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Editorial

A Retrospective Study of Covid-19-Related Gustatory and Olfactory Symptoms and ABO/Rh Blood Group - ə

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EDITORIAL

The swift universal spread of the novel coronavirus, SARS-CoV-2, has forced healthcare organizations to enhance testing, as well as distribution of vaccines to effectively care for and identify individuals most at-risk. After it was first presented by the CDC as a potential symptom of the disease, several publications have focused on the loss or reduced sense of smell and/or taste as an indicative symptom of the infection [1,2]. Given the significant mortality and morbidity associated with Covid-19, there have been concerns and a lack of knowledge present about possible clinical characteristics that might render patients more susceptible to infection. Accordingly, it has been previously suggested that blood type may affect the susceptibility of patients to the virus, as well as the risk of developing the more severe form of the infection. While previous studies have mainly focused on finding correlations between blood type and the clinical outcomes of Covid-19in terms of duration of hospitalization, intubation, and death [3,4], this paper aims to shed light on potential associations between Covid-19- related symptoms and patients' ABO/Rh blood group.

The present retrospective study was done at the department of Emergency medicine at Modarres Hospital, Saveh, Iran. A detailed questionnaire was given to 305 patients whose PCR diagnostic test was positive and had recovered (tested negative for and were clinically symptom-free) from Covid-19, 15±8. 6days prior to the study on average. All of the participants were previously hospitalized at the same facility. The survey was sent to the participants and each participant was walked through the questionnaire by atrained volunteer research assistant to ensure that the patient fully understood the questions. Eight blood types of A+, B+, AB+, O+, O-, AB-, A-, and B- were observed, clinically confirmed using laboratory testing, and examined as grouping variables. Data was gathered based on the patients' response to specific polar questions on previous medical history, comorbidities, and Covid-19-related symptoms as well as questions to test the duration of gustatory and olfactory dysfunction prior to recovery from Covid-19 (Table 1). Overall, among the participants of the study, 43 had reported gustatory and 71 had reported olfactory malfunction over the duration of their disease. Further, the median duration of olfactory and gustatory dysfunction experienced by the participants was found to be 7 and 10 days, respectively. Employing

Table 1: Clinical manifestations and past medical history of the study population based on the filled surveys.
ARDS: Acute Respiratory Distress Syndrome; DM: Diabetes Mellitus; HTN: Hypertension; CVD: Cardiovascular Disease; PND: Purulent Nasal Discharge; ICU: Intensive Care Unit

		Frequency	percentage
Gender	**Male**	189	62
	Female	116	38
Fever		158	51.8
Dry cough		63	20.7
Anorexia		63	20.7
Diarrhea		31	10.2
Pharyngalgia		18	5.9
Abdominal pain		13	4.3
Dizziness		16	5.2
Headache		43	14.1
Impaired consciousness		5	1.6
Ataxia		2	0.7
Myalgia		158	51.8
Fatigue		66	21.6
ARDS		10	3.3
Dyspnea		121	39.7
Sore throat		12	3.9
Arthralgia		14	4.6
Asthenia		57	18.7
Rhinorrhea		3	1
Sneezing		7	2.3
PND		2	0.7
Vomiting		36	11.8
Nasal congestion		2	0.7
Nasal stiffness		1	0.3
Facial fullness and sinus pain		3	1
Otalgia		5	1.6
Cheeks pain		2	0.7
Mild flu like symptoms lasting<24 hours		22	7.2

Delirium	2	0.7
Chest pain	50	16.4
Hoarse voice	1	0.3
Vertigo	9	3
Flu-like syndromes before anosmia	1	0.3
Parosmia	0	0
Phantosmia	2	0.7
Unilateral facial palsy	2	0.7
History of diabetes mellitus	55	18
History of hyperthyroidism	5	1.6
History of hypothyroidism	6	2
History of asthma	3	1
History of Hypertension	53	17.4
History of Cardiovascular disease	27	8.9
History of Immunocompromised Condition	3	1
Medicine use (aminoglycosides, tetracycline, opioids, cannabinoids, sildenafil, metronidazole, cholorpheniramine, allopurinol, methimazole, baclofen, levodopa, codein, morphin, carbamazepine, lithium, phenytoin, amphetamine, iron, vitamin D)	0	0
Use of corticosteroid spray to treat olfactory dysfunction	0	0
Olfactory dysfunction in family members	30	9.9
Gustatory dysfunction in family members	19	6.2
Smoking	14	4.6
Use of mask	123	40.3
The use of nasal drops for olfactory dysfunction	0	0
ICU admittance	11	3.6
Ventilator use during hospitalization	1	0.3

version 25 of SPSS, Fischer's exact test was used to identify any associations between the experiencing the Covid-19 symptoms and patients' blood-type. Importantly, among the tested symptoms, the incidence of hypogeusia and hyposmia were found to be significantly different among the examined blood groups (p-value = 0.005< 0.05; p-value = 0.026 < 0.05; 95% CI).

While the results of this study indicated a significant difference between the incidence of gustatory and olfactory malfunction with the patients' blood types, it has been previously found that around 33.9% to 85.6% of patients with SARS-CoV-2 infection experience hyposmia and hypogeusia [5]. Based on the findings of this study, this high variability may be clinically linked to factors such as the patients' blood type. Whereas it is difficult to always attribute olfactory malfunction symptoms only to upper airways obstruction, especially for patients with hyposmia and hypogeusia preceding systemic symptoms, the olfactory dysfunction may be clinically correlated to the Central Nervous System (CNS) entry of virus [5]. This hypothesis is relevant as it has previously been shown that Angiotensin Converting Enzyme 2 (ACE2), which is required for SARS-CoV-2 entry into the cells, demonstrates a widespread distribution in the neuroepithelium and neural cells [6,12]. Accordingly, ABO Blood group antigens have been shown to be involved in the development of olfactory nerve connectivity [7]. For instance, B antigens are expressed on primary sensory cells of the rat olfactory apparatus, while A antigens are associated with coordinating nerve fasciculation to regenerate olfactory accessory neurons [8]. Therefore, the absence of these surface antigens affects convergence of neurons and can ultimately disturb the nervous response. Also, the presence of A antigen in vomeronasal organ could be linked to the bitter taste receptors [7], which signals a link between the olfactory and gustatory dysfunction experienced by Covid-19 patients. Similar to the lack of association between blood type and composite intubation in Covid-19, there was no association noted between ABO/ Rh blood type and fever or dry cough which are considered as the most indicative symptoms of Covid-19 [9]. This is in contrast with previous research that demonstrated ABO blood-typing might play a role in multiorgan protective effect in Covid-19 and even introduced blood group as a biomarker for differential susceptibility and severity of Covid-19 [4].

Notably, blood types are unequally distributed across various ethnic groups, with enrichment of Rh-negative individuals among white and non-Hispanic groups [10]. Several studies have emerged to suggest ethnicity as a confounding factor of blood typing studies; hence, due to the disproportionate morbidity and mortality of Covid-19 among different ethnic groups, the full effects of ethnicity on Covid-19-related symptoms requires further research [11,12]. This study was limited first due to the relatively small sample sizes and variations among the different blood groups. Second, it inevitably suffers from some degree of recall bias as some of the patients may not have recalled experiencing Covid-19-associated hypogeusia and hyposmia. This may be due to the observation that olfactory and gustatory manifestations often represent an early marker of disease that precedes respiratory and systemic symptoms. Further, it has been shown that the subjective reporting of olfactory dysfunction, which is used in the present study due to its survey nature, is significantly

lower than using objective methods [13]. Finally, selection bias is a fundamental limitation of this study, since all of our effect estimates were conditional on patients who recently recovered from Covid-19. Although significant associations between ABO/Rh blood groups and olfactory and gustatory symptoms in Covid-19 patients were shown, no associations were found between the more prevalent symptoms such as fever, dry cough incidence and the patients' blood groups. Whereas the present study does not provide ample evidence for the associations found due to its observational nature, this paper presents a nuanced avenue worthy of consideration for further research into the potential correlation between the proposed symptoms and RBC antigens of Covid-19 patients.

REFERENCES

1. Hopkins C, Surda P, Vaira LA, Lechien JR, Safarian M, Saussez S, Kumar N. Six month follow-up of self-reported loss of smell during the COVID-19 pandemic. Rhinology. 2021 Feb 1;59(1):26-31. doi: 10.4193/Rhin20.544. PMID: 33320115.
2. Boscolo-Rizzo P, Polesel J, Spinato G, Menegaldo A, Fabbris C, Calvanese L, Borsetto D, Hopkins C. Predominance of an altered sense of smell or taste among long-lasting symptoms in patients with mildly symptomatic COVID-19. Rhinology. 2020 Oct 1;58(5):524-525. doi: 10.4193/Rhin20.263. PMID: 32683438.
3. Latz CA, DeCarlo C, Boitano L, Png CYM, Patell R, Conrad MF, Eagleton M, Dua A. Blood type and outcomes in patients with COVID-19. Ann Hematol. 2020 Sep;99(9):2113-2118. doi: 10.1007/s00277-020-04169-1. Epub 2020 Jul 12. PMID: 32656591; PMCID: PMC7354354.
4. Hoiland RL, Fergusson NA, Mitra AR, Griesdale DEG, Devine DV, Stukas S, Cooper J, Thiara S, Foster D, Chen LYC, Lee AYY, Conway EM, Wellington CL, Sekhon MS. The association of ABO blood group with indices of disease severity and multiorgan dysfunction in COVID-19. Blood Adv. 2020 Oct 27;4(20):4981-4989. doi: 10.1182/bloodadvances.2020002623. PMID: 33057633; PMCID: PMC7594392.
5. Bax F, Tascini C, Valente M, Marini A, Surcinelli A, Pellitteri G, De Carlo C, Gerussi V, Gigli GL. Hyposmia and Dysgeusia in COVID-19: Indication to Swab Test and Clue of CNS Involvement. Neurol Clin Pract. 2021 Apr;11(2):e92-e96. doi: 10.1212/CPJ.0000000000001029. PMID: 33842076; PMCID: PMC8032441.
6. Yavarpour-Bali H, Ghasemi-Kasman M. Update on neurological manifestations of COVID-19. Life Sci. 2020 Sep 15;257:118063. doi: 10.1016/j.lfs.2020.118063. Epub 2020 Jul 9. PMID: 32652139; PMCID: PMC7346808.
7. Mukherjee A, Basavarajegowda A, et al. Olfactory Function and Its Association with ABO Blood Group in Adults: A Cross-sectional Study. Global Journal of Transfusion Medicine. 2017.
8. Mollicone R, Trojan J, Oriol R. Appearance of H and B antigens in primary sensory cells of the rat olfactory apparatus and inner ear. Brain Res. 1985 Jan;349(1-2):275-9. doi: 10.1016/0165-3806(85)90154-3. PMID: 3986592.
9. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020 Feb 15;395(10223):507-513. doi: 10.1016/S0140-6736(20)30211-7. Epub 2020 Jan 30. PMID: 32007143; PMCID: PMC7135076.
10. Garratty G, Glynn SA, McEntire R; Retrovirus Epidemiology Donor Study. ABO and Rh(D) phenotype frequencies of different racial/ethnic groups in the United States. Transfusion. 2004 May;44(5):703-6. doi: 10.1111/j.1537-2995.2004.03338.x. PMID: 15104651.
11. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, Debenham L, Llavall AC, Dixit A, Zhou D, Balaji R, Lee SI, Qiu X, Yuan M, Coomar D, Sheikh J, Lawson H, Ansari K, van Wely M, van Leeuwen E, Kostova E, Kunst H, Khalil A, Tiberi S, Brizuela V, Broutet N, Kara E, Kim CR, Thorson A, Oladapo OT, Mofenson L, Zamora J, Thangaratinam S; for PregCOV-19 Living Systematic Review Consortium. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020 Sep 1;370:m3320. doi: 10.1136/bmj.m3320. PMID: 32873575; PMCID: PMC7459193.
12. Chen M, Shen W, Rowan NR, Kulaga H, Hillel A, Ramanathan M Jr, Lane AP. Elevated ACE-2 expression in the olfactory neuroepithelium: implications for anosmia and upper respiratory SARS-CoV-2 entry and replication. Eur Respir J. 2020 Sep 24;56(3):2001948. doi: 10.1183/13993003.01948-2020. PMID: 32817004; PMCID: PMC7439429.
13. Hannum ME, Ramirez VA, Lipson SJ, Herriman RD, Toskala AK, Lin C, Joseph PV, Reed DR. Objective Sensory Testing Methods Reveal a Higher Prevalence of Olfactory Loss in COVID-19-Positive Patients Compared to Subjective Methods: A Systematic Review and Meta-Analysis. Chem Senses. 2020 Dec 5;45(9):865-874. doi: 10.1093/chemse/bjaa064. PMID: 33245136; PMCID: PMC7543258.