ORIGINAL ARTICLES

PHILIPPINE JOURNAL OF OTOLARYNGOLOGY-HEAD AND NECK SURGERY VOL. 37 NO. 2 JULY – DECEMBER 2022

Quality of Life Among SARS-CoV-2 (COVID-19) Positive Patients with Anosmia Using the Short Version Questionnaire of Olfactory Disorders - Negative Statements Translated in Filipino (sQOD-NS Ph)

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ABSTRACT

Objective: To determine the quality of life among SARS-CoV-2 (COVID-19) positive patients with anosmia using the Short Version Questionnaire of Olfactory Disorders - Negative Statements translated in Filipino (sQOD-NS Ph).

Methods:

Design: Cross-Sectional Study

Setting: Tertiary Government Training Hospital

Participants: SARS-CoV-2 (COVID-19) RT-PCR positive patients aged 18 years old and above with COVID-19 symptoms and anosmia in a tertiary government hospital who consulted from March 2020 to August 2021 answered the short version of sQOD-NS Ph.

Results: Out of 108 participants with positive SARS-CoV-2 (COVID-19) RT-PCR test, 72 (66%) presented with anosmia, and sQOD-NS Ph scores ranged from 1 to 21 with a mean of 14.78. Thirty two (44%) encountered problems in eating while 21 (29%) had feelings of isolation due to loss of smell. There was an inverse correlation of -0.478 between recovery time of olfaction and QoL score, hence the longer the recovery time, the lower the QoL score, while the shorter the recovery time, the higher the QoL score ($p < .0001$).

Conclusion: Majority of COVID-19 patients with anosmia had mild or negligible impairment, while a small percentage had impaired quality of life. The low percentage may be due to high number of patients who may have recovered their sense of smell along the course of the disease.

Keywords: *COVID-19; olfaction; anosmia; quality of life; QOD-NS; smell; smell loss*

Olfaction plays an important role in protecting and conserving life. It is involved in food intake, social communication, reproductive behavior, and may influence working abilities.[1] It also helps in the early detection of fire, gas leaks, spoiled food or dangerous fumes. While these may be less important to a person's well-being, olfactory dysfunction may affect the individual's quality of

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Disclosures: The authors signed a disclosure that there are no financial or other (including personal) relationships, intellectual passion, political or religious beliefs, and institutional affiliations that might lead to a conflict of interest.

Presented at the Philippine Society of Otolaryngology Head and Neck Surgery virtual Analytical Contest November 10, 2021.

life (QoL) and functionality.[2] Patients with lost sense of smell showed significant impairment in eating, safety, personal hygiene and sex life.[3] Corollary to this, quality of life, safety issues, interpersonal relations and eating habits are severely altered in patients with olfactory disorders and patients with olfactory loss reported higher level of disability and lower QoL than those who recovered.[1]

Anosmia and dysgeusia have been identified among the many symptoms of COVID-19 infection. Patients who complain of anosmia and flu-like symptoms are more likely to test positive for COVID-19 infection.[4] Studies regarding the prevalence of smell loss and taste alteration in COVID-19 patients have been reported.[5-7] Our previous study showed 95% of patients with anosmia had a positive SARS-CoV-2 (COVID-19) RT-PCR test.[8] Another study found that out of 394 COVID-19 patients, 161 (41%) exhibited sudden olfactory and/or gustatory dysfunction, 66.2% suffered from anosmia and 88.8% reported gustatory disorders.[5] This olfactory dysfunction is believed to ensue from damages inflicted on the olfactory epithelium which prevent odors from binding to olfactory receptors.[9] With the advent of SARS-CoV-2 (COVID-19) infection that may compromise the sense of smell, an evaluation tool translated in Filipino is essential to assess the quality of life of patients affected along the clinical spectrum.

This study aims to determine how having an anosmic condition among SARS-CoV-2 (COVID-19) positive patients impacts the way they live or their quality of life using the Short Version Questionnaire of Olfactory Disorders - Negative Statements translated in Filipino (sQOD-NS Ph).

METHODS

This cross sectional study was approved by the Quezon City General Hospital Bioethics Committee. Patients aged 18 years old and above with symptoms of cough, colds, fever, difficulty of breathing, and anosmia with positive SARS-CoV-2 (COVID-19) RT-PCR test who consulted in COVID-19 tent screening areas or were admitted at the Quezon City General Hospital from July 2021 to August 2021 and who were able to accomplish the questionnaire were considered for inclusion. Patients with COVID-19 symptoms and anosmia with positive SARS-CoV-2 (COVID-19) RT-PCR test in the past who followed up in the study period were also considered. Informed consent was obtained from participants prior to inclusion.

Excluded were patients who had a past history of anosmia prior to the pandemic, those with chronic sinonasal conditions (sinusitis, septal deviation, nasal mass, nasal polyps, history of nasal trauma etc.), neuropsychiatric or mental illnesses and those with critical conditions.

The sample size was computed using a 95% level of confidence. With an estimated proportion of patients with anosmia among COVID-19 patients of 25%, based from the Al-Ani, *et al.*[10] at least 72 patients were needed at 10% error.

$$n = \frac{(z_\alpha)^2\, pq}{e^2}$$

Where:

n = is the number of participants/subjects needed
p = estimated proportion of patients with anosmia among COVID-19 patients = 60%=0.60
q = 1 – p = 1 – 0.60 = 0.40
Zα = 95% confidence level = 1.96
e = error of 10%

With permission for its translation and utilization in Filipino, the short version Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS) composed of a 7-item patient reported outcome questionnaire was translated and certified in Filipino language by the University of the Philippines *Sentro ng Wikang Filipino*. *(Figure 1)*

The sQOD-NS Ph incorporates the following items: 3 – from social subdomain involving impacts on patients' daily activities and feelings of isolation and anger; 2 – from eating subdomain regarding impacts on attending restaurants and food consumption; 1 – from anxiety subdomain inquiring on relaxation; and 1 – from annoyance subdomain involving adapting to changes in olfactory dysfunction. Each item is rated on a scale of 0 to 3, with higher scores reflecting better olfactory-specific QoL while a low score harbors poor QoL due to anosmia. The total score ranges from 0 (severe impact on QoL) to 21 (no impact on QoL).

The short version of the Questionnaire of Olfactory Disorders-Negative Statements translated in Filipino (sQOD-NS Ph) was initially administered to a group of 20 patients with or without anosmia to determine reliability. After Cronbach's alpha was computed, the questionnaire was then administered to SARS COV-2 (COVID-19) positive patients with anosmia.

Data on demographics (age, sex), date of COVID-19 diagnosis, signs and symptoms, whether admitted or quarantined at home, duration and recovery from anosmia and SARS-CoV-2 (COVID-19) RT-PCR results (from Department of Health (DOH) - approved testing facilities, the Philippine Genome Center, or St. Luke's Medical Center) were obtained. The questionnaire was administered to participants, assisted by a resident physician if needed. The data and questionnaires were then collated using MS Excel for Mac version 16.13 (Microsoft Corporation, Redmond, WA, USA) and the scores were tabulated and analyzed.

Cronbach's alpha was computed to measure the reliability of

Short version of Questionnaire of Olfactory Disorders-Negative Statements ***Maikling bersiyon ng kuwestiyonaryo ng Olfactory Disorders-Negative Statements***	**Agree** *Sumasang-ayon* **(0)**	**Partly Agree** *Sumasang-ayon* **(1)**	**Partly Disagree** *Bahagyang hindi Sumasang-ayon* **(2)**	**Disagree** *Hindi Sumasang-ayon* **(3)**
The changes in my sense of smell make me feel isolated. *Pakiramdam ko nag-iisa ako nang magbago ang aking pang-amoy.*				
Because of the changes in my sense of smell, I have problems with taking part in activities of daily life. *Nagkakaproblema ako sa pang-araw-araw na gawain dahil pagbabago sa aking pang-amoy.*				
The changes in my sense of smell make me feel angry. *Nagagalit ako dahil nagbago ang aking pang-amoy.*				
Because of the changes in my sense of smell. I go to restaurants less often than I used to. *Kumpara noon, bihira na akong pumunta sa mga restawran dahil sa pagbabago sa aking pang-amoy.*				
Because of the changes in my sense of smell, I eat less than I use to or more than I used to. *Mas kaunti o mas marami kaysa dati ang kinakain ko simula nang magbago ang aking pang-amoy.*				
Because of the changes in my sense of smell, I try harder to relax. *Mas sinisikap kong makapagpahinga o makapag-relax nang magbago ang aking pang-amoy.*				
I am worried that I will never get used to the changes in my sense of smell. *Nag-aalala ako na baka hindi ako masanay sa mga pagbabago sa aking pang-amoy.*				

Figure 1. Short Version Questionnaire of Olfactory Disorders - Negative Statements Translated in Filipino (sQOD-NS Ph) *(Original English statements are included for illustration).*

the questionnaire. Descriptive statistics were used to summarize the demographic characteristics of the patients. Frequencies and percentages were used for categorical data and means and standard deviations for normally distributed numerical variables. Spearman rank correlation was used to determine the correlation of the individual items with the over-all response. T-test was used to compare the age of patients according to QOL (impaired or not impaired). Chi-square test was used to compare the proportions. The IBM SPSS Statistics for Windows, Version 26.0, Released 2019 (IBM Corp., Armonk, NY, USA) was used for data processing and analysis.

RESULTS

Out of 108 subjects with positive SARS-CoV-2 (COVID-19) RT-PCR test, 72 (66.6%) presented with anosmia while 36 (33.3%) had normal sense of smell. Their ages ranged from 18 to 69 years with a mean of 35.75 years. Thirty-seven (51.4%) were male and 35 (48.6%) were female. Thirty-five (48.6%) were admitted while 37 (51.4%) were advised to undergo quarantine at home. Other clinical manifestations include fever (52.5%), colds (47.5%) and cough (40%).

Of these 72 SARS-CoV-2 (COVID-19) RT-PCR positive patients with anosmia, 52 (72.2%) recovered olfaction within 1 to 90 days with a mean duration of 7.56 days while 20 (27.8%) had anosmia at the time of enrolment in this study. The time between diagnosis and date of interview ranged from 0 to 490 days with a mean interval period of 73.36 days.

The translated version revealed a Cronbach's alpha of 0.875 which reflects good reliability and internal consistency of the questionnaire. The questionnaire was administered to 72 SARS-CoV-2 (COVID-19) RT-PCR positive patients with anosmia with the following responses: whether changes in their sense of smell made them feel isolated (Q1); 9 (12.5%), 12 (16.7%), 17 (22.2%) and 36 (48.6%), agreed, partly agreed, partly disagreed and disagreed, respectively. With regards to problems with taking part in activities of daily life (Q2); 8 (11.1%), 15 (20.8%), 10 (13.9%) and 39 (54.2%), agreed, partly agreed, partly disagreed and disagreed, respectively. When asked if changes in their sense of smell made them feel angry (Q3); 5 (6.9%) agreed and 9 (12.5%) partly agreed, while 8 (11.1%) and 50 (69.4%) partly disagreed and disagreed, respectively. Because of the changes in their sense of smell, 8 (11.1%) agreed that they went to restaurants less often than they used to (Q4), 5 (6.9%) partly agreed, 19 (26.4%) and 40 (55.6%) partly disagreed and disagreed, respectively. Eighteen (25%) agreed and 14 (19.4%) partly agreed that they ate less than they used to or more than they used to (Q5), while 11 (15.3%) and 29 (40.3%) partly disagreed and disagreed, respectively. When asked if they tried harder to relax because of changes in sense of smell (Q6); 13 (18.1%) each both partly agreed

and disagreed while 8 (11.1%) and 38 (52.8%) agreed and disagreed, respectively. Eight (11.1%) agreed that they were worried that they would never get used to the changes in their sense of smell (Q7), while 35 (48.6%) disagreed, and 14 (19.4%) and 15 (20.8%) partly agreed and partly disagreed, respectively.

Scores ranged from 1 to 21 with a mean of 14.78. Five (6.9%) had a score of 0 – 5, 11 (15.3%) 6 – 10, 17 (23.6%) 11 – 15, and 39 (54.2%) had a score of 16 – 21. A score of less than or equal to 10 reflects impairment in the quality of life comprising of 16 (22.2%), while a score of more than 11, composed of 56 (77.8%) respondents were classified with slight or negligible impairment.

There was no significant difference in the age of respondents ($p = .53$). Likewise, there was no significant difference in the proportion of males and females with impaired QoL ($p = .22$). On the other hand, there was a significant difference in the proportion of respondents with impaired QoL between those who were either admitted or home-quarantined. More respondents who were quarantined had impaired QoL than those who were admitted; 32.4% and 11.4%, respectively ($p = .03$).

Significant correlation was noted between recovery time of olfaction and the over-all QoL score as shown by the correlation coefficient of -0.478 ($p < .0001$). A negative correlation indicates an inverse correlation which means that the longer the recovery time of olfaction, the lower the over-all QoL score, while the shorter the recovery time of olfaction, the higher the over-all QoL score.

DISCUSSION

Our study showed that majority or 78% of SARS-CoV-2 (COVID-19) positive patients with anosmia had minimal or negligible impairment in quality of life, while 22% had impaired quality of life based on the scores of the respondents. In contrast, Lechien reported that COVID-19 patients with olfactory dysfunction had significantly lower scores in sQOD-NS which reflect impairment and deterioration of QoL after the onset of smell loss in 76% of patients.[6] In a study by Elkholi *et al.*, 73% reported negative effects pertaining to awareness to personal hygiene, interest in food, and drinks associated with significant reduction in health-related QoL.[11] Patients with olfactory loss disclosed difficulties in everyday activities and decrease in the quality of life.[12] In our study, problems encountered included eating less than they were used to and feelings of isolation due to loss of smell while only a few reported feelings of anger and going less often to restaurants. Olfactory deprivation becomes a problem if it persists for more than 2 months which may affect QoL. On the other hand 23% of patients with anosmia reported that it was beneficial since they were no longer bothered by unpleasant odors.[11]

There was no significant difference in the proportion of males and females with impaired QoL in our present study. On the contrary, there are reports that females are commonly affected[6,11] and have higher susceptibility to develop olfactory and gustatory dysfunctions.[6] Our current study also revealed that a higher proportion of patients who were advised quarantine at home had impaired quality of life 12 (32.4%) compared to those who were admitted 4 (11.4%). While it appears paradoxical that the quality of life of admitted patients was affected more compared to those advised to be quarantined at home, further investigation into possible reasons is beyond the scope of our study.

Regarding pathophysiology of anosmia, it has been hypothesized that the SARS-Cov2 virus does not directly affect the nerves, but other non-neuronal cells with ACE2 receptors including olfactory epithelium sustentacular cells, microvillar cells, Bowman's gland cells and others.[13]

The prevalence of anosmia in patients with COVID-19 infection ranges from 5 to 26, 32, 35, 48, and 79 percent.[7-8, 14-16] Alega and Cruz reported that 51% (60/117) of COVID-19 positive individuals reported loss of smell[8] while Regalado *et al.* reported an overall prevalence of 71% in a systematic review.[18] The prevalence rate of 66% in our present study is consonant with other reports that anosmia is associated with COVID-19 infection.

With regards to recovery from loss of smell, our present study showed a mean duration of 7.46 days; 52 (72.2%) had resolution of anosmia while 20 (27%) had olfactory dysfunction at the time of enrollment. This is comparable with Lechien who reported recovery of olfaction in 72.6% of patients within 8 days after resolution of the disease.[6] This may be apparent since the viral load decreased within 17 days following the beginning of olfactory dysfunction and complete recovery occurs after two weeks.[16, 19] The sense of smell improved in 28 and 21 days, with 98% and 79% recovering, according to Klopfenstein and Hopkins, respectively.[20, 21] In another study, the mean duration was 8 days in 60% of patients while 39% claimed to have persistence of loss of smell.[4] It may be presumed that the 20 (27%) patients who experienced anosmia during the interview developed infection a few days prior to inclusion in the study, and may have a higher viral load that may compromise olfaction. There was a negative or inverse correlation between recovery time of olfaction and the over-all QoL score which indicates that the longer the recovery time of olfaction, the lower the over-all QoL score or impaired QoL, while the shorter the recovery time of olfaction, the higher the over-all QoL score or less impaired QoL. It is worthwhile to consider Hopkins' observation that olfactory loss in COVID-19 patients is usually severe and abrupt in onset but is only transient or temporary and only about 10% may not recover within a month.[21]

There are other questionnaires dealing with QoL of patients affected by anosmia[12, 22, 23] but they have many items that need a lot

of time to answer and become tedious for respondents. Those written in a foreign language may not be easily understood in the local setting. Locally published olfactory tests and questionnaires dealing with nasal problems include the Sto. Tomas Smell Identification Test (ST-SIT) which uses 45 inhaled odorants,[24] the Nasal Obstruction Symptom Evaluation Scale (Nose-Ph) which addresses severity of nasal obstruction,[25] and the Filipino Sino-Nasal Outcome Test (SNOT 22) that evaluates quality of life in chronic rhinosinusitis.[26] The sQOD-NS Ph may be a valuable addition to evaluation tools dealing with quality of life of patients suffering from anosmia, being validated and translated in Filipino. Our questionnaire was derived from a brief version of the QOD-NS by Mattos to streamline clinical care and research, reducing 17 questions to only 7.[27] The shorter version was developed to increase the response rate and reduce the patient's mental processing when answering the questionnaire. It was translated in Spanish[28] and Italian[6] and was used to investigate impact of olfactory dysfunction on quality of life among COVID-19 patients.[29] The short version was used due to good reliability, ease of answering which requires a short amount of time, and relevance of the 4 subdomains covered.

Limitations of our current study include the lack of objective testing to evaluate olfaction and not performing nasal endoscopy to avoid prolonged exposure and risk of infection. Additional questionnaires dealing with psychological aspects like depression which might influence the perceived QoL in affected individuals in relation to the various domains were not measured. In some participants, the long interval between onset or span of time prior to responding to the questionnaire may have affected memory or recall of the specific time or day when anosmia developed and subsequently resolved. This is a continuous variable that may vary and is beyond our control in a cross-sectional study wherein the impact of a certain disease is observed over a given period. Some may contend that the responses may not be reliable since they may have negative RT-PCR at the time of inclusion in the study because they had infection way back in the past. While this may be so, they were included with a previous positive RT-PCR test for the simple reason that this study aimed to determine if anosmia improves, lingers, or persists afterwards. To our knowledge, there is no gold standard to compare with and evaluation tools or questionnaires for anosmia are varied and arbitrary because respondents' perceptions differ in many aspects and a standardized and universally accepted tool may take time to develop. The sQOD-NS was selected because of the attributes cited earlier and because it was already validated to evaluate anosmia in Covid-19 individuals in earlier studies.[27]

The results of this study are in agreement with the recommendation of other reports that anosmia should be included in the routine screening of COVID-19 patients' health declaration protocol. Patients who develop anosmia after COVID-19 infection can be advised that olfactory dysfunction may improve later. Olfactory retraining programs may help facilitate recovery for those with anosmia. Determination of QoL scores using sQOD-NS Ph or other questionnaires may be performed before and after recovery for comparison in future studies. Since the sQOD-NS Ph was not solely developed for patients with COVID-19 infection, the questionnaire may be used in clinic or other research settings to determine quality of life of patients with anosmia in general.

In summary, our study revealed a high prevalence of anosmia in confirmed COVID-19 patients in consonance with other reports[6-8, 17-18] with a good percentage of patients recovering from anosmia spontaneously. The majority of COVID-19 patients with anosmia had minimal or negligible impairment, while a small percentage had impaired quality of life. The low percentage of patients with impaired QoL may be due to high number of patients who may have recovered their sense of smell along the course of the disease.

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