics

In this study, two- thirds of the cases presenting with anosmia were female, and of those, 50% tested positive for COVID-19. This is consistent with findings in another study, where 73% of the subjects were indeed female [12]. Another study evaluating anosmia

and ageusia in COVID-19 patients had 72 subjects, of which 27 were males and 45 were females [20]. This could possibly be due to women being more aware of their sense of smell; a meta-analysis of 24 studies revealed that women tended to significantly outperform men in odor identification, but only in age groups 18-50 years [18]. As of yet, affection with COVID-19 hasn't been shown to discriminate based on gender, yet developing anosmia as a symptom of COVID-19 seems to be more commonly reported in females.

A meta-analysis done on total of twenty-four studies with data from 8438 test-confirmed COVID-19 patients from thirteen countries on the olfactory and gustatory dysfunctions among patients infected with COVID-19 revealed that increasing mean age correlated with lower prevalence of olfactory (coefficient = -0.076; p = .02) and gustatory (coefficient = -0.073; p = .03) dysfunctions [21]. Our study indicated that dysgeusia was noticed in 61.5% of positive cases (n = 24).

Most of the subjects enrolled in this study were married, three quarters of them had history of contact with an infected patient, and 48.7% had family members who were also affected, indicating that the virus spreads through close contact, which is in line with the WHO's recommendations to stay 3 ft apart to avoid transmission [22]. The rate of infection also appeared to be higher in employees, possibly due to them having to use public transportation and being in closed environments, as a study based in China has shown that the odds that a primary case transmitted COVID-19 in a closed environment was 18.7 times greater compared to an open-air environment [23].

This study revealed that most cases that were indeed positive (46.2%) were overweight. Obesity is known to cause a wide variety of chronic illnesses and may even negatively impact the immune system. Drawing upon past experience with virus pandemics, we can assume that obesity might be considered a risk factor for infection with COVID-19, as it was recognized as an independent risk factor for flu complications during the 2009 H1N1 pandemic [24]. The Centers for Disease Control and Prevention considers those with BMI ≥ 40 kg/m2 being at risk for flu complications [25]. The potency of flu vaccines could also be diminished in patients suffering from obesity, as a study shows that despite being vaccinated with IIV3, those with obesity were still twice as likely to get the flu [26].

The most frequent comorbidities among positive cases were hypertension (15.4%, n = 6), and diabetes mellitus (12.8%, n = 5). This is in line with reports from China and Italy, which showed that older patients with chronic diseases, including diabetes, were at higher risk for severe COVID-19 and mortality [27,28]. Therefore, diabetes and other comorbidities can be considered significant predictors of morbidity and mortality in patients with COVID-19. The results of this study suggest that female obese patients with co-morbidities of hypertension and diabetes were at higher risk of developing anosmia with COVID-19.

This study also found that symptomatic individuals with ABO blood group type A were more likely to test positive. The exact cause behind this isn't yet well understood, however another study revealed the same finding, with subjects with blood group A associated with a higher risk for acquiring COVID-19 compared with non-A blood groups, whereas blood group O was associated with a lower risk for the infection [29].

An interesting question is: has the prevalence of anosmia in general increased due to COVID-19, as compared to percentage of anosmia that was present before COVID-19 that was caused by other viruses? It is known that flu viruses can cause anosmia, and in fact 39% of anosmia is caused by upper respiratory infections [30]. However, not enough research has been done in this area to be able to compare them directly.

Regarding changes in sense of smell

38.5% of all positive cases had anosmia as a preliminary symptom, before developing any other symptoms. Therefore, it could possibly be a good predictor of COVID before the manifestation of other symptoms, and lead healthcare workers to be more attentive in wearing full PPE while dealing with anosmia patients. A comparable study that analyzed 237 entries, revealed that anosmia was noted in 73% of patients prior to COVID-19 diagnosis and was the initial symptom in 26.6% [17].

Ongoing researches suggest that the presence of anosmia could indicate a milder clinical course in COVID-19 positive patients [12,19]. Our study found that over half of our subjects who were presenting with anosmia also reported symptoms of fever (64.1%, n = 25), sore throat (53.8%, n = 21), fatigue (74.4%, n = 29), cough (64.1%, n = 25), headache (59%, n = 23), muscle ache (myalgia) (66.7%, n = 26), chest tightness (59%, n = 23), and diarrhea (61.5%, n = 24).

As for the associated ENT symptoms, we found that the most common were: allergic rhinosinusitis (12.8%, n = 5), dysgeusia (61.5%, n = 24), headache (59.3%), watery discharge (30.8%), burning, sneezing, and nasal obstruction were detected in 20.5% of cases (n = 8) for each symptom. Five patients had rhinorrhea (12.8%) and only 3 patients (7.7%) had itching. A meta-analysis that included 1773 COVID-19 laboratory-confirmed positive patients reported that the most common ENT manifestations of COVID-19 were sore throat (11.3%) and headache (10.7%), pharyngeal erythema (5.3%), nasal congestion (4.1%), runny nose or rhinorrhea (2.1%), upper respiratory tract infection (URTI) (1.9%), and tonsil enlargement (1.3%) [16].

We found that the average duration of anosmia was < 7 days for 55%, 7-14 days for 20%, and > 14 days for 25%. A study also carried out in Egypt by Amer et.al which followed the different recovery patterns of 96 anosmia patients showed 32 patients experiencing full recovery (33.3%) while, 40 patients showed partial recovery (41.7%) after a mean of 11 days while 24 patients (25%) showed no recovery within one month from onset of anosmia [31]. Another study conducted on 382 patients with anosmia through consecutive online surveys indicates that there appears to be significant improvement in the first 2 weeks but then the recovery rate appears to plateau. The overall recovery rate reported in those of 3 weeks duration or longer is 71%. Although only 15 patients in that study had been tested for SARS-CoV-2, 80% of those 15 tested positive [12]. Similarly, a cross-sectional survey-based study conducted in Italy, which followed the clinical course of 202 mildly symptomatic adults found that 89% of mildly symptomatic patients who presented with anosmia/hyposmia and altered sense of taste recovered from these symptoms after 4 weeks. It was evident that persistent loss of smell or taste was not associated with continued SARS-CoV-2 infection [32].

While all of our 81 subjects had gone through primary and secondary triage in our quarantine hospital and displayed signs and symptoms to fit the criteria of being suspected of having COVID-19 to require them to be sent to us for a PCR swab for confirmation, a surprising finding in our results was that while they all did suffer from anosmia, almost half of our subjects tested negative. This requires us to consider other causes of anosmia, rather than SARS-CoV-2. One study evaluating 278 consecutive patients classified the causes of olfactory loss as trauma (17%), URI (39%), sino-nasal disease (21%), idiopathic causes (18%), congenital anosmia (3%), and other causes (3%) [30]. However, since the focus for our study was new onset anosmia and none had history of trauma, this eliminates congenital anosmia and traumatic causes. Further investigation is needed to determine whether this finding was due to other viruses that cause anosmia such as the flu virus, or possibly allergies due to changing of the seasons. Further investigations are also needed to assess whether the overall rate of occurrence of anosmia has increased due to SARS-CoV-2 specifically.

During the course of our work, we encountered a few shortcomings in our research, such as:

- The method for detecting anosmia was self -reporting, which has good specificity, but poor sensitivity.
- There was no follow up with the patients to be able to see how many of them reached full recovery and to monitor the progression of their symptoms.
- This is a descriptive study, not an analytical one, therefore direct causality cannot be established.
- This study was conducted on a relatively small number of patients, and therefore not all variable had the chance to be significant.
- This is a hospital-based study, not done in a primary care setting, where full psycho-socio-demographic information can be taken from the patients.

On the other hand, we found that our study has several strengths, including:

- PCR testing for COVID-19 was done for all the subjects, and we were able to determine what percentage of patients presenting with anosmia were actually positive for the virus.
- The study took into consideration the socio-demographic aspects of the subjects.
- This was done in a quarantine hospital; therefore, many COVID-19 suspected patients were able to come for testing.
- This is a concurrent study, not a retrospective one, and therefore doesn't suffer from recall bias.

Conclusion

While anosmia has been proven to be an anecdotal finding in COVID-19 positive patients, the presence of new onset anosmia

in patients during the COVID-19 era cannot be fully explained by the SARS-CoV-2 virus. However, as healthcare workers, wearing full PPE while dealing with anosmia patients is recommended, as anosmia could be a preliminary symptom and this could prevent infection.

Recommendations

Further studies should be done to further assess the social and demographic characteristics of patients with COVID-19 related anosmia to determine whether any patterns emerge that could suggest causality. The high prevalence of anosmia in patients who tested negative for COVID-19 requires us to search for other causes. Studies should be carried out to specifically determine the percentage of anosmia caused by other flu viruses as compared to the percentage of anosmia caused specifically by SARS-CoV-2.

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