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(RESEARCH ARTICLE)

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# Chemosensory dysfunction, tobacco smoking and the need of hospitalization: how do they relate? - Data from COVID\_19 patients in Northwestern Greece

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## Abstract

**Background:** The aim of this study was to investigate the relation between tobacco smoking and chemosensory dysfunction in COVID-19 patients in Northwestern Greece. We also aimed to investigate if there is any association between smoking and the need of hospitalization, in the studied population of patients.

**Methods:** We used a questionnaire to select information about patient demographics, medical history, habits such as tobacco smoking and alcohol consumption and reported symptoms, during infection. In this study were included three hundred COVID-19 positive patients that were all undergone the RT-PCR test in the University Hospital of Ioannina, Grecce. A number of 150 patients recovered at home and 150 patients needed hospitalization. Statistical analysis based on IBM-SPSS Statistics 26.0.

**Results:** Data analysis in the total sample showed that there was no statistically difference between the subgroup of patients with loss of smell and tobacco smoking in the total sample, in the group of patients that recovered at home and in patients that needed hospitalization. No statistical association was found between the patients that used tobacco with loss of taste in the total sample, in the group of patients that recovered at home and in patients that needed hospitalization. The highest percentage of patients that were tobacco smokers was found in the subgroup of patients that recovered at home and was about 20% (n = 30). The lowest percentage was 8% (n = 12) in the subgroup of patients that needed hospitalization. There was a statistically difference between the subgroup of patients with the use of tobacco and decreased need for hospitalization.

**Conclusion:** There is no relation between chemosensory dysfunction during SARS\_COV2 infection and tobacco smoking. There is a statistically significant difference between active smokers with covid\_19 infection and decreased risk for hospitalization in this small number of patients.

Keywords: COVID-19; Olfactory dysfunction; Gustatory dysfunction; smoking; Northwestern Greece

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# 1. Introduction

It is now commonly accepted that olfactory and gustatory dysfunction caused by SARS\_COV2 have a significant impact on quality of life, as many studies improved loss of taste and smell during infection seem to be related to many factors, such as age, gender, ethnicity, co morbidities and tobacco smoking (1-16).

The role of the angiotensin converting enzyme 2 [ACE2] receptor has a key role as a pathway for chemosensory dysfunction in covid\_19 infection. The virus can also enter through neural olfactory epithelium cells directly to cerebrospinal fluid near to the olfactory bulb. Viral entry into the central nervous system along the olfactory tract seems to play an important role in this process. The extracellular domain of ACE2 is the cellular receptor for SARS-CoV-2 proteins that interacts causing virus endocytosis (17-26).

The aim of this study was to evaluate the relation between chemosensory dysfunction and the use of tobacco smoking, in Northwestern Greece, both in hospitalized and self-quarantined patients with SARS\_COV2 infection. We also aimed to investigate if the need for hospitalization during COVID\_19 infection was influenced by tobacco smoking in this population.

# 2. Methods

## 2.1. Participants

This is a prospective observational cohort study approved by the Research and Ethics Committee and the Scientific Council of University General Hospital of Ioannina. The total sample included 300 patients with COVID-19 infection, both men and women, aged from 18 to 80 years old that referred to the Emergency Department [ED] of Infectious Diseases or to the Outpatient Clinic of screening for SARS-COV2. All participants had a positive reverse transcription-polymerase chain reaction [RT-PCR] test result, between November 2020 and May 2021. An informed consent form was obtained from every patient.

The study population included two subgroups. The first subgroup of 150 patients recovered at home. These patients had a mild to moderate disease and did not need hospitalization. The other 150 patients had a severe disease and were hospitalized in the Infectious Diseases Unit [IDU] of the University General Hospital of Ioannina.

Specific exclusion criteria were used in order to determine the sample size of this research. We excluded every participant that had a previous sinus surgery, suffered from allergic rhinitis or chronic rhino sinusitis, undergone head and neck radiation therapy, had a history of head injury, psychiatric disorders, neurological diseases or medical history with olfactory and gustatory dysfunction. As these factors affect smell and taste, we considered that they should be excluded from our study.

## 2.2. Data collection

Data collection was performed during covid\_19, at the first days of infection, using a questionnaire. One hundred and fifty covid-19 positive patients with mild symptoms that recovered at home were informed in person at the time of diagnosis, by telephone, or by e-mail, following the safety measures provided by National Organization of Public Health of Greece. One hundred and fifty patients with moderate to severe symptoms that needed hospitalization were examined in person, by one of the main investigators of the study, in the Infectious Diseases Unit of the University General Hospital of Ioannina.

Patient demographics [name, age, sex, weight height] and contact details were recorded. Medical history, reported comorbidities, associated symptoms during infection, tobacco smoking and alcohol consumption were also recorded. The questionnaire was completed by the examinee, after providing a written consent form.

## 2.3. Statistical analysis

The statistical analysis approach regarding the categorical data was performed using the x2[chi-square] test or the Fisher's exact test in the case where at least one frequency in the contingency table was smaller than 5.

We estimated the percentage of patients that use tobacco smoking, in the total sample, in the subgroup of patients as well as in the two subgroups.

We investigated if there is statistically significant difference between the subgroup of patients with loss of smell and tobacco smoking during infection. This association was examined in the total sample, in the subgroup of patients that recovered at home and in hospitalized patients.

In a second analysis, we investigated if there is statistically significant difference between the subgroup of patients with loss of taste and tobacco smoking during infection. This association was examined in the total sample, in the subgroup of patients that recovered at home and in hospitalized patients.

We also examined the statistical association between tobacco smoking and hospitalization.

P-values and odds ratio [OR] were calculated for every feature that was statistically analyzed.

## 3. Results

A percentage of 14% of patients in the total sample were tobacco smokers. In the subgroup of patients that recovered at home, tobacco smokers were about 20%. This percentage was 8% in the subgroup of patients that needed hospitalization (Table 1).

**Table 1** Number and percentages of patients that were tobacco smokers, in the total sample, in the subgroup of patientsthat recovered at home and in the subgroup of hospitalized patients

	Total sample [n= 300]	Home- quarantine patients [n=150]	Hospitalized patients[n=150]
Tobacco smokers	42	30	12
Percentage %	14%	20%	8%

The percentage of tobacco smokers with loss of smell was 8,67% in the total sample, 13,33% in the subgroup of patients that recovered at home and 4% in the subgroup of hospitalized patients (Table 2).

**Table 2** Percentages of tobacco smokers with loss of smell/loss of taste, in the total sample, in the subgroup of patients that recovered at home and in the subgroup of hospitalized patients

Percentages%	Total sample [n=300]	Home-quarantine Patients [n=150]	Hospitalized Patients [n=150]
Tobacco smokers with loss of smell	8.67%	13.33%	4%
Tobacco smokers with loss of taste	13.33%	9.33%	4%

**Table 3** Statistical results between tobacco smoking and loss of smell, in the total sample, in the subgroup of patientsthat recovered at home and in hospitalized patients

Tobacco smoking	Total sample [n=300]	Hospitalized patients Home-quart [n=150] Patients [n=	
Loss of smell	26	6	20
No loss of smell	16	6	10
P-value	0.6	0.952	0.896
Odds Ratio	1.26637931	1.15625	0.962962963

[\*p < 0.050, \*\*p < 0.005, \*\*\*p < 0.001]; [OR > 1 means greater odds of association with the exposure and outcome; OR = 1 means there is no association between exposure and outcome; OR < 1 means there is a lower odds of association between the exposure and outcome]

Data analysis in the total sample showed that there was no statistically difference between the subgroup of patients with loss of smell and tobacco smoking in the total sample, in the group of patients that recovered at home and in patients that needed hospitalization (Table 3).

In addition, there is was no statistical association between the patients that used tobacco smoking and loss of taste in the total sample, in the group of patients that recovered at home and in patients that needed hospitalization (Table 4).

**Table 4** Statistically significant difference between tobacco smoking and loss of taste, in the total sample, in the subgroup of patients that recovered at home and in the hospitalized patients

Tobacco smoking	Total sample [n=300]	Hospitalized patients [n=150]	Home- quarantine Patients [n=150]
Loss of taste	20	6	14
No loss of taste	22	6	16
P-value	0.689	0.952	0.303
Odds Ratio	0.828282828	1.15625	0.603873239

[\*p < 0.050, \*\*p < 0.005, \*\*\*p < 0.001][OR > 1 means greater odds of association with the exposure and outcome; OR = 1 means there is no association between exposure and outcome; OR < 1 means there is a lower odds of association between the exposure and outcome]

Data analysis in the total sample showed that there was a statistical difference between the subgroup of patients with use of tobacco smoking and hospitalization [p=0,005], [OR=0,347826087] (Table 5).

Table 5 Statistically significant difference between tobacco smoking and hospitalization, in the total sample

Tobacco Smoking         12         30         0.005         0.347826087		Hospitalization	No Hospitalization	p-value	Odds Ratios
	Tobacco Smoking	12	30	0.005	0.347826087

[\*p < 0.050, \*\*p < 0.005, \*\*\*p < 0.001]; [OR > 1 means greater odds of association with the exposure and outcome; OR = 1 means there is no association between exposure and outcome; OR < 1 means there is a lower odds of association between the exposure and outcome]</p>

# 4. Discussion

Many studies have already shown that patients with a history of smoking and/or active smokers had significantly increased risk for severe COVID-19 disease (27-32). It is therefore critical to identify the reasons that this factor influences the course of the disease. The use of tobacco products is a potential risk factor, given its adverse effects on health and the high prevalence of use. These products have been shown to cause damage to the lungs and alter the immune system response. These effects leads to increased susceptibility to most respiratory viruses (33-36). Development of COVID-19-induced anosmia may be influenced by smoking behaviors, as many researchers had already shown (7, 37-40). However, we found no statistically significant association between tobacco smoking and olfactory and gustatory dysfunction, in this Northwestern Greek population. Of note, the sample size of our research, may serve as a limitation factor that affected this result.

Tobacco smoking was also shown to be a strong risk factor for hospitalization during COVID-19 pandemic. Daniel Puebla Neira et al., showed that significantly more former smokers were hospitalized and died from SARS\_COV2 than current or never smokers(41). Similar results were found by David Simons in his study(42), in contrary with George N. Ioannou where no relation between smoking and the need for hospitalization(43). In addition, another Spanish study concluded that both active and past smoking is an independent predictor of poor prognosis in patients with COVID-19 and is associated with higher intensive care unit [ICU] admissions and in-hospital mortality(44).

As smoking is a well-known risk factor associated with greater subsequent increased severity of respiratory infections, we expected that in a same way it would affect the majority of patients with COVID\_19. However, preliminary studies did not showed the expected results in real-world data (45)]. A chinese study found that the smoking prevalence among COVID-19 patients was 10.2%, (46), following the low prevalence of current smokers among hospitalized COVID-19 that is a common finding across several countries(46-49). In our study we investigated the association between active tobacco smokers and hospitalization. The percentage of smokers was 14% (n = 42) in the total sample and 20% (n = 30) in the subgroup of patients that recovered at home. The lowest percentage of smokers was noticed in the group of

patients that needed hospitalization (8%, n = 12). Aside this low percentage, we found that tobacco smoking was statistically significant associated with decreased risk of IDU admission similarly to other previously mentioned studies (46-48, 50).

However, our study is limited by the sample size that is not large enough to give an indicative result regarding the association between smoking and the need of hospitalization. The restriction to specific geographically isolated populations also limits the power of these findings'. So, the need for larger research trials that will investigate multiple racial groups should be a goal for the future.

# 5. Conclusion

The present study concluded that there is no relation between chemosensory dysfunction during SARS\_COV2 infection and tobacco smoking. There is a statistically significant difference between active smokers with covid\_19 and decreased risk for hospitalization. Our observations come to an agreement with previous studies.

## **Compliance with ethical standards**

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## Disclosure of conflict of interest

We do not have any competing interests that might bias the content of this work or its publication process.

## Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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