SELF-REPORTED OLFACTORY, GUSTATORY AND OTOLOGIC DYSFUNCTIONS AMONG COVID-19 POSITIVE ADULTS IN NIGERIA- A PRELIMINARY REPORT

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ABSTRACT

Introduction: The pathophysiology of COVID-19 is evolving. We investigated self-reported sudden loss of sense of smell and taste, and otologic disorders among COVID-19 patients.

Methods: This was a case-control olfaction, gustation and otology study of COVID-19 RT-PCR tested adults. The study took place at the isolation centres for COVID-19 positive individuals in Abuja and Ibadan, among the epicentres of the disease in Nigeria. The participants were 46 COVID-19 positive adults and 46 COVID-19 negative adults. They responded to a validated online questionnaire-based on olfactory, gustatory and auditory loss. Chi-square tests and correlation analysis was done. Level of significance was at P<0.05.

Results: Among cases, sudden loss of smell, taste and hearing were reported by 14 (30.4%), 8 (17.4%) and 5 (10.9%) cases respectively during the COVID-19 infection. First symptom was loss of smell in 7 (15.2%) and loss of taste in 2 (4.3%) cases. The controls did not present with any of the symptoms. There was no significant correlation between loss of smell and age (r = 0.023, p=0.879); sex (r = -0.132, p=0.382) and co-morbidities (r = -0.028, p = 0.857). Similarly, there was no significant correlation between loss of taste and age (r = 0.052, p = 0.732); sex (0.040, p = 0.792) and co-morbidities (r = -0.014, p = 0.925).

Conclusion: Sudden loss of smell and taste are commoner among COVID-19 positive adults than those without the infection in Nigeria. There is evidence of associated reduction in hearing acuity but further study with objective audiometric testing is recommended.

Keywords: Anosmia, Ageusia, Coronavirus, Chemosensory dysfunction, Hearing loss, Otology, COVID-19 pandemic, SARS-CoV-2

INTRODUCTION

Corona virus disease-2019 (COVID-19) is an RNA-viral syncytial respiratory disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). COVID-19 was first reported in Wuhan, China at the twilight of 2019 and declared a pandemic by the World Health Organisation (WHO) in March 2020. The epidemiology and management of this illness is still evolving resulting in the recent recognition of smell and taste disorders as "minor" clinical presentations in COVID-19 patients by the WHO, Centres for Disease Control and Prevention (CDC) and other global health organizations.[1]

Coronavirus is a highly virulent and contagious organism with an incubation period of about 2 weeks within which asymptomatic patients can transmit the disease. It is difficult to identify carriers and asymptomatic patients during the incubation period hence the prescribed stringent measures such as social distancing, hand washing, wearing of face masks, etc. to prevent, control, and contain its spread.[2]

Common symptoms of COVID-19 were fever, difficulty with breathing and cough. Early presentations with loss of smell (anosmia) and/or taste (ageusia) in mild and moderate cases of COVID-19 could be a red-flag and veritable tool for early diagnosis.[3] It is true that several diseases caused by viruses such as Herpes Simplex, Rhinoviruses, Measles, Epstein-Barr, Chicken pox and other Coronaviruses present with

varying degrees of anosmia, rhinorrhoea and nasal blockage.[4,5] Sometimes these triad is associated with ageusia. However, the anosmia and ageusia associated with COVID-19 is typically without rhinorrhoea or nasal blockage.[6] In addition, patients with COVID-19 have more than 10-fold chance of developing ageusia and anosmia compared to other flu-like diseases.[7] Variable reports on anosmia and ageusia in COVID-19 patients were documented in different parts of the world with the exception of Africa.[3,5-9]

SARS-CoV-2 infects human through the nasal cavity, oral cavity and conjunctiva. The respiratory epithelium and its supporting olfactory cells are rich in Angiotensin Converting Enzyme-2 (ACE2). This feature makes them serve as reservoir for the replication of the SARS-COV-2 virus because the spike (S) proteins on their cell walls called protease transaminase protease serine-2 (TMPRSS2) have strong affinity for ACE2.[3] This interaction initiates an inflammatory process in the olfactory and respiratory epithelium. Contiguous anatomical relationship and similarity in the epithelial cells of the nasal cavities/nasopharynx, the Eustachian tube and the middle ear strongly suggest a middle ear cleft susceptibility to COVID-19. Above all, SARS-COV-2 has been isolated in the middle ear spaces and mastoid cavities of COVID-19 patients.[10] The exact pathophysiology of loss of smell and taste in COVID-19 is not known. However, nasal mucosa inflammation, damage to olfactory receptors and infection of the olfactory bulb, nerve and smell centre in the brain have been suggested as the possible mechanisms.[11-13] Any or all of these three mechanisms may be possible for loss of smell and by extension taste in the COVID-19 though subject to further investigation. To the best of our knowledge, there has not been any clinical report on otologic manifestations of COVID-19 at the time of design of this research. To this end, we set out to explore the features of self-reported anosmia, ageusia and otological disorders among COVID-19 patients.

METHODS

This was a case-control olfaction, gustation and otology study of COVID-19 tested patients using real-time reverse transcription polymerase chain reaction (RT-PCR). Test cases were COVID-19 positive patients and controls were COVID-19 negative contacts. Criteria for testing by the test centres were based on either exhibition of symptoms or contact with a COVID-19 positive patient. The test centres were in Abuja which is one of the epicentres of the disease in Nigeria and Ibadan. Contact details of the participants who had undergone COVID-19 testing was collected from these centres after obtaining permission from the head of Isolation/Treatment Centre of University of Abuja Teaching Hospital, Gwagwalada and University of Ibadan. Thereafter, participants were contacted via telephone and only those who gave informed consent were recruited into the study. A structured, self-administered questionnaire was sent to them physically through the frontline workers at the centres to obtain their information on socio-demographics, travel history, symptomatology of COVID-19, the first symptom manifested and its duration, presence of loss of smell, taste, hearing, as well as medical comorbidities, treatment received, etc. Each participant subjectively graded his/her degree of loss of smell, taste and hearing on a visual analogue scale from 1 to 10. A score of 1 – 3 is regarded as mild, 4 – 7 is regarded as moderate and 8 – 10 is regarded as severe.

Data analysis/calculations

An anonymised database was used for analysis. Proportions were compared using Chi-square with Yates' correction or Fisher's exact tests. Normally distributed, continuous variables were compared by Student's t-test for independent group. The relationship between COVID-19 and loss of smell, taste and hearing was analysed using Pearson's correlation Coefficient. Descriptive data was presented and level of significance was determined at $P<0.05$, two-tailed level at 95% Confidence Interval (CI) and correlation coefficient (r).

RESULTS

Sociodemographic characteristics

Forty-six COVID-19 positive adults comprising 25 (54.3%) males and 21 (45.7%) females as well as 46 COVID-19 negative adults comprising 31 (67.4%) males and 15 (32.6%) females completed and returned the questionnaire. The mean age of 37.6±14.8 years in COVID-19 positive adults and 40.2±14.3 years in COVID-19 negative adults was similar. The country of residence in the preceding six months by the participants was shown in table 1; 15 (32.6%) cases had travelled outside Nigeria while all the controls have no abroad travel history. Majority 33(71.7) of the COVID-19 positive adults belong to the high socioeconomic class while only 13(28.3) controls belong to high socioeconomic class (Table 1). Social Classification was based on Oyedeji's Social Classification 2007.[14]

The symptomatology of the COVID-19 positive adults is shown in table 2. Sixteen (34.8%) of them presented with cough and body aches while fever, tiredness and difficulty with breathing were reported by 12 (26.1%), 8 (17.4%) and 4 (8.7%) cases respectively. Loss of smell

Table 1: Socio-demographic variables of the participants

Variables	Participants		Total
	Cases n=46 n (%)	Controls n=46 n (%)	n=92 n (%)
Age	37.6±14.8¥	40.2±14.3¥	
Male	25(54.3)	31(67.4)	56(60.9)
Female	21(45.7)	15(32.6)	36(39.1)
Country of Residence			
Nigeria	31(67.4)	46(100.0)	77(83.7)
UK	8(17.4)	0(0.0)	8(8.7)
USA	4(8.7)	0(0.0)	4(4.3)
Germany	1(2.2)	0(0.0)	1(1.1)
Turkey	1(2.2)	0(0.0)	1(1.1)
China	1(2.2)	0(0.0)	1(1.1)
Socioeconomic status			
High	33(71.7)	13(28.3)	46(50.0)
Middle	12(26.1)	18(39.1)	30(32.6)
Low	1(2.2)	15(32.6)	16(17.4)

¥*Mean±SD*

was reported by 14 (30.4%) and loss of taste was reported by 8 (17.4%) cases. The controls did not present with any of the symptoms in table 2.

The first symptom manifested by the cases was shown in table 3. Seven (15.2%) cases have either sudden loss of smell or cough as their first symptom. Fever was the first symptom in 6 (13%) cases, tiredness and sudden loss of taste were reported as first symptom in 2 (4.3%) cases.

Table 2: Clinical characteristics of the COVID-19 positive adults

Symptoms	Frequency(N=46)	Percent
Cough	16	34.8
Body aches Sudden	16	34.8
loss of smell Fever	14	30.4
Abdominal pain	12	26.1
Sudden loss of taste	11	23.9
Tiredness Loss	8	17.4
of appetite	8	17.4
Headache	6	13
Rhinorrhea	5	10.9
Difficulty with breathing	5	10.9
Chest pain	4	8.7
	1	2.2

Table 3: First symptom of COVID-19 as reported by the participant

Symptoms	Frequency (N=46)	Percentage
Sudden loss of smell	7	15.2
Cough	7	15.2
Fever	6	13
Body aches	5	10.9
Headache	4	8.7
Abdominal pain	4	8.7
Loss of appetite	4	8.7
Sudden loss of taste	2	4.3
Tiredness	2	4.3
Chest pain	1	2.2
Rhinorrhea	1	2.2
Difficulty with breathing	1	2.2
No response	2	4.3

Only few respondents reported medical comorbidities. Among the cases, only 2 (4.3%) respondents had history of hypertension while among the controls, 1 (2.2%) was asthmatic and 1 (2.2%) was diabetic.

Prevalence of loss of smell and taste among the participants

Loss of smell was reported by 14 (30.4%) cases while loss of taste was reported by 8 (17.4%) cases. None of the controls reported loss of smell or taste (Table 2). There was a significant difference between cases and controls in the loss of smell (<0.001) and taste (0.006). Among the cases, there was no significant correlation between loss of smell and age (r = 0.023, p=0.879); sex (r = -0.132, p=0.382) and co-morbidities

Table 4: Subjective rating of perception of smell, taste and hearing before and after COVID-19 infection

	Subjective rating of perception of sense of smell before diagnosis of COVID-19	Subjective rating of perception of sense of smell after diagnosis of COVID-19	Subjective rating of perception of sense of taste before diagnosis of COVID-19	Subjective rating of perception of sense of taste after diagnosis of COVID-19	Subjective rating of hearing acuity before diagnosis of COVID-19	Subjective rating of hearing acuity after diagnosis of COVID-19
Mean	7.86	6.08	8.92	6.90	7.6	7.2
Median	8.00	7.00	10.00	7.00	6	7
Mode	10	7	10	10	10	10
Std. Deviation	2.110	3.106	1.768	3.113	2.3	2.3

Table 5: Status of the sense of smell of COVID-19 positive adults

Progress of your sense of smell	Current COVID-19 status of participants				
	Active (n=15)	Recovering (n=14)	Recovered (n=4)	No response (n=13)	Tot
Improving	11	3	1	3	
Worsening	1	1	0	1	
No change	1	5	0	1	
No response	2	5	3	8	

**Recovering cases refer to COVID-19 positive cases whose symptoms are abating*
***Recovered cases are COVID-19 positive patients who have turned asymptomatic.*

Table 6: Status of the sense of taste of COVID-19 positive adults

Progress of your sense of taste	Current COVID-19 status of participants				
	Active (n=15)	Recovering(n=14)	Recovered(n=4)	No response (n=13)	Tot
Improving	6	3	0	0	
Worsening	0	2	0	2	
No change	6	5	2	3	
Resolved	2	2	2	0	
No response	1	2	0	8	

**Recovering cases refer to COVID-19 positive cases whose symptoms are abating*
***Recovered cases are COVID-19 positive patients who have turned asymptomatic*

(r = - 0.028, p = 0.0.857). Similarly, there was no significant correlation between loss of taste and age (r = 0.052, p = 0.732); sex (0.040, p = 0.792) and co-morbidities (r = -0.014, p = 0.925).

Only reduction in hearing acuity was reported by five (10.9%) cases during infection but none of the controls had otologic symptoms.

Table 4 showed the descriptive statistics of the cases' subjective rating of their perception of smell, taste and hearing before and after COVID-19 diagnosis There was an observed reduction in the mean score of their perception of smell, taste and hearing acuity after infection.

The status of sense of smell and taste as at the time of data collection was obtained from all the participants and shown in table 5 and table 6 respectively. There were 15 active cases, 14 recovering and 4 recovered COVID-19 cases.

DISCUSSION

In this present study, our observation showed that the COVID-19 infection in Nigeria has affected both genders without bias, which is similar to what had been

reported in the literature from other countries. The countries visited by the cases are locations where the burden of the disease is high.[14-16] To avoid transnational or transcontinental transmission during the pandemic international travels were banned to curtail spread. Nonetheless, the cases which had already entered the country unnoticed led to the surge observed in the community. In this present study, 32.6% of cases migrated to Nigeria during the pandemic. About three quarters of the cases belong to the high socioeconomic class (Table 1). This is the class that can afford overseas travels for tourism, vacation, health, conference attendance etc. It is the reason for the erroneous belief that COVID-19 is a disease of the rich hence the uninformed hardly adhere and comply with the measures put in place by health workers and government to curtail spread of the infection. This might have also contributed to the increase in new cases being identified and reported in Nigeria. The study has shown that COVID-19 also affected those in lower socioeconomic class (48.1%) thereby nullifying this belief (Table 1).

The symptomatology of COVID-19 (Tables 2-4) observed is similar to what had been reported in the literature.[3,17] The nasal cavities and oropharynx are the common portal of entry for SARS-COV-2 into the human body.[3] The interaction of the spike protein on the cell surface of the virus called protease transaminase protease serine 2 (TMPRSS2) and the Angiotensin Converting Enzyme 2 (ACE2 protein) receptor, which are abundantly expressed on the respiratory epithelium and its supporting olfactory cells in the nose allowed their adaptation, multiplication, invasion and propagation.[18,19] This partly explains the pathogenesis of the loss of smell in COVID-19 positive individuals. Patients with loss of smell usually complain of loss in taste. This is due to loss in contribution of smell to their perception of flavour. This hypothesis is implied in this report since there was no reported solitary case of loss of taste unlike loss of smell (Table 2 and 3). One could argue that taste loss in COVID-19 is due to smell loss rather than true pathologic taste loss as earlier posited by Fasunla and Ibekwe.[3] This evidence could explain the underlying pathogenetic mechanism of smell and taste loss in COVID-19. Underlying medical comorbidities have been shown to worsen the clinical course of COVID-19 by rapidly increasing the disease progression, making it to be more severe and often leading to death. In this study, there was no significant correlation between loss of smell or taste with medical comorbidities.[20]

The prevalence of loss of smell in this study is 30.4%. Meta-analysis done by Tong *et al.*[14] and Costa *et al.*[15] on loss of smell among COVID-19 positive individuals reported pooled prevalence of olfactory dysfunction to be 52.73% and 60.7% respectively. The actual proportion of COVID-19 positive individuals that reported olfactory dysfunction in the studies used for the metanalysis ranged from 5.1% by Mao *et al.*[21] to 98.3% from Moein *et al.*[22] Table 4 showed a decrease in the mean of subjective rating of smell perception by the participants. Sudden loss of smell was the first symptom developed by about one-third of the participants making it an important marker or screening tool during COVID-19 pandemic. Individuals with symptom of sudden loss of smell could self-isolate before availability of RT-PCR result to prevent COVID-19 transmission. Sense of smell plays a significant role in the enjoyment of food aroma, and also warns against danger especially with burnt cables, environment or spoilt food. In addition it plays a vital role in our sexuality and emotions. Loss of sense of smell has been demonstrated to affect adversely the quality of life of an individual.[23] The symptom may further worsen the wellbeing of COVID-19 positive individuals. Although the risk of developing loss of smell has been reported to increase with age[24], there was no significant correlation between loss of smell and age of COVID-19 positive adults.

The prevalence of loss of taste in this present study is 17.4%. The prevalence of loss of taste among COVID-19 positive individuals from different regions of the world ranged from 5.6% by Mao *et al.*[21] to 88.8% by Lechien *et al.*[8] Table 4 showed a decrease in the mean of subjective rating of taste perception by the participants. Optimal taste sensation is important in food enjoyment and compliance with medication which are essential in developing good immunity and satisfactory treatment outcomes. The wide range of proportion of COVID-19 positive individuals presenting with smell and taste loss from different studies might be related to different sample size and study designs. Olfactory training in those with loss of smell might also improve loss of taste as both have been shown to have a direct relationship.[25] This will also improve their wellbeing and quality of life.

Otologic symptom has not been documented among COVID-19 positive adults as at the time of our study. One could hypothesise that inflammation of the nasal mucosa caused by its invasion by SARS-COV-2 could spread through the eustachian tube to affect the middle ear with resultant middle ear pathology leading to otologic symptoms. About 11% of the COVID-19 positive adults reported reduction in perception of sound during the infection. In addition, Table 4 showed a decrease in the mean of subjective rating of hearing

acuity by the participants. The above finding is supported by a recent autopsy finding in two out of three deceased confirmed COVID-19 patients in the US, where SARS-COV-virus-2 was isolated in the middle ear and mastoid cavities.[10] The inflammatory process within the middle ear cleft could lead to exudate formation, otitis media with effusion (OME) and mastoiditis leading to conductive hearing loss. The limitation of this present study was the inability to clinically examine their ears for signs of OME and perform auditory test to confirm the reported hearing loss. Similarly, the virus is also known to be neurotropic and could therefore migrate into the inner ear to affect the vestibular or cochlear nerve with resultant hearing loss, tinnitus, dizziness or vertiginous spells. None of the cases presented with vestibular symptoms. The viral RNAs have also been isolated within the cerebrospinal fluid suggesting possible encephalitis which can affect the auditory center leading to a depreciated auditory perception.[26] It would have been better if this can be determined objectively. Further study on the hearing health of COVID-19 positive adults involving larger population and use of an objective audiological assessment method is hereby suggested.

CONCLUSION

Sudden loss of smell and taste are commoner among COVID-19 positive adults than those without the infection in Nigeria. There is an evidence of associated reduction in hearing acuity but further study with objective audiometric testing is recommended. Therefore, we recommend inclusion of sudden loss of smell and taste in the list of screening tools for identification of individuals with COVID-19 infection especially in sub-Saharan African where laboratory COVID-19 testing is still a challenge. Individuals with symptoms of sudden loss of smell and/or taste should be advised, as a matter of public health policy, to self-isolate prior to availability of RT-PCR result to prevent COVID-19 transmission in the community.

What is already known on the topic

- Loss of smell and taste has been reported among COVID-19 patients.
- They were either known to be first symptom or part of the clinical presentations of individuals with positive COVID-19 test result.
- Footprint of SARS-CoV-2 found within the middle ear mucosal specimen of COVID-19 patients

What this study adds

- To the best of our knowledge, it is the first scientific study on chemosensory function among COVID-19 positive individuals in Sub-Saharan Africa.
- Loss of smell and taste were also reported as first symptoms by some of these patients supporting the previous report.
- It also points to the possible involvement of the middle ear cleft by coronavirus infection which has been sparsely reported.

Competing interest

The authors declare no competing interest

Authors' contributions

(FAJ) Fasunla AJ was involved in the study design, data analysis & interpretation and drafting of the manuscript and final approval of the manuscript.
(TY) Thairu Y was involved in data collection, analysis and interpretation of results, manuscript review and correction as well as the final approval.
(SH) Salami H was involved in the data collection and analysis, manuscript review for contribution to knowledge and correction as well as the final approval.
(ITS) Ibekwe TS was involved in the study conception and design, data collection and analysis, manuscript review and correction for intellectual scientific knowledge as well as the final approval of the manuscript.

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