ABSTRACT

Objective: To determine the relationship between olfactory function threshold and quality of life (QOL) among adult Filipinos with perceived olfactory dysfunction (OD).

Methods:

Design: Cross-sectional Study
Setting: Tertiary Government Training Hospital
Participants: 98 adults who had self-perceived olfactory dysfunction described as "poor" or "no sense" of smell

Results: We analyzed data from 98 participants, with a mean age of 35.91 ± 12.58 years old, composed of 46 men (47%) and 52 women (53%), with 82 normosmic, six hyposmic and ten anosmic as categorized by their BTT scores. Twenty-seven percent (27%) identified themselves as having poor QOL based on Fil 17 QODNS. Differences were exhibited between sexes' BTT scores - [t(96) = -2.32; p = .022; females, M: 9.25; SD: 2.33 vs. males, M: 7.76; SD: 3.91], civil status - Fil17QODNS scores [t(96)= 3.05, p < .003; married M: 11.72, SD: 13.74 vs. single, M: 4.71; SD: 8.66], and the presence of ENT symptoms BTT [t(96) = -7.15; p < .0001; symptomatic, M: 5.62; SD: 4.54, vs. asymptomatic, M: 9.78; SD: 1.14] and Fil 17 QODNS scores [t(96) = 3.94; P < .00001; symptomatic, M: 14.86; SD: 13.97] vs. asymptomatic, M: 5.217; SD: 9.60]. Significant risk factors were the presence of ENT symptoms [OR= 0.15; 95% CI: 0.02-0.97; P = .046] for poor smell threshold, and comorbidities [OR= 3.36; 95% CI: 1.04-10.85; P = .043] for poor QOL. A negative correlation was observed between Fil-QOD-NS scores and BTT scores [r = -0.477, p < .001; r_s = -0.292, p = .004], signifying that the presence of olfactory dysfunction has an inverse relationship with the quality of life.
Conclusion: Individuals with olfactory dysfunction in this study population had poor quality of life as determined by the translated Filipino 17-item QOD-NS which has an inverse relationship with their smell threshold as represented by the BTT results. Among the factors studied, significant differences were found between sexes, civil status and presence of ENT symptoms in the BTT and Fil 17 QODNS scores. However, only presence of comorbidities and ENT symptoms are significant risk factors for quality of life and smell threshold, respectively, in this population.

Keywords: olfactory dysfunction, threshold, smell; quality of life; QOD-NS, BTT

The human olfactory sense is least studied among the senses. There are not many translational researches concerning it but the need becomes apparent once it is lost or malfunctions. The sense of olfaction evolved as an important element in identification of objects and potential threats into a crucial part in the social and emotional aspects of a person's well-being. Studies have shown links between olfactory dysfunction (OD) to different negative emotional states including mood changes, decreased appetite, reduced pleasure and, at the end of the spectrum, psychological disorders such as anxiety and depression. The recent coronavirus disease 2019 (COVID-19) pandemic brought an increased interest in the impact of smell loss on quality of life as it is one of the prominent symptoms of COVID-19, and highlighted its dysfunctional effects on quality of life (QOL).

Olfactory dysfunction -- defined as either a partial loss of smell (hyposmia), a complete loss of smell (anosmia), or even a distorted sense of smell (parosmia) -- is most commonly caused by disorders such as upper respiratory tract infection, sinus disease with or without nasal polyps, head trauma, tumors, and other neurodegenerative diseases such as Parkinson or Alzheimer disease. The pandemic exposed limited knowledge regarding OD as well as its impact on quality of life further necessitating the search for tools that help the general physician in quantifying and even monitoring olfaction-related quality of life. For the physician, the difficulty lies determining and diagnosing olfactory dysfunction, quantifying its impact on the quality of life and monitoring improvement over time with treatment. Various subjective and objective measures to establish olfactory dysfunction and determine the quality of life because of the loss of smell are usually used for management planning. Self-report questionnaires such as the 52-item Questionnaire for Olfactory Dysfunction (QOD) and a short version, the 17-item QOD-Negative statements (QOD-NS) have been developed and translated in many different languages. The purpose of this study is to determine how threshold olfaction is related to the quality of life of adult individuals using the Filipino translation of 17 item QOD-NS (Fil- 17 QOD-NS) and its association with the actual measured threshold of smell measured using the Butanol Threshold Test (BTT), among those who have perceived loss or poor smell.

METHODS

With IRB approval from the ‘Amang’ Rodriguez Memorial Medical Center Ethics Review Board (ARMMC-ERB No. R-2022-14-00), this cross-sectional study purposively recruited 120 potentially eligible adult patients with self-reported olfactory disorder and consulted at the Outpatient Department of the Amang Rodriguez Memorial Medical Center from August to October 2022. Excluded were individuals who were known cases of anosmia and psychiatric patients with an altered sense of smell. After explaining the procedures of the study, only 111 gave their consent. Butanol threshold test followed by accomplishing the Fil-17QOD-NS were performed on scheduled dates to abide by the strict protocols implemented for COVID-19.

Materials and Data Collection
Olfactory dysfunction screening using the Butanol threshold test (BTT)
Six participants failed to return during their scheduled dates for the BTT and quality of life assessment using the questionnaire. The 105 participants who came on schedule underwent the BTT. (Figure 1) Scores ranged from 0-10 where scoring was related to the patient's threshold compared to that of a normal subject. Patients were grouped into three categories based on BTT scores: normosmic for scores of 6 -10; hyposmic for scores of 2-5; and anosmic for scores of 0-1. Both the score and interpretation were disclosed to the participant. Those who were classified as hyposmic or anosmic were counseled and advised regarding management options. The procedure for performing the BTT is outlined in the study conducted by Rumeau et al. in 2016. Those who completed the BTT proceeded with answering the Fil-17 QOD-NS and were assisted by the research team in completing the questionnaire.

Filipino 17 item Questionnaire of Olfactory Disorders – Negative Statements (FIL-17 QOD-NS)
The previously validated modified version of the Questionnaire of Olfactory Disorders – Negative Statements (QOD-NS), developed by Frasnelli and Hummel, was translated into Filipino following the European Organization for Research and Treatment of Cancer evaluation of guidelines for translating quality-of-life questionnaires. The questionnaire was translated by an independent linguist and was translated back to English by an independent translator. The final Filipino translation was assessed by a panel consisting of 2 Otolaryngologists (1 General Ear Nose Throat surgeon and 1 Rhinologist). Reliability assessment was conducted through a test-retest method using the same group of participants. The Cronbach’s alpha coefficient was found to be 0.966 (r = 0.621; p < .01) indicating high internal consistency. Participants scoring above 12 on the Fil-QOD-NS were categorized as experiencing poor quality of life. The Filipino translated 17 item Questionnaire of Olfactory Disorders – Negative Statements (Fil-17QOD-NS) is shown in Figure 2.

Demographic profiles – age, sex and civil status; and clinical profiles – present ear, nose throat (ENT) symptoms, comorbidities, history of RT-PCR confirmed COVID-19, history of upper respiratory tract infection, sinonasal disease or tumor, previous head and neck surgery, neurologic disease, and history of substance abuse – were obtained from all participants together with their BTT and Fil-17QOD-NS scores.

Data Analysis

Demographic and clinical profiles, BTT scores, and Fil-17 QOD-NS scores were described using descriptive statistics (mean ± SD, range, frequencies and percentages, and ratios). Student t-test was performed...
to determine significant differences between BTT and Fil-17 QOD-NS scores based on the identified characteristics above while multiple regression analysis was used to determine relationships of these characteristics with their scores. Pearson correlation coefficient was utilized to determine the linear correlation between threshold scores and quality of life scores, and the Spearman rank correlation coefficient to cover for their monotonic relationship. All data were encoded in Microsoft Excel for Microsoft 365 MSO version 2306 (Build 16529.20182) (Microsoft Corp., Redmond WA, USA) while statistical analyses were performed using SPSS V22.0 (IBM SPSS Corp., Armonk NY, USA).

**RESULTS**

Of the 120 potentially eligible participants, 9 refused to consent after an explanation of the procedure, 6 did not arrive on their scheduled date for the test, and 7 failed to complete the BTT. The remaining 98 participants, with a mean age of 35.91 ± 12.58 years old, were composed of nearly equal males and females (46.94% vs 53.06%); 52.04% were single, 59.18% reported co-morbidities, and 61.2% did not have COVID-19 previously or at the time of the study.

In Table 1 we can see that based on BTT scores, 82 were classified as normosmic, 6 were hyposmic and 10 were anosmic. Among the normosmic group, 15 had poor quality of life based on their Fil 17 QODNS scores, while 4 and 8 had poor quality of life in the hyposmic and anosmic groups, respectively. Normosmic participants identified themselves as having a better quality of life based on sex (male 82%; female 81%), civil status (single 89%; married 73%); history of COVID-19 infection (74% with; 77% without); presence (73%) or absence (92%) of co-morbidities; and presence (73%) or absence (82%) of ENT symptoms. For the hyposmic and anosmic participants, all females identified as anosmic had poor QOL compared to 71% among the males, while 88% of the married anosmic participants also had poor QOL. Those who had co-morbidities (75% of hyposmics and 78% of anosmics), and presence of ENT symptoms (75% of hyposmics and 80% of anosmics), had poorer QOL compared to those without these clinical characteristics. All the hyposmics and anosmics who had a history of COVID-19 infection also identified themselves as having poor quality of life-based on their Fil 17 QOD NS Scores. (Table 1)

Analyzing scores of the study population as a whole using Student two tailed t-test, significant differences were found in BTT scores between sexes [t(96) = -2.32; p = .022] with females having better scores [M: 9.25; SD: 2.33] than males [M: 7.76; SD: 3.91]. For the Fil 17 QODNS scores, married participants had significantly [t(96) = 3.05, p < .003] higher QOL scores (M: 11.72; SD: 13.74) compared to single participants (M: 4.71; SD: 8.66), although their means can still be interpreted as having good QOL (< 12). For ENT symptoms, the BTT scores of all those with symptoms [M: 5.62; SD: 4.54] had statistically lower scores [t(96) = -7.15; p < .0001] compared to those without symptoms [M: 9.78; SD: 1.14]. The QOL scores were also significantly poorer [t(96)= 3.94; P < .00001] among those who were symptomatic [M: 14.86; SD: 13.97] compared to those who were symptom free [M: 5.217; SD: 9.60]. There were no significant differences in the BTT scores for civil status [married: M ± SD= 7.98 ± 3.78; vs single: M±SD= 9.08 ± 2.58; t(96)=

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Table 1. Butanol Threshold Test and Fil 17 QODNS scores based on specific characteristics among adult Filipinos with self-perceived olfactory dysfunction

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Butanol Threshold Test*</th>
<th>Fil 17 QODNS# scores (n=98)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normosmic (n=82)</td>
<td>Hyposmic (n=6)</td>
</tr>
<tr>
<td>FIL 17-QODNS Score &lt;12</td>
<td>1.676 ± 2.91</td>
<td>1.45 ± 2.72</td>
</tr>
<tr>
<td>FIL 17-QODNS Score ≥12</td>
<td>27.67 ± 13.65</td>
<td>25.60 ± 7.46</td>
</tr>
<tr>
<td>Total Population</td>
<td>67 (82%)</td>
<td>28 (82%)</td>
</tr>
<tr>
<td>Sex</td>
<td>0.08±0.19</td>
<td>2.15±3.42</td>
</tr>
<tr>
<td>Male (n=46)</td>
<td>0.08±0.19</td>
<td>2.15±3.42</td>
</tr>
<tr>
<td>Female (n=52)</td>
<td>2.15±3.42</td>
<td>1.00±2.31</td>
</tr>
<tr>
<td>Civil Status</td>
<td>0.80±1.91</td>
<td>21.00±12.02</td>
</tr>
<tr>
<td>Single (n=51)</td>
<td>21.00±12.02</td>
<td>0.80±1.91</td>
</tr>
<tr>
<td>Married (n=47)</td>
<td>21.00±12.02</td>
<td>0.80±1.91</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td>0.80±1.91</td>
<td>21.00±12.02</td>
</tr>
<tr>
<td>Present (n=58)</td>
<td>21.00±12.02</td>
<td>0.80±1.91</td>
</tr>
<tr>
<td>Absent (n=40)</td>
<td>0.80±1.91</td>
<td>21.00±12.02</td>
</tr>
<tr>
<td>History of COVID-19 infection</td>
<td>0.80±1.91</td>
<td>21.00±12.02</td>
</tr>
<tr>
<td>Present (n=38)</td>
<td>21.00±12.02</td>
<td>0.80±1.91</td>
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<tr>
<td>Absent (n=60)</td>
<td>0.80±1.91</td>
<td>21.00±12.02</td>
</tr>
<tr>
<td>ENT symptoms</td>
<td>0.80±1.91</td>
<td>21.00±12.02</td>
</tr>
<tr>
<td>Present (n=29)</td>
<td>21.00±12.02</td>
<td>0.80±1.91</td>
</tr>
<tr>
<td>Absent (n=69)</td>
<td>0.80±1.91</td>
<td>21.00±12.02</td>
</tr>
</tbody>
</table>

*Significance differences in scores between parameters were determined using 2 tailed student tests. Each parameter was analyzed if they were significant risk factors for scores using logistic regression.
1.70, p = .05), comorbidities [present: M ± SD = 7.93 ± 3.77; vs absent: M ± SD = 9.45 ± 1.99; t(96)= -2.33, p = .05], and history of COVID-19 [with history: M±SD= 9.00 ± 2.89; vs without history: M ± SD= 8.27 ± 3.44; t(96)= 1.09, p = .28]. No statistical differences were found also for Fil 17 QO DNS scores between sexes [male: M±SD = 26.02 ± 114.59; vs female: M ± SD = 6.90 ± 12.07; t(96)= -1.20, p = .05], comorbidities [present: M±SD= 11.05 ± 13.71; vs absent: M ± SD= 10.75 ± 6.53; t(96)= -1.34, p = .06], and history of COVID-19 [with history: M± SD = 29.74 ± 125.73; vs without history: M ± SD = 7.03 ± 11.266; t(96)= -1.39, p = .05] after analyses.

Regression analyses revealed that amongst all variables, exhibiting ENT symptoms was a risk factor for poor scores in BTT [OR= 0.15; 95% CI: 0.02-0.97; P = .046] while presence of comorbidities increased the odds of having a poor QOL [OR= 3.36; 95% CI: 1.04-10.85; P = 0.043] based on Fil17 QODNS in this study population.

The correlation analysis between QOD-NS total scores and BTT scores (n=98) revealed a significant negative correlation, with Pearson coefficient r = -0.477 (p < .001) and Spearman rho = -0.292 (p = .004). (Figure 3)

Figure 3. Graphical representation of the association between the BTT and FIL 17 QODNS Scores. The trendline sloping downwards indicates an inverse relationship between the QOL, Fil 17 QODNS scores, and smell threshold, BTT scores.

Discussion

Our study explored the relationship between olfactory function threshold and quality of life among adult Filipinos with perceived olfactory dysfunction (OD) using the data from 98 participants with comparable composition of male and female adults who exhibited varying degrees of olfactory dysfunction- normosmic (83.67%), hyposmic (6.12%) and anosmic (10.20%), with a mean BTT score of 1.5 ± 1.823 and reportedly poor quality of life, indicated by a mean Fil-17 QOD NS score of 19.06 ± 11.86.

As we analyzed our population’s smell threshold and quality of life based on test and questionnaire scores, significant findings were found between sex, civil status and ENT symptoms. Our data revealed that although statistical difference was found in BTT scores between sexes where females had better smell threshold than males, only a few were confirmed by BTT to have hyposmic and anosmic threshold levels. More males than females (11 vs. 4) with poor smell threshold capability were categorized as hyposmic and anosmic. This is similar to the findings of Sorokowski et al. where for each aspect of olfaction (namely identification, discrimination and threshold), women outperformed men. As shown by Yang and Pinto in 2016, with sex as a common risk factor for olfactory loss, males are more likely to suffer from smell loss probably due to their increased likelihood of exposure to hazardous environments particularly at work. They also added that among women, having estrogen and progesterone as their main hormones may be beneficial and protective to stem cells in the peripheral or central olfactory areas and may also contribute to slowing down their eventual losses once these hormone levels decline as they approach perimenopausal to menopausal stage.

Statistical differences were also found in the Fil 17 QODNS scores between married and single participants in our study. Having a married civil status was seen as a protective factor against some social and psychological problems especially among the elderly. However, this particular result can be attributable to aspects of security and stress, as some studies agree that having olfactory dysfunction in married individuals can affect their relationship in that anosmic women experience decreased security in their partnership; and that olfactory dysfunction can even affect the stress levels of a married subject as the body odor of their partner was seen to have the capability of altering an individual’s stress levels. This particular influence was not seen in our study population as the single and married participants comprising this group had almost equal numbers and distribution across the three levels of smell threshold. However, although small, the proportion of married participants identified as anosmic and having poor quality of life was greater compared to the proportion of anosmic single participants. Moreover, we could not determine any association with this difference in civil status because we had no data on whether the olfactory dysfunction occurred after or before marriage.
As it is commonly known, the presence of ENT symptoms, specifically nasal discharge and/or congestion can influence both the QOD-NS and BTT scores. The results of our study showed that the BTT scores were significantly lower and the FIL 17 QOD NS scores were significantly higher among those with ENT symptoms. It also increases the odds of having poor smell threshold based on our regression analysis [OR= 3.36; 95% CI: 1.04-10.85; P = .043]. Previous studies similarly showed decreased quality of life in patients with sinonasal disease. This paralleled the findings of the meta-analysis by Regalado et al. showing how self-reports of smell loss can approximate their objective test results. However, many studies still suggest that self-reported olfactory dysfunction should always be backed up with objective tests as reflected in our chosen methodology.

With the information on other characteristics, among those with comorbidities who were normosmic, 12 participants had poor quality of life compared to 3 participants without any comorbidity. Statistical differences were not established between BTT and Fil 17 QODNS in our study group. But logistic regression showed that comorbidities, if present, are factors in having a poor quality of life [OR = 3.36; 95% CI: 1.04-10.85; P = .043] among our participants. However, this is difficult to ascertain as the cause for the decrease in quality of life since it can be contributed by the olfactory concern or the comorbid disease itself. Croy et al. in 2014 noted that at least in their patients with olfactory dysfunction due to chronic rhinosinusitis, the decrease in the QOL may be attributable to decreased patency of the nasal airway which may confound the result.

Studies have shown the association between COVID-19 infection and decreased threshold and olfaction-related quality of life, but no significant differences were found between scores of those with and without history of COVID-19 infection, nor was it identified as a significant risk factor affecting the scores in our study. This may be attributed to the non-inclusion of information about the timing of positivity to COVID-19 and the duration of the olfactory dysfunction as part of the variables in our study.

In our study, Fil-17 QOD-NS scores negatively correlated with their corresponding BTT scores showing an inverse relationship between the two as shown in Figure 3. This means that as olfactory function becomes poorer indicated by the low BTT scores, their quality of life becomes poorer as well as seen in their high Fil-17 QOD-NS scores. Multiple studies reported a correlation of OD and olfaction-related QOL stating that loss of the sense of smell leads to disturbances in important areas of daily living such as the enjoyment of food, detection of harmful food, chemicals, and smoke, and also plays a role in social situations and even in work life. These studies also emphasize the impact of loss of smell linking them to anxiety, feelings of vulnerability, hygiene problems, reduced pleasure, and even depression, clearly demonstrating the relationship of smell loss to reduced quality of life. Similarly, a study on CRS-specific QOL noted that QOL and depression significantly affects the QOD-NS where a poorer olfactory status was associated with a negative impact on QOD-NS.

The results of our study exhibited the ability of the FIL-17 QOD-NS to determine quality of life in this population of adults with perceived olfactory dysfunction. It had a Pearson correlation of 0.621 significant at 0.01 level and a Cronbach alpha of 0.966 comparable with findings of other studies. Combined with an objective test such as the BTT to screen for presence of OD, it can help in assessing the degree of dysfunction, effect on patients’ quality of life and possibly useful in monitoring treatment and management of the condition.

Our study has several limitations. First, BTT limits its function to determining only the threshold of smell. The sensitivity and specificity of an ideal smell screening test may be improved if identification or discrimination elements were included such as a Sniffin Sticks’ test. Second, the recruitment method and the sample size in this study make the results valid for the study population alone, increasing the sample size with allotment for drop outs and employment of a stratified and randomly distributed recruitment among the members of the target population can improve the generalizability of results. Third, the history of COVID 19 infection, diagnoses of comorbidities, and appearance or resolution of ENT symptoms – the identified variables in this study, have temporal aspects in reference to their duration or interval from their occurrence or resolution to the period when the participants started to notice or perceive olfactory dysfunction symptoms. This temporal or time element should have been included as separate variables from the above mentioned or should have been controlled. In our analysis, we cannot make associations and firm references as to the effect of the three previously mentioned variables on smell threshold and quality of life since this time element may have confounding effects in our study.

In conclusion, individuals with olfactory dysfunction in this study population had poor quality of life as determined by the translated Filipino 17-item QOD-NS which has an inverse relationship with their smell threshold as represented by the BTT results. Among the factors studied, significant differences were found between sexes, civil status, and presence of ENT symptoms in BTT and Fil 17 QODNS scores. However, only presence of comorbidities and ENT symptoms are significant risk factors for poor quality of life and smell threshold, respectively, in this population.
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