Olfactory Bulb MRI Findings in Patients with Post-COVID Anosmia

Original Article

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ABSTRACT

Background: Olfactory dysfunction has been recognized as a key symptom of COVID-19. The pathogenesis of COVID-19 anosmia has not been fully defined. A dedicated MRI study allows assessment of olfactory bulb volume, morphology and signal intensity which is helpful to differentiate between different etiologies and predict prognosis of olfactory function recovery.

Objective: To investigate the MRI radiological changes of the olfactory bulb (OB) in patients with post-covid anosmia in comparison with a normal group of subjects for further identification of the underlying cause of anosmia.

Patients and Methods: In this study, we evaluated 50 patients with persistent COVID-19 olfactory dysfunction. All patients were anosmic at the time of imaging based on UPSIT scores. We noted a high percentage of olfactory bulb changes. There was reduction of olfactory bulb volumes, change in bulb shape, and signal abnormalities.

Results: Our results showed a marked decrease in OB volumes and hyperintensities in the patient group in comparison to the control group. This indicated that the cause of persistent anosmia in post-COVID-19 patients is highly suggestive due to nerve degeneration. Furthermore, we have correlated the degree of anosmia (by UPSIT score) with the degree of affection of the olfactory bulb indicating that a dedicated MRI study for OB could be used as a non-invasive objective method of assessment of anosmia.

Conclusion: In the current study, we revealed that there was a highly significant difference between cases and controls as regards results of MRI with lower mean right, left, and average bulb volume among cases. Similarly, the bulb flair signal and T1 signal on each side were significantly different between cases and controls. Also, we found that there was a highly significant positive correlation between Right, left, and average bulb volume, and UPSIT score among cases indicating that a dedicated MR study of the OB could be used for objective assessment of anosmia. Further studies with larger scales are needed to confirm our results.

Key Words: Anosmia, coronavirus disease, MRI, olfactory dysfunction.

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INTRODUCTION

Olfactory dysfunction (OD) is a commonly recognized symptom of coronavirus disease (COVID-19). OD has a sudden onset, may be accompanied by taste disturbances, and can vary in severity ranging from hyposmia to anosmia. OD can have a qualitative effect, such as parosmia or phantosmia, or quantitative effects like hyposmia or anosmia[1-3].

Since the recognition of the high prevalence of anosmia reported by COVID-19 patients, there has been much speculation regarding the underlying pathophysiological mechanism. Different theories have been proposed ranging from conductive loss due to obstruction of the olfactory cleft to central mechanisms relating to the known neurotropic properties of the human coronavirus[4].

Although hyposmia or anosmia has been reported in as many as 60% of patients who are symptomatic with COVID-19, imaging of the olfactory nerve is not routinely employed. The olfactory nerve is small and only well seen on dedicated skull base MRI, so prospective assessments of its changes have been lacking[5].

MRI dedicated to olfactory nerves is a useful anatomical imaging modality for the evaluation of olfactory dysfunction related to postviral infection, trauma, and neurodegenerative processes. A dedicated MRI study allows assessment of olfactory bulb volume, morphology, and signal intensity, the status of olfactory nerve filia, and signal intensity of primary olfactory cortex, which is helpful to differentiate between different etiologies and to predict the prognosis of olfactory function recovery[6].

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MR imaging is a useful and consolidated method for evaluating olfactory dysfunction. None- theless, to our knowledge, MRI-based evaluations of olfactory system alterations associated with COVID-19 are still limited to small investigational studies, case series, and case reports. Only a few studies performing systematic, quantitative olfactory system measurements have been published so far, but still on quite small populations[7].

AIM OF THE WORK

Our study aims to investigate the MRI radiological changes of the olfactory bulb in patients with post-covid anosmia in comparison with a normal group of subjects for further identification of the underlying cause of anosmia with prospection for effective treatment.

SUBJECTS AND METHODS

- **Type of Study:** Prospective cross-sectional study.

- **Study Setting:** Otorhinolaryngology and Radiodiagnosis department, Faculty of Medicine, Ain Shams University from year 2020 to 2024.

- **Study Population:**

Inclusion Criteria:

All adult patients (of both genders and between 20-60 years of age) non-smokers with post covid (confirmed by PCR) anosmia for more than 12 months.

Exclusion Criteria:

- Acute rhinosinusitis.
- Nasal polyposis.
- Chronic granulomatous inflammations.
- Neurodegenerative disorders.

Sampling Method:

The current study consists of:

- *Study group:* includes 50 patients diagnosed with postcovid anosmia. (30 female patients and 20 male patients)
- *Control group:* includes 50 subjects with normal smelling sensation. (30 female subjects and 20 male subjects).

Ethical Considerations:

All patients were subjected to the following protocol after taking their written consent.

Study Procedures:

All patients will be subjected to the following protocol:

- Full history taking and otorhinolaryngological examination of patients diagnosed with post covid anosmia, and to fulfill inclusion criteria.
- Endoscopic examination of the nasal cavity to exclude local causes of anosmia.
- Clinical evaluation of the degree of anosmia was assessed using the University of Pennsylvania Smell Identification Test (UPSIT) Arabic version. UPSIT is a test that is commercially available for smell identification to test the function of an individual's olfactory system. Known for its accuracy among smell identification tests it is considered to be one of the most reliable and trusted. The test has a total of 40 questions and consists of 4 different 10 page booklets. On each page, there is a different scratch and sniff strip which are embedded with a microencapsulated odorant. There is also a four choice multiple choice question on each page. The scents are released using a pencil. After each scent is released, the patient smells the level and detects the odor from the four choices. There is an answer column on the back of the test booklet, and the test is scored out of 40 items. The score is compared to scores in a normative database from 4000 normal individuals, this tells the level of absolute smell function. The score also indicates how the patient does in accordance to their age group and gender.

UPSIT Score	Outcome
6–18	Anosmia (complete loss of smell)
19–25	Severe microsmia
26–30 in women and 26–29 in men	Moderate microsmia
31–34 in women and 30–33 in men	Mild microsmia
>34 in women and 33 in men	Normosmia (normal smell appreciation)

High-resolution MRI dedicated to olfactory nerves was acquired with a 3 Tesla MRI unit (Acheiva, Philips medical system 2020 model USA, using Philips IntelliSpace 105 Portal workstation, version 8.0). Thin-section ultra-high-resolution coronal T2 images (TR: 6550ms; TE: 99ms; flip angle: 150°, slice thickness: 1mm; distance factor: 0; FOV: 100×100mm; matrix: 269×384; phase oversampling: 56%; bandwidth: 289Hz/pixel; voxel size: .6×.6×.6mm; time of acquisition: 8.19 minutes; turbo factor: 17) extending from the anterior pole of the olfactory bulb to the primary olfactory region were obtained. Coronal 3D T2 FLAIR images with the following parameters: repetition time/echo time 6002.0/126.9ms; inversion time, 1681.0ms; field of view, 215.3 108.7mm; and section thickness, 1.0mm.

Bulb volume and signal was calculated based on identifying sequential region of interest on consecutive slices using multi-planner reconstruction (MPR). Firstly, number of slices with clear visibility of the OB were selected. OB volumes were calculated by planimetric manual contouring. On each successive slice of brain, contours on left and right side of OB were manually delineated manually with an electronic cursor on the screen using the standard measurement tool option. For each

slice, the surface of the contoured area is given in mm^2. All surfaces are added to obtain a volume in mm^3. The proximal end of the OB was defined by the abrupt change in the diameter at the beginning of the olfactory tract. Two trained observers blind to the diagnosis and clinical characteristics of the subjects, calculated the volumes (in mm^3). Olfactory bulb signal was evaluated in FLAIR and T1 weighted sequences and compared to the cerebral cortex.

Fluid-attenuated inversion recovery (FLAIR) is an MRI technique that shows areas of tissue T2 prolongation as bright while suppressing (darkening) cerebrospinal fluid (CSF) signal, thus clearly revealing lesions in proximity to CSF.MRI 3D Drive was used as well. The3D-DRIVE sequence is a 3D T2-weighted driven equilibrium radio-frequency reset pulse for better visualization of fluids. The radiological data were measured and collected using RadiAnt DICOM viewer 2023.1 and PACS program (Picture archiving and communication system V.5260-1173).

Data Management and Analysis:

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

Descriptive statistics: Shapiro wilk's test was used to evaluate normal distribution of continuous data. Mean, Standard deviation (±SD), and range was used for parametric numerical data, while Median and InterquaRightile range (IQR) was used for non-parametric numerical data. Frequency and percentage of non-numerical data.

Analytical statistics: Student T Test was used to assess the statistical significance of the difference between two study group means. Fisher's exact test: was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells ANOVA test was used to assess the statistical significance of the difference between more than two study group means. Post Hoc Test is used for comparisons of all possible pairs of group means Correlation analysis (using Pearson's method): To assess the strength of association between two quantitative variables. The correlation coefficient denoted symbolically "r" defines the strength and direction of the linear relationship between two variables. The ROC Curve (receiver operating characteristic) provides a useful way to evaluate the Sensitivity and specificity for quantitative Diagnostic measures that categorize cases into one of two groups.

***P*- value:** level of significance: $P > 0.05$: Non significant (NS). $P < 0.05$: Significant (S). $P < 0.01$: Highly significant (HS).

RESULTS

There was no significant difference between cases and controls as regard age, however a highly significant difference was found between cases and controls as regard UPSIT score (Table 1).

There was a highly significant difference between controls (Figure 1,2) and cases (Figure 3,4) as regard results of MRI with lower mean right, left and average bulb volume among cases. Similarly, bulb flair signal and T1 signal on each side was significantly different between cases and controls (Figure 5) (Table 2).

Atypical findings were seen in some of the patients for example five cases showed complete atrophy of the olfactory bulb along its course (Figure 6), others showed olfactory bulb was atrophic along its anterior course only (Figure 7) and three patients shown prominent fascicular pattern in the olfactory bulb indicating microhemorrhages and nerve neuropathy (Figure 8).

There was significant difference in bulb volume between cases and controls (Figure 9).

Using roc curve (Figure 10), it was shown that Right bulb volume can be used to discriminate between cases and controls at a cutoff level $\leq 24.05 mm^3$ with 82% sensitivity, 90% specificity, 89.1% positive predictive value and 83.3% negative predictive value (Table 3).

Using roc curve (Figure 11), it was shown that left bulb volume can be used to discriminate between cases and controls at a cutoff level $\leq 27.1 mm^3$ with 80% sensitivity, 78% specificity, 78.4% positive predictive value and 79.6% negative predictive value (Table 4).

Using roc curve (Figure 12), it was shown that average bulb volume can be used to discriminate between cases and controls at a cutoff level $\leq 26.4 mm^3$ with 84% sensitivity, 80% specificity, 80.8% positive predictive value and 83.3% negative predictive value (Table 5).

There was no significant correlation between age and UPSIT score (Table 6).

There was a highly significant positive correlation between Right, left and average bulb volume, and UPSIT score among cases (Table 7).

There was a significant difference between cases with iso, hyper and atrophied bulb flair signal and T1 signal on each side and UPSIT score, where atrophied cases had lower mean UPSIT score compared to Iso and hyper cases (Table 8).

There was no significant correlation between duration of anosmia with bulb volume and UPSIT score (Table 9).

Table 1: Comparison between study group and controls as regards Age and UPSIT score:

	Group				*P*	Sig.
	Case *N*=50		Control *N*=50			
	Mean	±SD	Mean	±SD		
Age	38.90	12.40	35.20	10.22	1.00*	NS
UPSIT score	20.56	6.76	36.28	1.41	0.001*	HS

*: Student *t*-test.

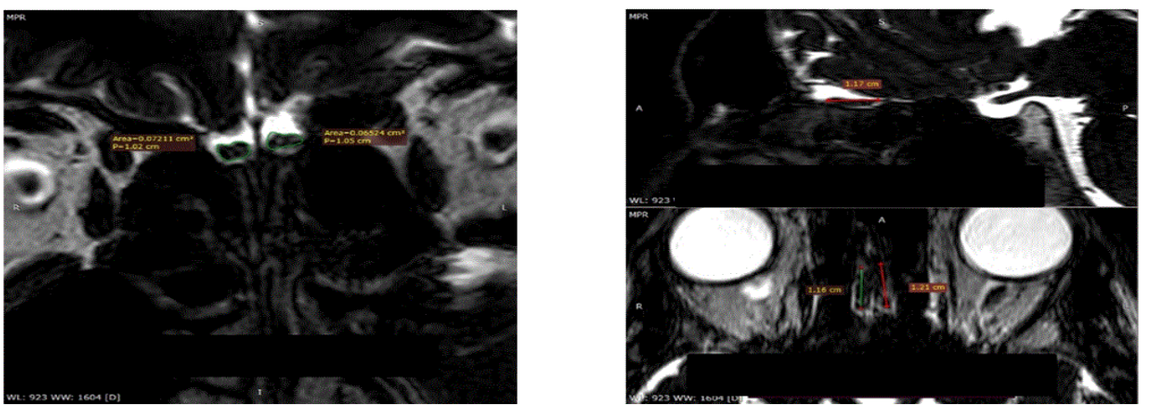

Figure 1: MRI 3D DRIVE coronal, sagittal and axial views showing no radiological abnormality in control no.3 (average olfactory bulb volume).

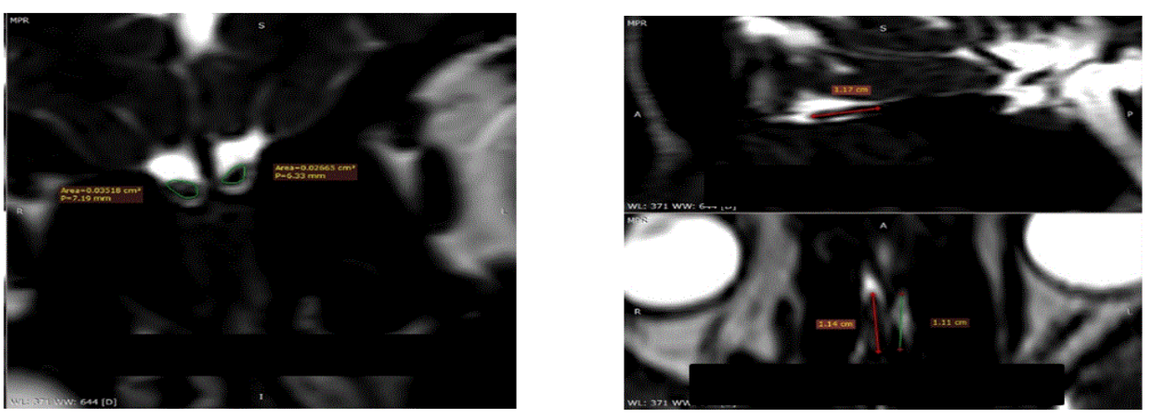

Figure 2: MRI 3D DRIVE coronal, sagittal and axial views showing no radiological abnormality in control no.3 (average olfactory bulb volume).

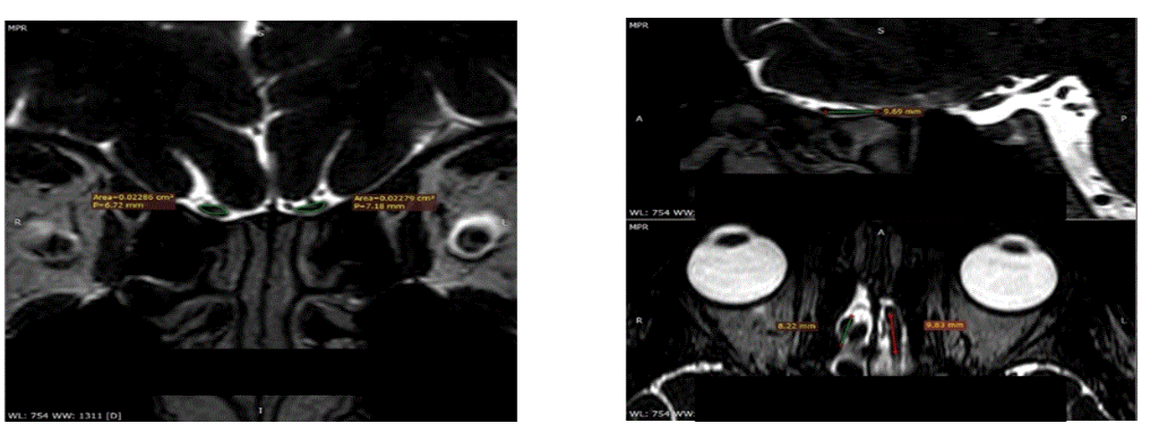

Figure 3: MRI 3D DRIVE sequence in coronal, sagittal and views showing bilateral atrophic olfactory bulbs in patient no.34 with UPSIT score 21.

Table 2: Comparison between study group and controls as regard results of MRI assessment of the olfactory system (*n*= 50):

		Group				*P*	Sig.
		Case		Control			
		Mean	±SD	Mean	±SD		
Right bulb volume(mm^3)		17.06	9.52	41.00	18.28	0.0001*	HS
Left bulb volume(mm^3)		17.94	11.95	38.51	13.89	0.0001*	HS
Average bulb volume(mm^3)		17.50	9.80	39.76	14.63	0.0001*	HS
Right bulb Flair signal	Iso	19	38.0%	50	100.0%	0.0001**	HS
	Hyper	29	58.0%	0	0.0%		
	Atrophied	2	4.0%	0	0.0%		
Right bulb T1 signal	Iso	23	46.0%	50	100.0%	0.0001**	HS
	Hyper	25	50.0%	0	0.0%		
	Atrophied	2	4.0%	0	0.0%		
Left bulb Flair signal	Iso	20	40.0%	50	100.0%	0.0001**	HS
	Hyper	27	54.0%	0	0.0%		
	Atrophied	3	6.0%	0	0.0%		
Left bulb T1 signal	Iso	26	52.0%	50	100.0%	0.0001**	HS
	Hyper	21	42.0%	0	0.0%		
	Atrophied	3	6.0%	0	0.0%		

*: Student t-test; **Fisher exact test.

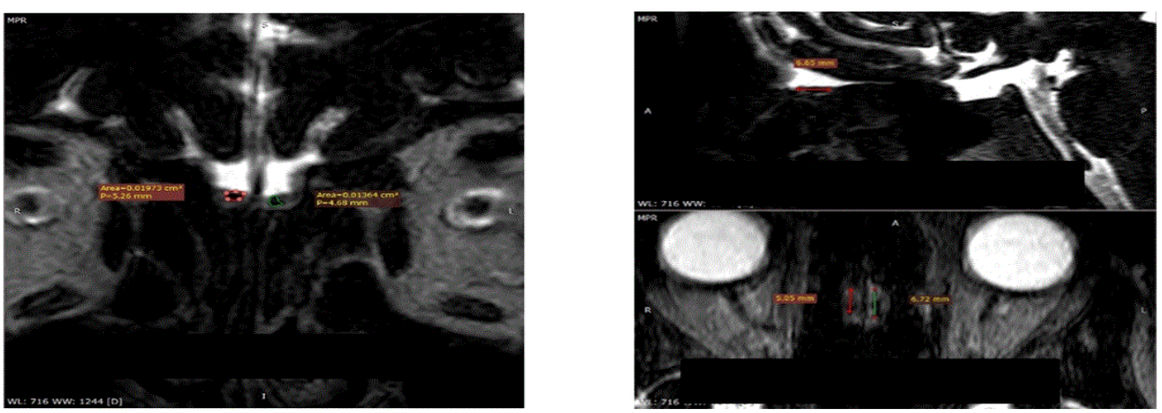

Figure 4: MRI 3D DRIVE sequence in coronal, sagittal and views showing bilateral atrophic olfactory bulbs in patient no.35 with UPSIT score 18.

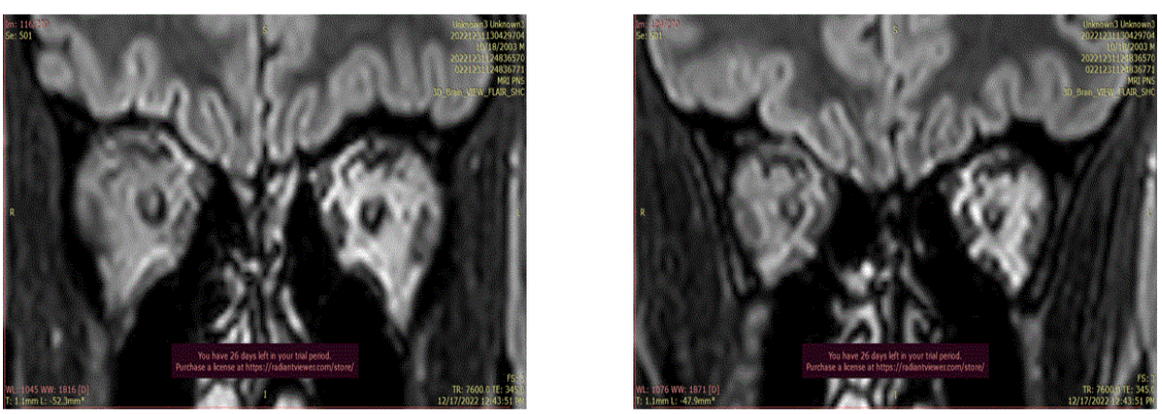

Figure 5: MRI 3D FLAIR sequence coronal view showing abnormal high signal in the left olfactory bulb [white arrow] (A) compared to the cerebral cortex and similar signal abnormality in bilateral olfactory tracts [yellow arrows] (B) in patient no.6 with UPSIT score 30.

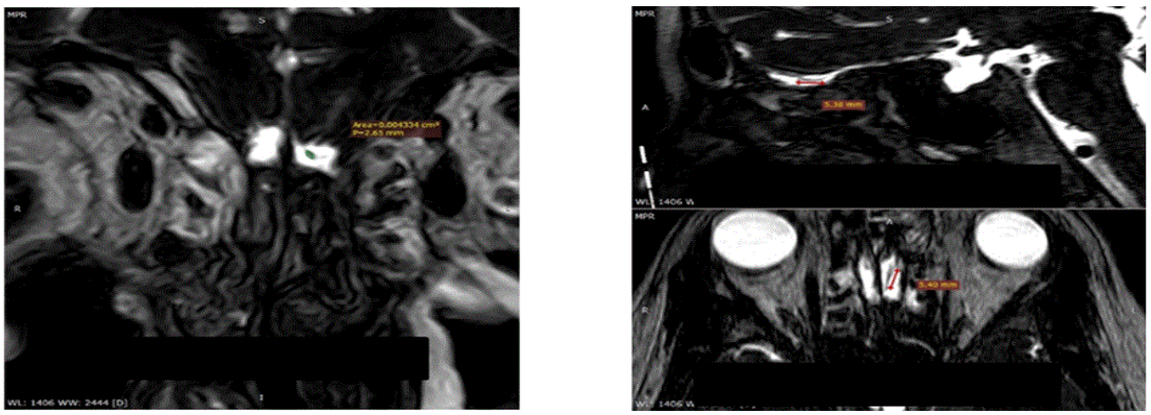

Figure 6: MRI 3D DRIVE sequence in coronal, sagittal and views showing bilateral atrophic olfactory bulbs in patient no.4 with UPSIT score 8.

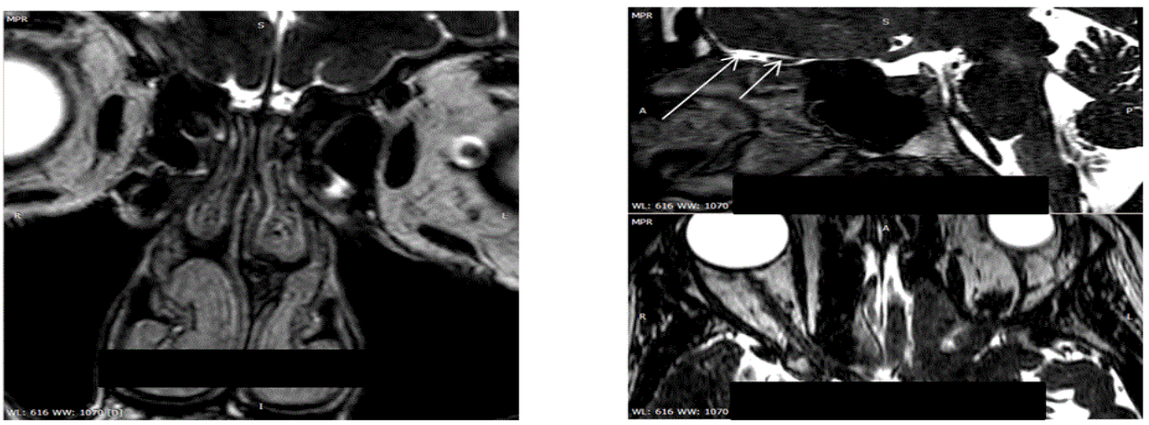

Figure 7: MRI 3D DRIVE sequence coronal, sagittal and axial showing olfactory bulbs are atrophic in the anterior course [long arrows] and average size but abnormal signal in the posterior course [short arrows] in patient no.14 with UPSIT score 23.

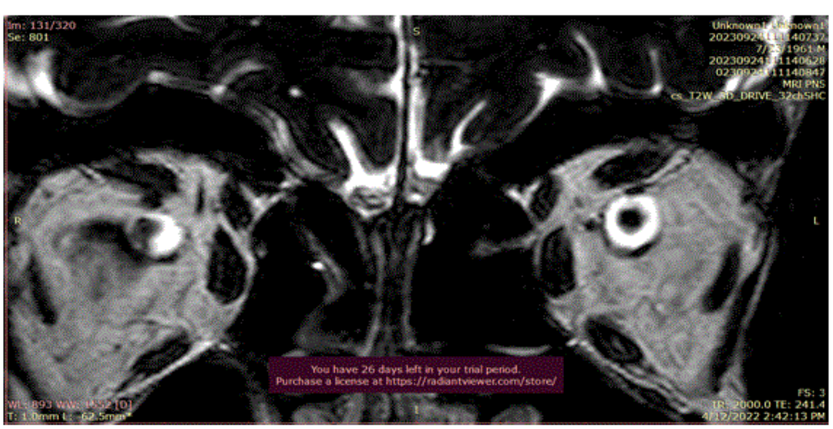

Figure 8: MRI 3D DRIVE sequence coronal view showing Bilateral prominent fascicular pattern [white arrow] in a patient no.41 with UPSIT score 31.

Table 3: ROC Curve using Right bulb volume to discriminate between cases and controls:

Cut off level.	Area under curve (CI)	Sensitivity	Specificity	PPV	NPV	P(Sig)
Right bulb volume ≤24.05 (mm^3)	0.918(0.846 to 0.963)	82.00	90.00	89.1	83.3	0.001(HS)

*: Confidence interval; **: Positive predictive value; **: Negative predictive value.

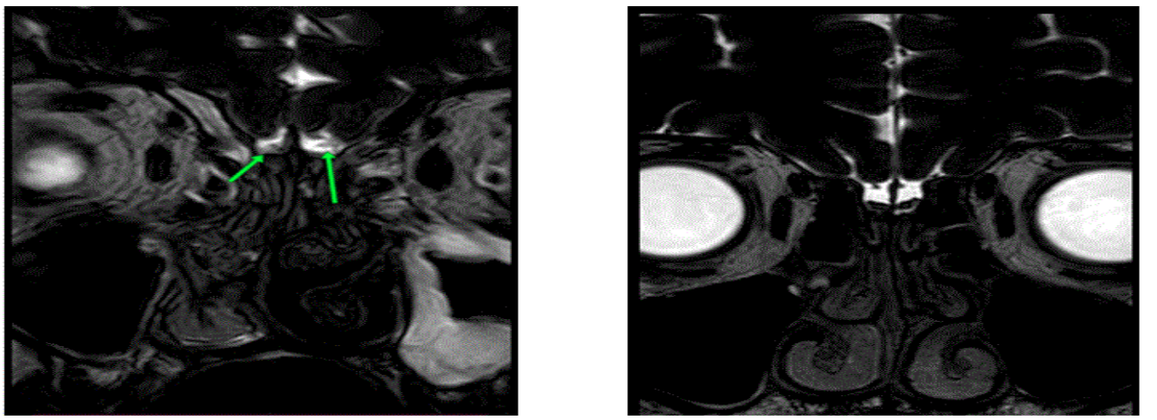

Figure 9: MRI 3D DRIVE sequence in coronal view showing bilateral atrophic olfactory bulbs in case no.6 (A) in comparison to normal olfactory bulbs volume in control no.5 (B).

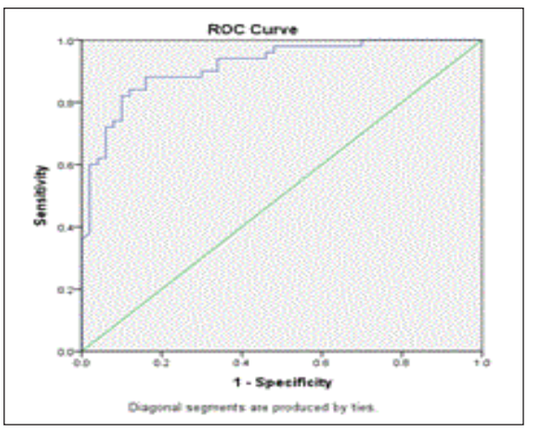

Figure 10: ROC Curve using Right bulb volume to discriminate between cases and controls.

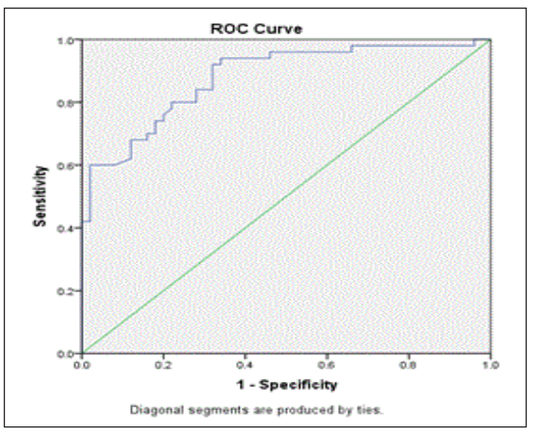

Figure 11: ROC Curve using Left bulb volume to discriminate between cases and controls.

Table 4: ROC Curve using Right bulb volume to discriminate between cases and controls:

Cut off level.	Area under curve (CI*)	Sensitivity	Specificity	PPV**	NPV***	P(Sig)
Left bulb volume ≤27.1 (mm^3)	0.879 (0.799 to 0.936)	80.00	78.0	78.4	79.6	0.001(HS)

*: Confidence interval; **: Positive predictive value; **: Negative predictive value.

Table 5: ROC Curve using Right bulb volume to discriminate between cases and controls:

Cut off level.	Area under curve (CI*)	Sensitivity	Specificity	PPV**	NPV***	P(Sig)
Average bulb volume ≤26.4 (mm^3)	0.924 (0.873 to 0.974)	84.00	80.00	80.8	83.3	0.001(HS)

*: Confidence interval; **: Positive predictive value; **: Negative predictive value.

Table 6: Correlations between age and UPSIT score:

		UPSIT score
Age	R*	0.079
	P	0.585
	Sig	NS

*: Pearson Correlation coefficient.

Table 7: Correlation between bulb volume and UPSIT score:

		UPSIT score
Right bulb volume (mm^3)	R*	0.879**
	P	0.0001
	Sig	HS
Left bulb volume (mm^3)	R*	0.818**
	P	0.0001
	Sig	HS
Average bulb volume (mm^3)	R*	0.926**
	P	0.0001
	Sig	HS

*: Pearson Correlation coefficient.

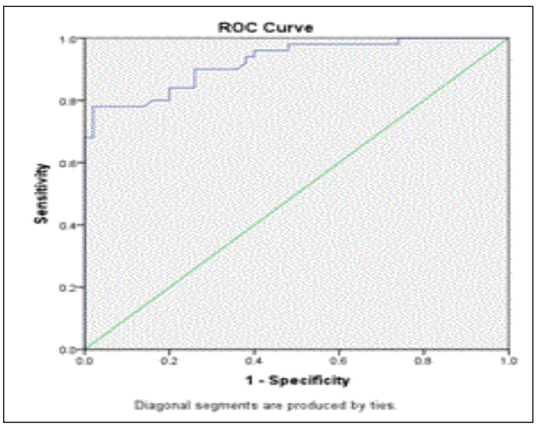

Figure 12: ROC Curve using average bulb volume to discriminate between cases and controls.

Table 8: Relation between bulb flair, T1 signal, and UPSIT score among cases:

		UPSIT score			
		Mean	**±SD**	***P***	**Sig**
Right bulb Flair signal	Iso	22.26	5.23		
	Hyper	20.34	6.95	0.01	S[a]
	Atrophied	7.50	0.71		
Right bulb T1 signal	Iso	21.30	6.60		
	Hyper	20.92	6.21	0.017	S[b]
	Atrophied	7.50	0.71		
Left bulb Flair signal	Iso	20.60	5.63		
	Hyper	21.96	6.47	0.001	HS[c]
	Atrophied	7.67	0.58		
Left bulb T1 signal	Iso	21.00	6.23		
	Hyper	21.86	6.05	0.002	HS[c]
	Atrophied	7.67	0.58		

*: ANOVA test; a: Atrophied Vs Iso (HS), Hyper (S); b: Atrophied Vs Iso(S), Hyper (S); c: Atrophied Vs Iso, Hyper (HS).

Table 9: Correlation between duration of anosmia with bulb volume and UPSIT score:

		Right bulb volume	Left bulb volume	Average bulb volume	UPSIT score
Duration of anosmia	R*	-.071	.101	.027	.068
	P	.623	.484	.852	.639
	Sig	NS	NS	NS	NS

*: Pearson Correlation.

DISCUSSION

Although coronavirus mainly targets the respiratory system, it can also spread from the respiratory tract to the central nervous system due to its neuroinvasive ability. So, patients with coronavirus disease 19 (COVID-19) may present neurological symptomatology with repercussions on imaging exams[8].

COVID-19-related olfactory dysfunction as an isolated symptom or in conjunction with other respiratory symptoms has been increasingly recognized. OD in COVID-19 has been reported up to 80% in some series and may be seen as an isolated symptom, precede the respiratory manifestations, or develop after onset of respiratory symptoms[9].

Olfactory dysfunction is of sudden onset in the majority of cases and is usually a transient entity with a median time to recovery ranging between 1 and 3 weeks. No significant association with sinonasal symptoms had been identified, suggesting that the pathogenesis of COVID-19 anosmia might differ from obstructive olfactory dysfunction seen in other viral upper respiratory tract infections[10].

Anosmia has been identified as one of the first or only recognizable symptoms of the severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2) infection, accounting for >50% of Western patients. It is now known that post-SARS-CoV-1 anosmia could persist for as long as 2 years[11].

Magnetic resonance imaging (MRI) is the gold standard in the etiological assessment of persistent olfactory dysfunction (OD). While the utility of imaging in COVID-19-related OD has yet to be established, MRI is recommended in all patients with persistent OD[12].

A dedicated MRI study allows assessment of olfactory bulb volume, morphology and signal intensity, status of olfactory nerve filia, and signal intensity of primary olfactory cortex, which is helpful to differentiate between different etiologies and predict prognosis of olfactory function recovery[13].

MR imaging is a useful and consolidated method for evaluating olfactory dysfunction. None- theless, to our knowledge, MRI-based evaluations of olfactory system alterations associated with COVID-19 are still limited to small investigational studies, case series, and case reports. Only a few studies performing systematic, quantitative olfactory system measurements have been published so far, but still on quite small populations[7].

The present study showed no significant difference between cases and controls as regard age; however, a highly significant difference was found between cases and controls as regard UPSIT score.

In agreement with our results, **Campabadal *et al.,***[14] aimed to study structural brain changes in patients with persistent olfactory dysfunctions after coronavirus disease 2019 (COVID-19). They reported that there was no significant difference between cases and controls as regard age, however, a highly significant difference was found between cases and controls as regard UPSIT score (P <0.001).

As well, our results were consistent with **Akkaya *et al.,***[15] who aimed to investigate whether the volume and morphology of the olfactory bulb are effective in the occurrence of anosmia in patients after COVID-19 infection. In this study, a total of 123 brain MRIs taken before the COVID-19 PCR (+) positivity, 59 belonging to the anosmia group and 64 to the control group, were retrospectively analyzed. The mean age was 54.5 (21–71) years for the anosmia group and 55 (19–80) years for the control group. There was no statistically significant difference in age between the two groups (p= 0.29).

In our study, we found that there was no significant correlation between age and UPSIT score.

In contrast with our results **Leedman *et al.,***[16] aimed to assess olfactory dysfunction in patients at 6 months after confirmed COVID-19 infection. They reported that Multivariable linear regression analysis of UPSIT scores at 6 months post-COVID-19 diagnosis revealed older age as statistically significant, with each year increase in age being associated with a 0.21-point reduction in UPSIT score (p <0.001; 95% CI [-0.28, -0.14]). This difference is explained by the wide range of age group in our study (20 – 60 years) as well as long duration of anosmia among study group (12 months).

Also, in contrast with our results **Callejón-Leblic *et al.,***[17] aimed to analyze the prevalence and predictive factors of long-lasting olfactory dysfunction in COVID-19 patients. A subgroup of 69 patients also underwent psychophysical evaluation of olfactory function through UPSIT. They reported that the correlation of UPSIT scores with age was also moderate (Pearson's r= −0.3486, p= 0.0033).

Moreover, **Saltagi *et al.,***[18] aimed to systematically review the literature on the diagnostic evaluation of anosmia to identify which diagnostic modalities of olfactory dysfunction have the strongest evidence, and to provide guidance to clinicians for approaching anosmia. They reported that age significantly correlated with UPSIT (ρ= −0.460).

In our study, we found that here was a highly significant difference between cases and controls as regards olfactory bulb volume with lower mean right, left, and average bulb volumes among cases indicating variable degrees of atrophy among study group. Similarly, the olfactory bulb flair signal and T1 signal on each side were significantly different between cases and controls showing hyperintense signals in 58% of study group and isointense signals in control group indicating neuropathy and microbleeding among study group.

Our results were consistent with **Elfeshawy *et al.,***[19] who aimed to assess the olfactory cleft and the olfactory bulb in post-COVID-19 anosmic patients with paranasal sinus CT, and MRI dedicated to the olfactory bulb. Regarding olfactory bulb volume, the mean volume of right-side OB volume was 38.3±12.03mm (17.06±9.5 in our study) with a minimum volume of 17.3mm and maximum volume of 57.2mm. As regard left-side OB volume, the mean volume of all studied patients was 35.6±9.1mm (17.94±11.95 in our study) with a minimum volume of 19.5mm and a maximum volume of 52.8mm. They found significant decreases in the values of investigated MR imaging parameters: right olfactory bulb volume, left olfactory bulb volume, right olfactory sulcus depth, and left olfactory sulcus depth.

Also, our results were consistent with **Chetrit *et al.,***[20] who aimed to evaluate magnetic resonance imaging of COVID-19 anosmic patients reveals abnormalities of the olfactory bulb. They found that statistical analysis of the Signal Intensity Ratio of the OB showed significant differences between the anosmic group (mean= 1.73±0.23) and the normosmic group (mean= 1.27±0.04; p <0.0001). Signal intensity ratio in loss of smell and the control group,

revealing a statistically higher T2/FLAIR Signal Intensity Ratio of the olfactory bulb in the loss of smell group (p <0.001).

As well, **Altunisik *et al.,***[21] aimed to compare quantitative measurements of olfactory anatomic structures between patients diagnosed with COVID-19 associated with persistent olfactory dysfunction and healthy controls. The measured values were compared between the patient and control groups. The right, left, and total OB volume values were significantly lower in the patient group (41.57 [SD, 16.96], 40.76 [SD, 15.93], and 82.34 [SD, 31.29] mm3, respectively) compared with the control group (66.12 [SD, 16.86], 65.38 [SD, 18.80], and 131.50 [SD, 32.27] mm3, respectively; P, .001, P, .001, and P, .001). They found significant decreases in the values of all investigated MR imaging parameters (right OBV, left OBV, total OBV, right OTL (olfactory tract length), left OTL, right OSD (olfactory sulcus depth), and left OSD) in the case group compared with the control group. In addition to an increase in focal intensity in 7 patients in the patient group.

Also, **Altundag *et al.,***[21] aimed to investigate the differences in olfactory cleft (OC) morphology in coronavirus disease 2019 (COVID-19) anosmia compared to control subjects. This study comprises 91 cases, including 24 cases with anosmia due to SARS-CoV-2, 38 patients with olfactory dysfunction due to viral infection other than SARSCoV-2, and a control group of 29 normosmic cases. They reported that as regards the results of the MRI assessment of the olfactory system, there was a highly significant difference between cases and controls with lower mean right, left, and average bulb volume among cases.

Furthermore, **Ammar *et al.,***[22] reported that the mean values of OB volumes significantly decreased from baseline (49.22±10.46mm^3) to 6-month follow-up (43.70±9.88mm^3), with a mean variation of -10.30±13.01% (p= 0.006)

In contrast with our results, **Akkaya *et al.,***[15] found that there was no significant difference between patients with anosmia and 64 controls without anosmia as regards results of MRI of mean right, left, and average bulb volume among cases mostly due to differences in severity of anosmia as well as the duration of anosmia was 1 month (12 months in our study).

In our study, we found that using the ROC curve, the Right bulb volume can be used to discriminate between cases and controls at a cutoff level ≤24.05 with 82% sensitivity, 90% specificity, 89.1% positive predictive value, and 83.3% negative predictive value. Left bulb volume can be used to discriminate between cases and controls at a cutoff level ≤27.1 with 80% sensitivity, 78% specificity, 78.4% positive predictive value, and 79.6% negative predictive value. Average bulb volume can be used to discriminate between cases and controls at a cutoff level ≤26.4 with 84% sensitivity, 80% specificity, 80.8% positive predictive value, and 83.3% negative predictive value.

Our results were consistent with **Sherif *et al.,***[23] who aimed to assess the utility of MR Imaging in the detection of olfactory bulb dysfunction in COVID-19-related anosmia. It was performed in 62 patients with COVID-19-related anosmia and 23 controls. The threshold of fractional anisotropy and mean diffusivity to differentiate a diseased from a normal olfactory bulb were 0.22 and 1.5, with sensitivities of 84.4% and 96.8%, respectively, and a specificity of 100%.

As well, our results were consistent with **Kim *et al.,***[24] who reported that the area under the summary ROC curve was 0.8. Olfactory and/or taste changes had a low sensitivity (0.57; 95% CI, 0.47–0.66) but moderate negative (0.78; 95% CI, 0.69–0.85] and positive (0.78; 95% CI, 0.66–0.87) predictive values and a high specificity (0.91; 95% CI, 0.83–0.96).

In our study, we found that there was a highly significant positive correlation between olfactory bulb volume and UPSIT score among cases. This may open up great horizons and prospects for using a dedicated MRI study as a noninvasive objective method for assessment of anosmia and know its prognosis.

Our results were consistent with **Bispo *et al.,***[25] who found a positive correlation between total olfactory bulb volume and the Sniffin' Sticks smell identification test performance in the study sample (n= 53) (rho= 0.281, p= 0.014).

CONCLUSION

After thorough investigation and well calibrated statistics this study revealed that there was a highly significant difference between study and control groups as regards results of MRI showing lower bulb volume and hyperintensity of the bulb FLAIR signals among study group. This indicates that the anosmia in post COVID-19 patients is mainly due to central affection (nerve neuropathy, microbleeding and atrophy) prospecting that treatment of post COVID-19 anosmia is to be conducted by systemic medication rather than local sprays. Furthermore, we found that there was a highly significant positive correlation between bulb volume and UPSIT score among study group prospecting that a dedicated MRI study of the OB could be used for objective assessment and prognosis of anosmia. We recommend further studies with larger scales and different durations to confirm or negotiate our results and prospections for this important topic.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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