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ORIGINAL PAPER

Ear/Nose/Throat

Clinical, sinonasal, and long-term smell and taste outcomes in mildly symptomatic COVID-19 patients

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Abstract

Introduction: Coronavirus 2019 disease (COVID-19) has variable clinical, sinonasal, and smell/taste outcomes.

Methods: Observational study was conducted at a tertiary hospital in Amman, Jordan. Demographic data, clinical presentation and smoking status were collected. Sinonasal symptoms, using Sino-Nasal Outcome Test (SNOT-22) Questionnaire, were evaluated. Smell/taste dysfunction was followed for three months.

Results: Ninety-Seven patients had satisfactory responses. Eighty-six patients were symptomatic (41 at presentation, and 45 during admission). Among those patients, 59.3% had cough, 52.3% sore throat and 48.8% fever. The most common initial symptom was sore throat. Shortness of breath and smell/taste dysfunction were significantly higher in females. Surprisingly, shortness of breath was more common in non-smokers. Smell/taste dysfunction affected 25.6% of patients, but was the first symptom in only one patient. Fourteen of 22 symptoms in SNOT-22 had significant increase. The overall average of symptoms scores increased from 0.472 to 1.034, with smell/taste dysfunction to have the most increment. The latter symptom recovered completely in 81% and dysgeusia developed in 9.5% at three months, and it recovered completely in all patients at six months.

Conclusion: Although COVID-19 may produce severe lower airways disease, it has modest effect on nose and paranasal sinuses. Moreover, smell/taste dysfunction is a prominent symptom, but it usually recovers dramatically.

What's known

- Coronavirus 2019 disease (COVID-19) has variable clinical, sinonasal, and smell/taste outcomes
- As the virus is transmitted from human to human by contact and droplets, sinonasal presentation can occur, with the smell and taste dysfunction being the most prominent symptoms.

What's new

• This is the first clinical study in Jordan that was conducted to recognise the most common presenting symptoms in our patients, focus on the sinonasal symptoms and analyse the severity of different rhinologic symptoms in affected patients.

 Long-term follow-up of the smell and/or taste dysfunction showed complete recovery in all affected patients within 6 months.

1 | INTRODUCTION

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A novel coronavirus caused an epidemic of severe acute respiratory syndrome (SARS) in humans in Wuhan, China on December 12, 2019, and is of probable bat origin.¹ It was officially named SARScoronavirus 2 (SARS-CoV-2), and the disease was called coronavirus disease 2019 (COVID-19). The World Health Organization (WHO) on March 11, 2020, has declared the novel coronavirus (COVID-19) outbreak a global pandemic.²

Coronaviruses are enveloped positive strand RNA viruses.^{3,4} Six coronavirus species are known to cause human disease. Four viruses, 229E, OC43, NL63 and HKU1, usually cause common cold symptoms in immunocompetent individuals. The two other strains, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are zoonotic in origin and can sometimes be fatal.^{5,6} The 2019 novel coronavirus (2019-nCoV) is the seventh member of the family of coronaviruses that infect humans.⁶

SARS, MERS and COVID-19 infections commonly present with fever and cough, which frequently lead to lower respiratory tract disease with poor clinical outcomes associated with older age and underlying health conditions. World Health Organization (WHO) reported 62 195 274 confirmed cases of COVID-19, and 1 453 355 deaths by the end of November, 2020 globally.⁷ This results in mortality rate of 2.34%. In comparison to SARS-CoV and MERS-CoV, it has less fatality rate but higher speed of spread.⁸

Confirmation of infection requires nucleic acid testing of respiratory tract samples (eg nasal and throat swabs), but clinical diagnosis may be made based on symptoms, exposures and chest imaging.^{9,10} However, COVID-19 disease can present as asymptomatic carriage, acute respiratory distress and pneumonia.¹¹ Asymptomatic patients can spread the virus, and careful monitoring of the natural course of the disease and contact history may only identify them. It is unknown whether these patients are only asymptomatic initially after contracting the disease or they are asymptomatic throughout the course of the disease.⁸

Although the virus is transmitted from human to human by contact and droplets,^{8,12} few sinonasal symptoms are documented, including nasal congestion and smell/taste changes.^{13,14} Nasal congestion developed in up to 4.8%.¹⁵ Earlier data showed loss of smell as a key symptom that occurred in 5%-70% of patients.^{14,16}

This is the first clinical study in Jordan that was conducted to recognise the most common presenting symptoms in our patients, focus on the sinonasal symptoms and analyse the severity of different rhinologic symptoms in affected patients.

2 | METHODS

2.1 | Study participants

This is an observational study that included 116 consecutive patients who were admitted to Prince Hamza Hospital (PHH), a tertiary centre that is affiliated to Hashemite University, and it was designated to be the major COVID-19 centre in Amman, Jordan. Patients who were positive by real-time reverse transcription Polymerase Chain Reaction (RT-PCR) nasopharyngeal swab test were admitted to the hospital for isolation regardless of their symptom status. Exclusion criteria were patients at Intensive Care Unit (ICU) and paediatric patients less than 10 years of age; as they would not be able to answer the questions and fill the questionnaire. The data were collected between March 26 and March 28, 2020.

2.2 | Study design

Demographic data, including age and gender, were collected. Smoking status, type of smoking (eg cigarette, shisha, e-cigarettes), amount and duration were all assessed. Admission variables such as days from RT-PCR and the reason for the test were documented. The latter was categorised into "Developed symptoms", "Travel from abroad", "Was in contact with COVID-19 positive person" and "Other reason".

The patients self-reported different symptoms, such as fever, sore throat, dry cough, wet cough, shortness of breath and others. In addition, the first symptom that the patient felt was documented. Furthermore, the symptoms were arranged in chronological order as recalled by the patient. The patients' preference regarding isolation was requested as "Hospital isolation", "Home isolation" and "Others".

Sinonasal symptoms were documented by the patients using Sino-Nasal Outcome Test (SNOT-22) Questionnaire was used as a platform. It is a valid outcome measure for patients with rhinosinusitis; it describes the health burden and is sensitive to clinical change.^{17,18} In this test, each of the 22 symptoms was graded according to severity into "0" for "No Problem", "1" for "Very Mild Problem", "2" for "Mild or Slight Problem", "3" for "Moderate Problem", "4" for "Severe Problem" and "5" for "Problem as bad as it can be". A validated Arabic form was used.¹⁹ Each patient filled out two copies of the questionnaire; one for the symptoms during COVID-19 disease, and one form represented the symptoms within a year before COVID-19. Furthermore, patients who reported smell/taste dysfunction were followed at 6 weeks by phone call, and those who were partially recovered were contacted after 3 months and 6 months by phone.

2.3 | Ethical approval and statistics

Institutional Review Boards (IRB) approval was obtained from Prince Hamza Hospital (Approval Code 5/2019/2020). The study was conducted in accordance with the Declaration of Helsinki. Data were analysed using IBM SPSS version 24. Data were described using percentages. In addition, Chi-square test was used, and results were considered statistically significant when the P value was <.05.

3 | RESULTS

3.1 | Characteristics of participants

A total of 116 patients were invited to participate in the study. Of those, 97 (83.6%) patients (51 men and 46 women) agreed to participate in the study and completed the study questionnaires. Their age ranged between 12 and 74 years, with median of 38 years in males and 34 years in females. Patients were interviewed within 1-14 days of the diagnosis (median of four days).

Of the 95 patients who responded to isolation preference, 43.2% preferred hospital isolation, 51.6% preferred home isolation and 4.2% preferred other options (eg hotel isolation). Any smoking status was considered as "smoker". About 56.9% of males were smokers compared to only 23.9% in females (P = .002).

The reason for undergoing RT-PCR test was "developed symptoms" in 15 (15.5%) patients, travelled from abroad in 16 (16.5%) patients, was in contact with COVID-19 positive person in 33 (34%) patients, and other reason such in 6 (6.2%) patients, and combined responses in 27 (27.8%) patients. In total, 41 (42.3%) patients had symptoms at time of RT-PCR.

Although only 41 (42.3%) patients had symptoms at time of RT-PCR, 45 (46.4%) patients developed symptoms later during the admission. The rest (11.3%) did not report any symptoms.

The symptomatic and non-symptomatic groups were compared at time of RT-PCR and also at the time of study, and were not significantly different in gender and smoking status distributions at both times.

3.2 | General symptoms

The most common first single symptom was sore throat (26.7%), followed by fever (22.1%) and cough (9%) (Table 1). However, the symptoms distribution changed with hospitalisation course. Cough affected (59.3%) of patients (without sputum in 32.6%, and with sputum in 26.7%), followed by sore throat (52.3%), and fever (48.8%) among overall symptomatic patients (Table 2). Smell/taste dysfunction was the first symptom in only one patient, while it occurred in 25.6% of overall symptomatic patients. Among those who developed smell/taste dysfunction, 63.6% were younger than 40 years, and 68.2% were females.

Of all symptoms, shortness of breath and smell/taste dysfunction were significantly more common in females compared to males **TABLE 1** The relative frequency of the first symptoms reported by symptomatic patients (N = 86)

Symptom	Ν	%
Sore throat	23	26.7
Fever	19	22.1
Cough	8	9.3
Arthralgia/Myalgia	6	7
Fatigue	5	5.8
Rhinorrhea	4	4.7
Chills	2	2.3
Shortness of breath	1	1.2
Nasal congestion	1	1.2
Smell/taste dysfunction	1	1.2
Combined symptoms	16	18.6

(37% in females vs 13.7% in males, P = .015 and 32.6% in females vs 13.7% in males, P = .048, respectively).

Considering smoking status, shortness of breath was more common among non-smokers (33.3% in non-smokers vs 12.5% in smokers, P = .035). None of other symptoms differed between smokers and non-smokers significantly. Of the 40 smoker patients, nine developed dry cough and eight had wet cough. There was no significant difference regarding dry cough (P = .351) and wet cough (P = .633) between smokers and non-smokers.

When patients aged "less than 40 years" (n = 55) were compared to patients "40 years and above" (n = 42), gender difference was not significant (P = .321). In the latter group, males were more smokers than females (64% vs. 11.8%, P = .002). In addition, symptom development was not significantly different between both age groups at time of RT-PCR (38.2% younger group vs older group 47.6%, P = .469, respectively) and at time of study (85.5% younger group vs 92.9% older group, P = .414, respectively). Although females were fairly more likely, but not significantly, to have symptoms than males in patients less than 40 years at time of RT-PCR (51.7% vs 23.1%, P = .057), both genders did not otherwise differ significantly for symptom development.

3.3 | Sinonasal symptoms

SNOT-22 Questionnaire showed increased average values of all the symptoms during the COVID-19 disease compared to same symptoms 'within a year before COVID-19'. The difference in the severity of symptoms between the two time periods was significant (P < .05) for the following symptoms: cough, postnasal discharge, dizziness, decreased sense of smell/taste, difficulty falling asleep, wake up at night, lack of a good night's sleep, wake up tired, fatigue, reduced productivity, reduced concentration, frustrated/restless/irritable, sad and embarrassed. Amongst all, 'decreased sense of smell/taste' was the main symptom to increase (Table 3).

Although smokers had more severe symptoms in both time periods, same trend in symptoms severity difference was found;

TABLE 2	The relative frequency of the symptoms reported by		
patients who developed symptoms ($N = 86$)			

Symptom	Ν	%
Cough	51	59.3
Sore throat	45	52.3
Fever	42	48.8
Shortness of breath	24	27.9
Smell/taste dysfunction	22	25.6
Myalgia/arthralgia	17	19.8
Headache	16	18.6
Fatigue	13	15.1
Rhinorrhea	7	8.1
Diarrhea	6	7
Flu-like	6	7
Dizziness	5	5.8
Chest pain	4	4.7
Chills	4	4.7
Nasal congestion	3	3.5
Eye pain	2	2.3
Vomiting	2	2.3
Sweating	2	2.3
Loin pain	1	1.2
Palpitations	1	1.2
Nausea	1	1.2
Sneezing	1	1.2

however, fatigue was the main symptom to increase, followed by 'decreased sense of smell/taste', and then reduced productivity. During the current COVID-19 disease, the symptoms did not change significantly between different smoking habits, except for more ear fullness for the shisha group (P = .023).

3.4 | Smell/taste dysfunction

The patients who reported smell/taste dysfunction were followed at six weeks by phone call. One patient lost to follow-up. This symptom improved in all other patients (n = 21), with complete recovery in 71.4%, and self-reported (50-90) % improvement in the rest (Table 4). Most patients had their smell and taste recovered within two weeks, the shortest was three days. Only one patient needed ICU admission due to decreased oxygen saturation, but she did not require mechanical ventilation, and her condition was stable afterwards. Furthermore, 3-month follow-up was performed for the smell/taste dysfunction "partially recovered" group. Of six patients, two had total recovery, and four patients had better, but incomplete recovery. It is noteworthy to state that two out of the four latter patients developed dysgeusia along with hyposmia. One described the taste as "spicy-like" and the other felt "earth-like" taste. Those four patients were contacted by phone after 6 months of their illness, and all of them had complete recovery of their smell and taste senses.

TABLE 3 The average score (standard deviation) among patients for each symptom of the SNOT-22 Questionnaire. Scores for both periods "During COVID-19" and "Within a year before COVID-19" are presented

Symptom	During COVID-19	Within a year before COVID-19	P-value
Need to blow nose	0.72 (1.151)	0.6 (1.017)	.398
Nasal blockage	1.01 (1.394)	0.73 (1.126)	.095
Sneezing	0.45 (0.817)	0.63 (1.002)	.094
Runny nose	0.57 (1.061)	0.59 (1.004)	.87
Cough	1.35 (1.608)	0.62 (0.952)	<.001 [†]
Post-nasal discharge	1.02 (1.559)	0.43 (0.903)	<.001 [†]
Thick nasal discharge	0.43 (0.940)	0.31 (0.732)	.33
Ear fullness	0.49 (1.220)	0.41 (0.993)	.544
Dizziness	0.89 (1.531)	0.29 (0.735)	.001†
Ear pain	0.4 (1.196)	0.28 (0.731)	.38
Facial pain/pressure	0.18 (0.610)	0.10 (0.337)	.239
Decreased sense of smell/taste	2.04 (2.060)	0.30 (0.827)	<.001 [†]
Difficulty falling asleep	1.41 (1.725)	0.46 (1.047)	<.001 [†]
Wake up at night	1.12 (1.684)	0.49 (1.099)	.002†
Lack of a good night's sleep	1.51 (1.754)	0.67 (1.184)	<.001 [†]
Wake up tired	1.53 (1.741)	0.70 (1.159)	<.001 [†]
Fatigue	1.77 (1.802)	0.68 (1.124)	<.001 [†]
Reduced productivity	1.40 (1.795)	0.42 (0.998)	<.001 [†]
Reduced concentration	1.22 (1.647)	0.40 (0.909)	<.001 [†]
Frustrated/restless/ irritable	1.17 (1.594)	0.66 (1.160)	.003†
Sad	1.34 (1.775)	0.47 (0.954)	<.001 [†]
Embarrassed	0.73 (1.407)	0.14 (0.549)	<.001 [†]

[†]Means significant value (<.05).

4 | DISCUSSION

COVID-19 disease is a worldwide pandemic, Jordan is not an exception. First documented Jordanian case was on March, 2020. We present here the first clinical study in Jordan to describe the common presenting symptoms in non-severe COVID-19 patients, and some variables that affect them. In general, our patients developed

	After 6 weeks (N = 21)		After 3 months (N = 6)		After 6 months (N = 4)	
Variable	Complete recovery	Partial recovery	Complete recovery	Partial recovery	Complete recovery	Partial recovery
Gender						
Males	5	1	1	0	0	0
Females	10	5	1	4	4	0
Smoking						
Yes	6	1	1	0	0	0
No	9	5	1	4	4	0
Age (years)						
<40	10	3	2	1	1	0
≥40	5	3	0	3	3	0

TABLE 4Smell/taste dysfunctionprogression after 6 weeks, 3 months and6 months of the COVID-19 disease

fever, cough, and sore throat as common symptoms. Females and non-smokers interestingly were more prone to some symptoms. Among sinonasal symptoms, smell/taste dysfunction was the most prominent. Although females younger than 40 years were fairly, but not significantly, more likely to have symptoms at presentation (P = .057), both genders would be symptomatically similar with disease progression.

In the study sample, only 42.3% had symptoms at time of RT-PCR; however, 88.7% were symptomatic at time of data collection. This indicates that there is high risk of being carrier to the virus despite having no symptoms, which increases the risk of transmissibility. Furthermore, most patients develop symptoms over the course of the disease. As the virus can be present in 63% of nasal swabs and 32% of pharyngeal swabs of affected patients,²⁰ and knowing that the viral load can be similar in both asymptomatic and symptomatic patients,²¹ healthcare providers that deal with nasal and oral cavities (eg otolaryngologists, dentists) are at higher risk, and the precautions have to be followed.

The most common presenting symptom was sore throat (26.7%), whereas cough (59.3%), sore throat (52.3%) and fever (48.8%) were the commonest among overall symptoms. A review by Lovato and Filippis showed pooled values of different symptoms, such as 85.6% fever, 68.7% cough, 12.4% sore throat (pharyngodynia).²² In Jordan, all patients get admitted regardless of their symptom status, and this might explain less fever and cough among current subjects. Higher sore throat might indicate higher viral load and, hence, more inflammation in the pharyngeal mucosa early in the disease.

The common cold syndrome has been defined as a short mild illness with early symptoms of headache, sneezing, chilliness and sore throat. Later symptoms of common cold syndrome include nasal discharge, nasal obstruction, cough and malaise. The influenza syndrome is typically of sudden onset and is characterised by fever, headache, cough, sore throat, myalgia, nasal congestion, weakness and loss of appetite.²³ It seems that COVID-19 has much similar presentation as influenza syndrome, but with more lower airway sequelae. However, it has more rate of spread of the infection which is measured by a factor called Basic Reproduction Number (R_o). The influenza virus has an R_{\circ} of ~1.3 whereas the SARS-CoV-2 virus has an R_{\circ} of ~2.3. 24

Although Vardavas and Nikitara found that smoking is most likely associated with the negative progression and adverse outcomes of COVID-19,²⁵ smoking was not associated with more symptoms in general in our study. However, shortness of breath was, surprisingly, more common in non-smokers. Females were significantly less smokers than males (P = .002), and this might explain why women had more shortness of breath. Furthermore, smoking had no effect on sputum production in patients with cough, and wet cough and dry cough were almost similar in both smokers and non-smokers. Although our sample size was small and did not include intubated patients, our findings raise the question about the impact of smoking on non-severe cases.

More than half the patients preferred home isolation, as they had mild symptoms, more anxiety and less quality of sleep at hospital, and they can take care of offspring better at home. In contrast, those who preferred hospital isolation wanted to protect their close unaffected contacts and were feeling safer under direct medical supervision. The right answer should be tailored to each country's capabilities and needs, and probably to the overall numbers, severe cases, ICU admissions, and mortality rate.

Despite the fact that SNOT-22 questionnaire was devised to evaluate the social and emotional consequences of chronic rhinosinusitis, we used it in this study to quantitatively assess the severity of different sinonasal symptoms. Statistically, 14 of the 22 symptoms increased significantly. However, the average score of all symptoms increased only from 0.472 to 1.034, and 'decreased sense of smell/taste' was the most to change. Furthermore, in smoker subpopulation, same trend in symptoms severity change was found, and the overall symptom score increased from 0.64 to 1.552. Fatigue was the main symptom to change, followed by 'decreased sense of smell/taste', and then reduced productivity. These findings suggest that COVID-19 disease, apart from smell/ taste dysfunction, has mild sinonasal presentation. Moreover, ear fullness was more in shisha smokers, possibly due to Eustachian tube dysfunction.

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It has been suggested that anosmia and ageusia are common findings in COVID-19,¹³ and that smell dysfunction can be considered a biomarker.²⁶ In their study, Spinato et al found smell/taste dysfunction affected 64.4% of their patients, and it was the only or initial symptom in 14.9%.²⁷ In contrary, only one patient (1%) presented with smell/taste dysfunction initially in our study. Nevertheless, 25.6% of patient complained of smell/taste dysfunction later on, suggesting that it is not necessary to have this symptom at first presentation. Despite that, the authors agree with the trend of considering this symptom as part of the screening symptoms in ambulatory individuals with influenza-like symptoms.²⁸ In addition, it should not be considered as a prominent feature of the disease; as the prevalence of olfactory disorders caused by upper respiratory tract infection (URTI is stated to be as high as 11-40%,²⁹ and the culprit viruses may include parainfluenza virus type 3, herpes simplex virus type 1, corona mouse hepatitis virus and rabies virus. The olfactory dysfunction is likely due to direct damage to peripheral epithelium, while the effect on central olfactory pathways cannot be ruled out.²⁹

The relationship of olfaction with sex hormones is significant.³⁰ Women are known to have a lower threshold than men in smell identification and detection. This matches our results; as females had significantly more smell/taste dysfunction. Although chronic cigarette smoking was associated with increased odds of self-reported olfactory alterations, directly and indirectly via olfactory-related pathologies,³¹ no difference was found between smokers and non-smokers in our study (P = .377). This could be due to small sample size.

Whether olfactory dysfunction during COVID-19 is part of neurological disease or a sinonasal disorder remains a question. According to Butowt and Bilinska, respiratory epithelial cells express both SARS-CoV-2 human proteins required for host cell entry, namely, Angiotensin Converting Enzyme 2 (ACE2) and TRMPSS2 transmembrane proteases, which will facilitate SARS-CoV-2 binding, replication and accumulation. Furthermore, neuronal and non-neuronal expression of host receptors might act like a nasal cavity olfactory epithelium reservoir and olfactory nerve route of transport.³² It has been reported that by using nasal cytology the only modification evidenced in samples of COVID-19 patients was a partial rarefaction of the hyperchromatic supranuclear stria.³³ However, disruption of sensorineural pathways could affect smell and taste, as nasal obstruction is relatively uncommon.^{34,35} In addition, Aragao et al reported olfactory bulb microbleeding or abnormal enhancement on magnetic resonance imaging, which could reflect injury.³⁶ These findings and mechanisms need further elaboration in future experimental and clinical studies.

It is still controversial whether smell/taste dysfunction is associated with more severe course of the disease.^{37,38} In our group, smell/ taste dysfunction is unlikely to predict severity of the disease; as only one patient (4.8%) needed ICU admission during the course of the disease. In contrary, this symptom improved dramatically in all patients within six weeks, either completely or partially. These findings are consistent with other studies.^{39,40} Two of the six partially recovered patients developed dysgeusia with less hyposmia after three months, which might be interpreted as either recovery from injury or a neurological deficit. However, it seems that this injury is transient and resolves completely within six months. To the best of our knowledge, this is the longest follow-up of smell/taste dysfunction for the published data until the end of November, 2020. However, further long-term large-scale studies are needed.

5 | CONCLUSIONS

Although COVID-19 affects lower airways mainly, it does affect the nose and paranasal sinuses, but probably in less severe form compared to other viral upper respiratory tract infections. However, smell/taste dysfunction is a prominent symptom that usually recovers dramatically, and its mechanism needs further evaluation. Moreover, studies need to be conducted to investigate the interaction between the virus and smoking, and to further elaborate the clinical presentation in different genders and age groups.

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DISCLOSURES

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Amjed Tarifi: Conceptualisation; Methodology; Investigation; Data curation; Writing-review and editing; Visualisation; Supervision; Project administration. Amjad A. Al Shdaifat: Conceptualisation; Methodology; Data curation; Writing-review and editing; Visualisation; Supervision. Abdel-Ellah M. Al-Shudifat: Methodology; Investigation; Writing-original draft preparation; Supervision. Mohammed Azab: Methodology; Writing-review and editing; Supervision. Ja'far Ismail: Investigation; Data curation; Writing-original draft preparation; Visualisation. Rand Bashir: Investigation; Data curation; Writing-original draft preparation; Visualisation. Aous Amro: Investigation; Data curation; Writing-original draft preparation; Visualisation. Ahmad Altarifi: Conceptualisation; Writing-review and editing. Yousef Khader: Formal analysis; Writing-review and editing. All authors have read and agreed to the published version of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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