Acta Pharm. Sci. Vol 61:(2), 2023
DOI: 10.23893/1307-2080.APS6111

Parosmia and COVID-19 from the lens of google trends: infodemiology study

Nilay AKSOY[1*], Nur OZTURK[1]

[1] Department of Clinical Pharmacy, Faculty of Pharmacy Altınbaş University, İstanbul, Türkiye

ABSTRACT

Parosmia is a subcategory of olfactory hallucinations and refers to a distorted ability to detect the right smell in the presence of a stimulus. The study aims to investigate the relationship between COVID-19 and parosmia by calculating the interest search volume of parosmia using google trends. Google trends was used to investigate trends in searches regarding parosmia and to track these search engine terms against the coronavirus outbreak in France, Sweden, the United States [USA], and Türkiye. The terms utilized in the search were "Parosmia" and "anosmia" and the data were collected between March 20, 2020, to July 25, 2021. Parosmia searches increase with time in all the countries and the correlation significance values were obtained for France, Sweden, USA, and Türkiye to be Rs 0.660, P-value 0.0038 "Moderate correlation"; Rs 0.566, P-value 0.017 "Moderate correlation"; Rs 0.842, P-value 0.0001 "Strong correlation"; Rs 0.800, P-value 0.0001" Strong correlation" respectively. Relative search volume of parosmia and anosmia changed significantly with time may point out that there are some late COVID-19 complications that haven't been detected yet, and with the pandemic still ongoing, more complications could be discovered by analyzing the trends.
Keywords: Olfactory disorders, quality of life, disease severity, COVID-19

INTRODUCTION

The occurrence of olfactory dysfunction following viral infections is a common phenomenon that can affect an individual's sensory perceptions and cognitive abilities from mood swings to suppressing the ability to detect danger, impairing the gustatory system and by extension food enjoyment, to influencing overall health and quality of life [1,2].

*Corresponding Author: E-mail: nilay.aksoy@altinbas.edu.tr,
ORCIDs:
Nilay AKSOY: 0000-0002-6990-1945
Nur OZTURK: 0000-0002-0356-3744
(Received 21 Dec 2022, Accepted 01 Mar 2023)

Among the most common olfactory dysfunctions that affect patients' post-viral infections are parosmia and phantosmia; both conditions affect 56% of patients following viral infections. The SARS-CoV-2 virus trigger an outbreak of the coronavirus disease, which the World Health Organization (WHO) declared a pandemic on March 11, 2020 [3]. Olfactory disorders before the covid-19 pandemic were largely unrecognized, and often underestimated by researchers. During the COVID-19 pandemic, about 52.73% of cases result in loss of smell "anosmia" [4]. Although a large proportion of them recovered within weeks, some of the patients reported persistent problems including parosmia and phantosmia which aren't always associated with additional nasal disorders such as nasal obstruction and rhinorrhea [5]. While sufficient evidence remains scarce regarding the relationship between COVID-19 and olfactory dysfunction; the plethora of report studies and self-reports exchanged on social media platforms show that there's a direct bond between the two.

All olfactory dysfunctions fall into two categories, quantitative olfactory disorders which environ anosmia and hyposmia and qualitative olfactory disorders which environ parosmia and phantosmia. Anosmia is an olfactory dysfunction that refers to a complete loss of the smelling sensation, whereas hyposmia refers to a decrease in the ability to detect scents. On the other hand, there's parosmia, which is a subcategory of olfactory hallucinations and refers to a distorted ability to detect the right smell in the presence of a stimulus. Parosmia can present itself as either pleasant scents referred to as troposmia or unpleasant scents referred to as euosmia. Similarly, phantosmia is another type of olfactory hallucination that triggers the detection of scents in the absence of a stimulus. Both parosmia and phantosmia typically exist in relation to quantitative olfactory dysfunctions, however, they can also exist individually, although rarely [6].

At the start of the COVID-19 pandemic, many studies from all over the globe noted the frequent occurrence of olfactory dysfunction in patients affected by the disease [7]. For instance, some case reports indicate that some perfectly healthy individuals experienced olfactory hallucinations post recovering from COVID-19 where they express their perception of all smells as dirty, rotten, sewage, or smoky [8]. These complications imply the presence of a condition referred to as the Rare Late Complication of COVID-19, which is still unpopular.

The mechanism by which viruses impair or distort olfactory sensations is through damaging the neurons responsible for olfactory sensations and the upper respiratory tract. As for the olfactory dysfunction following a COVID-19 infection, there are a few possible hypotheses that attempt to explain the formation after treatment from the disease. The first hypothesis attributes the

damage to mechanical obstruction suggesting that the formation of inflammation surrounding the olfactory cleft prevents odors from binding to the receptors [9]. The second hypothesis proposes that the direct infection of the ACE-2 cells by the SARS-CoV-2 is the reason [10] and the 3rd hypothesis refers the reason to the direct invasion of olfactory neurons by COVID-19 virus, which impedes the mechanism of conducting olfactory sensations [11].

While the estimated number of cases that reported parosmia post recovering from COVID-19 has been limited by a lack of either reliability or availability of testing; there are several anecdotal reports that conclude the presence of sudden olfactory changes after recovering from COVID-19. For instance, many patients reported having a distorted sense of smell, some of them displayed a persistent smell of a burnt rubber scent, while others displayed the persistent presence of an onion odor [12].

Under times of pressure in a rapidly spreading viral outbreak around the world, the need for equally rapid and fast-paced research technologies and real-time data collection becomes clear. Google Trends is an online tracking system of the biggest search engine that proved to be a powerful tool for epidemiologic surveillance in previous studies specifically in the rhinology field [13]. The study aims to investigate the relationship between COVID-19 and parosmia by calculating the interest search volume of parosmia using google trends.

METHODOLOGY

Google Trends is the master of the materials employed in this research which is a system that tracks internet activity relevant to any topic on Internet hit-search volumes. The selection of searches is predetermined by the portal to be inclusive of user-specified terms searched on Google. Relative search volume (RSV) is a tool from Google trends that suggest the query share of a specific term at a certain location during a certain time period; executed on a scale of 0 to 100 that is later normalized in opposition to the highest query share of the given term over a specific duration. Each individual point has divided by the highest point, which is conventionally 100 to generate the final graph values [14].

Google trends have been used to investigate trends in searches regarding parosmia and to track these search engine terms against the coronavirus outbreak in France, Sweden, the United States (USA), and Türkiye. To make the data comparison process three different countries besides Türkiye were selected randomly using a computer program as it's difficult to collect and cover all the countries around the world.

The terms utilized in the search were "Parosmia OR change of smell" and "anosmia OR loss of smell" for (USA and Sweden), "Parosmi OR kokuları farklı

algılama" and "Anozmi OR ansomi OR koku kaybı" for Türkiye. Lastly, "Parosmie" and "anosmie" for France. All the used data were collected between March 20, 2020 to July 25, 2021 in the countries mentioned previously.

The results were displayed as a monthly search volume score and to investigate the correspondence between parosmia and anosmia, a null hypothesis was constructed, and the p-values was established. A Spearman's correlation was then employed to evaluate the potential significance of the score trends between the relative search volume (RSV) of parosmia and time progression. The data entered was assessed using IBM SPSS (Statistical Package for the Social Sciences) version 20.

RESULTS AND DISCUSSION

Using the search terms "Parosmia" "anosmia", trajectories for the frequency of the search items were examined from March 20, 2020 to July 25, 2021. Figure 1 - 4 shows the total monthly RSVs during the duration mentioned above in the selected countries.

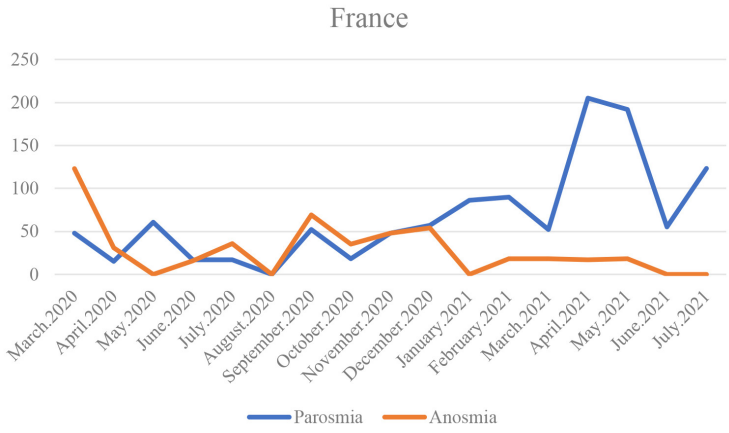

Figure 1. The total monthly RSVs between March 20, 2020 to July 25, 2021 in France

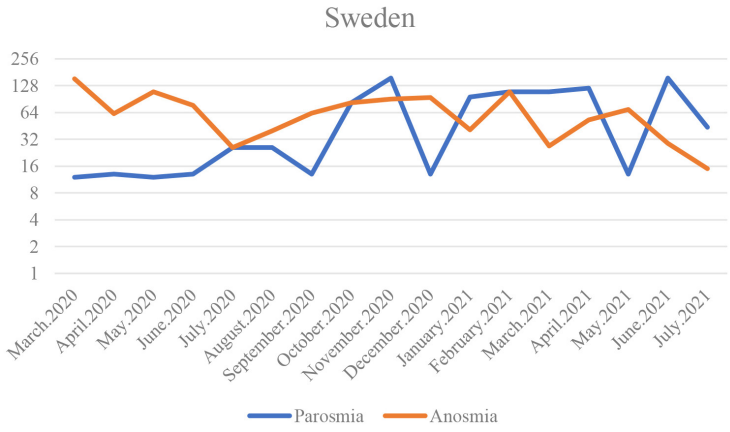

Figure 2. The total monthly RSVs between March 20, 2020 to July 25, 2021 in Sweden

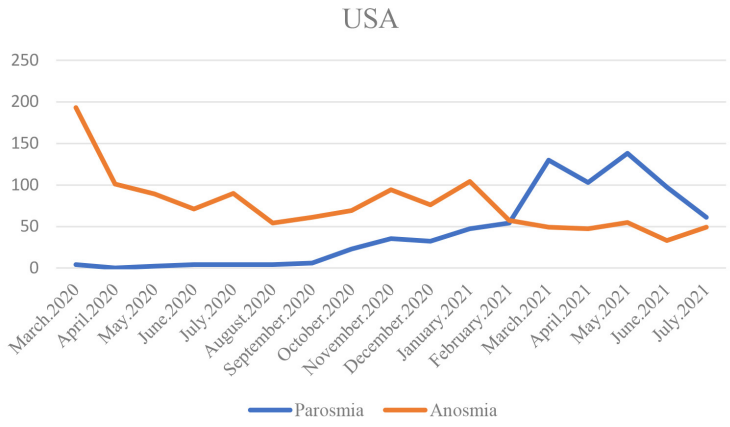

Figure 3. The total monthly RSVs between March 20, 2020 to July 25, 2021 in Unites States

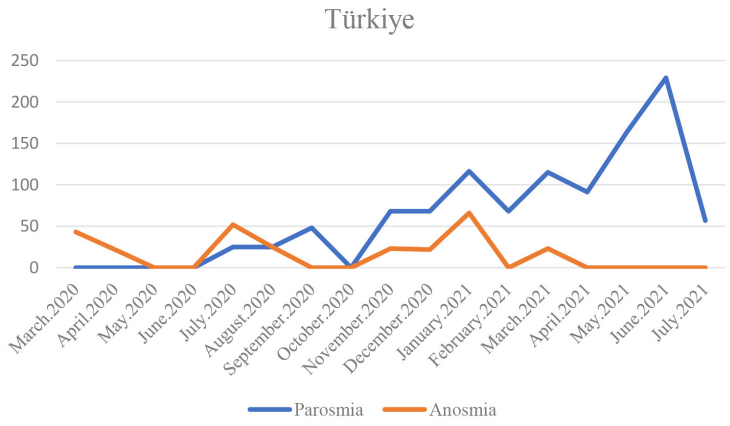

Figure 4. The total monthly RSVs between March 20, 2020 to July 25, 2021 in Türkiye

In regards to hypothesis testing on a population proportion, the null hypothesis HO was rejected indicating the presence of a statistically significant impact between parosmia and anosmia in France, USA, and Türkiye. However, in Sweden the null hypothesis HO has been accepted for the data implying the absence of a statistical significance between parosmia and anosmia.

All the data procured from varying countries indicate the presence of a statistically significant difference ($p<0.05$) between anosmia and parosmia during the pandemic with the exception of Sweden's data. Table1 shows the *P*-values between the selected terms in all the selected countries.

Table 1. Determining the significant difference between the parosmia and anosmia during Covid-19 between March 20, 2020 to July 25, 2021

	France		Sweden		USA		Türkiye	
	Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value
Parosmia	66.82 ± 58.49	0.023*	59.58 ± 54.13	0.63	43.76 ± 46.85	0.03*	63.11 ± 64.67	0.007*
Anosmia	28.41 ± 32.00		67.11 ± 36.79		76.00 ± 36.67		16.23± 21.03	

*Significant at the 0.01 level (2-tailed); SD = standard deviation; mean= average search volume per month

=In order to investigate the correlation between the escalating RSV of parosmia and the progression of time, the Bivariate Spearman correlation coefficient was calculated. The correlation significance values obtained for France, Sweden, USA and Türkiye were Rs 0.660, P-value 0.0038 "Moderate correlation"; Rs 0.566, P-value 0.017 "Moderate correlation"; Rs 0.842, p-value 0.0001 "Strong correlation"; Rs 0.800, P-value 0.0001 "Strong correlation" respectively. All countries in the study displayed a significant correlation. Table 2 shows the correlation between the selected variables.

Table 2. Correlations between the time progression and parosmia RSV

	France		Sweden		USA		Türkiye	
	Rs	P-value	Rs	P-value	Rs	P-value	Rs	P-value
Parosmia	0.660	0.0038*	0.568	0.017*	0.842	<0.001*	0.801	<0.001*
Anosmia	-0.474	0.055	-0.509	0. 037	-0.680	0.003	-0.314	0.219

*Correlation is significant at the 0.01 level (2-tailed); Rs = Spearman's correlation;
Corelation done between total monthly RSV and the time progression which ranges between March 20, 2020 to July 25, 2021

By collecting and analyzing data using Google Trends, this study was able to uncover the link between COVID-19 and parosmia as a late COVID-19 consequence. The consequences are far-reaching. There is already good evidence supported by a statistically significant effect from Italy, South Korea and China that significant numbers of patients with proven COVID-19 infection have developed anosmia/hyposmia. In Germany, it is reported that anosmia affects more than two out of every three verified cases [7]. While most people with COVID-19 olfactory dysfunction recover rapidly "within four weeks for 79 % of people" [15,16], some with long COVID-19 smell disorders are detected unpleasant scents after recovery [17].

Our findings show that the RSV of parosmia and anosmia changed significantly with time. This suggests that, around the time the coronavirus first appeared in the world, there was an upsurge in the number of people looking for information about the loss of their sense of smell. Although the RSV of anosmia was decreasing with time, the RSV of parosmia was increasing. This could be supported by a study done in 2021 concluded that, the onset of parosmia started within 3 – 5 months after the smell disorder[12], whereas reporting of anosmia onset began 4.4 days after infection initiation. According to Klopfenstein et al, the average duration of anosmia was 8.9 days, and 98 percent of patients recovered by 28 days[18]. The increase of the parosmia RSV and decrease in the anosmia search volume could be explained clearly via the results of the mentioned studies, as the onset of anosmia begins and ends entirely in 28 days,

whereas the onset of parosmia begins after 3 months of recovery. That's why people have started to search for parosmia term lately while the anosmia term RSV has increased since the initial days of the Covid-19 outbreak.

According to our findings, there is a statistically significant difference $p < 0.05$ present between anosmia and parosmia across all the selected countries except Sweden. A study has been done on 268 patients reported that all patients suffered from parosmia, they were suffering from hyposmia or anosmia prior to developing it. This supports our hypothesis that there is a statistically significant and unambiguous relationship between anosmia and the development of parosmia later on[16].

Our data illustrates a clear strong to moderate correlation in all the countries between the increase of the google search volume about parosmia regarding the time progression. That's could be explained as there is a directly proportional relation between time progression and parosmia given the strength and consistency of the Rasheed et al. study outcomes that patients with COVID-19 started to suffer from parosmia after 3.434 ± 0.4886 months after the disappearance of anosmia or getting better from COVID-19 [16]. Another study of COVID-19 patients found that after 8 weeks of follow-up, 30.9 percent of the study group had developed parosmia[19].

This finding could point to the fact that there are some late Covid-19 complications that haven't been detected yet, and with the SARS-CoV-2 pandemic still ongoing, more complications could be discovered by analyzing the trends or waiting for future case reports.

Despite all our efforts, our findings must be interpreted with caution as the data was collected regarding the RSV. Any data analysis based on electronic search volume must admit the inherent bias of a population sample drawn specifically from those who are educated, have enough money to access the internet, and use Google as their search engine of choice.

Our study suggests that members of the public have noticed a change in their sense of smell and have been obliged to look for answers on google and it shows that the interpretation of Google Trends data could have been useful to investigate the medical issues that the population might be suffering from around the world. Olfactory dysfunction is a remarkable problem that happened in the patient during and after Covid-19. Healthcare providers should play a role in the pandemic by following up with patients to report post-Covid-19 complications and assist patients in overcoming olfactory dysfunction in order to improve their quality of life.

STATEMENT OF ETHICS

No need.

CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

AUTHOR CONTRIBUTIONS

All authors contributed to the concept and design of the study. Material preparation, data collection, analysis and the draft of the manuscript were performed by [N.A] and [N.O]. The final manuscript has been reviewed and approved by all writers.

ACKNOWLEDGMENTS

None.

REFERENCES

1. Kershaw JC, Mattes RD. Nutrition and taste and smell dysfunction. World J Otorhinolaryngol Head Neck Surg. 2018;4(1):3-10. https://doi.org10.1016/j.wjorl.2018.02.006.

2. Scangas GA, Bleier BS. Anosmia: Differential Diagnosis, Evaluation, and Management. Am J Rhinol Allergy. 2017;31(1):e3-e7. https://doi.org/10.2500/ajra.2017.31.4403.

3. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. Acta Biomed. 2020;91(1):157-160. https://doi.org/10.23750/abm.v91i1.9397.

4. Tong JY, Wong A, Zhu D, Fastenberg JH, Tham T. The Prevalence of Olfactory and Gustatory Dysfunction in COVID-19 Patients: A Systematic Review and Meta-analysis. Otolaryngol Head Neck Surg. 2020;163(1):3-11. https://doi.org/10.1177/0194599820926473.

5. Keller A, Malaspina D. Hidden consequences of olfactory dysfunction: a patient report series. BMC Ear Nose Throat Disord. 2013;13(1):8. https://doi.org/10.1186/1472-6815-13-8.

6. Hüttenbrink KB, Hummel T, Berg D, Gasser T, Hähner A. Olfactory dysfunction: common in later life and early warning of neurodegenerative disease. Dtsch Arztebl Int. 2013;110(1-2):1-7. https://doi.org/10.3238/arztebl.2013.0001.

7. Hopkins C, Surda P, Kumar N. Presentation of new onset anosmia during the COVID-19 pandemic. Rhinology. 2020;58(3):295-298. https://doi.org/10.4193/Rhin20.116.

8. Meng X, Deng Y, Dai Z, Meng Z. COVID-19 and anosmia: A review based on up-to-date knowledge. Am J Otolaryngol. 2020;41(5):102581. doi: https://doi.org/10.1016/j.amjoto.2020.102581.

9. Stenner M, Vent J, Hüttenbrink KB, Hummel T, Damm M. Topical therapy in anosmia: relevance of steroid-responsiveness. Laryngoscope. 2008;118(9):1681-6. https://doi.org/10.1097/MLG.0b013e31817c1368.

10. Butowt R, von Bartheld CS. Anosmia in COVID-19: Underlying Mechanisms and Assessment of an Olfactory Route to Brain Infection. Neuroscientist. 2020:1073858420956905. doi: https://doi.org/10.1177/1073858420956905.

11. Gane SB, Kelly C, Hopkins C. Isolated sudden onset anosmia in COVID-19 infection. A novel syndrome? Rhinology. 2020;58(3):299-301. https://doi.org/10.4193/Rhin20.114.

12. Duyan M, Ozturan IU, Altas M. Delayed Parosmia Following SARS-CoV-2 Infection: a Rare Late Complication of COVID-19. SN Compr Clin Med. 2021:1-3. doi: https://doi.org/10.1007/s42399-021-00876-6.

13. Carneiro HA, Mylonakis E. Google trends: a web-based tool for real-time surveillance of disease outbreaks. Clin Infect Dis. 2009;49(10):1557-64. doi: https://doi.org/10.1086/630200.

14. Support.google.com. 2021 [cited 9 August 2021]. Available from: https://support.google.com/trends/answer/4365533?hl=en&ref_topic=6248052

15. Hopkins C, Surda P, Whitehead E, Kumar BN. Early recovery following new onset anosmia during the COVID-19 pandemic - an observational cohort study. J Otolaryngol Head Neck Surg. 2020;49(1):26. doi: https://doi.org/10.1186/s40463-020-00423-8.

16. Rashid RA, Alaqeedy AA, Al-Ani RM. Parosmia Due to COVID-19 Disease: A 268 Case Series. Indian J Otolaryngol Head Neck Surg. 2021:1-8. https://doi.org/10.1007/s12070-021-02630-9.

17. Hopkins C, Surda P, Vaira LA, Lechien JR, Safarian M, Saussez S, et al. Six month follow-up of self-reported loss of smell during the COVID-19 pandemic. Rhinology. 2021;59(1):26-31. https://doi.org/10.4193/Rhin20.544.

18. Klopfenstein T, Kadiane-Oussou NJ, Toko L, Royer PY, Lepiller Q, Gendrin V, et al. Features of anosmia in COVID-19. Med Mal Infect. 2020;50(5):436-439. https://doi.org/10.1016/j.medmal.2020.04.006.

19. Amanat M, Rezaei N, Roozbeh M, Shojaei M, Tafakhori A, Zoghi A, et al. Neurological manifestations as the predictors of severity and mortality in hospitalized individuals with COVID-19: a multicenter prospective clinical study. BMC Neurol. 2021;21(1):116. https://doi.org/10.1186/s12883-021-02152-5.