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Abstract

Covid-19 is a pandemic that has changed the very structure of the world in the past year. Anosmia was not mentioned as a symptom during the first wave of the pandemic. Still, recent literature from both Western and Chinese started describing anosmia as an early symptom along with other flu-like symptoms. This paper discusses whether anosmia can be used as an early diagnostic symptom and if there is a female predominance of anosmia in Covid-19 patients. We used 290 Covid-19 positive patients from Government Mohan Kumaramangalam Medical College Hospital, Salem, Tamil Nadu, India. The results of our study demonstrated that there is a female predominance of anosmia in Covid-19 patients. Anosmia can be used as an initial diagnostic tool for the infection.

Introduction

Covid-19, an emerging pandemic, has caused a vast disaster throughout the world and substantially has a massive impact on our global healthcare and economy. There has been newer evidence that Covid-19 has frequently been reported with neurologic symptoms such as anosmia and ageusia. Although Covid-19 initially has not been reported with anosmia alongside typical symptoms such as fever, cough, fatigue, and myalgia, Coronavirus, in general, is known to cause neurologic, gastrointestinal, and hepatic dysfunction in humans and animals. Evidence from newer research [7] has suggested that olfactory dysfunctions are widely reported throughout the world. Detection of mild olfactory dysfunction before severe dysfunction such as respiratory distress, cardiac arrest, and thrombosis can be helpful for timely treatment and management of the patient.

Additionally, Anosmia during Covid-19 infection has a higher predisposition towards the female gender than male Covid-19 patients. This paper focuses on the early detection of Covid-19 disease to help avoid severe untreated complications and establish that female patients are more likely to present with anosmia during their infection period. However, the exact pathologic mechanism or differences in inclination towards the female gender has not been addressed in this paper.

Methods

This is a retrospective observational study of 290 patients infected with Covid-19 between June 1, 2020, to July 1, 2020, in GMKMC, Salem, India. All patients described as having anosmia had a complete loss of smell during the period as per the medical records. The patients underwent a Sniffin-sticks smell test to identify anosmia.

Due to the pandemic restrictions, not all patients underwent smell testing during their stay in the hospital. Patients included in this study are aged between 18 to 80 years, with complete medical records, and the genders are female and male. Patients excluded were with prior neurologic diseases and patients previously diagnosed with anosmia.

Results

Two hundred and ninety patients were included in this study. Most of the patients were males; 65% (186 patients) and 35% (104 patients) were females.

Based on **table 1**, Out of a total number of 290 patients, 102(35.2%) reported having anosmia before getting admitted to the hospital - 37 (36.3%) of the 102 patients recovered from anosmia in a few days after admission. Additionally, 89 (30.7%) patients developed anosmia during their stay in the hospital.

Table 1. Distribution of patients with anosmia before admission and during their stay in the hospital.

	Present	Not Present
Before Admission	102	188
During Hospital Stay	154	136

A chi-square test of independence was performed to examine whether anosmia could be used as an early diagnostic symptom. The relation between these variables was significant, $\chi^2(1, N = 290) = 18.9082, p = .000014$. Anosmia can be used as an early diagnostic symptom.

Based on **table 2**, 66% (69) of the female and 46% (85) of the male population associated anosmia as a symptom during their Covid-19 infection, identified by the Sniffin-sticks smell test. The difference signifies that female patients predominantly present with anosmia than male patients during their infection period.

Table 2. Percentage distribution of Covid-19 infected females and males with anosmia during their stay in the hospital.

	Not Present	Presented with anosmia
Males	101	85
Females	35	69

A chi-square test of independence was performed to examine the relationship between gender and anosmia during Covid-19 infection. The relation between these variables was significant, $\chi^2(1, N = 290) = 11.4185, p = .000727$. Female gender predisposes to have anosmia during Covid-19 infection.

Discussion

Seven known coronavirus variants cause infections in humans, including SARS-COV 2 (Covid -19). SARS COV-2 enters through the ACE-2 receptor by binding its spike protein S1 [2]. The expression and distribution of ACE-2 receptors throughout the nervous system serve as an entry point for SARS-COV-2 to cause numerous neurological dysfunctions. Evidence from studies has shown olfactory dysfunction as the most common sign of Covid -19 infection [6]. The olfactory dysfunction in Covid -19 has caught the attention of otolaryngologists all over the world. Anosmia has been reported as the first symptom or following mild symptoms such as cough, fever, fatigue, or developed gradually accompanying pulmonary dysfunction during their hospital stay.

The mean age of our patients included in this study population was 48 years, 65% were males, and 35% were females. The prevalence of anosmia was significantly higher in female patients (66%) than male patients (46%). The patients included in anosmia predominance in the female gender were chosen with impaired olfactory dysfunction during their inpatient stay with moderate to severe infection. The study is similar to Klopfenstein et al. [5]; A retrospective study showed 47% presented with anosmia. The study states that 67% of patients reported with anosmia were female patients [5]. The study also found that olfactory dysfunction is often accompanied by dysgeusia in Covid -19 patients [5].

A systematic review and meta-analysis conducted by Agyeman et al. [1] describe a high prevalence of olfactory and gustatory dysfunction in patients infected with Covid -19, and 41% of 8438 patients had anosmia. Our study also found out that 65.9% of the patients have had anosmia either before or during the hospital stay. Another survey by Printz and Constanidis [9], concludes that anosmia is more prevalent in Covid -19 patients than in patients suffering from other respiratory infections. 95% of the taste disorders are disorders of the olfactory system [7]. A study by Vinayachandran and Balasubramanian [10] states that the loss of taste could be secondary to anosmia rather than a problem in the gustatory system. So patients presenting with ageusia should also be tested for anosmia. A study by Hornuss et al. [4] states that anosmia was the sole symptom present for many patients, so primary care physicians and otolaryngologists should be aware of this putative presentation.

Thus, it should be mandatory to make anosmia a tool for initial diagnosis or to create a suspicion of Covid -19 infection and isolate the particular patient. Giacomelli et al. [10] also agree with our study that more research should be done in nonhospitalized infected patients if anosmia can be used as a clinical screening tool. Since Covid-19 is highly transmissible, isolation of the patient results in the most significant curb of the spread of disease. In developing countries and underdeveloped countries, the amount of RT-PCR tests are limited; Anosmia can be used as a tool by patients to isolate themselves and contact the respective Covid-center or a Covid-clinic for further support.

The female patients should be prioritized for neurologic care while dealing with Covid-19

infection. The female gender potentially is linked to developing other neurologic dysfunctions since ACE-2 receptor expression is throughout the nervous system. Female patients with previously diagnosed neurologic impairment should be cautious since serious complications such as acute encephalopathy are reported in Covid -19 infection [11]. Future studies should potentially study the morphologic differences for this prevalence of anosmia in the female gender.

We were only able to get the data of 290 patients. Since the number of infections is still increasing, the values of the results might change for a different sample size. The entire data was taken from a single hospital because of the limited resources. If the sample taken was much more extensive and diverse, there might be some changes in the results. The amount of research previously done on this topic is also significantly less than other areas of interest related to Covid -19 infection. We believe that many more researchers should take up this topic and try to find the answers on a larger scale so that it could help in a better understanding of anosmia in Covid -19 patients and maybe help decide the treatment plan and prognosis of the infection.

Conclusion

Anosmia in Covid-19 is a crucial symptom to be considered in Covid -19 infection. Covid-19 infection accompanies olfactory dysfunction in more than half of the cases. Potentially an initial symptom for clinical diagnosis. Additionally, Women with Covid -19 infection have a higher degree of developing anosmia.

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