Deviated nasal septum in COVID-19 patients: A case control study in DHQ Teaching Hospital, Mirpur, Azad Jammu and Kashmir Pakistan.

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ABSTRACT... Objective: The following study aimed to correlate the prevalence of COVID-19 and the rhino pathological conditions simultaneously in the population visiting the hospital of Mirpur, Azad Jammu and Kashmir. Study Design: Case Control Study. Setting: DHQ Teaching Hospital, Mirpur, Azad Jammu and Kashmir. Period: April to July 2020. Material & Methods: Patients visiting the DHQ teaching hospital, Mirpur, Azad Jammu and Kashmir for their COVID-19 related symptoms were included in the study. Demographic data was obtained. Prevalence of DNS was recorded for further statistical analysis of the symptoms in the population. Results: The results demonstrated that these rhino pathological conditions exists with the prevailing COVID-19 or may even aggravate the situation. Although DNS is not among the typical symptoms of the COVID-19 but it may add to the results of PCR testing following swab testing. Conclusion: Rhino pathological conditions may alter or obstruct the airway passages hence making the test for COVID-19 by swab difficult and unapproachable.

Key words: Coronavirus, COVID-19, Case Control Study, DNS.

INTRODUCTION
The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for global health emergency. Since the beginning of this year, the number of infections and deaths reported every day around the world has been increasing. We must urgently pay attention to the new SARS-CoV-2 pandemic, caused by a β-coronavirus associated to SARS-CoV. Some general symptoms of COVID-19 comprise fever, cough, dyspnea, malaise, myalgia and gastrointestinal diseases.¹ In addition, olfactory dysfunction (OD) or anosmia has also been testified in COVID-19 patients.² Previously, most studies investigating OD in COVID-19 have used retrospective questionnaires or patient self-reported symptoms.³ These evaluation methods are prone to reporting bias and may not be able to identify subtle ODs. Therefore, it is necessary to objectively measure the olfactory function of COVID-19 patients. In addition, the olfactory function of COVID-19 patients has not been compared with healthy controls, which is a necessary condition to prove that COVID-19 patients have impaired sense of smell. There is also a lack of systematic assessment of the sternness, occurrence, etiology and extent of OD in COVID-19 patients.⁴

One of the most communal complaints faced by otolaryngologists in daily practice is nasal obstruction. Deviation of the nasal septum is the most common cause of nasal congestion. It can lead to changes in air flow dynamics, causing a lot of histopathological alterations in the nasal mucosa. DNS causes mouth breathing, wheezing and peripheral nasal deformities. Perhaps, it may affect the airflow subtleties of the nasal cavity and inappropriate ventilation of the paranasal sinuses that cause sinusitis. These changes in airflow, hypertrophy of the concave nasal mucosa as a compensation is often found.⁵ Additional variations caused by changes in airflow dynamics are mucociliary dysfunction, lymphocyte infiltration along with squamous metaplasia. Though these deviations are visible on either sides of the nasal...
mucosa, they are more severe on the concave side.\textsuperscript{6} Correcting the DNS surgically can avoid all these changes. The deviation of the nasal septum can source indications such as nasal congestion, oral breathing, and other signs such as headaches and olfactory disturbances. In the nasal cavity, the dynamic airflow is affected by the degree, position and form of the nasal septum deflection.

COVID-19 infection can be analyzed through a diversity of upper and lower respiratory tracts, including oropharynx (OP), nasopharyngeal (NP), sputum, and bronchial fluid.\textsuperscript{7} Generally, COVID-19 can be detected most sensitively by gathering and testing upper and lower respiratory tract samples.\textsuperscript{8} However, bronchoscopy is an extremely technical procedure that requires advanced tools for diagnosis and well-trained staff, and these tools are not always accessible. In addition, the collection of sputum through bronchoscopy, especially BAL, will increase the risks related to biosafety of medical staff by generating aerosol droplets. Upper respiratory tract specimens, such as OP and NP swabs, are comparatively easy to obtain, particularly when resources are inadequate. They must be obtained within the initial few days of the onset of symptoms, because the RNA positive rate peaks in upper respiratory tract samples 7 to 10 days after the onset of symptoms, and then gradually declines. The correct collection of nasopharyngeal swabs that reach the area of the posterior nasopharyngeal tonsil seems very important.\textsuperscript{9} This means that there is a regular bottom of the nasal cavity. Few anatomical alterations, such as a deflection of the nasal septum, can prevent the nasopharynx from reaching and consequently accumulate suitable samples. Numerous studies of nasal septum deflection have shown its widespread prevalence. Among adults, a current global study found that the prevalence is about 90%. It is also reported as clinically relevant interval unconventionality prevalence of 15% to 25%.\textsuperscript{10} Hence, keeping in view the prevailing pathological conditions, a definite diagnosis is a matter of concern.

OBJECTIVES
To associate nasal pathological conditions with the prevalence of COVID-19 in Mirpur, Azad Jammu and Kashmir. To affirm the relationship of proper diagnosis of a positive COVID-19 case with symptomatic patients.

The following study was conducted in order to evaluate the prevalence of COVID-19 in the people of Mirpur, Azad Jammu and Kashmir particularly focusing on the symptoms that are observed during the illness. DNS along with SARS-CoV-2, was highlighted among the patients having positive and negative tests for COVID-19. The age of the patients was also considered to correlate the effect of illness on the patients of different age groups.

MATERIAL & METHODS
A cross sectional study was conducted in the locality of Mirpur, Azad Jammu and Kashmir, Pakistan. Division Head Quarter (DHQ) teaching hospital, Mirpur was targeted and the influx of patients with COVID-19 symptoms were monitored. For the confirmation of the disease, PCR testing was carried out in PCR Lab Microbiology Division Department of Pathology DHQ Teaching Hospital Mirpur, Azad Jammu and Kashmir. Sampling was done by microbiology department whereas examination was made by ENT department of the hospital. Frequency distribution of the demographics were calculated. T-test was applied for the calculation of p-values using statistical software such as IBM SPSS Statistics 25. The study was approves by ethical review board (17154/MS/2020).

RESULTS
Demographics of patients with COVID-19 symptoms.

| Age of patients | Gender of Patients | Total |
|-----------------|--------------------|-------|
|                 | Male | Female |       |
| <15             | 1    | 6      | 7     |
| 15-30           | 59   | 21     | 80    |
| 30-45           | 76   | 23     | 99    |
| 45-60           | 33   | 8      | 41    |
| 60-75           | 12   | 2      | 14    |
| >75             | 1    | 3      | 4     |
| Total           | 182  | 63     | 245   |

Table-I. Demographics of patients participated in the study.
Among the patients visiting the hospital, it was observed that 28.8% had a presentation of DNS while the rest 71.2% were presented without physical symptoms of DNS. The distribution if depicted in figure below.

![Deviated nasal septum](image)

**Figure-1. Frequency distribution of patients with DNS.**

Correlation of prevailing condition of DNS with COVID-19.

| Remarks of PCR test for COVID-19 | Deviated Nasal Septum | Total | P-Value |
|----------------------------------|-----------------------|-------|---------|
|                                  | Yes                   | No    |         |
| Negative                         | 58                    | 153   | 211     | 0.000056 |
| Positive                         | 12                    | 25    | 37      | 0.002541 |
| Repeat                           | 2                     | 0     | 2       | 0.292893 |
| Total                            | 72                    | 178   | 250     |         |

**Table-II. Relationship between the DNS prevalence with PCR test results of COVID-19.**

SARS-CoV receptor ACE2 is used by the SARS-CoV-2 to enter cells, and uses serine protease TPRRSS2 for its S protein priming. According to reports, the nasal expression of ACE2 is higher than that in the throat tissue. In fact, compared to throat swabs obtained from patients infected with COVID-19, a higher viral load of SARS-CoV-2 was detected in the nose, which is attributed to the ACE2 between the two tissues. With the differences in expression, in fact, associated to throat swabs attained from patients infected with COVID-19, a higher SARS CoV-2 viral load was detected in nose. This is due to the modification in the ACE2 expression between the two organizations. Recently, in a study that compared with the lower respiratory tract, the upper respiratory tract shows more SARS-CoV 2 into the genes ACE2 and TPRRSS2. In addition, Hou et al. lately established that the main cell type that expresses ACE2 in nasal tissues are multiciliated cells and is affected with SARS-CoV-2. In addition, Sungnak et al. analyzed single-cell RNA sequencing data of human nasal epithelial cells and demonstrated that ACE2 and TPRRSS2 are co-expressed in the nasal epithelium involving the genes responsible for carrying host innate immunity, which refers to the possible part of nasopharyngeal carcinoma. These cells can cause SARS CoV-2 infection. Therefore, as these receptors might not be upregulated after infection, the level of SARS CoV-2 receptors in nasal tissues may regulate the level of virus infectivity.

**DISCUSSION**

The study was conducted to evaluate the relationship between the rhino pathological conditions and their effects in the development, progress and testing of serious infections such as COVID-19. It was observed from the study that only 12 of a total 250 patients had DNS along with a positive COVID-19 test. While for the rest either the test was negative or the prevalence of DNS was not existing. The results suggested no significant correlation between the already existing pathological conditions of the rhinus and progression of COVID-19. However, in some studies a justifiable mechanism is presented to correlate the two.
the world, the pathogenic mechanism related to human infection as well as intracellular entry, the continuous transmission in the body along with the factors that ultimately control the difference among them. One patient developed asymptomatic infection or mild infection, and another patient developed a fatal disease. Certainly, the age and health status of the diseased individual (including hypertension, diabetes and cardiovascular disease) serves a crucial part in the clinical course of COVID. We instantly need to find an appropriate treatment. On the one hand, we may need to have enough masks and social isolation, on the other hand, we need to be vaccinated. SARS-CoV-2 is highly contagious and can cause 2019 coronavirus disease (COVID-19) infection.18

Understanding how the virus successfully infects an individual and first enters the outer surface cells and begins to replicate is critical, as this may provide a treatment in the coming time. The patient’s main entrance is obviously the nose and nasopharynx. An investigation of infected patients confirmed that the SARS-CoV-2 viral load is expected to be more in the nose than in the throat.19 In addition, painful lessons were a part of daily news from many healthcare professionals (especially otolaryngology) and ENT where the expert died of COVID-19.20 Nasal surgery of an infected patient has proven to put the surgeon at risk along with the personnel in the operating room is at risk, especially when using drill bits and endoscopes and forming aerosols during the operation cases.21

CONCLUSION

The present study was conducted in order to develop a relationship between COVID-19 and rhinopathies. Despite being a significant relationship, there lies a chance of misleading results of swab testing as these rhinopathies obstruct the airway hindering the path. Therefore, while carrying out a confirmation test for the infection it is important to consider the chances of rhinopathies in patients beforehand.

REFERENCES

1. Bilgin S, Kurtkulagi O, Kahveci GB, Duman TT, Tel BM. Millennium pandemic: A review of coronavirus disease (COVID-19). Experimental Biomedical Research. 2020 Mar 29; 3(2):117-25.

2. Chung TW, Sridhar S, Zhang AJ, Chan KH, Li HL, Wong FK, Ng MY, Tsang RK, Lee AC, Fan Z, Ho RS. Olfactory dysfunction in coronavirus disease 2019 patients: Observational cohort study and systematic review. In Open Forum Infectious Diseases 2020 Jun (Vol. 7, No. 6, p. ofaa199). US: Oxford University Press.

3. Bagheri SH, Asghari AM, Farhadi M, Shamshiri AR, Kabir A, Kamrava SK, Jalessi M, Mohebbi A, Alizadeh R, Honarmand AA, Ghalehbaghi B. Coincidence of COVID-19 epidemic and olfactory dysfunction outbreak. MedRxiv. 2020 Jan 1.

4. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, Le Bon SD, Rodriguez A, Dequanter D, Bleiscic S, El Afia F, Distinguin L, Chekkoury-Idrissi Y. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): A multicenter European study. European Archives of Oto-Rhino-Laryngology. 2020 Apr 6:1-1.

5. Higuera S, Lee EI, Cole P, Hollier Jr LH, Stal S. Nasal trauma and the deviated nose. Plastic and reconstructive surgery. 2007 Dec 1; 120(7):64S-75S.

6. Reitzen SD, Chung W, Shah AR. Nasal septal deviation in the pediatric and adult populations. Ear, Nose & Throat Journal. 2011 Mar; 90(3):112-5.

7. Laidlaw TM, Mullol J, Fan C, Zhang D, Amin N, Khan A, Chao J, Mannent LP. Dupilumab improves nasal polyp burden and asthma control in patients with CRSwNP and AERD. The Journal of Allergy and Clinical Immunology: In Practice. 2019 Sep 1; 7(7):2462-5.

8. Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. American journal of rhinology & allergy. 2013 Nov; 27(6):473-8.

9. Vultaggio A, Agache I, Akdis CA, Akdis M, Bavbek S, Bossios A, Bousquet J, Boyman O, Chaker AM, Chan S, Chatzipetrou A. Considerations on biologicals for patients with allergic disease in times of the COVID-19 pandemic: an EAACI Statement. Allergy. 2020 Jun 5.

10. Settipane GA. Nasal polyps: Epidemiology, pathology, immunology, and treatment. American Journal of Rhinology. 1987 Sep; 1(3):119-26.
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11. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA. SARS-CoV-2 cell entry depends on ACE2 andTMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020 Mar 5.

12. Ziegler CG, Allon SJ, Nyquist SK, Miano IM, Miao VN, Tzouanas CN, Cao Y, Yousif AS, Bals J, Hauser BM, Feldman J. SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues. Cell. 2020 Apr 27.

13. Chan JF, Zhang AJ, Yuan S, Poon VK, Chan CC, Lee AC, Chan WM, Fan Z, Tsol HW, Wen L, Liang R. Simulation of the clinical and pathological manifestations of Coronavirus Disease 2019 (COVID-19) in golden Syrian hamster model: Implications for disease pathogenesis and transmissibility. Clinical Infectious Diseases. 2020 Mar 26.

14. Lukassen S, Chua RL, Trefzer T, Kahn NC, Schneider MA, Muley T, Winter H, Meister M, Veith C, Boots AW, Hennig BP. SARS-CoV-2 receptor ACE 2 andTMPRSS 2 are primarily expressed in bronchial transient secretory cells. The EMBO journal. 2020 May 18; 39(10):e105114.

15. Hou Y, Zhao J, Martin W, Kallianpur A, Chung MK, Jehi L, Sharifi N, Erzurum S, Eng C, Cheng F. New insights into genetic susceptibility of COVID-19: An ACE2 and TMPRSS2 polymorphism analysis. BMC medicine. 2020 Dec; 18(1):1-8.

16. Chang ET, Adami HO. The enigmatic epidemiology of nasopharyngeal carcinoma. Cancer Epidemiology and Prevention Biomarkers. 2006 Oct 1; 15(10):1765-77.

17. Sungnak W, Huang N, Bécavin C, Berg M, Queen R, Litvinukova M, Talavera-López C, Maatz H, Reichard D, Sampaziotis F, Worlock KB. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. Nature medicine. 2020 May; 26(5):681-7.

18. Wang LS, Wang YR, Ye DW, Liu QQ. A review of the 2019 Novel Coronavirus (COVID-19) based on current evidence. International journal of antimicrobial agents. 2020 Mar 19:105948.

19. Yu F, Yan L, Wang N, Yang S, Wang L, Tang Y, Gao G, Wang S, Ma C, Xie R, Wang F. Quantitative detection and viral load analysis of SARS-CoV-2 in infected patients. Clinical Infectious Diseases. 2020 Mar 28.

20. Kowalski LP, Sanabria A, Ridge JA, Ng WT, de Bree R, Rinaldo A, Takes RP, Mäkitie AA, Carvalho AL, Bradford CR, Paleri V. COVID-19 pandemic: effects and evidence-based recommendations for otolaryngology and head and neck surgery practice. Head & neck. 2020 Jun; 42(6):1259-67.

21. Basso D, Aita F, Navaglia F, Franchin E, Fioretto P, Moz S, Bozzato D, Zambon CF, Martin B, Dal Prà C, Crisanti A. SARS-CoV-2 RNA identification in nasopharyngeal swabs: Issues in pre-analytics. Clinical Chemistry and Laboratory Medicine (CCLM). 2020 Jun 22; 1(ahead-of-print).

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