# Magnetic Resonance Imaging pearls in the Diagnosis of Coronavirus associated rhino-orbital-cerebral fungal infection : Retrospective Imaging Analysis of 80 Patients

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**Abstract**

**Background:** Rhino-orbital-cerebral mucormycosis has emerged as a major opportunistic infection in patients with COVID-19 and shows tremendous increase during second wave of the COVID-19 pandemic. High clinical suspicion and prompt imaging are crucial for early diagnosis and management as it leads to pernicious morbidity /mortality result

**Objectives:** This study's goal is to describe the different MRI findings of COVID-19 associated rhino-orbital-cerebral mucormycosis (CA-ROCM) , to be familiar with the wide imaging variety which is crucial for early diagnosis and management

**Patients and Methods**: In this retrospective study, which included 178 patients confirmed with COVID-19 through March 2020 and February 2022.After reviewing the pateints' imaging data, only 80 patients were included. Medical records with a special emphasis on MRI were reviewed regarding the severity of sinuses and nasal cavity affection, orbital and cerebral invasion.

**Results**: We reported findings in 80 patients with (CA-ROCM). The study cohort had 12 patients with isolated sino-nasal involvement( stage I) , 28 patients with sino-nasal-orbital involvement ( stage II), and 40 patients with intracranial involvement (stage III).The most frequently involved sinuses were ethmoid & maxillary sinuses represented in 75 patients (93.7 %) .Black turbinate sign and non-enhancing sino-nasal mucosa were observed in 63 patients (87.7 %). Sixty two patients (77.5 %) presented with orbital extension. Thirty one (38.7 %) patients had thickening and enhancement of dura, cerebritis was reported in 24patients (30 %). Cerebral ischemic infarcts were seen in 12 (15 %) patients. Post contrast MRI results was correlated with operative data and revealed that MRI had higher sensitivity and specificity in stage III disease (100 % , 100%) rather than stage II (94 % , 96%) and stage I disease (85%, 89%).

**Conclusions**: MRI findings of CA-ROCM significantly vary from mild mucosal thickening of paranasal sinuses up to intracranial and orbital invasion. MRI with contrast can early detect subtle inflammatory changes outside the paranasal sinuses as early diagnosis of nasal/orbital/cranial invasion would reduce individuals' mortality and morbidity rates.

**Keywords:** MRI; COVID 19; CA-ROCM.

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## Introduction

The term "Mucormycosis" refers to a variety of fungal infection syndromes, the most frequent of which represents in the form of severe type of rhino-orbital-cerebral or respiratory infections. **(Mekonnen et al., 2021).**

COVID 19 may have a variety of illness patterns as it may be accompanied with fungal and bacterial life-threatening opportunistic coinfections in high risk patients because of their comorbid conditions (such as diabetes mellitus and chronic obstructive pulmonary disease) and in immune-compromising circumstances (such as corticosteroid use, ICU stays, and ventilation) **(Mehta and Pandey 2020).**

Massive pulmonary disease and consequent alveolo-interstitial affection are common complications of COVID 19 disease which increase the risk for aggressive fungal infections affecting airways lungs and paranasal sinus , In addition to the immunological dysregulation condition associated with COVID 19, makes the innate immunity modified (**Sen et al., 2021).**

The spread along the nasolacrimal duct and medial orbital wall causes orbital involvement. Fungal spread to the brain parenchyma by vascular invasion may cause thrombosis, infarction and necrosis (**Hmaied et al., 2005).**

Debridement procedures (such as enucleation) are the only choice for certain individuals, leaving a significant portion of them blind. Hence, the radiologist's role is helpful in knowing such a case and alerting the treating physician as soon as possible (**Sethi et al ., 2021**).

Thickening of mucosa without air fluid levels is the initial disease presentation seen on a CT scan..MRI with contrast has been shown to be very helpful in assessing complications such as orbital cellulitis, ICA thrombosis, cavernous sinus thrombosis, and brain abscess (**Byale and Pattanshetti, 2022**).

Fat stranding in the orbits, face, and retro-antral region are the first indicators of aggressive progression. The disease's more severe variant has early brain involvement, as shown in a few reports **(Silverman and Mancuso, 2005**)

Physicians should be aware of the danger of (ROCM) after COVID-19 illness and be aware about the use of CT and MRI together because early detection of the disease by imaging is important for effective therapy **(White et al .,2021)**.

Our aim in this research is to stress on the importance of MRI in the diagnosis of ROCM since early detection and management are required to avoid transmission of disease, assist in effective treatment, and enhance patients' outcomes.

## Patients and methods

### *Patients*

After institutional ethics committee approval (No 35971) was obtained, this retrospective study was done in Tanta University Hospital in the period between March 2020 and February 2022 by reviewing the MRI data of patients confirmed to have acute CA-ROCM (by histology or fungus smears) .

All patients had history of COVID-19 exposure and their first pre-operative MRI of the paranasal sinus and brain were included. To confirm the exposure to COVID-19 infection ; a positive reverse transcription-polymerase chain reaction (RT-PCR) from nasopharyngeal swab was used and/or the patients had characteristic COVID-19 Reporting and Data System (CO-RADS) category-5 based upon their CT chest imaging findings. A full clinical examination; including a

nasal endoscopy, demographic information, a medical history of additional comorbidities, laboratory and histological results, a treatment plan, were all evaluated.

A total of 178 CA-ROCM patients were included for the first assessment. Eighty of them who had pre-operative enhanced MR imaging were included in the final analysis (**Fig.S1**).

***Inclusion criteria***

- Confirmed patients of COVID infection .
- Confirmed patients of COVID associated maxillary , orbital , sinus and intracranial fungal infection.
- Patient with pre-operative enhanced MR imaging of the paranasal sinus , orbit and brain .

***Exclusion criteria***

- Non confirmed COVID patients.
- Non histological confirmed fungal infection patients.
- Patients with non available post operative data .
- Unsuitable Patients for pre-operative enhanced MRI ; Claustrophobic, poor renal functions patients and Patients with metallic implants.

***Ethics approval***

The local ethics committee gave its approval to this study.

***Informed consent***

*All participants in this study provided their informed consent.

***Subject confidentiality:***

*To ensure subject confidentiality, none of the assessment forms, reports, or other documents include unique personal information.

***Methods***

**A) Image acquisition & reconstruction**

All MRI exams were performed using a 1.5 T (Signa16 channel, Excite, GE Healthcare, Milwaukee, WI, USA machine) with head-neck coil.

***Brain sequence***: T1weighted images parameters ((TR/ TE/ 400–644 ms/8–20 ms/)) T2-weighted images parameters (TR: 6672 ms, TE: 147 ms); FLAIR (TR: 7432, TE: 118.6, inversion time (TI): 2200); field of view (FOV) 22 × 18 mm;diffusion-weighted imaging (DWI) and ADC with the following parameters B = 0, B = 1000 s/mm2 TR/TE = 10,000 ms/76.8 ms ;matrix, 310 × 620; slice thickness, 5 mm; and slice gap, 0.4 mm.

***Orbit and paranasal sinus protocol***: T1WI (TR/ TE/ 400–644 ms/8–20 ms/), T2WI fat-saturated (TR/ TE/, 3200–5000 ms/85–129 ms). Slice thickness/gap/ FOV = 2–3 mm/0.5 mm/18 cm), diffusion-weighted imaging (DWI) and ADC with the following parameters B = 0, B = 1000 s/mm2 TR/TE = 10,000 ms/76.8 ms, slice thickness, 0.3 mm slice gap.

***Post contrast series***: were obtained 20–30 s after intravenous administration of 0.1 mmol/kg gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany).

All patients' signal characteristics and the degree of sinus opacification were observed; .The mucosal disease was scaled on a 5-pointscore (0 = subtle mucosal thickening, 1 < 25% opacified,2 = 25%: < 50% opacified, 3 = 50%: < 75% opacified,
4 = 75%:100% opacified, 5 = mucocele (100% opacified with expansion)

The signal intensity (SI) of the sinus content was measured in comparison to the SI of the cerebral cortex. The absence of nasal turbinates and mucosal enhancement was the definition of the black turbinate sign. The extra-sinus soft tissue invasion was characterized by the smudging of healthy fat/fat stranding and the infiltration of soft tissue into the retro-

antral fat pad along the maxillary sinus's posterior wall. The masticator space, orbit, and pterygopalatine fossa.

To assess intracranial extension and perineural dissemination, post-contrast T1 WI was utilized (absence or presence of enhancement of the dura, infiltration of cavernous sinus, cerebritis, intracerebral infarcts or abscess formation)

The intensity of the condition was divided into three stages depending on the radiological extent. Stage I disease was limited to the nasal cavity and paranasal sinuses. Extension into the orbits was considered as stage II disease, while intracranial extension indicated stage III.

**B) Image analysis**

Three radiologists interpreted the images in conjunction One reader (S.N) had 13 years of experience interpreting, the second reader (S.B) had 13 years of experience & the third one (A.R) had 12 years of experience

**Statistical analysis**

The statistical analysis was performed using SPSS, version 23.0. Age, gender, co-morbidities, and imaging characteristics are examples of qualitative variables that were represented using frequency and percentages. The Pearson correlation test was used to determine the degree of association between the CTSI, the HbA1c values, the use of steroids, the use of oxygen therapy, and the disease stage. If the P-value was less than 0.05, the results were deemed statistically significant.

**Results**

Twelve participants in the research group had solitary sino-nasal involvement in stage I **(Figs. 1-3**), 28 participants had sino-nasal-orbital affection in stage II (**Figs. 4 and 5**), and forty participants had intracranial invasion in stage III **(Figs. 6 and 7), (Table .1).**

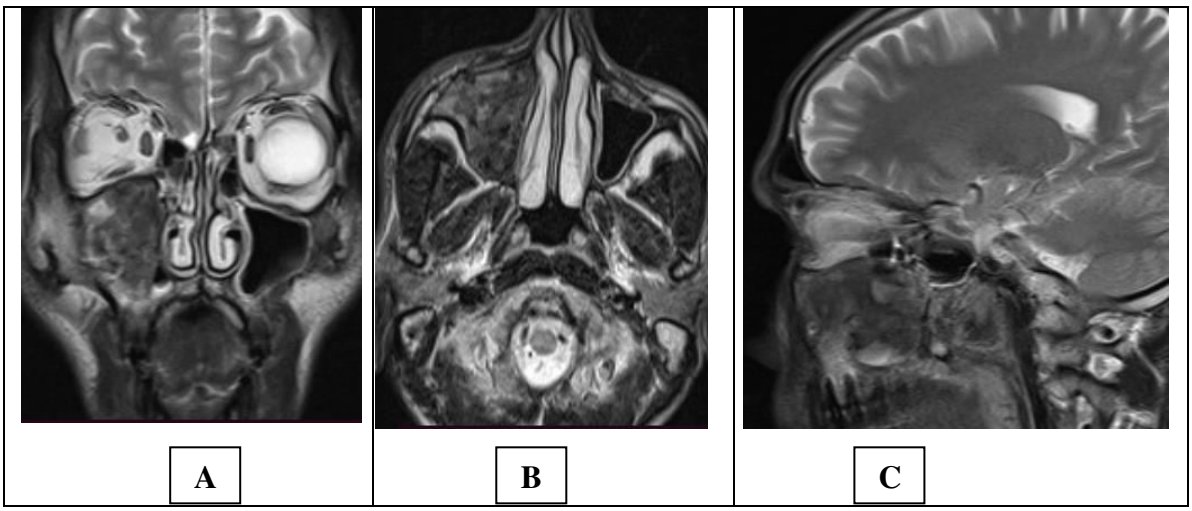


**Fig.1.** A) Coronal ; B)Axial ; C)Sagittal T2 WIs show dark right maxillary signal with no evidence of intraorbial /intra cranial invasion

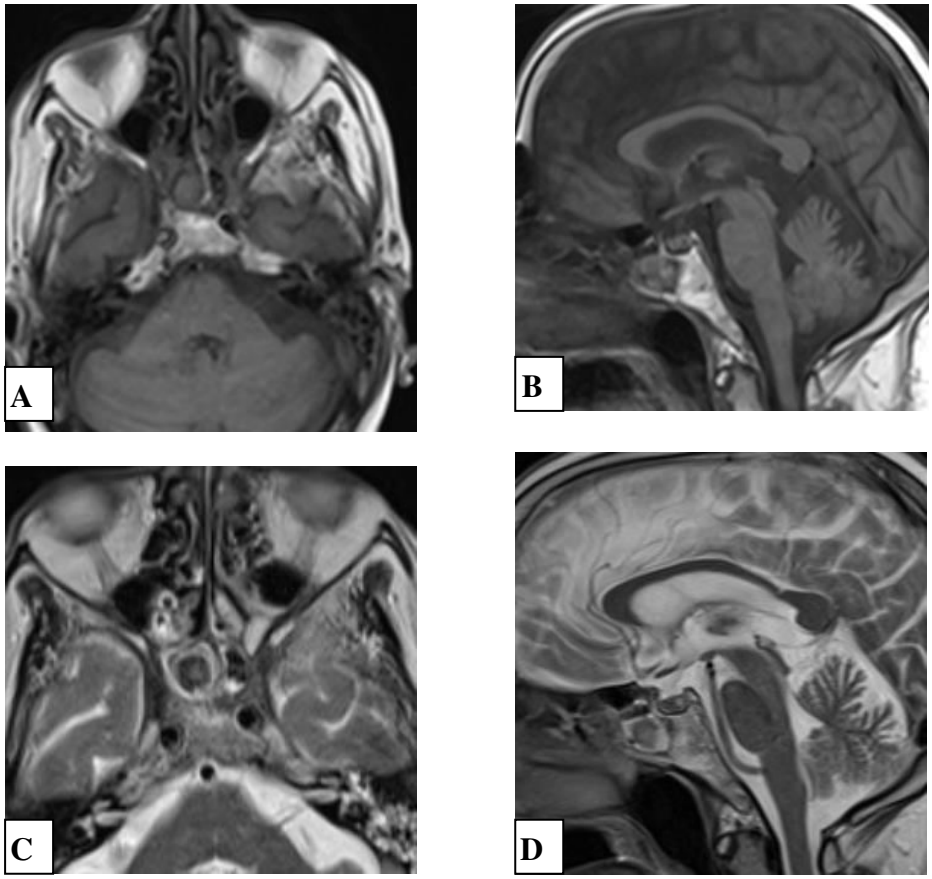


**Fig.2.** A&B)axial and sagittal T1WIs show right sphenoidal intermediate signal; C&D) axial and sagittal T2WIs show right sphenoidal dark signal

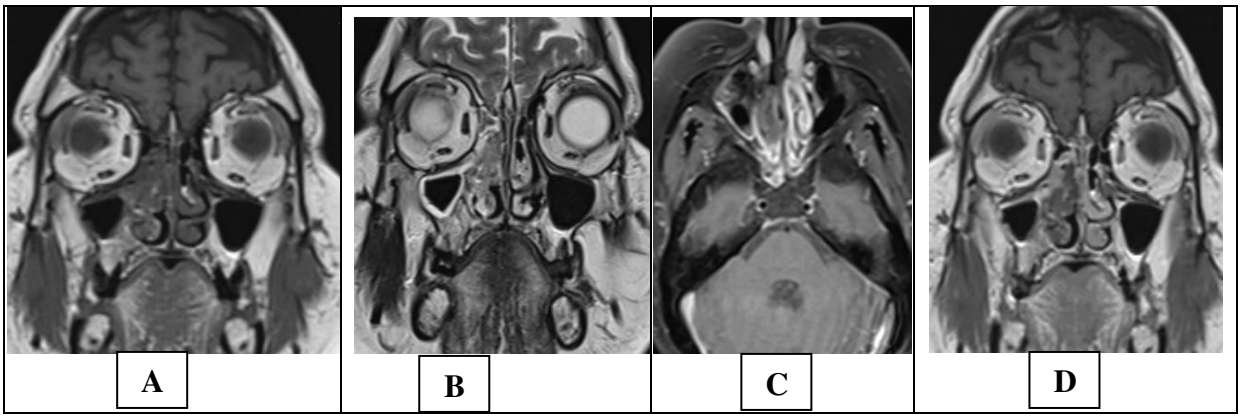


**Fig3**. A & B) axial T1 &T2 WIs shows The mucosal covering the right middle and inferior turbinate displaying low signal in T1 WI and T2 W I with in C & D ) axial & coronal post contrast shows no post contrast enhancement giving black turbinate sign

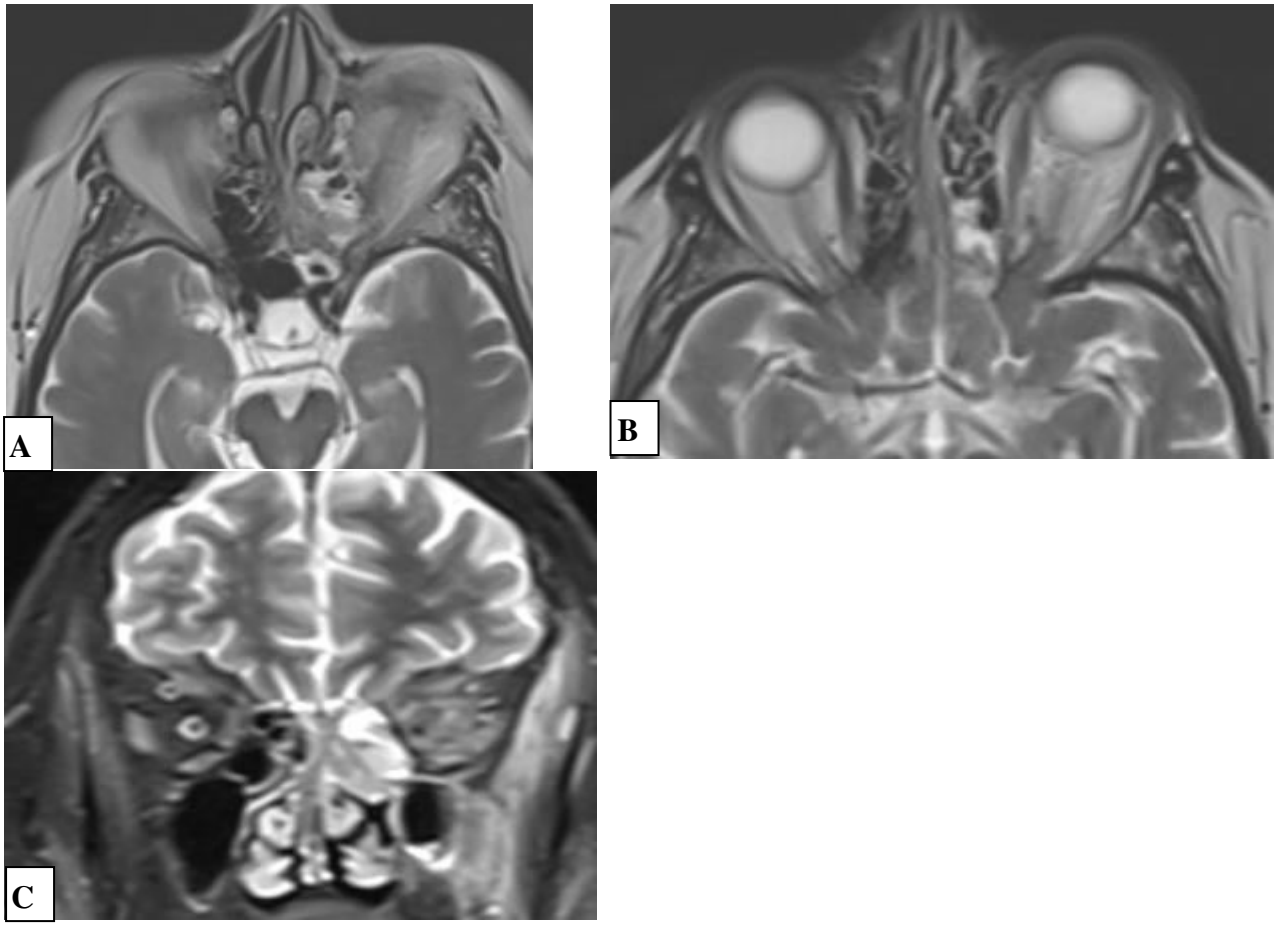


**Fig.4.** A & B) axial T2 WI and C) coronal STIR shows Left posterior ethmoidal obliteration by ill-defined soft tissue lesion together with left side intra-orbital fat stranding& orbital proptosis

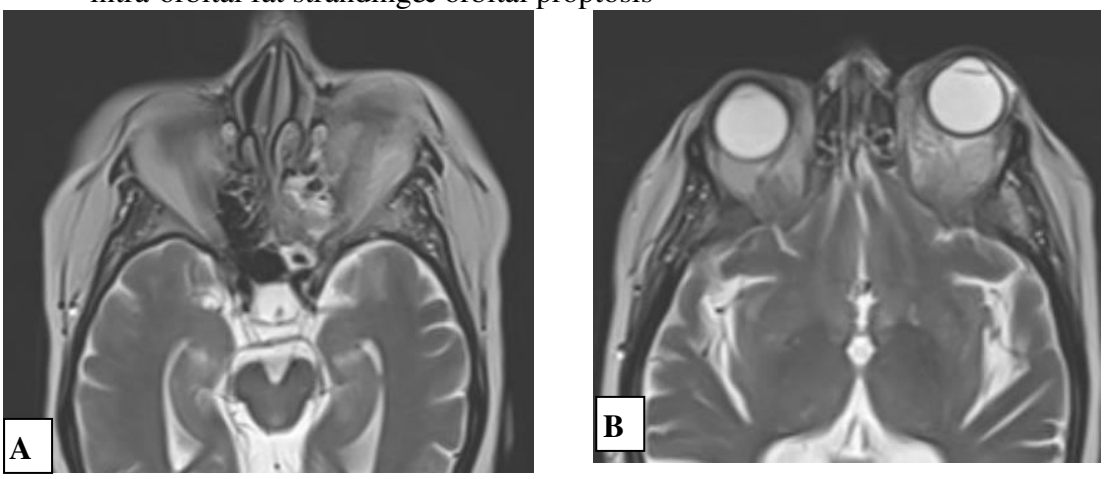


**Fig.5**. Axial T2WI in different planes shows left posterior ethmoidal mucosal thickening with dark signal denoting fungal sinusitis together with left orbital proptosis with dirty fat planes

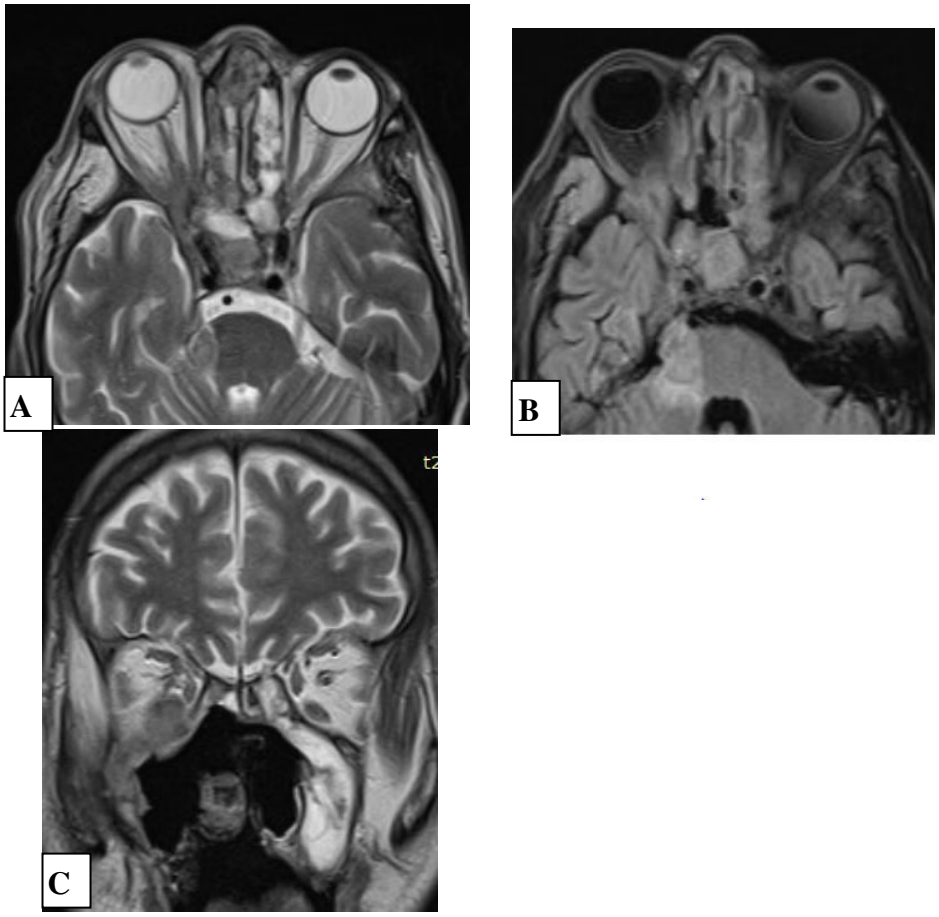


**Fig. 6.** A)axial T2 b)axial flair & c) coronal T2 WI shows abnormal soft tissue thickening is seen involving the ethmoidal , sphenoidal and frontal sinuses extending to right para-sellar region encasing the ICA and the cavernous sinus , with intra orbital extension .

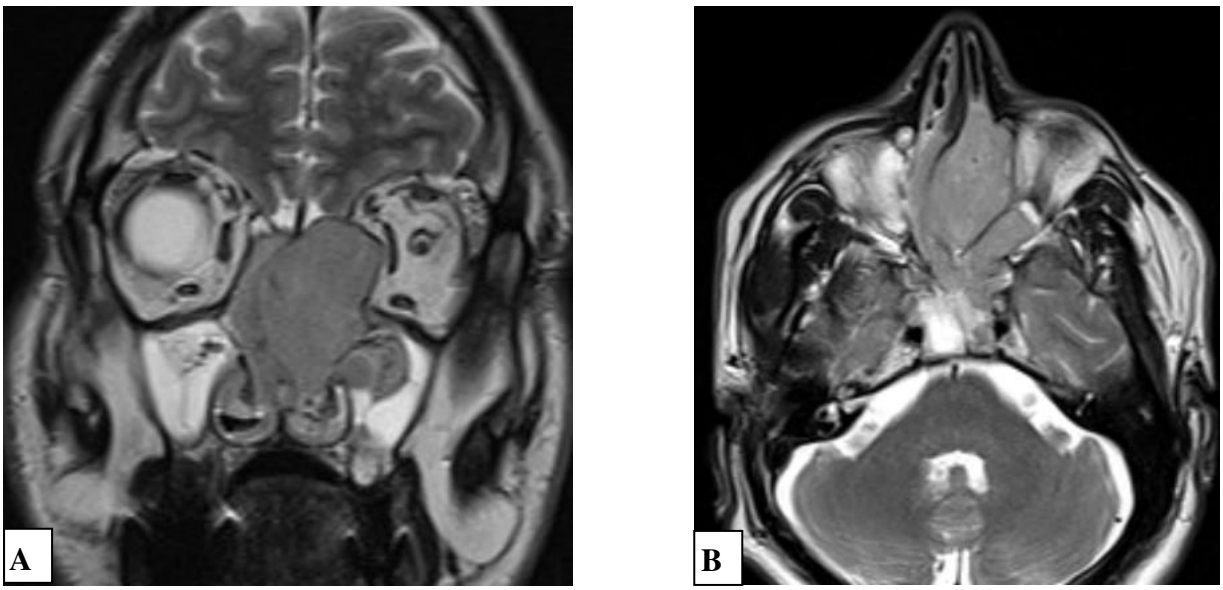


**Fig.7.** A) coronal T2 WIs b) axial T2 WIs show: Large soft tissue polypoidal mass lesions totally obliterating both ethmoidal air cells, both nasal cavities partially extending into the left maxillary and left sphenoid sinuses. The upper part of the septum is destructed. The lesion is seen extending into the left orbit through the

lamina paperacia with medial deviation of the medial rectus and left side proptosis. Superiorly the mass is extending intra-cranially through the cribriform plate into anterior cranial fossa subfrontal.

**Table 1. Stages for Coronavirus disease-2019 associated Rhino-orbito-cerebral Mucormycosis (CA-ROCM) among the studied group**

| Stage | N | % |
|---|---|---|
| **Stage I** | 12 | 15.00 |
| **Stage II** | 28 | 35.00 |
| **Stage III** | 40 | 50.00 |
| **Total** | 80 | 100.00 |

Out of eighty patients included in this analysis, 51 participants were male (63.7%), and their mean age was 60.125 ± 10.511 years (range from 40 - 77 years). The mean CT severity score (CTSI) was 19 ± 3.197.

Thirty seven patients (46.2%) had a prior hospitalization history, 38 patients (47.5%) and 31 patients (38.7%), had a history of steroid use and oxygen supplementation respectively. The average interval between the COVID-19 diagnosis and the imaging for CA-ROCM was 15.2 ± 6.2 days. **(Table.2)**

Thirty two patients had previously received a diagnosis of type 2 diabetes (DM); 25 of them had was poorly controlled glycemic index that (high random blood sugar levels > 200 mg/dl or HbA1c > 6.5). 36 patients had just recently been diagnosed with diabetes at the time of presentation (according to increased HbA1c readings of > 6.4%). Nine of the remaining 12 patients were prediabetic (HbA1c between 6% and 6.4%). Only three cases had good glucose control, while one of them had an immunodeficiency as a result of a prior liver transplant.

**Table 2. Demographic data and risk factors for Coronavirus disease-2019 associated Rhino-Orbito-Cerebral Mucormycosis (CA-ROCM)**

| Variables | | Stage | | | | | | | | | ANOVA | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Stage I | | | Stage II | | | Stage III | | | F | P-value |
| **Age** | Range | 40 | - | 48 | 46 | - | 66 | 54 | - | 77 | 141.884 | <0.001* |
| | Mean ±SD | 43.667 | ± | 2.535 | 55.036 | ± | 4.566 | 68.625 | ± | 5.614 | | |
| **Chi-Square** | | N | | % | N | | % | N | | % | $X^2$ | P-value |
| **Sex** | Male | 8 | | 66.67 | 19 | | 67.86 | 24 | | 60.00 | 0.492 | 0.782 |
| | Female | 4 | | 33.33 | 9 | | 32.14 | 16 | | 40.00 | | |
| **Diabetes** | Negative | 2 | | 16.67 | 1 | | 3.57 | 0 | | 0.00 | 6.539 | 0.038* |
| | Positive | 10 | | 83.33 | 27 | | 96.43 | 40 | | 100.00 | | |
| **Steroid use** | Negative | 9 | | 75.00 | 15 | | 53.57 | 14 | | 35.00 | 6.559 | 0.038* |
| | Positive | 3 | | 25.00 | 13 | | 46.43 | 26 | | 65.00 | | |
| **Oxygen** | Negative | 12 | | 100.00 | 23 | | 82.14 | 13 | | 32.50 | 26.324 | <0.001* |
| | Positive | 0 | | 0.00 | 5 | | 17.86 | 27 | | 67.50 | | |
| **HbA1c** | Range | 5.5 | - | 7.8 | 7 | - | 11.1 | 10 | - | 12.1 | 146.627 | <0.001* |
| | Mean ±SD | 6.358 | ± | 1.044 | 9.119 | ± | 1.228 | 11.335 | ± | 0.631 | | |
| **Hospitalization** | Negative | 10 | | 83.33 | 20 | | 71.43 | 13 | | 32.50 | 15.011 | 0.001* |
| | Positive | 2 | | 16.67 | 8 | | 28.57 | 27 | | 67.50 | | |
| **CTSI** | Range | 11 | - | 18 | 16 | - | 22 | 16 | - | 25 | 38.338 | <0.001* |
| | Mean ±SD | 14.333 | ± | 2.348 | 18.571 | ± | 1.687 | 20.850 | ± | 2.617 | | |

A positive association between disease stage and HbA1c level was present with (r = 0.849, p-value < 0.001). Mean HbA1c in stage 1, stage 2, and stage 3 were (6.358 ± 1.044, and 9.119 ±1.228 and 11.335± 0.631) respectively, (**Table. 2)**

The correlation between the patient's age and illness stage (r= 0.868 and P-value <0.001), a history of steroid usage (P-value =0.038), oxygen therapy (P-value < 0. 001), and the CTSI ((r = 0.645 and P-value < 0.001), hospitalization (P-value =0.001) was statistically significant **(Table. 2 and 3)**.

**Table 3. Correlation between stage of disease and various patient parameters**

| Correlations | | |
|---|---|---|
| Spearman's rho | Stage | |
| | R | P-value |
| Age | 0.868 | <0.001* |
| HbA1c | 0.849 | <0.001* |
| CTSI | 0.645 | <0.001* |

Clinical presentation was variable with sinusitis, nasal discharge and fascial pain are the most common presenting symptoms with percentage (100%), (97.8%) and (97.5%), extension into the orbit resulting in proptosis (56.2 %), ophthalmoplegia (60%) even visual loss (15 %), Cerebral extension resulted in symptoms of cerebral infraction (15%) and cerberitis (30%) **(Table 4)**

**Table 4. Clinical presentations of CO-ROCM patients**

| **Clinical persentaion** | **PERCENTAGE** |
|---|---|
| **Sinusitis** | **100 %** |
| **Nasal discharge** | **97.5%** |
| **Fever** | **94.3%** |
| **Toothache** | **80.4%** |
| **Facial swelling** | **89.4 %** |
| **Facial pain** | **97.8 %** |
| **Epitaxis** | **87.7 %** |
| **Proptosis** | **56.2%** |
| **Opthalmoplegia** | **60%** |
| **Loss of vision** | **15%** |
| **Meningeal signs** | **38.7%** |
| **Cerebral infraction symptoms** | **15%** |
| **Cerberitis symptoms** | **30%** |
| **Cavernous sinus involvement** | **32.5%** |

Surgical debridement was the main line of treatment as followed ; 23.2% of patients had external debridement, 25.8 % had endoscopic debridement, and 24% had combined open and endoscopic debridement .six patients (8.1 %) underwent maxillectomy 14 patients (18.9%) underwent orbital exenteration **(Fig.8)**.

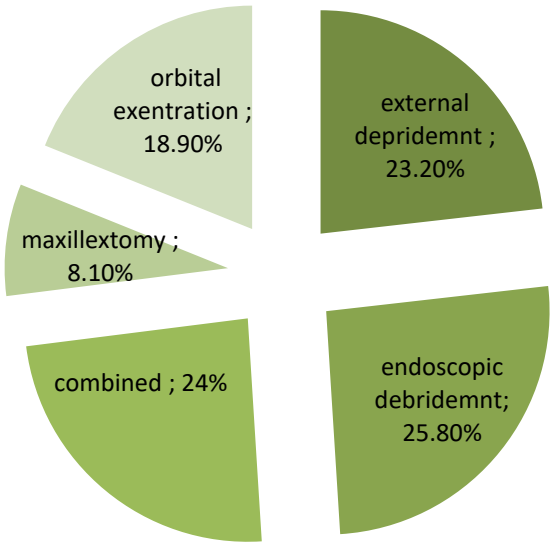


**Fig. 8.Types of surgical treatment of CO-ROCM patients**

As regards to MRI findings ; degree of mucosal opacification of the paranasal sinuses , nasal cavity and nasopharynx was reported ; 12.3 % of the patients showed subtle mucosal alteration.**(Table .5).**

**Table 5. Degree of mucosal opacification of the paranasal sinuses , nasal cavity and nasopharynx**

| Degree of sinus opacifictaions | Percentage |
|---|---|
| Subtle mucosal opacifctaions | 12.3 % |
| 25% opacified | 22.2 % |
| 25—50% opacified | 20.4 % |
| 50-75% opacfied | 21.8% |
| 75-100 % opacified | 23.3 % |

The maxillary and ethmoid sinuses were the most affected in 75 patients (93.7 %) then sphenoid sinus in 67 patients (83.7 %), and the frontal sinuses was the least involved in 46 patients (57.5 %).

Upon post contrast sequences 63 patients (87.7%) had the black turbinate sign and non-enhancing sino-nasal mucosa while 100% of patients showed sinonasal soft tissue infarction at endoscopy/surgery (**Fig.3**).

In 68 cases (85%), there was bone erosion or destruction. The maxilla was the most frequently affected bone in 35 individuals (43.7%), followed by the lamina papyracea in nine cases (11.2%) .60 individuals (5%) had periantral soft tissue involvement.

Sixty two patients ( 77.5%) had orbital extension including all patients in stage II and 34 individuals in stage III; 45 patients (56.2%) had proptosis, which was more often observed on the right side (29/45). All cases with orbital involvement had extraocular muscle involvement, with the inferior rectus being the most frequently affected muscle in 32 patients (40%) and the medial rectus in 30 individuals (37.5%). Involvement of the orbital apex was observed in 38 cases (47.5%).

In 20 individuals (25%), the optic nerve had diffusion restriction. In 9 patients (11.2%), conical deformity of the posterior ocular globe caused by significantly elevated intra-orbital pressure was seen.

The most frequent location of perisinus extension was seen in the pterygopalatine fossa in 54 individuals (67.5%), followed by the infratemporal fossa in 53 cases (66.3%).

Twenty six patients (32.5%) had cavernous sinus involvement, with bilateral involvement in 8 instances and only unilateral right-sided involvement in 18 cases. The most prevalent intracranial abnormality seen in 31 patients (38.7%) was dura thickening and enhancement, which was followed by cerebritisin 24 patients (30%). Only 12 patients (15%) had cerebral ischemia infarcts as a result of vascular invasion.**(Table. 6).**

**Table 6. MRI imaging findings of (CA-ROCM) patients**

| **Imaging features** | **Number (out of 80) (Percentage)** |
|---|---|
| **Non enhancing sino-nasal mucosa /Black Turbinate sign** | **87.7 %** |
| **Bone erosion or destruction** | **85 %.** |
| **Peri-antral inflammation of the soft tissue** | **75 %** |
| **Proptosis** | **56.2%** |
| **Extra-ocular muscle involvement** | **77.5%** |
| **Orbital apex invovlment** | **47.5%** |
| **Diffusion restriction of optic nerve** | **25 %** |
| **Pterygopalatine fossa involvement** | **67.5 %** |
| **infratemporal fossa involvement** | **66.3 %.** |
| **Cavernous sinus** | **32.5 %** |
| **Pachymeningeal involvement** | **38.7 %** |
| **Cerebritis/early abscess formation** | **30 %** |
| **Cerebral ischemic Infarct** | **15 %** |

Post contrast MRI results was correlated with operative data and revealed that MRI had higher sensitivity and specificity in stage III disease ( intracranial extension ) rather than stage II and stage 1 disease.**(Table .7)**

**Table 7. Correlation between post contrast MRI findings and operative data**

| Stages | Sensitivity | Specificity |
|---|---|---|
| **Stage I** | **85 %** | **89 %** |
| **Stage II** | **94 %** | **96 %** |
| **Stages III** | **100%** | **100%** |

## Discussion

ROCM is an invasive fungal sinusitis that could be acute or chronic **(Deshazo et al., 1997)**, mucor was the most commonly isolated fungal pathogensis , it is inoculated mainly by inhalation, where it colonizes the paranasal sinuses then the orbit and brain through soft-tissue, perineural, or perivascular pathways, or by bone invasion. **(Yadav et al., 2022).**

Only 9% to 20% of immunocompetent people have been reported to have mucormycosis, which mostly affects immunosuppressed patients. **(Adulkar et al., 2019).**

On stride of Yadav et al **(Yadav et al., 2022)** we grouped our patients into 3 grouped according to the sage of invasion. The majority of our cases presented initially by orbital (stage II) and intracranial (stage III) lesions, suggesting an aggressive & invasive course of the disease which may explained by the immune-compromised factors of most of the cases, such as; poor glycemic control (the mean HbA1 c levels was 9.870 ± 2.054 ) , high CT severity score (The mean CTSI was19 ± 3.197 ) steroids usage, oxygen therapy, prolonged hospitalisation, his is in consistent with Yadav et al **(Yadav et al., 2022) ,** Shaban E etal **(Shaban et al.,2022)** Malleshappa et al. (**Malleshappa et al., 2020)** as they stated in their researches that most of their patients suffered from predisposing condition as diabetes mellitus

The most common presenting features of patients were nasal congestion & discharge, facial pain & swelling as well as fever in agreement with Turner et al. **(Turner et al., 2013)** who reported facial swelling (64.5%), nasal congestion (52.2%) andfever (62.9%). In our study 50 patients presented with deterioration in vision & proptosis which is considered as sign of orbital invasion and increased intra-orbital pressure due to inflammatory process in retro-orbital fat and orbital apex.**(Chan et al ., 2000).** This is in concordance with Agrawal et al (**Agrawal et al ., 2022**).

The orbital invasion of disease is also explained by ; Firstly, perineural dissemination.(**Theoret et al., 2011)** which is considered as one of the most important route for disease spread wiyh trigeminal nerve divisions ( maxillary and ophthalmic) are the most often affected nerves.(**Turgut et al., 2019** ). Secondly; contiguous spread from the neighboring maxillary & ethmoidal sinuses(**Chan et al., 2000).** Thirdly ; vascular invasion as mucormycosis pathobiology is characterized by the angio-invasive proliferation of the hyphae within the elastic lamina of large to intermediate sized arteries (**Turgut et al., 2019** ).these include the internal carotid, ophthalmic, and pterygopalatine branches of the internal maxillary artery respectively.(**Mazzai et al., 2022**)

Imaging features of the patients in the current study show wide variety. Sino-nasal disease shows variable radiological patterns, ranging from nodular mucosal thickening to opacification by high intensity content in absence of fluid level, its content mostly shows low T2SI due to the presence of paramagnetic elements as manganese and iron components in composition of fungi this is in agreement with Sreshtaetal 2020**&**Yadav et al 2022**.** (**Sreshtaetal, 2020 &Yadav et al .,2022).**

In our study maxillary and ethmoid sinuses were the most frequently affected sinuses followed by the sphenoid and frontal ones. This is consonance with Yadav et al who reported 46 (92%) patients followed by sphenoid 41 (82%), and frontal sinuses 28 (56%) in their study **(Yadav et al., 2022)** and Agrawal et al**(Agrawal et al., 2022)** as they recorded in their work that maxillary and ethmoid sinuses were affected in 95.83% and 89.17% of patients, respectively while sphenoid and frontal sinuses came in the 2nd place in 75% and 45.83% of patients, respectively.

Bone erosion / destruction was noted in 85% of the cases . The maxilla was the most frequently affected bone followed by the lamina papyracea , this is agreed with Agrawal et al. how stated that 60% of their patients diagnosed with bony erosion or marrow edema . Maxillary antrum and orbital walls erosions, allowing extension of the disease to retromaxillary soft tissue and orbit, respectively. **(Agrawal et al., 2022)**

MRI with post contrast enhancement permits delineation of subtle invasion, thrombosis of cavernous sinus structures, and identification of necrosis. (**Shaban et al., 2022).** It plays crucial role in the diagnosis as the “Black turbinate Sign” ,which is referred to sustained non-enhancement of the nasal turbinates on post-contrast imaging, and it is considered as an early MRI sign denoting nasal mucormycosis. **(Yadav et al., 2022)**.Sixty three patients in current study suffers from Black turbinate sign while 43 patients shows sinonasal mucosal non enhancement which denotes devitalized and necrotic tissue due to microvascular invasion**.**

Pterygopalatine fossa fungal infiltration may occur either by direct erosion of the sinus wall, perivascular, or perineural spread. Pterygopalatine involvement considered as an infection route to the cavernous sinus and middle cranial fossa (**Mathur et al., 2007).** In current study 54 individuals (67.5%) shows pterygopalatine extension

In our study 45 patients (56.2%) had proptosis, all of them show extraocular muscle involvement, with the inferior rectus being the most frequently affected muscle in 32 patients (40%) this is in concordance with Chan et al as they reported in their work 33 cases with inferior rectus muscle involvement & explained by contiguous spread from the neighboring maxillary & ethmoidal sinuses**(Chan et al., 2000).**

Restricted diffusion of optic nerve present in 25% of cases, unfortunately it is considered as bad omen for irreversible vision loss. This is may be caused by ophthalmic artery encroachment at the apex of the orbit or the optic canal (**Theoret et al ., 2011**).

In our study, pachymeningeal enhancement and thickening followed by cavernous sinus invasion and cerebritis were the most frequent signs denoting intracranial involvement with anteromedial temporal and basifrontal regions being the most affected sites. This is as long with Agrawal et al who reported that

meninges were the most commonlyinvolved intracranial structure and appeared thickened with abnormal Enhancement(**Agrawal et al., 2022**).

Invasive fungal disease affects common arteries in the apex of the orbit, cavernous sinus, and pterygomaxillary fissure, these include the internal carotid, ophthalmic, and pterygopalatine branches of the internal maxillary artery respectively **(Mazzai et al., 2022)**, The mucormycosis pathobiology is characterized by the angio-invasive proliferation of the hyphae within the elastic lamina of large to intermediate sized arteries (**Turgut et al ., 2019 )**.

The degree of sinonasal as well as nasopharyngeal mucosal opacification had relatively poor sensitivity and specificity .The correlation between mucosal opacification and infiltrations was very weak in operative data correlation in contrary to other orbital & intra cranial findings which correlate with surgical data . This is along with Shaban et al **(Shaban et al., 2022)**, as they reported 61% of their patients with subtle/insignificant nasal / nasopharyngeal mucosal thickening while 100% of the patients showed sinonasal soft tissue infarction at endoscopy/surgery

Our study had some limitations:1st, it was a single institutional study. 2nd, patient selectivity possibly be biased because of rapid disease progression and poor prognosis. 3rd, the lack of an indicator control group limited the findings. 4th, long-term clinical outcomes wasn't available. The international longitudinal study is necessary for future studies.

**Conclusion**

A severe invasive fungal sinusitis called rhino-orbital-cerebral mucormycosis associated with COVID-19 had a life-threatening course.

It is crucial to watch out for the modest but crucial initial imaging abnormalities as reported in a Confirmed COVID-19 incident with symptoms of sinusitis since patients with immune compromised situations are more likely to develop more serious infections.

Comprehensive imaging assessment is essential to assess the level of affection and consequences in order to direct operation. MRI with contrast can early detect subtle inflammatory changes inside of the orbital or face soft tissue, outside of the paranasal sinuses and cerebral involvement which allows early diagnosis and intervention to prevent disease transmission thus reducing individuals mortality & morbidity and improve patients ` outcome.

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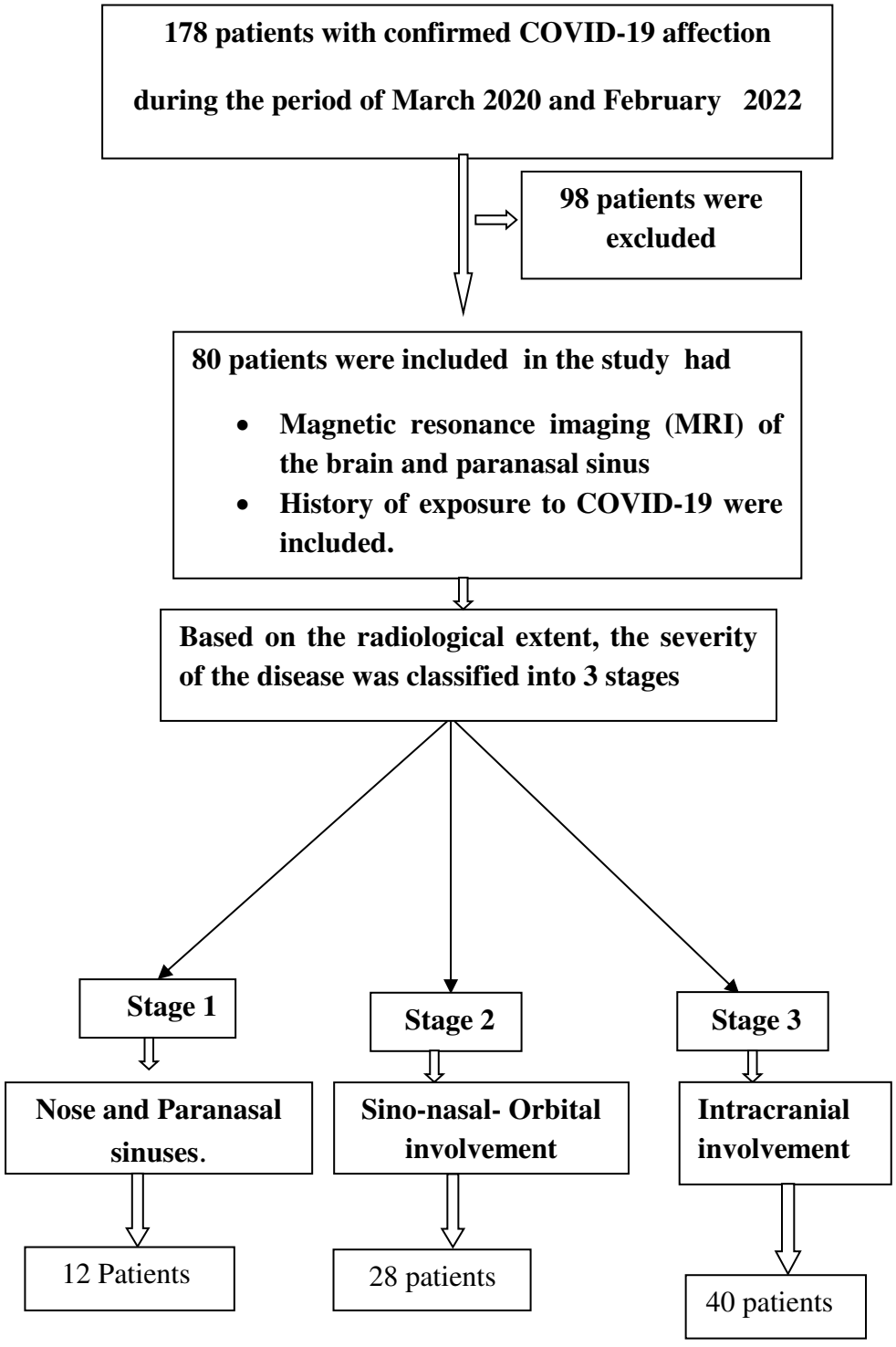


**Fig.S1. Study flow chart**