# Anosmia, a Hidden Sign for COVID-19? A Case Report and Literature Review

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**Case Report**

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# Abstract

**Background** The coronavirus disease 2019 (COVID-19) is an ongoing viral pandemic that is actively affecting 210 countries worldwide, with a total of more than 1.5 million cases and 106 000 deaths. Symptoms associated with COVID-19 are mainly fever, cough, dyspnea and sore throat. The current indication for COVID-19 testing includes presence of these symptoms with a positive history of travel to affected countries or contact with COVID-19 patients. Anosmia has been recently reported anecdotally over the past weeks as an emerging symptom of the COVID-19 but has yet to gain recognition as a symptom for COVID-19 by the World Health Organization (WHO) and Centre for Disease Control and Prevention (CDC). This case report highlights a case of isolated sudden onset of anosmia as a presenting symptom of COVID-19 and relevant literature review supporting the incidence of anosmia in COVID-19. This is a first case report of anosmia in COVID-19 occurring in pregnancy.

**Case Presentation** A 30-year-old pregnant lady at 11 weeks of gestation presented with sudden onset of anosmia for one day with no other accompanying symptoms. She had just recovered from a mild cold a day prior to the development of anosmia. She had a history of travel by land to Singapore 14 days prior to onset of anosmia. There was no known close contact with a COVID-19 patient or attended any mass gatherings prior to development of her symptom. She underwent nasopharyngeal and oropharyngeal swab sampling which was then tested using reverse transcription polymerase chain reaction (RT-PCR) method and confirmed infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

**Conclusion** Clinicians should be aware regarding anosmia as a presenting symptom of COVID-19 especially in the presence of risk factors such as travel to affected countries and having close contact with COVID-19 positive patients. If testing is not done, these patients should be advised for home quarantine to reduce the risk of transmission. Healthcare workers must always adhere to infection control and prevention protocol as well as personal protective equipment.


# Background

The coronavirus disease 2019 (COVID-19) is an ongoing viral pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has taken the lives of more than 106 000 people globally (1). The transmission of disease has increased exponentially across many countries within a very brief period. WHO and CDC has recommended that testing for COVID-19 be done for patients who presented with fever, cough, dyspnea or other symptoms compatible to COVID-19 with relevant epidemiological factors under the sound judgement of clinicians (1, 2).

Recently, olfactory dysfunction such as hyposmia and anosmia in the absence of other symptoms has been highlighted as an emerging symptom among COVID-19 positive patients and statements have been released by several otorhinolaryngology societies (3, 4). This symptom however has yet to be recognized by the WHO or CDC as a symptom of COVID-19. The intent of this case report is to generate awareness among the public and clinicians regarding the possibility of anosmia as a silent marker of COVID-19 and to prompt the international scientific community to consider this clinical manifestation in the current case testing and management guidelines while awaiting more vigorous evidence.

This case report highlights a case of isolated sudden onset of anosmia as a presenting symptom of COVID-19 and relevant literature review supporting the incidence of anosmia in COVID-19. This is a first case report of anosmia in COVID-19 occurring in pregnancy.

# Case Presentation

A 30-year-old, gravida 1 lady at 11 weeks of gestation visited the antenatal care clinic at a private hospital for her routine check-up. However, she complained of having sudden onset of anosmia on the day of presentation to the antenatal care clinic. Two days prior, she had fever, mild runny nose and non-productive cough which resolved a day before the development of anosmia. On the day of onset of anosmia, she did not have any fever, cough, runny nose, nasal congestion, shortness of breath, sore throat, vomiting, diarrhea, myalgia, abdominal pain or fatigue. She had no other comorbidities.

She had a history of travel by land in her own vehicle from Johor, Malaysia to Singapore and returned to Johor on the same day 14 days prior to development of anosmia. Her timeline of travel and symptomatology are as in Figure 1. She had no close contact

with any known COVID-19 positive patients or attended any mass gatherings prior to development of her symptoms. She lives with her husband who was well.

Upon examination, she was afebrile with normal blood pressure, pulse, respiratory rate and oxygen saturation under room air. She was comfortable and did not appear to be in respiratory distress. Her lung auscultation was clear. She underwent nasopharyngeal and oropharyngeal swab sampling immediately after consultation at the facility which was then tested using reverse transcription polymerase chain reaction (RT-PCR) method. Healthcare workers attending her wore adequate personal protective equipment (PPE) and adhered to infection control protocol.

As per local guidelines, her symptoms did not fulfil the criteria for being a person under investigation (PUI) (5). Thus, she was allowed discharge from the facility with advice for home surveillance.

After approximately 48 hours, her RT-PCR results confirmed the SARS-CoV-2 infection. She was then referred and admitted to the designated COVID-19 hospital for further management. None of the healthcare workers who had contact with her prior to testing developed any COVID-19 symptoms or anosmia up to date. Her husband was tested negative.

## Discussion And Conclusion

The current symptoms for suspicion of COVID-19 as outlined by WHO are fever with at least one sign or symptom of respiratory disease such as cough, shortness of breath alongside a history of travel to or residence in a location reporting community transmission of COVID-19 or having been in contact with a confirmed COVID-19 patient or PUI during the 14 days prior to symptom onset (1). The CDC has noted that most persons with COVID-19 will experience fever, fatigue, anorexia, shortness of breath, sputum production and myalgias while less than ten percent of the COVID-19 patients had atypical presentations such as headache, confusion, rhinorrhea, sore throat, haemoptysis, vomiting and diarrhea (2).

Olfactory dysfunctions such as anosmia and hyposmia as a symptom of COVID-19 on the other hand has been anecdotally reported and described by very few studies. It has yet to receive recognition as a symptom to raise suspicion or become a testing indication for COVID-19. The British Rhinological Society, American Academy of Otolaryngology-Head and Neck Surgery and the French Society of Otorhinolaryngology has recently issued expert statements suggesting that anosmia could be a potential feature of COVID-19 (3, 4, 6). A few studies have been conducted which provides support for the suggestion. The limitations of these studies are mostly due to the state of emergency of the disease, including some not being peer-reviewed, use of unvalidated questionnaires as well as lack of verification of symptoms by clinical examinations. Findings of the relevant studies are as summarized in Table 1.

**Table 1** Summary of literature review

| Author | Number of participants | Country | COVID-19 status | Findings relevant to anosmia/hyposmia |
|---|---|---|---|---|
| Mao et al., 2020 (1) | 214 | Wuhan | Positive | • 11 out of 214 patients (5.1%) had hyposmia<br>• 3 were severe cases, 8 not severe<br>• Finding was not significant (p=0.338) |
| Vaira et al., 2020 (2) | 320 | Italy | Positive | • Estimated that chemosensory dysfunction is present in 19.4%<br>• No true statistical data due to state of health crisis in country |
| Giacomelli et al., 2020 (3) | 59 | Italy | Positive | • 20 (33.9%) had at least one taste or olfactory disorder and 11 (18.6%) had both.<br>• 12 patients had the symptoms prior to hospitalization while 8 of them started experiencing the symptoms during the hospital stay.<br>• Females reported these symptoms more frequently than males [ 10 out of 19 females (52.6%); 10 out of 40 males (25%); p=0.036] |
| Lechien et al., 2020 (4) | 417 | 12 European hospitals (Belgium, France, Italy, Spain) | Positive | • 357 patients (85.6%) had olfactory dysfunction.<br>• Anosmia was present in 284 patients (79.6%) while hyposmia was present in 72 patients (20.4%).<br>• Females were found to be more affected by anosmia or hyposmia than males.<br>• 72.6% regained olfactory function within the first 8 days following disease resolution |
| Bagheri et al., 2020 (5) | 10069 | Iran | Uncertain -the study enrolled all with hyposmia/anosmia within 1-month (since the start of COVID-19 epidemic in Iran) No information provided if they were then tested | • There was a surge of olfactory dysfunction coinciding with the COVID-19 epidemic in Iran<br>• The correlation between anosmia with the number of COVID-19 positive patients was significant (Spearman correlation coefficient 0.87; $p < 0.001$)<br>• The onset of anosmia was sudden in 76.24%<br>• 83.38% had decreased taste sensation in association with anosmia. |
| Menni et al., 2020 (6) | 1 573 103 | United Kingdom | Only 1702 tested, 579 were positive, 1123 negative | • Loss of smell and taste was reported in 59% of the those tested positive and 18% of those tested negative (OR 6.59; 95% CI 5.25 to 8.27; $p=1.9x10^{-59}$)<br>• Combination of loss of smell and taste, fever, persistent cough, fatigue, diarrhea, abdominal pain and loss of appetite is predictive of COVID-19 positive test with sensitivity 0.54, specificity 0.86 |

To date, within the limitations of our search, there were very few case reports published regarding sudden onset anosmia who were then confirmed to have COVID-19 by RT-PCR testing. A summary of the case reports is presented in Table 2. There were no case reports retrieved regarding anosmia among COVID-19 positive pregnant patients.

**Table 2:** Summary of case reports

| Literature | Age (years) | Sex | Onset of anosmia | Duration of anosmia prior to presentation | Other symptoms | Comorbidities | PCR testing for COVID-19 |
|---|---|---|---|---|---|---|---|
| Gane et al.,2020 (7) | 45 | Male | Sudden | 72 hours | None | None | Positive |
| Villalba et al.,2020 (8) | 85 | Male | Sudden | 4 days | Fatigue | Hypertension, Ischaemic heart disease and Diabetes Mellitus type II | Positive |
| Villalba et al.,2020 (8) | 80 | Female | Unknown | 5 days | Ageusia, fatigue | Hypertension, heart failure and end stage renal failure | Positive |

The cause of anosmia in COVID-19 is yet to be ascertained. Nasal endoscopy still possesses a high risk to doctors during this pandemic and deferment of the procedure has been recommended. It has been hypothesized that anosmia could be due to an insult occurring at the neuro epithelium of the olfactory receptor cells in the nasal roof or central olfactory routes (7, 15). A study investigating human and mouse data sets found that olfactory epithelial support cells, stem cells and nasal respiratory epithelium cells expresses the two key genes, angiotensin converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) which enables proteins production. These proteins then enable the attachment of SARS-CoV-2 onto cells (15). This discovery evokes a probable mechanism of anosmia in COVID-19 and warrants further research for validation.

In relation to our case, the symptoms of COVID-19 in pregnancy has been reported to be similar with the non-pregnant adults which are fever, sore throat, malaise, dyspnea and cough (16). The COVID-19 severity is also equivalent to the non-pregnant population with the majority cases being mild (17). There are currently no data suggesting an increased risk of miscarriage or early pregnancy loss however, those who develop pneumonia were found to have a higher incidence of preterm labour, preterm birth, prelabour rupture of membranes, pre-eclampsia and caesarean delivery for abnormal fetal heart tracings (18). Vertical transmission of COVID-19 is yet to be established but studies have shown that samples of amniotic fluid, cord blood, breastmilk and neonatal throat swabs were negative for SAR-CoV-2 (19). As of time of this writing, there are no reported cases of maternal death due to COVID-19.

The patient in our case has been allowed discharge from the COVID-19 designated hospital after her repeated RT PCR after 72 hours was negative. She did not develop any respiratory distress or experienced any signs of miscarriage or pregnancy loss. She has been advised for home quarantine for 14 days. She was pleased that the attending physician who first saw her was aware of anosmia being a probable symptom of COVID-19 and tested her despite not fulfilling the criteria for testing (5). She is thankful that COVID-19 was promptly detected, and she was referred for further management by a multidisciplinary team.

COVID-19 is still a very new, challenging disease and research gaps are still present. Future studies might want to consider exploring the anosmia predilection towards females, it’s recovery as well as treatment modalities.

Globally, most countries are yet to begin testing patients with complaints of anosmia for COVID-19. These patients with isolated anosmia could represent the submerged part of the COVID-19 iceberg as they might be vectors of the virus. Until anosmia has gained recognition as a COVID-19 symptom and becomes an indication for RT-PCR testing, patients with isolated sudden onset of anosmia should be advised for home quarantine with daily monitoring of clinical progress via telemedicine. Healthcare workers must always wear appropriate PPE and adhere to infection control protocols to minimize risk of transmission.

## List Of Abbreviations

COVID-19: coronavirus disease 2019

WHO: World Health Organization

CDC: Centre for Disease Control and Prevention

RT-PCR: reverse transcription polymerase chain reaction

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

PPE: personal protective equipment

PUI: person under investigation

ACE2: angiotensin converting enzyme 2

TMPRSS2: and transmembrane serine protease 2

# Declarations

### Ethics approval and consent to participate

Ethics committee approval for a case report was considered unnecessary because, under Malaysian law, it is only required for clinical trials. The patient gave her written informed consent to the medical procedures used for treatment purposes.

### Consent for publication

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

### Availability of data and materials

Data will be made available upon reasonable request.

### Competing interests

The authors declare that they have no competing interests.

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### Authors' contributions

KC, MMZ and ND contributed to the design and implementation of this case report. KC acquired data, undertook the literature search and review as well as drafted the manuscript. MMZ and ND critically revised the manuscript. All authors approved the final manuscript.

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# Figures


**Figure 1**

Patient's timeline from history of travel to development of anosmia

# Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1BMCanosmia.docx
- Table2BMC.docx