

A Retrospective Study on Smell Dysfunction in COVID-19 Patients Presenting to a Tertiary Care Teaching Hospital in Northern India

Aditya Singhal, Akshay Jain, Shradha Agarwal

Department of ENT, Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India

Abstract

Introduction: The smell dysfunction in COVID-19 patients has remained an unexplained topic. The blood parameters' variability in COVID-19 patients with anosmia has been studied in few literatures. The study is aimed to find the association of anosmia with the blood grouping and C-reactive protein (CRP) levels in coronavirus-infected patients. **Materials and Methods:** Database from Medical Records Department of a Tertiary Care Teaching Hospital in Northern India was searched from July 2020 to December 2020. Every fifth file was selected using the stratified random sampling. Laboratory-confirmed COVID-19 cases by reverse transcription-polymerase chain reaction files were included. Blood grouping and CRP levels were assessed and statistically correlated. **Results:** A total of 103 patients of coronavirus-associated infection with anosmia were included among which 52 (50.48%) patients were from moderate category of AIIMS-ICMR joint task Force's clinical guidelines. A total of 44 (42.71%) patients had moderate levels of elevated CRP. The blood Group B-type was found most commonly in 35 (33.98%) patients. The correlation of severity of COVID-19 infection with CRP was found to be statistically significant (Chi-square test statistic was 31.203 and $P = 0.00023$) in patients presenting with smell dysfunction. **Conclusion:** Anosmia was found to a suggestive symptom for the early identification of coronavirus-infected cases. In this study, CRP levels showed statistically significant association with anosmia in COVID-19 patients. Predilection for specific blood groups serves as platform for further research.

Keywords: ABO grouping, COVID-19, C-reactive protein levels, olfactory dysfunction

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 variant causing COVID-19 infection is the deadliest infection of this century till date.^[1] The pandemic has impacted not only health-care system but also a multidimensional global loss.^[2,3] Anosmia is one of the common presenting complaints in COVID-19-infected individual.^[4,5] The upper airway is considered foci of infection and a mainstay harbor site for the virus. The virus is transmitted through respiratory droplets. Transmission is by sneezing, coughing, or by direct near contact. The virus was first detected in Wuhan, China from where it has rapidly spread to rest of the world.^[6]

Clinical manifestations range from mild flu-like symptoms to severe respiratory distress syndrome involving immediate

medical attention.^[7,8] The incubation time studied in the different waves of the COVID-19 infection ranges from as early as few days up to 3 weeks. COVID-19 infection is considered contagious even during the latency period of the disease.^[9-11] Ear, Nose, and Throat (ENT)-related symptoms involve throat and nasal complaints with olfactory dysfunction as a concerning, identifiable, and early symptom. The mechanism of olfactory dysfunction is either conductive or due to neural predilection of the virus. The virus seems to invade the epithelial and neuronal mucosa of the olfactory nerve.^[12-14] Prospective studies of high planar MRI have shown involvement of olfactory nerve.^[7,15-17]

Address for correspondence: Dr. Akshay Jain,

Department of ENT, Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India.
E-mail: meetakshayjain@gmail.com

Submitted: 17-Jul-2023 Revised: 16-Oct-2023

Accepted: 18-Oct-2023 Published: 22-Dec-2023

Access this article online

Quick Response Code:



Website:
www.actamedicainternational.com

DOI:
10.4103/amt.amit_57_23

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Singhal A, Jain A, Agarwal S. A retrospective study on smell dysfunction in COVID-19 patients presenting to a tertiary care teaching hospital in Northern India. Acta Med Int 2023;10:117-20.

C-reactive protein (CRP) is a biomarker of inflammation, acute phase reactant synthesized from liver in response to interleukin-6. CRP has shown to be elevated in COVID-19 patients.^[18,19] However, only few studies have been done to find the relation between CRP levels and anosmia in coronavirus-infected individuals. ABO blood grouping has also been studied to find its association with various illnesses including many bacterial and viral infections in the past.^[20-23] There have been some studies which have tried to correlate the association of blood grouping with COVID-19.^[23-25] However, limited work has been done correlating it to olfactory dysfunction in COVID-19 patients. In this study, our primary aim has been to correlate olfactory dysfunction with the ABO blood typing of the patients. In this study our primary aim is to correlate Covid 19 patient's (presenting with smell dysfunction) ABO blood typing and CRP levels with the severity of the disease. These findings can support in future endemic breakouts as a screening tool for early detection and further management.

MATERIALS AND METHODS

Study design

The study design was a retrospective observational study.

Study place

The study was conducted at a Tertiary Care Teaching Hospital and Medical College in Northern India.

Study duration

The study was conducted from July 2020 to September 2020.

Sampling method

Every 5th file of 3147 files was screened for olfactory dysfunction, using stratified random sampling.

Inclusion criteria were the presence of anosmia in COVID-19 cases confirmed by reverse transcription-polymerase chain reaction test. Exclusion criteria included patients who underwent any nasal surgery in the past and previous history of smell-and-taste disorder or those with nasal allergies.

Data collection

A total of 103 cases were identified. The ICMR criteria were used for the categorization of severity of the disease. The age and gender distribution of the cases was assessed.

Data entry

It was done in Microsoft Excel format and analysis done using latest version of IBM SPSS. IBM Corp. Released 2021. IBM SPSS Statistics for Windows, (Version 28.0. Armonk, NY: IBM Corporation).

Data analysis

The blood parameters such as ABO grouping and CRP were assessed, and statistical association with the severity of disease was inferred using the Chi-square test.

Ethical clearance

Institutional Review Board approval was obtained with no. IRB/100/2023.

RESULTS

Out of the total 103 case sheets included during the timeframe for analysis, there were 58 (56.31%) males and 45 (43.68%) females as shown in Figure 1. A maximum number of patients belong to age group of 21–30 years [Figure 2].

A total of 83 patients [Figure 3] had ageusia along with smell dysfunction.

In this study, case severity distribution according to the ICMR guidelines is shown in Table 1.

The CRP levels was found to be moderately elevated in most patients ($n = 44$). A total of 36 patients had mildly elevated CRP levels as shown in Table 2.

The blood group distribution along with the Rhesus factor of the cases was assessed [Figure 4]. Correlating the severity of the disease with blood group distribution in anosmia patients, most patients had B blood group and least belonged to AB blood group as depicted in Table 3. The Chi-square statistic is 3.6718, with $P = 0.720996$ which was found to be insignificant.

Correlation of the severity of the disease with CRP levels in anosmia patients was done. The contingency Table 4 provides the information, where the Chi-square statistic is 31.203 and $P = 0.00023$ (statistically significant).

DISCUSSION

The predilection of the coronavirus to the nonneuronal structures of the olfactory nerve was found to be the most likely pathological mechanism, according to Cazzolla *et al.* The study reports high prevalence of olfactory dysfunction in coronavirus-infected patients.^[4]

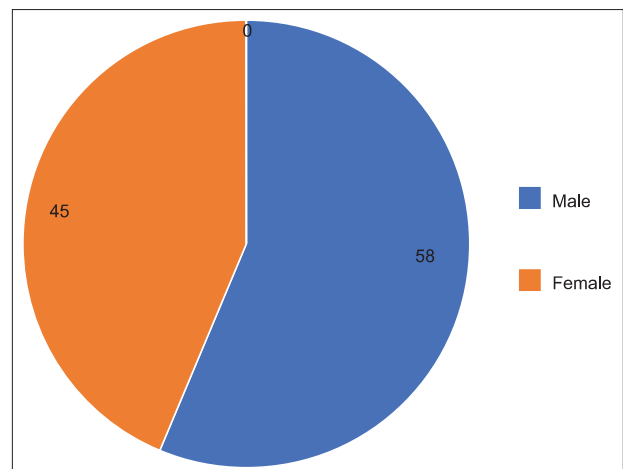


Figure 1: Sex distribution

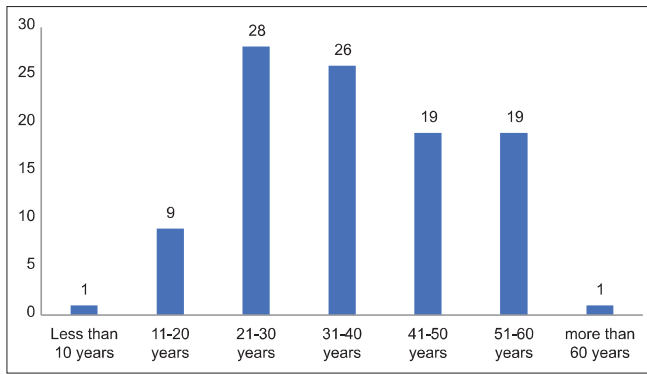


Figure 2: Age distribution

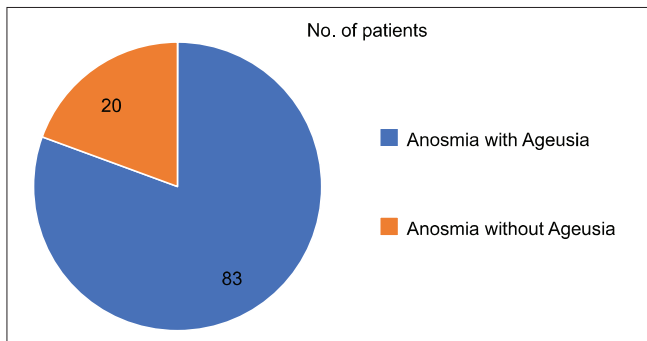


Figure 3: Relation with Ageusia (loss of taste)

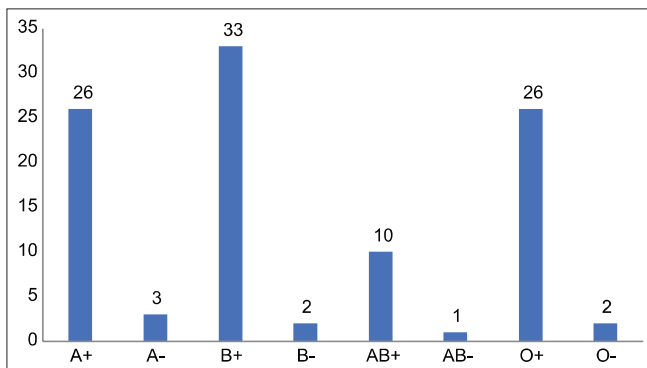


Figure 4: Blood group distribution

Dicpinigaitis concluded that anosmia is associated with other viral illnesses as well; however, the association of blood parameters with anosmia in coronavirus infection is less understood.^[6] Kavaz *et al.* in his study have concluded that olfactory disturbances are due to increased inflammation of the nonneuronal mucosa, which serves as a basis to study the inflammatory markers in anosmia.^[9] The blood grouping and its association with bacterial and viral diseases have been done since long time.^[26-28] In a study conducted by Mahmud *et al.*, most number of patients of coronavirus infection belonged to blood Group A, also these patients had delayed seroconversion. In this study, the association is maximum with B type of blood group.^[10,28] El-Anwar *et al.* concluded that most common presenting complaints were fever and

Table 1: Case distribution according to severity

Severity	Number of patients (%)
Mild	33 (32.03)
Moderate	52 (50.48)
Severe	18 (17.47)

Table 2: C-reactive protein levels distribution

CRP levels	Number of patients (%)
Normal (<3 mg/dL)	8 (7.77)
Mildly elevated (3–10 mg/dL)	36 (34.95)
Moderately elevated (10–100 mg/dL)	44 (42.71)
Marked elevated (>100 mg/dL)	15 (14.56)

CRP: C-reactive protein

Table 3: Correlation of severity with blood grouping in anosmia patients

Severity	A	B	AB	O
Mild	11	9	4	9
Moderate	14	18	4	16
Severe	4	8	3	3
Total, n (%)	29 (28.16)	35 (33.98)	11 (10.68)	28 (27.18)

Table 4: Correlation of severity with the C-reactive protein levels in anosmia patients

Severity	Normal	Mildly elevated	Moderately elevated	Severely elevated
Mild	6	20	6	1
Moderate	1	13	30	8
Severe	1	3	8	5

cough.^[29] Porta-Etessam *et al.* proposed that the olfactory and gustatory dysfunction was a good prognostic factor of disease and also said increase in CRP imply a worse prognosis of the patient.^[26,30,31]

CONCLUSION

In this study, more male patients presented with anosmia and they were mainly in their third and fourth decades of life. Maximum patients who presented with anosmia had B blood group, followed by A and O with almost similar incidence (The Chi-square statistic is 3.6718 with $P=0.720996$ which was found to be insignificant). The CRP is found as a good predictor of association of anosmia with COVID-19 infection (Chi-square statistics is 31.203 and $P=0.00023$). In our study, most patients with anosmia were came under the moderate COVID-19 categories.

A study on a larger scale is further required for getting a more accurate result and serves a platform for further research.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Maxmen A. Wuhan market was epicentre of pandemic's start, studies suggest. *Nature* 2022;603:15-6.
- Hariyanto TI, Rizki NA, Kurniawan A. Anosmia/hyposmia is a good predictor of coronavirus disease 2019 (COVID-19) infection: A meta-analysis. *Int Arch Otorhinolaryngol* 2021;25:e170-4.
- Burges Watson DL, Campbell M, Hopkins C, Smith B, Kelly C, Deary V. Altered smell and taste: Anosmia, parosmia and the impact of long COVID-19. *PLoS One* 2021;16:e0256998.
- Cazzolla AP, Lovero R, Lo Muzio L, Testa NF, Schirinzio A, Palmieri G, *et al.* Taste and smell disorders in COVID-19 patients: Role of interleukin-6. *ACS Chem Neurosci* 2020;11:2774-81.
- Lechien JR, Chiesa-Estomba CM, De Siaty DR, Horoi M, Le Bon SD, Rodriguez A, *et al.* Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): A multicenter European study. *Eur Arch Otorhinolaryngol* 2020;277:2251-61.
- Dicpinigaitis PV. Post-viral Anosmia (loss of sensation of smell) did not begin with COVID-19! *Lung* 2021;199:237-8.
- Zheng J, Wong LR, Li K, Verma AK, Ortiz ME, Wohlford-Lenane C, *et al.* COVID-19 treatments and pathogenesis including anosmia in K18-hACE2 mice. *Nature* 2021;589:603-7.
- Roy D, Ghosh R, Dubey S, Dubey MJ, Benito-León J, Kanti Ray B. Neurological and neuropsychiatric impacts of COVID-19 pandemic. *Can J Neurol Sci* 2021;48:9-24.
- Kavaz E, Tahir E, Bilek HC, Kemal Ö, Deveci A, Aksakal Tanyel E. Clinical significance of smell and taste dysfunction and other related factors in COVID-19. *Eur Arch Otorhinolaryngol* 2021;278:2327-36.
- Mahmud R, Rassel MA, Monayem FB, Sayeed SK, Islam MS, Islam MM, *et al.* Association of ABO blood groups with presentation and outcomes of confirmed SARS CoV-2 infection: A prospective study in the largest COVID-19 dedicated hospital in Bangladesh. *PLoS One* 2021;16:e0249252.
- Saussez S, Lechien JR, Hopkins C. Anosmia: An evolution of our understanding of its importance in COVID-19 and what questions remain to be answered. *Eur Arch Otorhinolaryngol* 2021;278:2187-91.
- Neta FI, Fernandes AC, Vale AJ, Pinheiro FI, Cobucci RN, Azevedo EP, *et al.* Pathophysiology and possible treatments for olfactory-gustatory disorders in patients affected by COVID-19. *Curr Res Pharmacol Drug Discov* 2021;2:100035.
- Chabot AB, Huntwork MP. Turmeric as a possible treatment for COVID-19-induced anosmia and ageusia. *Cureus* 2021;13:e17829.
- Hjermstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, *et al.* Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: A systematic literature review. *J Pain Symptom Manage* 2011;41:1073-93.
- Chiu A, Fischbein N, Wintermark M, Zaharchuk G, Yun PT, Zeineh M. COVID-19-induced anosmia associated with olfactory bulb atrophy. *Neuroradiology* 2021;63:147-8.
- Kandemirli SG, Altundag A, Yildirim D, Tekcan Sanli DE, Saatci O. Olfactory bulb MRI and paranasal sinus CT findings in persistent COVID-19 anosmia. *Acad Radiol* 2021;28:28-35.
- Yazdanpanah N, Saghaizadeh A, Rezaei N. Anosmia: A missing link in the neuroimmunology of coronavirus disease 2019 (COVID-19). *Rev Neurosci* 2020;31:691-701.
- Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. *J Infect* 2020;80:e14-8.
- Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, *et al.* Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: Prospective cohort study. *BMJ* 2020;369:m1966.
- Bhatkar D, Utpat K, Desai U, Joshi JM. Bilateral tuberculous otitis media: An unique presentation. *Indian J Tuberc* 2017;64:334-6.
- Chakrani Z, Robinson K, Taye B. Association between ABO blood groups and *Helicobacter pylori* infection: A meta-analysis. *Sci Rep* 2018;8:17604.
- Lesky E. Viennese serological research about the year 1900: Its contribution to the development of clinical medicine. *Bull N Y Acad Med* 1973;49:100-11.
- Guillon P, Clément M, Sébille V, Rivain JG, Chou CF, Ruvoën-Clouet N, *et al.* Inhibition of the interaction between the SARS-CoV spike protein and its cellular receptor by anti-histo-blood group antibodies. *Glycobiology* 2008;18:1085-93.
- Wu B, Gu D, Yu J, Yang J, Shen W. Since January 2020 Elsevier has Created a COVID-19 Resource Centre with free Information in English and Mandarin on the Novel Coronavirus COVID-19. The COVID-19 Resource Centre is Hosted on Elsevier Connect, the Company's Public News and Information; 2020.
- Li H, Liu L, Zhang D, Xu J, Dai H, Tang N, *et al.* SARS-CoV-2 and viral sepsis: Observations and hypotheses. *Lancet* 2020;395:1517-20.
- El-Shitany NA, El-Hamamsy M, Alahmadi AA, Eid BG, Neamatallah T, Almukadi HS, *et al.* The impact of ABO blood grouping on COVID-19 vulnerability and seriousness: A retrospective cross-sectional controlled study among the Arab community. *Int J Environ Res Public Health* 2021;18:276.
- Ishaq U, Malik A, Malik J, Mehmood A, Qureshi A, Laique T, *et al.* Association of ABO blood group with COVID-19 severity, acute phase reactants and mortality. *PLoS One* 2021;16:e0261432.
- Komal A, Noreen M, Akhtar J, Imran M, Jamal M, Atif M, *et al.* Analyses of ABO blood groups with susceptibility and symptomatic variations of COVID-19 infection, a questionnaire-based survey. *APMIS* 2021;129:579-86.
- El-anwar MW, Elzayat S, Ahmed Y. Since January 2020 Elsevier has created a COVID-19 Resource Centre with Free Information in English and Mandarin on the Novel Coronavirus COVID-19. The COVID-19 Resource Centre is Hosted on Elsevier Connect, the Company's Public News and Information; 2020.
- Kabrah SM, Abuzerr SS, Baghdadi MA, Kabrah AM, Flemban AF, Bahwerth FS, *et al.* Susceptibility of ABO blood group to COVID-19 infections: Clinico-hematological, radiological, and complications analysis. *Medicine (Baltimore)* 2021;100:e28334.
- Porta-Etessam J, Núñez-Gil IJ, González García N, Fernandez-Perez C, Viana-Llamas MC, Eid CM, *et al.* COVID-19 anosmia and gustatory symptoms as a prognosis factor: A subanalysis of the HOPE COVID-19 (health outcome predictive evaluation for COVID-19) registry. *Infection* 2021;49:677-84.