

Review Article

Olfactory dysfunction and anosmia awareness in coronavirus disease 2019 pandemic

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ABSTRACT

Raise awareness of anosmia association in Coronavirus pandemic. Current finding about Coronavirus infection and its association with olfactory dysfunction and anosmia is reviewed. The exact mechanism of Coronavirus on the Olfactory system is still unresolved. The olfactory dysfunction is due to local inflammation of the nasal cavity or viral-induced olfactory nerve damage or both. Screening of all patients coming with anosmia should be done to early diagnose the disease and isolate and treat accordingly. Olfactory dysfunction is the most common clinical feature of coronavirus disease 2019 with anosmia being the most distinguished sign with patient may present with sudden onset anosmia as single clinical feature or in association with taste dysfunction and / or dry cough, sore throat, pharyngitis, fever. Clinician should be alert of anosmia and diagnose, isolate and treat patients accordingly.

Keywords: SARS-CoV 2, COVID-19, Pandemic, Olfactory dysfunction, Anosmia

INTRODUCTION

Severe Acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for Coronavirus disease 2019 (COVID-19).¹ Corona virus causes upper and lower respiratory tract infections the severity can be mild, example common cold, and can be even lethal, like SARS (Severe acute respiratory syndrome), MERS (Middle East respiratory syndrome), and COVID-19 (Corona virus disease 2019). This disease was first identified in December 2019 in Wuhan, the capital of China's Hubei province (Hui DS et al).^{2,3} The virus predominantly spread by close contact in the form of small droplet produced while coughing, sneezing and talking.^{4,5} Bioaerosol transmission occurs while doing intubation and cardiopulmonary resuscitation. Fomite transmission is also feasible.⁴ The virus is most contagious when people are symptomatic, but spread is possible even before symptoms appear.⁴ The patient may be asymptomatic or present with

flu like symptoms like fever, cough, sneezing, fatigue, shortness of breath. Blood tests may reveal lymphocytopenia and HRCT chest may denote ground glass appearance. The disease may progress to pneumonia, multi-organ failure, and even death (Chen et al, Hessen et al, Michael et al).⁸⁻¹¹ The incubation period is five to six days, may range from two to 14 days. The virus survives for hours to days on surfaces. Olfactory dysfunction is increasingly seen in COVID-19 patients. Anosmia can solely be the presenting symptom or it may be associated with dry cough (Marchese-Ragona et al).¹⁴ Otolaryngologists and health care staff are at high risk of COVID-19 infection, hence appropriate protective and hygiene measures are utmost importance (van Doremalen et al).^{6,7} The risks seem to be more high in the field of rhinology and endoscopic endonasal surgery (Ramakrishna et al, Workman et al).^{12,13} Nasal endoscopy and flexible laryngoscopy examination of patients in out patient clinic and during surgery is especially risky as the

virus resides primarily in the nasal cavity and nasopharynx.

METHODS

COVID-19 disease has become pandemic all over the world causing huge disaster throughout. There is increasing incidence of COVID-19 with anosmia and olfactory dysfunction. Anosmia relating to COVID-19 is gathered from various literatures written in Centers for Disease Control and Prevention (CDC), Web of Science, PubMed, Google Scholar. The review outlines Anosmia and olfactory dysfunction in this COVID-19 disease and its possible mechanism of association of it with the disease.

COVID-19 AND OLFACTORY DYSFUNCTION

Olfactory dysfunction is currently the most common clinical feature of COVID-19 (Lechien et al).¹⁵ Anosmia is the most distinguished sign of COVID-19 disease with patients presenting with anosmia of sudden onset (Heidari et al).¹⁶

Klopfenstein et al study showed 54 (47%) out of 114 COVID-19 positive patients had clinical features of anosmia and patients principally developed anosmia 4.4 days after the outset of the SARS-CoV-2 infection. 98 % patients recovered of anosmia within 28 days.¹⁷

Olfactory dysfunction is frequently accompanied by dysgeusia in COVID-19 patients (Klopfenstein et al; Luers et al).^{17,18} Incidence of Olfactory dysfunction in COVID-19 patients ranging from 33.9 to 68% along with associated smell disorders was reported. (Giacomelli et al; Yan et al; Bagheri et al; Menni et al; Spinato et al).¹⁹⁻²³

Incidence of smell disorders are seen higher in COVID-19 patients (Giacomelli et al; Yan et al; Spinato et al).^{19,20,23}

Moein et al executed olfactory function test (OFT) of 60 COVID-19 positive patients and 60 subjects as control group having similar age and gender of the patient's group and it concluded that COVID-19 patients presented with marked olfactory dysfunction.²⁴

Another investigation was done using self-reported questionnaire which surveyed the prevalence of taste and / or smell disorders in COVID-19 and influenza patients (Beltran-Corbellini et al).²⁵ The study showed that incidence rate in COVID-19 cases (39.2%) was significantly higher than in influenza cases (12.5%).²⁵

Mayo Clinic analyzed the symptoms and signs of COVID-19 infection by using artificial intelligence which revealed that the prevalence of anosmia or dysgeusia in COVID-19 positive patients was 28.6 fold more than that of COVID-19 negative patients and the study also disclosed that

anosmia or dysgeusia was one of the earliest presentation of COVID-19 infection (Shweta et al).²⁶

GENOTYPE RELATION OF OLFACTORY DYSFUNCTION IN COVID-19 DISEASE

COVID-19 infection can have some association host genotype with heritability for anosmia upto 47% (95% confidence intervals 27-67) (Williams et al).²⁷ Olfactory dysfunction has a high incidence rate in COVID-19 cases in some American and European countries, but it hardly occurs in Chinese patients (Williams et al; Lovato et al).^{27,28} This can be due to genotype mutation.

Forster et al found change in amino acid in three central variants. The A and C genotype of SARS-Cov-2 presents remarkably in Americans and Europeans, with B type being most common genotype in East Asian. Type A and C genotype seem to have a high pathogenicity for human nasal cavity, thus favoring increased prevalence of olfactory dysfunction in American and European countries (Forster et al).²⁹

COVID-19 INFECTION AND ITS ETIOLOGY

In humans it has been found that there are 7 types of coronaviruses namely severe acute respiratory syndrome coronavirus (SARS-CoV-2), Middle East respiratory syndrome coronavirus (MERS-CoV), HCoV-NL63, HCoV-OC43, HCoV-229E and HCoV-HKU1 (Wu et al).³⁰

SARS-CoV-2 genome is a 29,903 bp single-stranded RNA coronavirus (Baig et al).³¹

NASAL CAVITY AND COVID-19 INFECTION

SARS-CoV-2 virus bears a spiny protein named S1 which adheres to the ACE2 receptors present on host cell membrane (Baig et al).³¹

ACE2 receptors are distributed in the central nervous system.⁵

The olfactory system has olfactory bulb and nerve, viruses can invade this olfactory system via cibriform plate to involve the central nervous system (Koyuncu et al; Baig et al).^{33,34}

SARS-CoV-2 mainly resides in ciliated cells and goblet cells in the nasal mucosa, thus transmission occurs primarily through droplets (Sungnak et al).³⁵ SARS-CoV-2 virus can pass from nasal cavity via nasolacrimal duct to eyes, hence it can be detected in tears (Gengler et al).³⁶

Olfactory dysfunction following COVID-19 infection is believed to be caused by either damage to the olfactory epithelium or central olfactory system pathways (Hummel et al).³⁷

DISCUSSION

After reviewing this study it is concluded that olfactory dysfunction, mainly anosmia is the most common earliest symptom of COVID-19 infection. Anosmia sometimes goes unnoticed in this COVID-19 scenario and one must emphasise on a detailed history in these patients. It is often associated with loss or altered taste sensation. Olfactory dysfunction is more common in COVID-19 cases particularly patients in American and European countries, but it hardly occurs in Chinese patients, depicting association of genotype variation. The A and C genotype of SARS-Cov-2 presents in Americans and Europeans and B type being most common genotype in East Asian. Type A and C genotype seem to have a high pathogenicity for nasal cavity of the humans, thus favoring increased prevalence of olfactory dysfunction in American and European countries. The exact reason for olfactory dysfunction is still unresolved. Thus more studies and research regarding olfactory dysfunction is yet to be carried out.

Post-viral anosmia amounts upto 40% cases of anosmia. Viruses that give rise to common cold are familiar to cause post-infectious loss. Coronaviruses accounts for 10 - 15% cases. It is therefore evident that novel COVID-19 virus would also cause anosmia. In South Korea, China, Iran, US, France, Germany and Italy many COVID-19 infected patients have developed anosmia or hyposmia as a single symptom or in association with other symptoms. The exact catastrophic mechanism of SARS-CoV-2 virus on the Olfactory system is still unresolved. It is ambiguous whether olfactory dysfunction is due to local inflammation of the nasal cavity or viral-induced olfactory nerve damage or both. Rhesus monkey can be used to study the physiological and pathological effect of the olfactory system by SARS-CoV-2 virus. Olfactory epithelium of COVID-19 positive patients can be biopsied for better delineation of the pathology of Olfactory dysfunction in COVID-19 patients (Jafek et al).³⁸

CONCLUSION

Sudden onset anosmia is a very and earliest clinical feature of COVID-19 infection. It can be associated with taste dysfunction and/or dry cough, sore throat, pharyngitis, fever. Olfactory dysfunction can be due to local inflammation of the nasal cavity or viral-induced olfactory nerve damage or both, although the reason is still ambiguous. Detailed studies of the pathogenesis of olfactory dysfunction need to be done in COVID-19 positive patient. Anosmia and hyposmia often occur unnoticed in COVID-19 patients. Some patients may present solely with anosmia, thus primary physicians and Otolaryngologists need to be aware of this presentation. Otolaryngologists should screen all patients coming with anosmia with real-time reverse transcription polymerase chain reaction (rRT-PCR) for COVID-19 and/or HRCT

chest to avoid any delay in diagnosis, with prompt isolation and treatment of patient.

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