Real-world observational data on olfactory dysfunction of the Smell & Taste Clinic of UZ Leuven (Belgium) from 2021-2024

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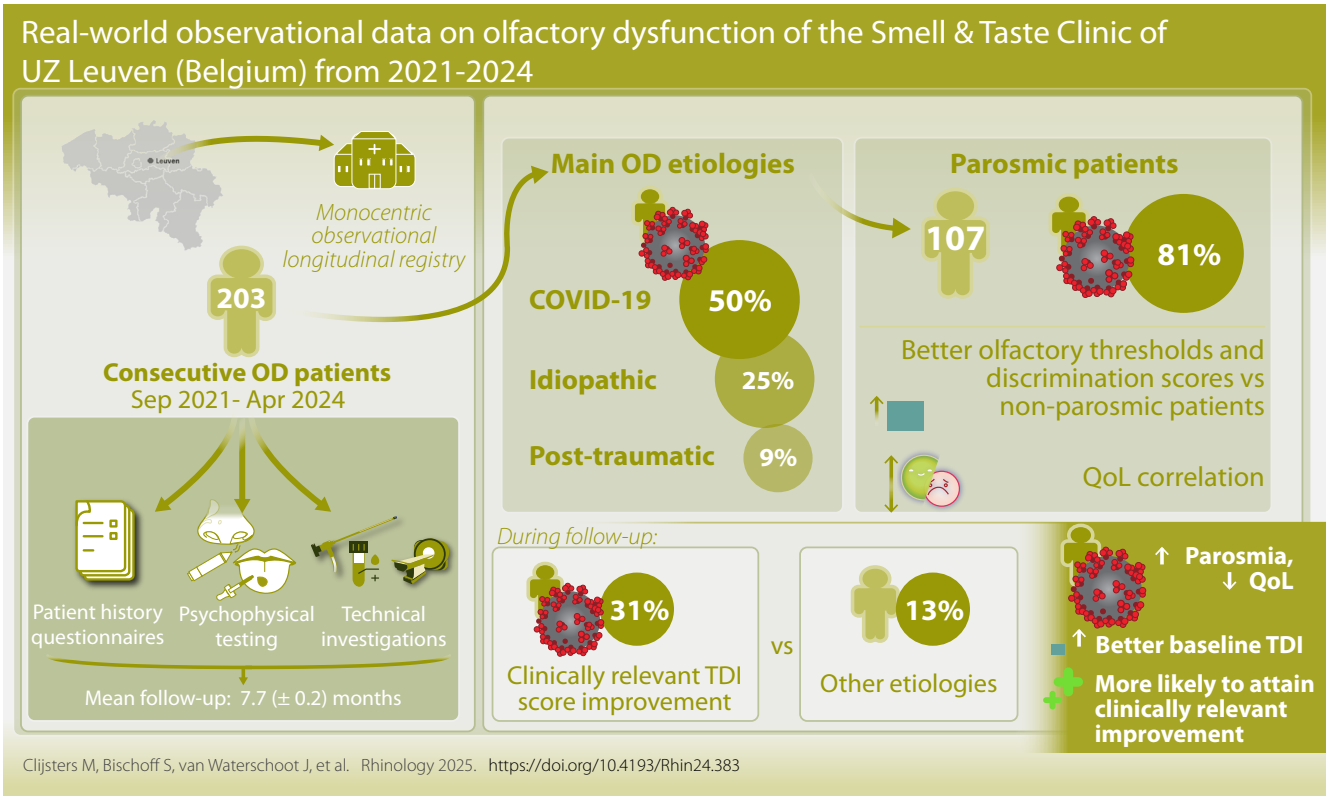

Abstract

Background: The COVID-19 pandemic led to a surge in olfactory dysfunction (OD), increasing the need for specialized care. This study explores the prevalence, characteristics, and clinical implications of OD in a specialized Smell & Taste Clinic established at the ENT-HNS department of the University Hospitals Leuven (UZ Leuven) in 2021.

Methodology: We included consecutive patients with OD in the observational longitudinal ProspeRo'Scent registry at UZ Leuven between September 2021 and April 2024. Chemosensory assessment was done with psychophysical tests (Sniffin' Sticks TDI and Taste sprays) and questionnaires.

Results: Of the 203 unique, consecutive patients, COVID-19-associated OD (C19OD) was the predominant etiology (50.2%), followed by idiopathic (25.1%), and post-traumatic (8.9%) OD. Parosmia was present in 60.2% of patients, with the highest prevalence in C19OD cases (80.9%). Sniffin' Sticks TDI testing indicated that patients with parosmia had better olfactory thresholds and discrimination scores than patients without. During follow-up (n=116; average 7.7 months), 31% of C19OD patients exhibited clinically relevant improvement in TDI scores, compared to 13% for the other etiologies. Quality of life, as assessed by sQOD-NS, was not significantly different between etiologies but correlated with higher parosmia scores.

Conclusions: C19OD patients suffered more from parosmia, correlating with worse quality of life, but had better baseline TDI scores and demonstrated a higher likelihood of clinically relevant improvement over time compared to other etiologies.

Key words: anosmia, COVID-19, olfaction disorders, smell

Introduction

The senses of smell, taste, and chemesthesis—collectively known as the 'chemosensory system' or 'chemical senses'—enable us to perceive molecules that enter our nose or mouth. Through multisensory integration, the chemical senses create the perception of flavor when we eat and drink. Chemosensory impairments can have a substantial impact on various aspects of daily life, including safety, nutritional status, quality of life, and mental health. Yet, our clinical knowledge and expertise regarding chemosensory disorders remains inadequate [1].

Of all chemosensory disturbances, olfactory dysfunction (OD) is the most common. The overall prevalence of OD in the general population is estimated to be over 20% and increases significantly with age [2,3]. OD encompasses both quantitative dysfunction (changes in intensity) and qualitative dysfunction (distorted perception). Qualitative OD, such as parosmia and phantosmia tend to have a more profound effect on quality of life than quantitative changes such as hyposmia or anosmia [4]. Of all causes of OD, sinonasal disease, viral infections, and traumatic injury account for nearly two-thirds of cases in the Western world [5,6]. In many clinical cases, the etiology of OD cannot be identified formally, and studies suggest that 16% to 24% of OD cases are idiopathic [7,8].

Giving rise to a large cohort of COVID-19 associated PIOD (C19OD) patients, the SARS-CoV-2 pandemic has prompted the establishment or expansion of smell and taste centers around the globe but also presented a unique chance to study OD. It has highlighted the existing knowledge gaps and brought renewed focus to the field of olfaction and chemosensory dysfunction [9]. While various common cold viruses, including rhinovirus, coronavirus, influenza, and parainfluenza, have long been associated with PIOD [10,11], the incidence of C19OD patients is unparalleled.

In response, the Smell & Taste Clinic was set up at the Ear-Nose-Throat (ENT) department of UZ Leuven in 2021 to provide a healthcare trajectory for patients with chemosensory disorders. This study aims to provide a detailed profile of patients consulting the clinic, including the frequency of various etiologies, associated chemosensory characteristics, the impact on quality of life and the evolution over time.

Materials and methods

Setup and implementation of the Smell & Taste Clinic care pathway and registry

The ProspeRo'Scent (Prospective Registery of Smell & Taste Clinic ENT-HNS) study is an observational, longitudinal, ambidirectional cohort study conducted at the Smell & Taste Clinic of the ENT department of University Hospitals Leuven (UZ Leuven), Belgium. Considering the increased incidence of chemosensory disorders associated with the COVID-19 pandemic, we established a clinic for smell and taste disorders at UZ Leuven in 2021. The design of the clinic is based on the best practice frameworks for patients with OD and insights from established centers [3,8]. A data registry was set up to include all patients with chemosensory dysfunction visiting our clinic since the opening of the clinic in September 2021 (retrospectively) and prospectively since December 2022. The data registry study protocol was approved by the Ethics Committee of UZ Leuven (local ethical committee number: S67158) and registered at clinicaltrials.gov (NCT06456008). Written informed consent was obtained from participants prior to prospective inclusion.

Participants and sample size

Patients consulting for chemosensory dysfunction were recruited from the outpatient Smell & Taste Clinic of UZ Leuven between September 2021 and April 2024. Exclusion criteria included severe cognitive impairment that precluded the completion of psychophysical tests or questionnaires.

Clinical procedures and chemosensory assessment

All participants underwent a standardized clinical trajectory to diagnose and manage chemosensory dysfunction. This trajectory included a comprehensive assessment comprising patient history, clinical examination including nasal endoscopy, psychophysical olfactory and gustatory testing, and when indicated, additional diagnostic investigations to elucidate the underlying etiology of OD (allergy testing, imaging, blood sample, referral to neurologist/psychiatrist). Based on this comprehensive assessment, an etiologic diagnosis was made according to the groups defined in the 2023 position paper [3]. For the PIOD cases, only patients with a clear link with the SARS-CoV-2 infection (or vaccination) were considered as C19OD; all other PIOD cases were considered as non-COVID-19-associated PIOD.

Olfactory testing

The Sniffin' Sticks test (Burghart®) was used to assess olfactory function. This test assesses Threshold (the lowest concentration of an odor that the patient can detect), Discrimination (the ability to discriminate between different odors), and Identification (the ability to correctly identify various odors) testing, each scored on a maximum of 16. The total TDI score on 48 is calculated by the sum of these three test components [12,13].

Gustatory testing

Screening with Taste Sprays and extensive testing with Taste Strips (Burghart®), were used to evaluate gustatory function, based on a similar workflow described in other centres [14]). Taste sprays are a whole-mouth suprathreshold test, and a quick and easy screening tool to assess the patient's ability to identify basic taste qualities [15]. The patient needs to identify sweet, sour, salty, bitter and water/tasteless, hereby generating a score ranging from 0 to 5. If the patient had a score below 3/5, and/or

Table 1. Patient baseline characteristics.

	All patients	C19OD	Idiopathic	Post traumatic	Non-COVID PIOD	Toxic exposure	Sinonasl disease	Congenital
	N = 203	N = 102	N = 51	N = 18	N = 14	N = 7	N = 6	N = 5
Patient characteristics								
Demographics								
Gender(% female)	126 (62)	71 (70)	27 (54)	11 (61)	9 (64)	1 (14)	3 (50)	3 (60)
Age (y)	46 (±17)	41 (±15)	53 (±16)	49 (±16)	54 (±14)	51 (±15)	59 (±16)	22 (±17)
Smoking(%)	31 (21)	11 (14)	8 (25)	4 (29)	5 (42)	1 (14)	1 (25)	0 (0)
Chemosensory dysfunction								
Qualitative olfactory dysfunction								
Parosmia(%)	107 (61)	77 (82)	16 (40)	5 (38)	7 (54)	2 (40)	0 (0)	0 (0)
Parosmia score †	11 (±3)	10 (±3)	12 (±3)	13 (±3)	12 (±3)	12 (±4)	11 (±5)	16 (±0.5)
Quantitative olfactory dysfunction								
TDI diagnosis								
• Normosmia(%)	32 (16)	23 (23)	4 (8)	0 (0)	3 (21)	1 (14)	1 (17)	0 (0)
• Hyposmia(%)	119 (59)	67 (66)	28 (56)	9 (50)	6 (43)	4 (57)	2 (33)	2 (40)
• Anosmia(%)	52 (26)	12 (12)	18 (36)	9 (50)	5 (36)	2 (29)	3 (50)	3 (60)
TDI score	22 (±8)	25 (±7)	21 (±7.5)	18 (±7)	21 (± 8)	21 (±9)	20 (± 10)	16 (±8)
• Threshold(max.16)	4 (±3)	5 (±3)	4 (±3)	3 (±2)	4 (±3)	3 (±2)	5 (±5)	4 (±4)
• Discrimination(max.16)	9.6 (±3)	10 (±3)	9 (±3)	9 (±3)	10 (±4)	8 (±4)	6.5 (±3)	7 (±3)
• Identification(max.16)	8.5 (±3)	9 (±3)	8 (±3)	7 (±3)	8 (±3)	9 (±3)	8 (±4)	6 (±3)
Gustatory dysfunction								
Taste Spray score(max. 5)	4.5 (±0.8)	4.4 (±0.8)	4.3 (± 0.9)	4.7 (± 0.6)	4.5 (± 0.9)	4.4 (± 1.5)	4.8 (±0.4)	4.6 (± 0.5)
• Normogeusia(%)	179 (91)	88 (91)	44 (90)	17 (94)	12 (86)	6 (86)	6 (100)	5 (100)
• Hypogeusia(%)	17 (9)	9 (9)	4 (8)	1 (6)	2 (14)	1 (14)	0 (0)	0 (0)
• Ageusia(%)	1 (0.5)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Impact of the disorder								
Time since onset(months)	33 (±66)	16 (±12)	69 (± 122)	17 (±20)	16 (± 10)	34 (± 32)	80 (±76)	200 (± 0)
Weight loss(%)	36 (24)	20 (27)	6 (18)	2 (13)	4 (33)	2 (29)	1 (25)	0 (0)

Patient characteristics at baseline – defined as first presentation at the Smell & Taste Clinic – classified by the etiology of their olfactory dysfunction. Continuous variables are expressed as averages and standard deviation. All other variables are expressed as percentages. † Four-item parosmia scale according to Landis et al. [17].

gustatory complaints, more extensive testing with Taste Strips was performed. Taste Strips are filter papers impregnated with various tastants (bitter, sweet, salty, and sour) in four concentrations each, to be placed on the patient's tongue [16].

Questionnaires

To assess qualitative OD and perceived severity of chemosensory deficits, Visual Analog Scales (VAS) and standardized questionnaires, including the 4-item questionnaire by Landis et al. [17], were utilized. For qualitative OD, patients were asked about the nature, frequency and triggers of distorted smells. Quality of life was assessed using the short version of Olfactory Dysfunction Questionnaire (sQOD-NS) [18,19].

C19OD – SARS-CoV-2 variant of concern (VOC) determination

The determination of VOCs for C19OD cases was done based on the date of onset of the OD. The cut-off dates were defined by the periods in which at least 80% of sequenced cases in Belgium were attributable to a specific VOC.

Data management and analysis

For more efficient and failproof data collection, the clinic utilizes Microsoft Infopath® for systematic and structured data entry by healthcare staff. Patient-reported data and self-assessment of chemosensory function are recorded using MyNexuz Health (nexuzhealth NV). Both systems are integrated into the electro-

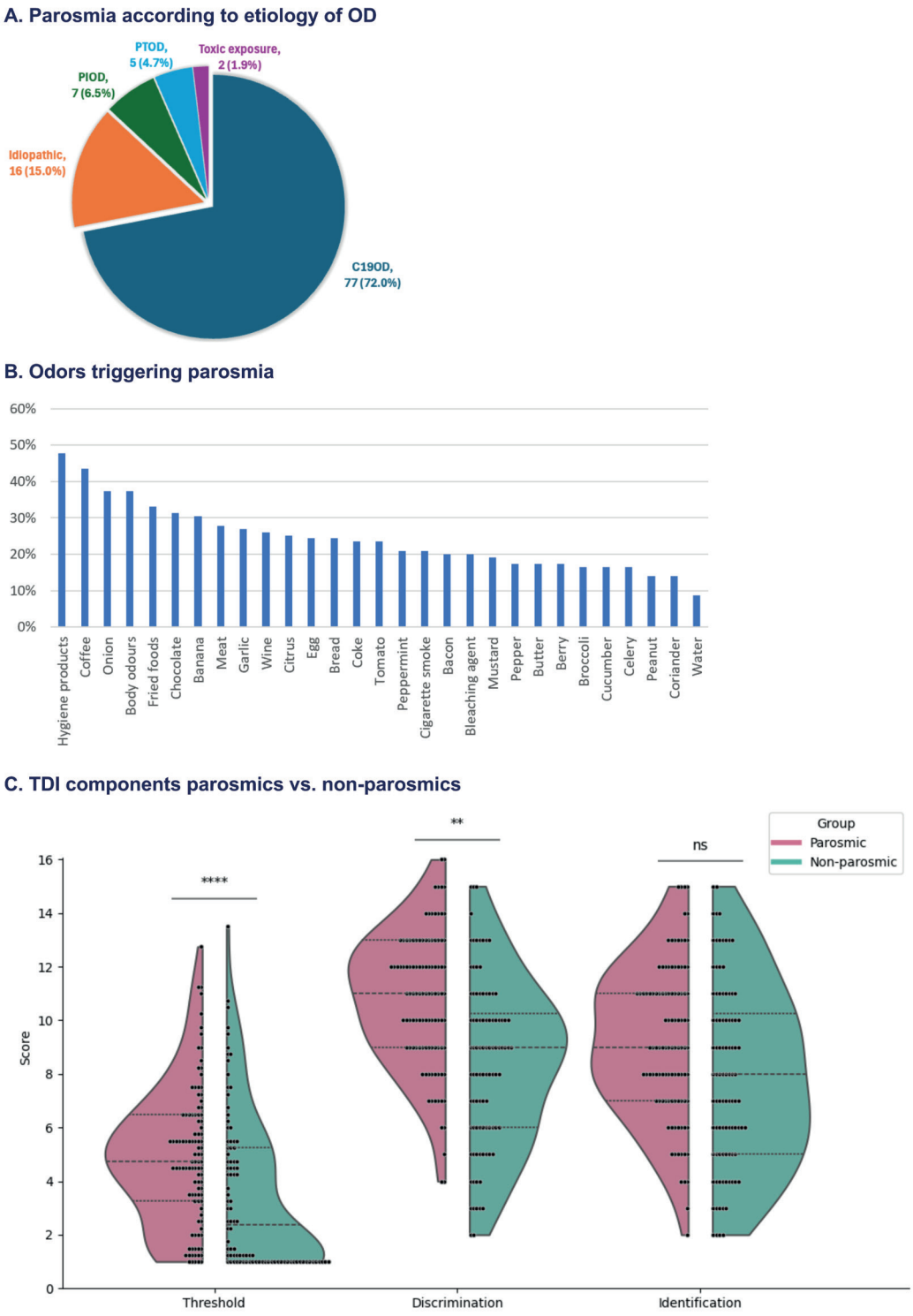

Figure 1. Characteristics of parosmia symptoms in patient cohort. (A) Pie chart showing the distribution of parosmia according to etiology of olfactory dysfunction (n=107). Categories with no parosmia cases (congenital and sinonasal disease) were excluded from the visualization for clarity. (B) Parosmia triggering items. Bar graph showing the percentage of patients who scored an item as a trigger for their parosmia. (C) Violin plots of the TDI-scores of patients with parosmia (n=107) and without parosmia (n=96). The plots are divided into the subcomponents of the test: Threshold (in red), Discrimination (in green), and Identification (in blue). The dashed and dotted lines indicate the median and Q1 and Q3, respectively.

nic health records of the patient, stored on UZ Leuven servers, with access restricted to authorized personnel. Descriptive statistics were used to summarize patient characteristics (Table 1). Depending on the questionnaire version and completeness of

the responses provided by patients, some of the patient parameters were calculated on a subtotal of the cohort. Statistical analyses were performed in GraphPad Prism®.

Results

Patient demographics and baseline characteristics

The ProspeRoScent registry included a total of 203 unique, consecutive patients presenting with OD at the outpatient Smell & Taste Clinic of the ENT-HNS department of UZ Leuven, Belgium between September 2021 and April 2024 (Table 1). Patients were categorized according to the etiology of OD, with most cases being C19OD (n=102, 50.2%), followed by idiopathic (n=51, 25.1%), post-traumatic (n=18, 8.9%) and non-COVID-19 PIOD (n=14, 6.9%) causes. Toxic exposure (n=7, 3.4%), sinonasal disease (n=6, 3%), and congenital (n=5, 2.5%) were less frequent causes.

The overall demographic distribution showed a relatively balanced representation across sex, and a wide range of ages. A predominance of female patients was observed in the post-infectious OD groups, with 71 females (/31 males) for C19OD and 9 females (/5 males) for PIOD.

The average delay before patients presented at our clinic was 33.4 months (SD: ±66.1, range: 1.7 months – 52.3 years) after the onset of OD. Patients with PIOD, including both non-COVID-19 (15.7 months) and C19OD (16.1 months) cases, and those with posttraumatic OD (17.1 months) were the earliest to seek consultation.

Psychophysical assessments, using Sniffin' Sticks and taste sprays, were performed to investigate the olfactory and gustatory function. Less than 10% (n=18) of all patients had concomitant gustatory dysfunction, and only 1 patient (0.5%) from idiopathic etiology, had ageusia. Of the 9% of all patients with hypogeusia (n=17), most common etiologies were PIOD (n=2, 14%), C19OD (n=9, 9%), toxic exposure (n=1, 14%), and idiopathic OD (n=4, 8%).

Patients with a post-traumatic etiology (mean TDI score 18.3 ±7.2) or a congenital (mean TDI score 16.2 ±8.1) etiology showed a higher percentage of anosmia compared to other etiologies. Parosmia was reported in 60.8% of all patients (107 out of 176 patients). The highest prevalence of parosmia was observed in the C19OD group (82%), significantly higher compared to other groups. This higher prevalence was also reflected in the lower score in C19OD cases (10.4 ± 3.3) on the 4 questions used for differentiating parosmia [17]. Likely distribution of variant of concerns in the C19OD is, in chronological order, 38% ancestral strains (n=38), 1% alpha (n=1), 16% delta (n=16), 5% omicron (n=5) and 40% unknown or other (n=41).

Parosmia symptoms

Of all patients that reported parosmia (n=107), C19OD accounted for 77 (72%) of the total cases (Figure 1A).

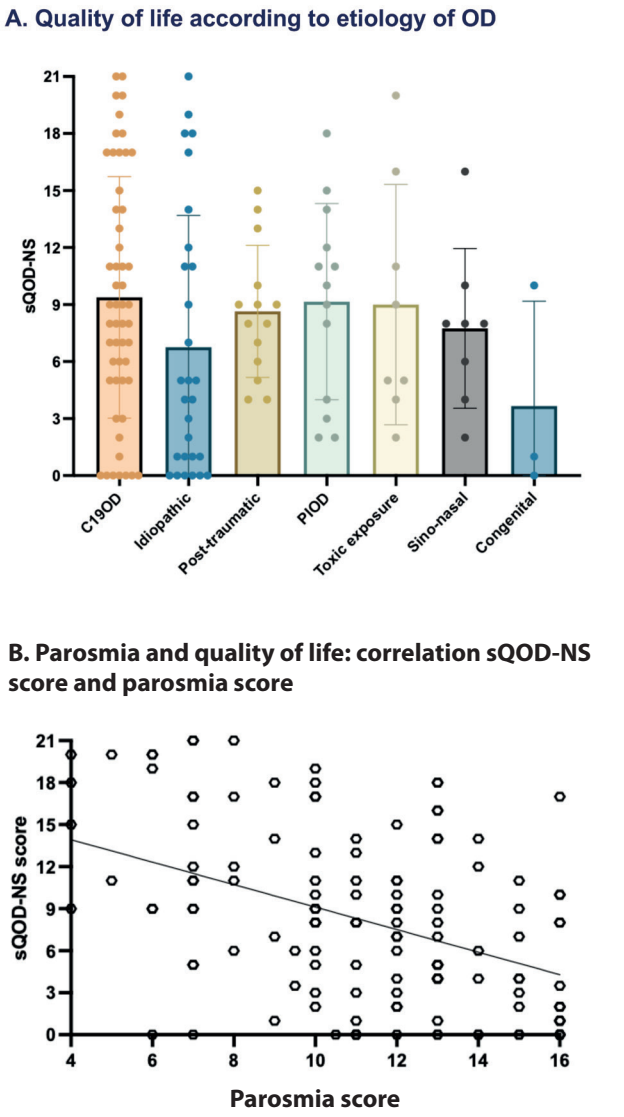

Figure 2. OD related quality of life evaluated by the sQOD-NS scale. (A) sQOD-NS scores across etiologies. The bar chart displays the distribution of sQOD-NS scores across various etiologies of olfactory dysfunction. The bars represent the mean sQOD-NS score, the error bars the standard deviation. Abbreviations used: C19OD = COVID-19 associated olfactory dysfunction. PIOD = post-infectious olfactory dysfunction. (B) Correlation of parosmia score and sQOD-NS Score. Linear regression analysis between parosmia score and the sQOD-NS (short Olfactory Dysfunction Questionnaire – Negative Statements). Each point represents an individual observation. The linear regression line is fitted to the data.

Parosmic distortions are triggered by certain items [20], and ((From a list of items that had previously been reported to trigger parosmic distorions [20])) personal hygiene products (perfumes, deodorants), coffee, onion, body odors and fried foods were the most reported items in our cohort (Figure 1B). Examining the subcomponents of the TDI score (Threshold,

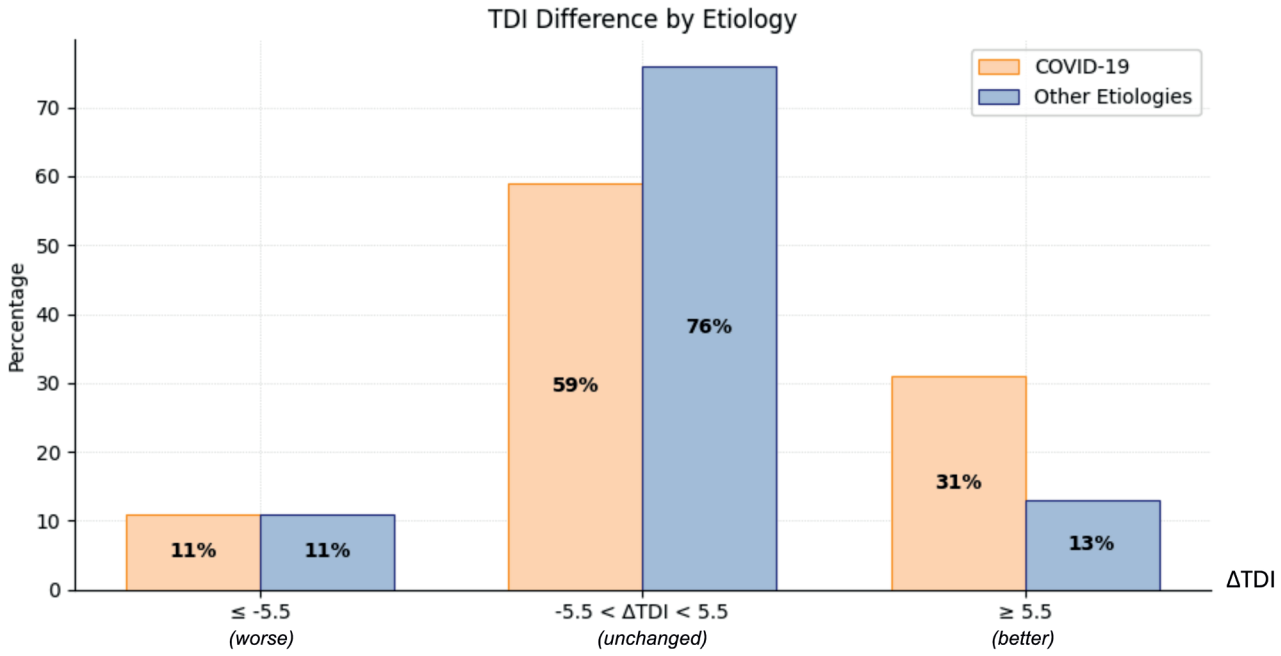

Figure 3. Clinically relevant changes in TDI score according to etiology. Clinically relevant changes in TDI score between baseline and follow-up visit among patients with C19OD compared to patients with OD of other etiologies. Changes in TDI scores are grouped into three categories: a clinically relevant decrease of more than 5.5 points (≤ -5.5), changes within ±5.5 points (-5.5 < ΔTDI < 5.5), and a clinically relevant increase of more than 5.5 points (≥ 5.5).

Discrimination, and Identification) between parosmics (n=107) and non-parosmics (n=96) (Figure 1C), patients with parosmia exhibited a significantly higher mean threshold score (4.9 ± 2.6) compared to non-parosmics (3.5 ± 2.9), indicating a stronger ability to detect odors at lower concentrations among parosmics (p=0.0002). Similarly, the mean discrimination score was higher in parosmics (10.8±2.5) than in non-parosmics (8.4±3.1), suggesting that – although qualitatively disturbed –, parosmics still had a better capacity to differentiate between different odors (p=0.0072). However, no significant difference was found in the identification scores between parosmics (9.2±2.8) and non-parosmics (7.9±3.4).

Quality of life assessments

Although no significant differences were observed across etiologies, COVID-19-associated and non-COVID-19 post-infectious OD had a trend towards higher scores, corresponding with a more severe impact on the quality of life (Figure 2A).
The sQOD-NS score correlated (p<0,0001, n=134) with the score used for differentiating parosmia symptoms. The more the score indicated parosmia symptoms, the greater the impact on quality of life (Figure 2B).

Longitudinal follow-up of TDI scores

Of the 203 OD patients included in the ProspeRo'Scent registry, 116 patients (54.7%) completed a follow-up visit by April 2024, with an average follow-up duration of 7.7 months. For longitudinal analysis of TDI scores, patients were categorized into two groups based on the etiology of OD: C19OD and other etiologies (Figure 3). A clinically relevant difference was determined as a change in TDI score of ±5.5 points [21]. Of the 61 patients with C19OD that had a follow-up visit, 31% (n=18) were shown to have a clinically relevant improvement in olfactory function, compared to only 13% (n=7) in the group of 55 patients with OD from other etiologies (Figure 3). The improvement was irrespective of any treatment protocol. The percentage of patients with C19OD that deteriorated (decline in TDI score of ≥ 5.5) is consistent with other causes of OD (11%).

Discussion

In this observational study conducted at the Smell & Taste Clinic of University Hospitals Leuven (UZ Leuven) between September 2021 and April 2024, we investigated the prevalence, characteristics, and clinical implications of olfactory dysfunction (OD) in a cohort of 203 patients. Longitudinal analysis was conducted on a subcohort of 116 patients with at least one follow-up visit. Patients presented at our clinic with an average delay of 33 months after onset of OD, with PIOD and C19OD patients presenting earlier (around 16 months) than all other etiologies. The long delay before presentation may be related to the relative clinical neglect and difficulty for patients to find medical advice for their OD. Indeed, patients with OD often face challenges

when seeking medical advice and treatment [22], and even in ENT departments, proper chemosensory assessment for OD is generally neglected [22]. This neglect stems from the perceived insignificance of the consequences of OD, the frustration about the lack of successful management options, the need for financial and staffing resources, and the time-consuming nature of lege artis olfactory testing [22]. Additionally, methodological issues—such as a lack of consensus on appropriate testing methods and inherent difficulties in sampling olfactory tissue—impede translational research [23].
However, proper diagnostic assessment is crucial in the clinical work-up of patients with chemosensory impairment. Self-assessment is often unreliable and underestimates the true extent of OD [3,24]. Moreover, self-reported measures often fail to adequately distinguish between disturbances in olfaction, gustation, and chemesthesis [3]. Proper olfactory assessment should include psychophysical testing with validated tools (such as Sniffin' Sticks® for olfaction and Taste Strips® for gustation), providing a detailed and reliable assessment of chemosensory function, enabling adequate monitoring of quantitative function [3,14].

In our cohort of patients presenting at the Smell & Taste Clinic of UZ Leuven (2021 –2024), the most common etiology was C19OD, comprising 50% of cases. In the pre-COVID era in specialized smell and taste centers, PIOD was already a leading cause, accounting for 31% of cases, as reported by a center in Denmark [8]. Our data registry shows a substantial increase of PIOD causes, now comprising 57% of cases (including COVID-19 and non-COVID-19), underscoring the impact of the SARS-CoV-2 pandemic on the incidence of olfactory disorders. Existing research suggests that as much as half of the COVID-19 patients experienced OD following SARS-CoV-2 infection, but estimates vary based on assessment methods, geographical location, and SARS-CoV-2 variant [3,9,25].
Although sinonasal disease is a leading cause of OD, the prevalence of OD due to sinonasal disease reported in our cohort is low. Main reason for this underestimation, is that chronic rhinosinusitis patients are referred to and managed by our general ENT division, and therefore less likely to present at the Smell & Taste Clinic.

Despite considerable efforts, long-term effective treatments for OD are generally lacking. Many suggested pharmacological treatments (such as phosphodiesterase inhibitors or intranasal calcium buffers) lack evidence to support their use [3]. The prognosis of OD varies significantly based on the underlying etiology. Only in select cases, such as OD due to sinonasal disease, can the underlying cause be treated. Olfactory training is recommended for various etiologies of OD, but evidence is largely based on post-infectious OD (PIOD) and treatment adherence to olfactory training is often low [26].

Chemosensory dysfunction in C19OD

The chemosensory profile of C19OD has been widely studied since the onset of the pandemic. In line with our findings, patients with C19OD are typically younger, and more often women than men [3]. Although subjectively taste dysfunction is a common complaint, most patients are normogeusic when tested [27,28]. Most people define their ability to taste as the extensiveness of flavors they perceive in food, while the actual taste function comes down to just the basic tastes (sweet, sour, salty, bitter and umani). This is why when asked about their taste function, people with OD will incorrectly report their taste as reduced or even absent [3]. Similarly, we found that gustatory dysfunction was found in less than 10% of C19OD cases. Although the nature of OD in C19OD was initially thought to be mainly quantitative, it has become increasingly evident that qualitative dysfunction, and particularly parosmia, frequently occurs in the course of persisting C19OD. In our cohort, the prevalence of parosmia in C19OD was 82%, which is significantly higher than reported in previous studies, where rates ranged from 32% [29], 40% [27] to 58% [30].

Parosmia characteristics

Although attempts have been made to objectively/psychophysically assess parosmia, such as SSParOT [31], the diagnosis is usually made from the patient history and can be supported with the use of questionnaires [3,17]. In our cohort, almost 78% of patients that reported parosmia were diagnosed with PIOD (either C19OD or non-C19OD); idiopathic accounted for 15% and post-traumatic for 5%. When asking about odorants that are perceived as parosmic, patients interestingly often report a similar set of items, as previously reported in PIOD [32]. We used a list of items that were frequently reported as triggers for parosmia in C19OD patients, adapted from Parker et al. [20], and found that over a third of patients with parosmia reported hygienic products, coffee, onion and body odours as trigger for parosmia. Specific patterns of parosmia and substances triggering it, could contribute to our understanding of its pathophysiology. The 'mis-wiring' hypothesis – which poses that altered odor quality is the consequences of incomplete or incorrect Olfactory Sensory Nerve (OSN)-signal integration – could fit with such patterns when incomplete or preferential OSN regeneration leads to partial odour maps.
Psychophysical olfactory assessments using Sniffin' Sticks TDI revealed that parosmics had significantly better TDI scores, particularly olfactory thresholds and discrimination scores compared to non-parosmics, though their identification abilities were similar. In contrast, Li et al. found that C19OD patients with parosmia exhibited significantly worse odor identification scores compared to non-parosmic patients, both orthonasally and retronasally [31]. Similar to our findings, a more recent study from Dresden, Germany showed that parosmia was more prevalent

in patients with a higher olfactory function, compared to those without parosmia, with significant differences in threshold and discrimination, but not identification [33].

Quality of life

An extensive study that investigated well-being using the WHO-5 scale in patients with OD [34], found that poor well-being was most pronounced in patients with sinonasal disease for the group of patients with hyposmia, but when looking at the group of anosmia patients alone, they could not find any significant differences between the different etiologies. Using the olfactory specific sQOD-NS questionnaire, we found no significant differences in QoL between etiologies.

Mai et al. also investigated the differences in well-being between patients with and without parosmia and found that severe parosmia significantly impacted well-being compared to patients without parosmia or with mild to moderate parosmia [34]. Similarly, we found that severity of parosmia assessed with questionnaire from Landis et al. [17], correlated with worse quality of life assessment with sQOD-NS.

Longitudinal follow-up of TDI scores

Most C19OD patients recover spontaneously within a few weeks, and meta-analytic work suggests that approximately 5% to 30% have persistent OD after six months [35,36]. In our study, follow-up TDI scores showed that a clinically relevant improvement was indeed more common in the C19OD group compared to other etiologies, while the potential for deterioration remains consistent with other causes of OD. Of all C19OD patients, 31% had a clinically relevant improvement in TDI score, defined as an increase in TDI score of at least 5.5 points [21].

Few other studies investigating persistent C19OD report on the clinically relevant difference. A retrospective analysis of 791 patients with PIOD found that 35% to 46% of anosmic and hyposmic patients respectively, exhibited a clinically significant improvement [37]. Reporting on 1-year psychophysical follow-up data of 37 C19OD patients, Tervo et al. suggested that improvement in TDI score is mainly mediated by improvement in threshold score [38]. Although the improvement in overall TDI score was statistically significant, the clinically important difference of 5.5 could not be reached.

Conclusion

The findings from this study underscore the substantial impact of COVID-19 on the prevalence of OD within a specialized clinical setting. With C19OD as a predominant etiology, our study documents the increased incidence of parosmia. Although there can be some improvement in olfactory function over time, particularly among C19OD patients, the overall prognosis of OD remains poor. This situation calls for targeted management strategies and further research into the pathophysiology of OD. The establishment of dedicated clinics and comprehensive patient registries, as exemplified by the Smell & Taste Clinic at UZ Leuven, are practical steps toward better understanding and managing OD in the post-pandemic era.

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Authors' contributions

Under the supervision, guidance and support of LVG and MJ; MC conceived the ProspeRo'Scent project and registry, and Smell & Taste Clinic. SB, EH, VN, JvW and MC were responsible for data collection and psychophysical testing. SB assisted in the analyses of Figure 1 and 2. MC wrote the original draft of the manuscript. LVG revised the manuscript. All authors approved the submitted manuscript.

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Conflicts of interest

The authors declare no conflict of interest.

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