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# Post Covid Rhino-Orbito-Maxillary Mucormycosis- Proposed Diagnostic Protocol

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***Abstract-*** *Aims & objective- To evaluate rhino-orbito-maxillary (ROM) mucormycosis (MM) in post covid patients and grading them in 3 phases based on patient's complaints and clinical-radiographical findings. Methods- The study included 203 patients of ROM MM diagnosed clinically and radiographically. Demographic profile, vaccination status, covid history and other risk factors responsible for covid 19 infection and MM were analyzed in detail. Patients complaints, clinical and radiographical findings were studied in detail and graded in 3 phases. Results- Statistical analysis showed complaints and clinical findings related to oral cavity has significant role to categorized them into three phases. Radiographic findings related to oral cavity and all paranasal sinuses has valuable role for grading of ROM MM. Conclusion- Grading of ROM MM through clinical and radiographic findings helps in early detection & prevention of ROM MM.*
***Keyword-*** *ROM, MM, Post COVID, clinical & radiographical*

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## I. Introduction

Coronavirus disease 2019 (COVID-19) caused by SARS coronavirus continues to be significant problem worldwide and has been associated with wide range of opportunistic bacterial and fungal infections. Opportunistic infection is defined as infection caused by non-pathogenic microorganisms which become pathogenic when immune system is impaired by an unrelated disease. [1] Mainly aspergillosis, Candidiasis and mucormycosis(MM) have been reported as main fungal pathogens for co-infection. [2,3] MM also known as Zygomycosis and phycomycosis & used to refer to any fungal infections of order mucorales, which belongs to class Zygomycetes commonly found in soil and among decaying vegetation. [4] Paltauf in 1885 was first to describe MM and later term coined by Baker in 1957. [5,6] Most frequently reported pathogens in MM are Rhizopus, Mucor and Lichtheimia species. These microbes may be cultured from oral cavity, nasal passage, throat and stools of healthy patients. [6,7] The disease may manifest in six different ways depending on route of entry & type of pathogen: rhino cerebral, pulmonary, cutaneous, gastrointestinal, central nervous system, and disseminated form. [4,8]

Rhino-orbital-cerebral(ROC) is most common form of infections, predominately occurring in patients with uncontrolled diabetes mellitus(DM) & use of corticosteroids.[8,9] This variant usually results from inhalation of spores through nose and spore begins to germinate in nasal mucosa or sinus mucosa and spreads inferiorly to invade palate and maxilla, extends posteriorly and laterally to paranasal sinuses and orbit, spreading via angular, lachrymal, ethmoid vessels and nasolacrimal duct as well as by direct extension and cranially to invade cavernous sinus and brain. [4,8,10,11]. Pulmonary MM often occurs in neutropenic patients with cancer undergoing chemotherapy, can spread into other organs. Cutaneous and soft tissue MM are most common forms in immunocompetent patients, primarily after skin disruption due to trauma, surgery or burns. Primary gastrointestinal disease is a rare manifestation of MM that can present with symptoms similar to other gastrointestinal disease and commonly manifests in neonates, malnourished children and individuals with hematological malignancies. MM in one organ can spread hematogenously to other organs & most common in lungs. [12,13]

In normal functioning immune cells, spores and hyphae are readily taken by mononuclear and polymorphonuclear phagocytes. Low phagocyte counts or impaired phagocyte function due to any risk factors leads to invasive MM. [14] Risk factors for ROC MM include uncontrolled diabetes, systemic corticosteroid use, neutropenia, hematologic malignancies, stem cell transplant, and immunocompromised individuals. [15,16] Typical clinical presentations include extraoral painful mid facial swelling, nasal discharge & stuffiness, severe headache and eye complaints like periorbital swelling, discharge from eye and changed vision. Intraorally sudden mobility of maxillary teeth and buccal/palatal swelling with or without pus draining sinuses, erosion, ulceration or perforation with or without slough formation may be present. [17] Post covid MM has same features with more aggressive, severe and widespread involvement. [18]

Imaging modalities used to diagnose invasive MM are OPG, PNS, CT PNS, CBCT and MRI. Radiographic findings of MM were first described by green et al, in 3 typical signs- nodular thickening of sinus lining, absence of fluid level and spotty destruction of bony walls of sinus. [5,19] Other investigations used to diagnose MM through nasal cavity and oral cavity are nasal endoscopy and crust sampling, KOH, GMS or PAS staining, fungal culture, histopathology and frozen section to see the presence of fungal element, type of fungi and extension of disease. [12] Due to poor drug penetration in devitalized tissue mandates the need of aggressive surgical debridement of all necrotic tissue along with intravenous antifungal agents and control of precipitating cause. [18,20] There is high mortality (25-80%) even after aggressive approach. [5,6]

The study is aimed to evaluate rhino-orbito-maxillary (ROM) MM in post covid patients regarding demographic data, complaints, clinical & radiographic findings & underlying predisposing factors. An attempt has been made to grade ROM MM in 3 phases based on patient's complaint, clinical findings & radiographic involvement.

## II. Material And Method

The study was conducted on 203 cases of ROM MM attended dental OPD in institution from December 2020 to May 2021. The study protocol was approved by the IEC. A written informed consent was obtained from each subject.

Patients included in study had chief complaint related to oral cavity, mostly maxilla and maxillary teeth along with swelling of mid-face region. Other complaints were associated with nose, maxillary sinus, orbit & in few cases related to neurogenic complaints. All subjects whether suspected or proven for ROM were enrolled in the study. Suspected cases were confirmed histopathologically for MM. Once enrolled in the study, demographic details, medical history regarding covid, DM, hypertension, long standing respiratory disease, heart disease, kidney related disease, malignancies or haematological disorders were recorded then covid history was evaluated in detail for severity, type of isolation, medication, as well as vaccination. Questions related to medications, especially corticosteroids, antiviral, antibiotics, as well as medications related to systemic disease were asked in detail and recorded. If hospitalized, patients were asked about, ICU admission, oxygen therapy and ventilation. History of multiple hospitalization were also noted. General condition of patients attending dental OPD was so weaken and compromised that almost all patients came by wheel chair.

Patients were asked about eye, nose, sinus and oral cavity complaints according to table 1. All complaints were recorded with duration and progress (ODP) and entered in tabulated form. A thorough extra oral and intraoral examination was carried out. Lymph nodes were also examined. Clinical findings were analysed in detail.

OPG & PNS were carried out in all cases. CT/ MRI/ CBCT findings were recorded & analysed in detail. Based on complaints and clinical-radiographic findings study patients were graded in three phases i.e., phase I (acute maxillary sinusitis), phase II (pre-necrotic) and phase III(necrotic) as shown in table 1(master table A & B) and in figure 1, 2 and 3.

**Statistical analysis**

Categorical variables were compared by Chi-square test. A two tailed P value of less than 0.05 is considered as statistically significant between the categorical variables. Statistical analysis was performed using SPSS software (IBM Corp 2013; Version 22.0; Armonk, NY). Statistical tables are prepared by using M.S office 2010 software.

## III. Result

In this study, out of 203 patients of ROM MM, 59.1% were reported in phase II, followed by phase III (26.1%) and phase I (14.8%). [p value= 0.011] Non-significant results were found in correlation with age & sex, type of isolation in covid, medications taken for covid treatment, risk factors and vaccination taken as shown in table 2, 4, 5, 6 & 8. Significant results were found in correlation with type of occupation and type of mask usage as shown in table 3 & 7. In present study distribution of clinical & radiographical findings according to side involvement shows highly significant results in nose & orbit region while maxillary and other sinus showed non-significant results. (Table 9) Clinical findings were more significant in relation to orbit and oral cavity while radiographical findings were more significant in relation to nose, maxillary sinus and other sinuses (master table A & B).

## IV. Discussion

The first outbreak of COVID-19 occurred in Wuhan, Hubei Province in Dec 2019 where several patients with viral pneumonia were found. On 30th January 2020, WHO declared an outbreak, a Public Health Emergency of International Concern and on Feb 2020, WHO officially named this outbreak as COVID-19 [2]

While whole world is battling against COVID-19, the issue of post COVID mucormycosis has emerged as significant problem and India is severely suffering, having life-threatening risk & high mortality. [21]

In present study maximum 48.8% patients were reported in age range of 46-60 in both genders. Youngest patient affected from ROM MM was 24-year-old male. Similar findings were reported in other studies. (4,19,22,23,24,25) No significant correlation is noted between age & sex which shows post covid ROM MM does not depend on age or gender of patients. In present study MM was equally reported in patients working outside as well as in patients staying at home that showed not only soil but poorly ventilated area, frequent travel and other factors such as covid severity (26), hospitalization and treatment given may play a significant role to cause MM.

The most important risk factor for ROM MM is COVID-19 itself as well as uncontrolled diabetes mellitus and was reported with maximum no. of patients in age group 46-60 years. ROM MM was more commonly reported in mild & moderate grades of covid as severe grade of covid patients had more complications related to eye & brain. (26) In uncontrolled diabetes mellitus & ketoacidosis, chronically elevated blood glucose levels & acidic pH will lead to defect in the motility and killing of bacteria and fungi by an impaired neutrophil function. It is believed that as the pH becomes acidic, the iron-protein complexes dissociate, which allows for the fungal cells to use the increased free iron. Recently, there have been reports of new-onset diabetes following infection with SARS-COV2 mainly due to weight gain following disordered diet and exercise during lockdown, mental stress, and unwarranted use of dexamethasone for mild to moderate cases of COVID. SARS coronavirus has a direct diabetogenic potential by entering target cells with angiotensin converting enzyme 2(ACE2) receptor on the pancreas, that is also present on the pancreatic beta-cell.

The covid patients reported in this study were mostly treated by antibiotics, steroids, antiviral & oxygen therapy and whether hospitalized or home quarantined. Use of steroids is proved as lifesaving medication to increase survival rate in COVID-19 patients but unfortunately it has considered as one of the major cause for immunosuppression & hence deep seated fungal infection. Hospital environment like overwhelmed hospitals and lack of mask hygiene, vents, oxygen system and humidifiers can be considered as causative factor for MM. Systemic disease like hypertension, heart disease and other immunocompromised state were also considered as one of important risk factors. Present study had one patient of hairy cell leukemia, even though pulmonary MM are common in hematological malignancy. As no significant results were found in covid grades, distribution of risk factors and type of isolation this shows not only single risk factor but together all cumulative factors are responsible for causing ROM MM and the most vulnerable age group is 46-60 years as maximum patients were reported in this group related to all risk factors. (3,7,11,25,27)

In present study mostly patients were using cloth mask this shows that N-95 mask is more helpful in restricting the COVID-19 infection and might also be in inhaling MM spores. Unhygienic masks or improper wash of masks may aid in contracting the spores of MM. During 2$^{nd}$ phase maximum (78.3%) patients were non-vaccinated, proving the role of vaccine in building antibodies. Vaccinated individuals are at lesser risk to develop covid and MM or if occurs it might have less severity as compared to non-vaccinated patients.

As significant results were found in grading of ROM MM, hence each and every patient should be graded according to phases of ROM MM (table 1) & according to chief complaints and findings. In phase I clinical examination revealed signs and symptoms of acute inflammation of sinus so named as acute sinusitis. Maximum cases reported with complaint related to maxillary sinus like heaviness/numbness, mid face swelling followed by oral complaint like sudden pain in maxillary teeth (premolars and molars). As when spores are inhaled they first lodge into nasal or paranasal sinuses and start to germinate affecting the mucosal lining giving first symptoms related to it. Mid face swelling may present, due to infiltration of infection into periantral fat planes and subcutaneous tissue while teeth pain due to their close proximity to floor of maxillary sinus. Other complaints like nasal stuffiness & nasal discharge was present due to mucosal thickening in nasal meatus, headache due to pressure changes in sinuses or closure of infundibulum and frontonasal opening leading to a vacuum or negative pressure and eye complaints like redness and conjunctivitis due to inflammation of periorbital soft tissue. Radiographic imaging showed mucosal thickening at floor of maxillary sinus & other sinuses, PDL widening and altered alveolar bone pattern due to early spread of infection.

In phase II i.e pre necrotic phase because there was not complete devitalization of tissue and bone & was between inflammation and necrosis. Maximum complaints were recorded related to oral cavity like acute pain and sudden mobility of teeth followed by palatal swelling and buccal/gingival swelling with pus discharging sinus than others complaints. Sudden mobility of teeth may be because of hyperglycemia causing damage to connective tissue, with reduced synthesis of fibroblast, resulting in loss of PDL fibers and alveolar bone. Palatal swelling occurs when floor of maxillary sinus or nasal cavity affected as infection spreads through marrow spaces of palatal bone. All other findings related to eye, nose and paranasal sinus were increased in severity due to further involvement and necrosis like discoloration of facial skin, due to spread of infection causing necrosis into subcutaneous tissue and periorbital swelling, change in vision due to erosion and destruction of lamina papyracea. Radiographic imaging showed erosion and thinning of sinus walls, orbital margin, palatal and alveolar bone and also generalized PDL widening, multiple periapical radiolucency

involving maxillary teeth was very characteristics radiologic finding as fungal hyphae grow occupying the whole sinus and eroding the walls of it. In present study, a 44-year-old male patient showed phase II involvement through clinical findings, but radiographic features showed moth eaten appearance of alveolar ridge and palate eliciting the chronic nature of lesion.

In phase III i.e., necrotic phase dead or devitalized bone was clinically visible and radiographically there was complete loss/destruction of bony walls. It showed severe and aggressive involvement of orbit, nose, maxillary sinus and other PNS and oral cavity, as mucor hyphae further progresses to involve remaining areas of maxillofacial region. Complaints like self-exfoliation of maxillary teeth and involvement of whole maxilla was present due to complete necrosis leads to destruction of periodontium and alveolar support leads to exfoliation of teeth. Radiographically complete erosion with destruction of all walls of maxillary sinus along with other PNS and nasal turbinate's were noted. Palatal bone destruction was very characteristic finding in necrotic phase. Palatal bone involves earlier than maxillary alveolus because of direct extension to palate from sinus and nose and also rich blood supply to maxilla leads to late necrosis from angioinvasion and subsequent thrombosis. Present study reported one unique case of ROM MM having complete exposed palatal bone with empty sockets and necrosis of all soft tissue. The aggressive behavior of MM was unable to establish as patient was only 28-year-old male without any systemic co-morbidities with mild grade of COVID-19 infection.

Clinical findings were more significant in relation to orbit and oral cavity while radiographical findings were more significant in relation to nose, maxillary sinus and other sinuses this shows that clinical examination should always be followed by radiological examination for early detection of ROM MM and also when grade increases severity increases in extraoral clinical findings, but individual involvement of sinus, nose and eye depends on path of spread of infection as disease progresses. On comparing unilateral & bilateral involvement clinically & radiographically in all phases, radiographically more patients had ROM MM as compared to clinical involvement in nose, orbit, maxillary sinus & other sinuses. Also radiographically bilateral involvement was more commonly found in above mentioned sites although clinically there was unilateral involvement. Thus, radiographic diagnosis is must to see exact phase & involvement in ROM MM.

Clinical findings of ROM MM other than above mentioned were reported like ulcerations (2.4%) and superficial candidiasis (24.5%) over labial and buccal mucosa other than palate in phase III due to severe immunosuppression & being most common opportunistic fungi to grow as white plaque scrapable lesion. (Figure 4). This should be considered as new findings because with treatment of MM the ulcer size was decreased. Neurologic complication such as facial palsy was reported only in phase II (2.5%) and in phase III (9.4%). Facial palsy with fungal rhinosinusitis due to septic cavernous sinus thrombosis and diabetic polyneuropathy should be suspected. Similar findings reported in other studies. (4) Covid infection showed suppress immune system like decrease lymphocyte counts as COVID-19 acts on lymphocytes and increase neutrophil count due to damage induce innate inflammation in body. (28)

Diagnostic laboratory strategies employed- microscopic examination of fresh clinical specimens or histopathological preparations; culture of the etiologic agent from clinical material; serology and skin testing; radiographic techniques; polymerase chain reaction methods to detect specific fungal DNA in clinical specimens. KOH investigations had done for fungal elements in suspected cases before admission to institution. Then biopsy tissue was taken from nasal cavity if only involvement of sinus and no necrosis or mobility of teeth present & was performed from oral cavity when necrosis of palatal and alveolar bone or mobility of teeth present.

Treatment of phases I, II and III depends of extension of lesion, involvement of vital structures and remaining healthy bone. Reversal of underlying immunocompromised state is one of the most important factors had been done by strict glycemic control and stabilizing the metabolic state to improves the survival rates. In all phases, urgent drainage, aeration and aggressive debridement of involved sinus until clear bleeding margins were exposed. IV Liposomal Amphotericin B for atleast 21 days and patients had kidney related disease had given with tab or syrup form posaconazole. In phase II and III surgical approach had taken under general anesthesia for removal of necrotic tissue and bone (like radical maxillectomy) along with mobile teeth.

## V. Conclusion

A high suspicion must be considered in post COVID patients with age group of 46-60 years and having uncontrolled diabetes and history of steroid intake during COVID-19 infection. Such patients should be kept under periodical examination regarding ROM MM and diabetes must be controlled. Early diagnosis of ROM MM is utmost important in phase I for better prognosis as slight delay in diagnosis can be proven to be fatal disease. OMR specialist plays most significant role in diagnosing phase I stage as most of the patients are unaware of symptoms. One should get aware of early signs as oral complaints are misdiagnosed more often. SOP prepared from the study as shown below.

**Declaration of conflicts of interest-**

The authors declare that there are no conflicts of interest

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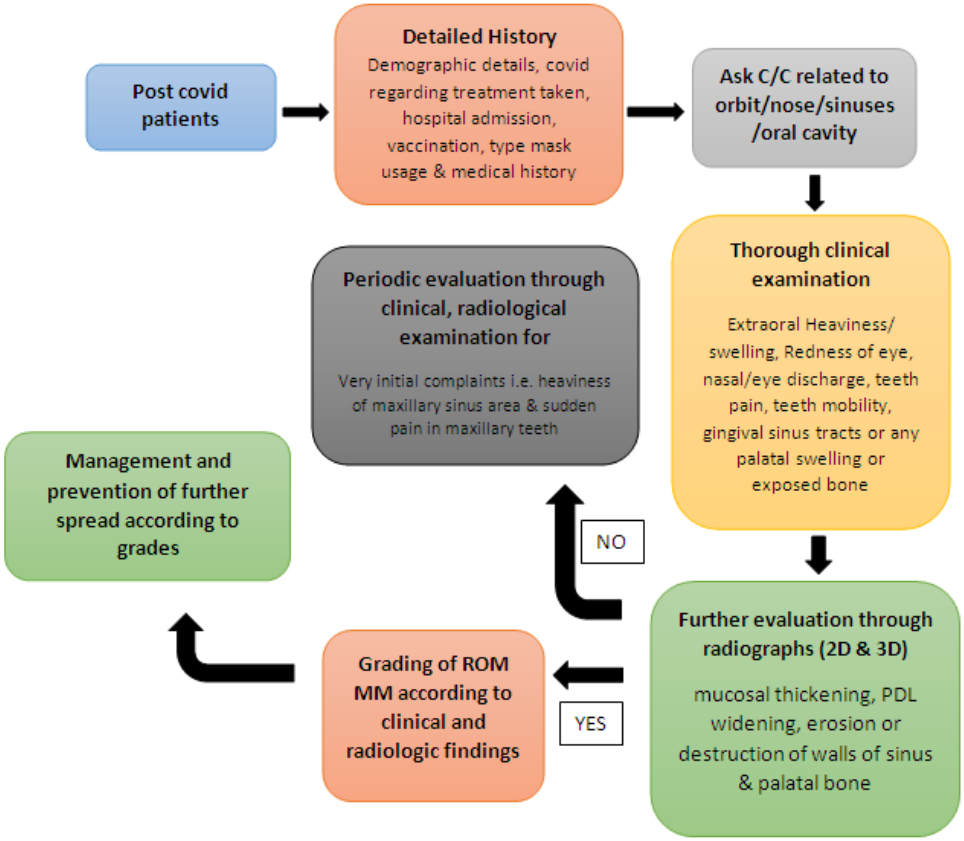
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**SOP for early detection & prevention of ROM MM**

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**Legends of figures-**

**Figure 1-** showing normal extraoral & intraoral appearance. Patient was having only pain in upper teeth. OPG shows PDL widening in maxillary anterior teeth. PNS & MRI showing mucosal thickening involving left & right (L>R) maxillary sinus & nasal cavity with partial haziness on left maxillary sinus without any erosion. (Phase Ⅰ)

**Figure 2-** showing periorbital swelling & facial swelling on right side of face. Intraorally well defined multiple swelling on hard palate with pus discharge & multiple gingival swelling with sinus tract formation. PNS & CT scan showing involvement of right & left maxillary sinus (L>R), bilateral ethmoidal sinus with erosion of walls & erosion seen on the midpalatine region. (Phase Ⅱ)

**Figure 3**- showing black discoloration of facial skin on left midface & crusting on right side of nose. Intraorally exposed whole maxilla & exposed left palatal bone is seen. Radiographically PNS & CT showing destruction of palatal bone, medial wall & floor of bilateral maxillary sinus. (Phase Ⅲ)

**Figure 4**- showing super added candidiasis on dorsal surface of tongue & right buccal mucosa (a, b) & ulceration on lower lip & hard palate ( c, d) in ROM MM patients.

**Figure 1**

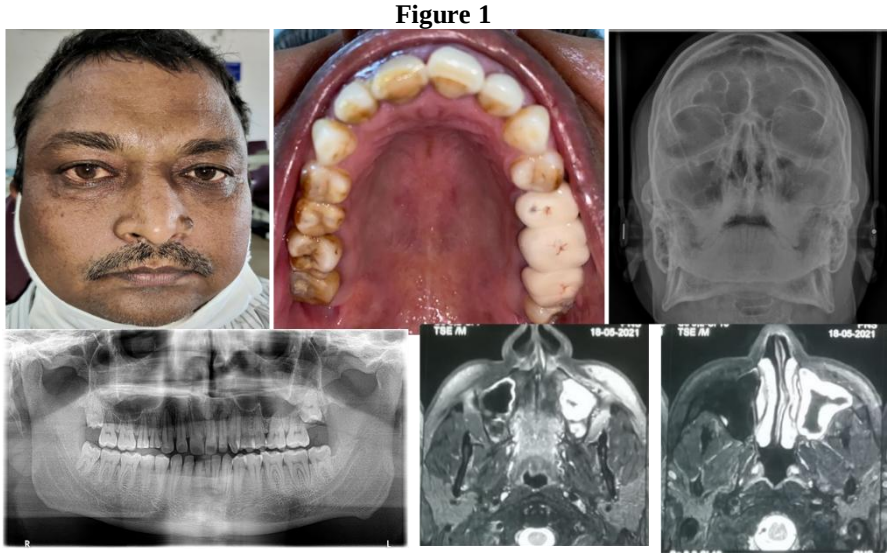


**Figure 2**

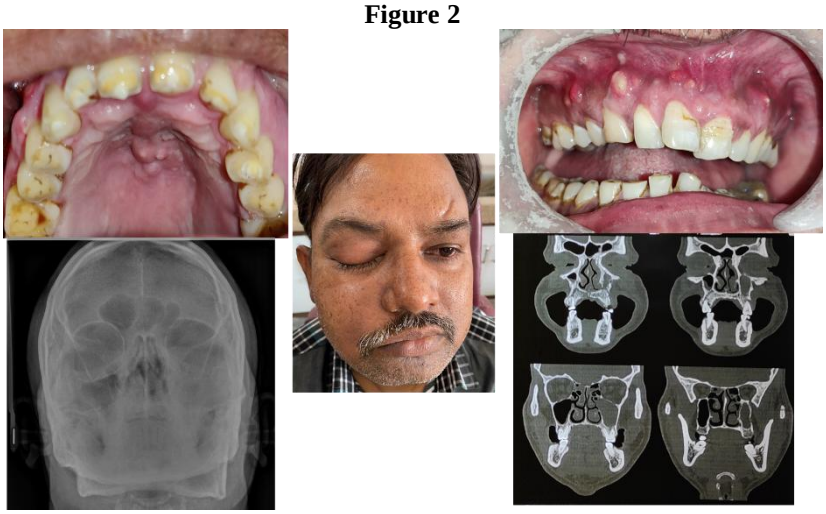
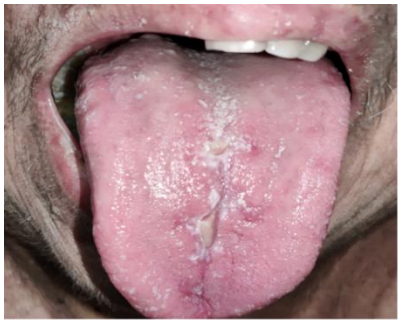


**Figure 3**

**Figure 4**

a



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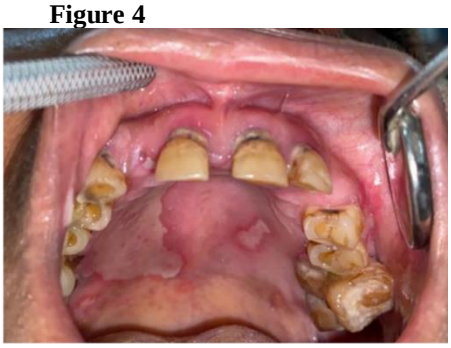

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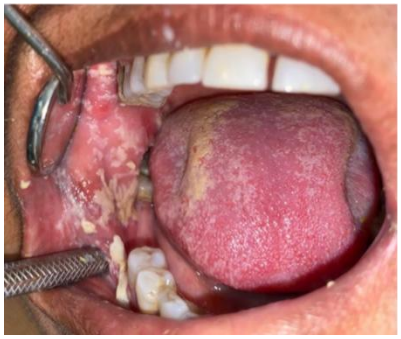
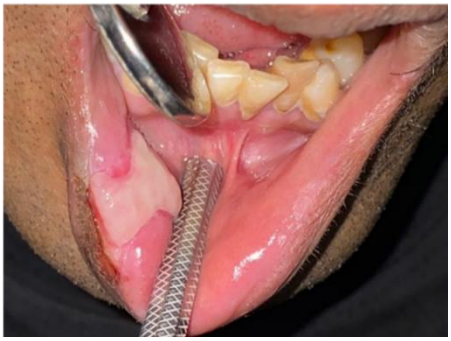
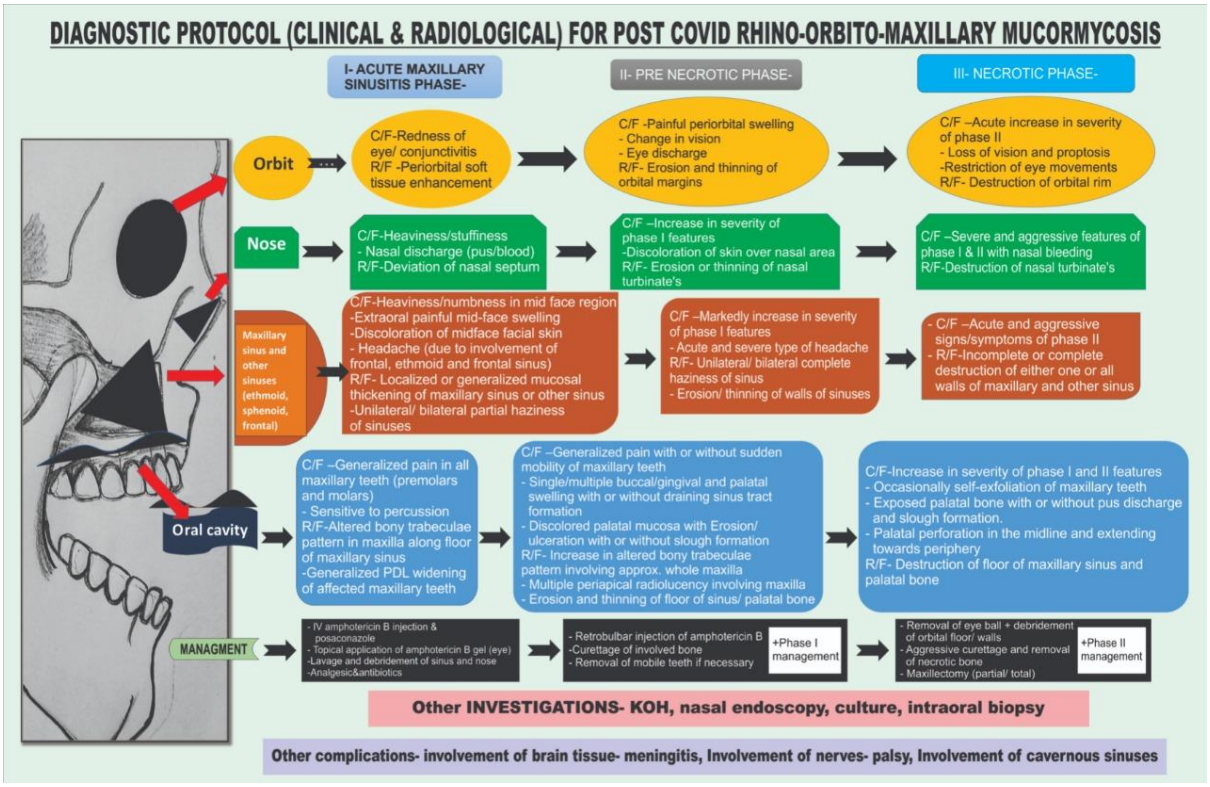




d

**Table-1**




| Table 2: Distribution of study patients according to age & sex (n=203) | | | |
|---|---|---|---|
| **Age in Years** | **Male (n=134) (66.1%)** | **Females (n=69) (33.9%)** | **Total (n=203)** |
| Below 20 years | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| 21-30 years | 4 (3.0) | 1 (1.4) | 5 (2.5) |
| 31-45 years | 38 (28.4) | 15 (21.7) | 53 (26.1) |
| 46-60 years | 58 (43.3) | 41 (59.4) | 99 (48.8) |
| Above 60 years | 34 (25.4) | 12 (17.4) | 46 (22.7) |
| **Chi-square value = 4.913 P value =0.178 NS** | | | |

| Table 3: Distribution of study patients according to occupation (n=203) | | | |
|---|---|---|---|
| **Occupation** | **Male (n=134) (66.1%)** | **Females (n=69) (33.9%)** | **Total (n=203)** |
| staying at home | 41 (30.6) | 57 (82.6) | 98 (48.3) |
| Working outside | 54 (40.3) | 2 (2.9) | 56 (27.6) |
| Farmer | 39 (29.1) | 10 (14.5) | 49 (24.1) |
| **Chi-square value = 52.646 P value =0.000 HS** | | | |

| Table 4 A: Distribution of study patients according to type of isolation in covid (n=203) | | | |
|---|---|---|---|
| **Age in Years** | **Home isolation (n=82) (40.3%)** | **Hospitalization (n=115) (56.6%)** | **ICU (n=06) (2.9%)** |
| 21-30 years | 3 (3.7) | 2 (1.7) | 0 (0.0) |
| 31-45 years | 21 (25.6) | 32 (27.8) | 0 (0.0) |

| | | | |
|---|---|---|---|
| 46-60 years | 45 (54.9) | 52 (45.2) | 2 (33.3) |
| Above 60 years | 13 (15.9) | 29 (25.2) | 4 (66.7) |
| **Chi-square value = 12.339 P value = 0.055 NS** | | | |

**Table 4 B: Distribution of study patients according to medications taken for covid treatment (n=203)**

| Age in Years | Corticosteroids (n=124) (61.0%) | Antivirals (n=124) (61.0%) | Antibiotics (n=140) (68.9%) | Oxygen therapy (n=64) (31.5%) |
|---|---|---|---|---|
| 21-30 years | 4 (3.2) | 3 (2.4) | 4 (2.9) | 1 (1.6) |
| 31-45 years | 33 (26.6) | 32 (25.8) | 35 (25.0) | 15 (23.4) |
| 46-60 years | 55 (44.4) | 63 (50.8) | 72 (51.4) | 31 (48.4) |
| Above 60 years | 32 (25.8) | 26 (21.0) | 29 (20.7) | 17 (26.6) |
| **Chi-square value = 2.792 P value = 0.972 NS** | | | | |

**Table 4 C: Distribution risk factors in study patients (n=203)**

| Age in Years | Diabetes mellitus (n=143) (70.4%) | | Hypertension (n=51) (25.1%) | Heart Disease (n=26) (12.8%) | Haematological disease (n=01) (0.4%) | Renal disease (n=01) (0.4%) | Liver disease (n=01) (0.4%) | Thyroid (n=01) (0.4%) |
|---|---|---|---|---|---|---|---|---|
| | Pre existing (n= 105) (73.4%) | Newly diagnosed DM (n= 38) (26.6%) | | | | | | |
| 21-30 years | 2 (1.9) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| 31-45 years | 21 (20.0) | 13 (34.2) | 12 (23.5) | 2 (7.7) | 1 (100.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| 46-60 years | 59 (56.2) | 17 (44.7) | 24 (47.1) | 11 (42.3) | 0 (0.0) | 1 (100.0) | 1 (100.0) | 1 (100.0) |
| Above 60 years | 23 (21.9) | 8 (21.1) | 15 (29.4) | 13 (50) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| **Chi-square value = 13.828 P value = 0.877 NS** | | | | | | | | |

**Table 5 A: Distribution of study patients according type of mask usage (n=203)**

| Type of mask | Total (n=203) | % |
|---|---|---|
| N 95 | 11 | 5.4 |
| Cloth | 183 | 90.1 |
| Disposable | 9 | 4.4 |
| **Chi-square value = 442.345 P value = 0.000 HS** | | |

**Table 5 B: Distribution of study patients according to vaccination (n=203)**

| Age in Years | 1st Dose (n=40) (19.7%) | 2nd Dose (n=4) (1.9%) | Non-vaccinated (n=159) (78.3%) |
|---|---|---|---|
| 21-30 years | 0 (0.0) | 0 (0.0) | 5 (3.1) |
| 31-45 years | 5 (12.5) | 1 (25.0) | 46 (28.9) |
| 46-60 years | 19 (47.5) | 2 (50.0) | 79 (49.7) |
| Above 60 years | 16 (40.0) | 1 (25.0) | 29 (18.2) |

**Chi-square value = 11.473 P value =0.075 NS**

| **Master table A: Clinical findings of ROM MM (n=203)** | | | | **Chi-square value** | **P value** |
|---|---|---|---|---|---|
| | **Phase Ⅰ (n=30) (14.7%)** | **Phase Ⅱ (n=120) (59.1%)** | **Phase Ⅲ (n=53) (26.1%)** | | |
| **Orbit** | | | | | |
| - Redness/Conjunctivitis | 07(23.3%) | 20(16.7%) | 02(3.8%) | 41.042 | **0.000 HS** |
| - Painful periorbital Swelling | 02(6.7%) | 21(17.5%) | 29(54.7%) | | |
| - Proptosis | 0 (0.0%) | 10(8.3%) | 16(30.2%) | | |
| - Change in vision | 03(10%) | 15(12.5%) | 16(30.2%) | | |
| - Loss of Vision | 0 (0.0%) | 05(4.2%) | 07(13.2%) | | |
| - Eye Discharge | 02(6.7%) | 16(13.3%) | 22(41.5%) | | |
| - Restrictions in eye movements | 0 (0.0%) | 10(8.3%) | 19(35.8%) | | |
| **Nose** | | | | | |
| - Heaviness/stuffiness | 05(16.7%) | 38(31.2%) | 25(47.2%) | 1.551 | **0.956 NS** |
| - Nasal Discharge | 05(16.7%) | 19(15.8%) | 16(30.2%) | | |
| - Discoloration of skin over nasal area | 0 (0.0%) | 02(1.7%) | 01(1.9%) | | |
| - Nasal bleeding | 01(3.3%) | 06(5%) | 04(7.5%) | | |
| **Maxillary Sinus& other sinuses(Ethmoidal, Sphenoidal & Frontal)** | | | | | |
| - Heaviness/Numbness | 23(76.7%) | 79(65.8%) | 38(71.7%) | 6.682 | **0.351 NS** |
| - Extraoral painful midfacial swelling | 18(60%) | 94(78.3%) | 44(83%) | | |
| - Discoloration of skin in midfacial area | 03(10%) | 02(1.7%) | 04(7.5%) | | |
| - Severe Headache | 08(26.7%) | 32(26.7%) | 17(32.1%) | | |
| **Oral Cavity** | | | | | |
| - Pain in all maxillary teeth | 19(63.3%) | 62(51.7%) | 25(47.2%) | 379.359 | **0.000 HS** |
| - Sensitivity on percussion | 23(76.7%) | 70(58.3%) | 28(52.8%) | | |
| - Sudden mobility of maxillary teeth | 0 (0.0%) | 82(68.3%) | 28(52.8%) | | |
| - Buccal/Gingival Swelling | 0 (0.0%) | 68(56.7%) | 14(26.4%) | | |
| - Palatal swelling | 0 (0.0%) | 86(71.7%) | 16(30.2%) | | |
| - Pus discharging sinuses | 0 (0.0%) | 35(29.2%) | 08(15.1%) | | |
| - Discolouration of Palate | 0 (0.0%) | 42(35%) | 31(58.5%) | | |
| - Erosion/Ulceration/Necrotic slough | 0 (0.0%) | 53(44.2%) | 50(94.3%) | | |
| - Exposed bone (Buccal/Palatal) | 0 (0.0%) | 0 (0.0%) | 53(100%) | | |
| o Only in midline | 0 (0.0%) | 0 (0.0%) | 51(96.2%) | | |
| o Whole maxilla | 0 (0.0%) | 0 (0.0%) | 02(3.8%) | | |
| - Self exfoliation of maxillary teeth | 0 (0.0%) | 0 (0.0%) | 07(13.2%) | | |
| - **Others** | | | | | |
| o Palsy | 0 (0.0%) | 03(2.5%) | 05(9.4%) | 0.414 | **0.813** |

| | | | | | |
|---|---|---|---|---|---|
| o Oral ulcerations | 0 (0.0%) | 02(1.7%) | 03(5.7%) | | **NS** |
| o Candidiasis | 0 (0.0%) | 09(7.5%) | 09(17%) | | |

| **Master table B: Radiographical Findings of ROM MM (n=203)** | | | | **Chi-square value** | **P value** |
|---|---|---|---|---|---|
| | **Phase Ⅰ (n=30) (14.7%)** | **Phase Ⅱ (n=120) (59.1%)** | **Phase Ⅲ (n=53) (26.1%)** | | |
| **Orbit** | | | | | |
| - Periorbital Soft Tissue Enhancement | 03(10%) | 24(20%) | 31(58.5%) | 5.106 | **0.277 NS** |
| - Erosion And Thinning Of Orbital Margins | 0 (0.0%) | 05(4.2%) | 10(18.9%) | | |
| - Enhancing Soft Tissue Mass At Orbital Apex And Cavernous Sinus | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | | |
| - Destruction Of Orbital Rim | 0 (0.0%) | 0 (0.0%) | 05(9.4%) | | |
| **Nose** | | | | | |
| - Deviation of nasal septum | 12(40%) | 66(55%) | 26(49.1%) | 36.484 | **0.000 HS** |
| - Erosion or thinning of nasal turbinate's | 0 (0.0%) | 40(33.3%) | 30(56.6%) | | |
| - Destruction of nasal turbinates' | 0 (0.0%) | 0 (0.0%) | 13(24.5%) | | |
| **Maxillary Sinus& other sinuses(Ethmoidal, Sphenoidal & Frontal)** | | | | | |
| **Mucosal Thickening** | | | | | |
| **Maxillary sinus** | 29(96.7%) | 120(100%) | 53(100%) | | |
| - Localized | 07(23.3%) | 100(83.3%) | 53(100%) | 88.555 | **0.000 HS** |
| - Generalised | 22(73.3%) | 20(16.7%) | 0 (0.0%) | | |
| **Ethmoidal sinus** | 23(76.7%) | 107(89.2%) | 51(96.2%) | | |
| - Localized | 07(23.3%) | 67(55.8%) | 51(96.2%) | 39.469 | **0.000 HS** |
| - Generalised | 15(50%) | 40(33.3%) | 0 (0.0%) | | |
| **Sphenoidal Sinus** | 10(33.3%) | 56(46.7%) | 31(58.5%) | | |
| - Localized | 10(33.3%) | 55(45.8%) | 20(37.7%) | 22.476 | **0.000 HS** |
| - Generalised | 0 (0.0%) | 01(0.8%) | 11(20.8%) | | |
| **Frontal sinus** | 10(33.3%) | 48(40%) | 33(62.3%) | | |
| - Localized | 10(33.3%) | 48(40%) | 17(32.1%) | 34.120 | **0.000 HS** |
| - Generalised | 0 (0.0%) | 0 (0.0%) | 16(67.9%) | | |
| **Haziness Of Sinus** | | | | | |
| **Maxillary sinus** | 25(83.3%) | 120(100%) | 53(100%) | | |
| - Partial | 25(83.3%) | 20(16.7%) | 02(3.8%) | 95.302 | **0.000 HS** |
| - Complete | 0 (0.0%) | 100(83.3%) | 51(96.2%) | | |
| **Ethmoidal sinus** | 15(50%) | 102(85%) | 51(96.2%) | | |
| - Partial | 15(50%) | 35(29.2%) | 0 (0.0%) | 58.021 | **0.000 HS** |
| - Complete | 0 (0.0%) | 67(55.8%) | 51(96.2%) | | |
| **Sphenoidal Sinus** | 0 (0.0%) | 10(8.3%) | 15(28.3%) | | |
| - Partial | 01(3.3%) | 10(8.3%) | 14(26.4%) | 0.763 | **0.683 NS** |
| - Complete | 0 (0.0%) | 0 (0.0%) | 01(1.9%) | | |
| **Frontal sinus** | 02(6.7%) | 25(20.9%) | 18(33.9%) | | |
| - Partial | 02(6.7%) | 23(19.2%) | 04(7.5%) | 23.392 | **0.000 HS** |
| - Complete | 0 (0.0%) | 02(1.7%) | 14(26.4%) | | |
| **Erosion/ Thinning Of Walls Of Sinuses** | | | | | |
| Maxillary sinus | 0 (0.0%) | 120(100%) | 0 (0.0%) | -- | -- |
| Ethmoidal sinus | 0 (0.0%) | 107(89.2%) | 0 (0.0%) | | |
| Sphenoidal Sinus | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | | |
| Frontal sinus | 0 (0.0%) | 10(8.3%) | 0 (0.0%) | | |
| **Destruction Of Either One Or All Walls** | | | | | |
| Maxillary sinus | 0 (0.0%) | 0 (0.0%) | 53(100%) | -- | -- |
| Ethmoidal sinus | 0 (0.0%) | 0 (0.0%) | 51(96.2%) | | |
| Sphenoidal Sinus | 0 (0.0%) | 0 (0.0%) | 05(9.4%) | | |
| Frontal sinus | 0 (0.0%) | 0 (0.0%) | 20(37.7%) | | |
| **Oral Cavity** | | | | | |
| - PDL widening | 02(6.7%) | 17(14.2%) | 01(1.9%) | 177.831 | **0.000 HS** |
| - Periapical radiolucency | 01(3.3%) | 09(7.5%) | 02(3.8%) | | |
| - Altered alveolar bone pattern | 03(10%) | 58(48.3%) | 42(79.2%) | | |
| - Erosion And Thinning Of Floor Of Sinus/ Palatal Bone | 0 (0.0%) | 100(83.3%) | 0 (0.0%) | | |
| - Destruction Of Floor Of Maxillary Sinus And Palatal Bone | 0 (0.0%) | 0 (0.0%) | 53(100%) | | |

**[NS= not significant, S= significant, HS= highly significant]**

**Table 6: Distribution of clinical & radiographical findings according to side involvement (n=203)**

| | **Phase Ⅰ (n=30) (14.7%)** | | **Phase Ⅱ (n=120) (59.1%)** | | **Phase Ⅲ (n=53) (26.1%)** | | **P Values** | |
|---|---|---|---|---|---|---|---|---|
| | **Clinical** | **Radiographical** | **Clinical** | **Radiographical** | **Clinical** | **Radiographical** | **Clinical** | **Radiographical** |
| **Nose** | Y=11 | Y=12 | Y=54 | Y=80 | Y=39 | Y=45 | **0.004 (H.S)** | **0.000 (H.S)** |
| Unilateral | 10 (90.9) | 12 (100%) | 50 (92.6) | 73 (91.2%) | 35 (89.7) | 10 (22.2%) | | |
| Bilateral | 1 (9.1) | 0 | 4 (7.4) | 07 (8.7%) | 4 (10.3) | 35 (77.7%) | | |
| **Orbit** | Y=09 | Y=03 | Y=34 | Y=24 | Y=35 | Y=31 | **0.000 (H.S)** | **0.000 (H.S)** |
| Unilateral | 9 (100.0) | 3 (100.0) | 34 (100.0) | 24 (100.0) | 33 (94.3) | 29 (93.5) | | |
| Bilateral | - | - | - | - | 2(5.7) | 2 (6.5) | | |
| **Maxillary Sinus** | Y=28 | Y=29 | Y=109 | Y=120 | Y=53 | Y=53 | **0.193 (N.S)** | **0.204 (N.S)** |
| Unilateral | 25 (89.3) | 8 (27.6) | 98 (89.9) | 33 (27.5) | 45 (84.9) | 16 (30.2) | | |
| Bilateral | 3 (10.7) | 21 (72.4) | 11 (10.1) | 87 (72.5) | 8 (15.1) | 37 (69.8) | | |
| **Ethmoidal Sinus** | - | Y=23 | - | Y=107 | - | Y=51 | - | **0.090 (N.S)** |
| Unilateral | - | 11 (47.8) | - | 44 (41.1) | - | 20 (39.2) | | |
| Bilateral | - | 12 (52.2) | - | 63 (58.9) | - | 31 (60.8) | | |
| **Sphenoidal Sinus** | - | Y=10 | - | Y=56 | - | Y=31 | - | **0.131 (N.S)** |
| Unilateral | - | 5 (50.0) | - | 24 (42.9) | - | 18 (58.1) | | |
| Bilateral | - | 5 (50.0) | - | 32 (57.1) | - | 13 (41.9) | | |
| **Frontal sinus** | - | Y=10 | - | Y=48 | - | Y=33 | - | **0.020 (S)** |
| Unilateral | - | 9 (90.0) | - | 29 (60.4) | - | 21 (63.6) | | |
| Bilateral | - | 1 (10.0) | - | 19 (39.6) | - | 12 (36.4) | | |

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