IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 1 Ser.8 (January. 2022), PP 23-31
www.iosrjournals.org

"A clinico-pathological study of fungal rhinosinusitis, in post-covid patients, at a tertiary care hospital, in coastal districts of Andhra Pradesh, India."

[1]Dr.P.RamanaKumari, [2]Dr.K.Madhavi, [3]Dr.M.Rajani, [4]Dr.K.ChandraSekhar, [5]Dr.B.V.RamaReddy, [6]Dr.G.Sailabala, [7]Dr.Jahnavi Manisha, [8]Dr.BhanuSree, [9]Dr.Rinsha Surendranath.

[1]Associate Professor
[2]Assistant Professor
[3]Associate Professor
[4]Assistant Professor
[5]Professor & HOD
[6]Professor
[7]Post graduate
[8]Post graduate
[9]Post graduate
Department of Pathology.
Government Siddhartha Medical College, Gunadala, Vijayawada,
Andhra Pradesh, India- 520008

Abstract:
Aims & Objectives: *To study the clinic-pathological spectrum of fungal rhino-sinusitis, in post-covid patients and categorize the histopathological findings.*
Materials and Methods: *A total of 153 consecutive cases, during a period of 2 months, with a provisional diagnosis of post-covid fungal rhinosinusitis are studied. Clinical features, associated co-morbid conditions and radiological findings are recorded. The tissue samples are obtained from FESS debridements, maxillectomies and orbital exenterations. The samples are rapidly processed, manually and the tissue sections stained with H & E and PAS are studied under microscope.*
Results: *The study included … males and … females with age ranging from ..-… years. On histopathological examination, fungal morphology with broad, asptate hyphae with near right angle branching were identified as Mucorales species. Co-infection with Aspergillus species was observed in 4 cases. The associated findings included dense suppurative inflammation, foreign body granulomas, necrosis, infarction, angioinvasion, ulcerated sinus epithelium, invasion into adjacent soft tissue, bone and congested dilated blood vessels were noted.*
In conclusion*, fungal rhinosinusitis in post-covid patients is due to Mucorales species, in the background of uncontrolled diabetes and steroid therapy. Early diagnosis and treatment is essential to minimize the morbidity and mortality. Yield of organisms in culture is sub-optimal. Hence, histopathological examination plays a critical role in establishing the diagnosis and provides evidence of tissue invasion.*
Key words: *Fungal rhino-sinusitis, Clinico-pathological spectrum, Post COVID -19*

Date of Submission: 01-01-2022 Date of Acceptance: 12-01-2022

I. Introduction:

The disease pattern of global pandemic COVID-19 caused by the novel corona virus /SARS-Cov 2 ranges from mild to life threatening pneumonia, with associated bacteria and fungal co-infections [(1)].

Due to associated co-morbidities and immunocompromised conditions , these patients are prone to develop severe opportunistic infection.

Mucormycosis is emerging as an aggressive, angioinvasive infection in post-covid patients.

It is a fulminant form of Zygomycosis and caused by Mucorales species of phylum Zygomycota [(2)].

Mucormycosis generally develops secondary to immunosuppression or debilitating diseases. The fatality rate of mucormycosis is 46% globally [(3)].

The fatality can be as high as 50-80% in intracranial and orbital involvement [(4)] .

Mucormycosis is difficult to diagnose, which affects the outcome and leads to poor prognosis.
Early diagnosis and treatment are essential.
However, clinical features and imaging studies are non-specific.
Definite diagnosis requires demonstration of characteristic hyphae in tissue or recovery of the organism in the culture. Yield of organisms in culture is sub-optimal [(5)] .
Hence, Histopathological examination plays a critical role in establishing the diagnosis and provides evidence of tissue invasion.
The aim of the present study is to analyze the clinico-pathological spectrum of fungal rhino-sinusitis , in post covid patients and to assess the role of histopathology in the early diagnosis and to categorize the histopathological findings, basing on the type of inflammation, invasion into soft tissues, type of spread and presence of infarction/necrosis.

II. Materials and Methods:

The present study is done in the Department of Pathology, attached to a tertiary care hospital, in coastal districts of Andhra Pradesh, India, for a period of 2 months (1^{st} May to 30^{th} June 2021).
All the biopsy samples, with a provisional diagnosis of fungal rhinosinusitis are included in the study, which include FESS samples, maxillectomies, enucleation of eye and brain abscesses.
A total of 153 consecutive cases of post covid cases, with provisional diagnosis of fungal rhinosinusitis are studied.
Clinical history, including, age, gender, past history of covid illness, associated co-morbid conditions, treatment taken, oxygen inhalation, denovo diabetes, other co-morbidities, clinical features and radiological findings are recorded.
Inclusions criteria: All biopsy samples ,from post covid cases, with a provisional diagnosis of fungal rhinosinusitis, are included in the study, during the period of May 2021 to June 30^{th} 2021.
Exclusion criteria: Inadequate biopsy material and samples from repeat debridement cases are excluded from the study.
The samples are rapidly processed manually, with descending grades of alcohol (4 changes-each 1 hr) followed by clearing with Xylol (2 changes-each 20mts) and impregnated with paraffin (2 changes each 1hr). The tissues are embedded in paraffin, 4 microns thick sections are cut and stained with Hematoxylin and Eosin and also PAS (Periodic acid Schiff stain).
The sections are studied under microscope, for evidence of fungal elements and other associated histomorphological changes. The presence and type of inflammation(suppurative/granulomatous; sparse/absent), invasion into soft tissues(muscle, adipose tissue), type of spread(angio/perineural) and presence of infraction/necrosis are noted.
Fungal morphology delineated by H and E and PAS as broad pauci/aseptate hyphae with irregular/right angle branching were identified as Mucorales species.
Presence of mixed infection were noted.

III. Results:

In the present study, the histomorphological changes in 153 consecutive cases, with a provisional diagnosis of fungal rhino-sinusitis, in Post-COVID-19 patients are analyzed.
The study included 92 males and 61 females with age ranging from 24 to 68 Years(median 45 years).
All the 153 patients were diabetic, out of which 87 were denovo diabetes. Other co-morbidities included hypertension in 68 cases, HbS Ag in 2cases, Post renal transplant 2cases , post CABG 2 cases and known HIV 2 cases.
The clinical syndromes and radiological findings included 60 cases of rhino-orbital , 38ases of rhinocerebral and 55Cases of rhino-orbito-cerebral sinusitis.
Pansinusitis was recorded in all the 153 cases, basing on radiological findings.

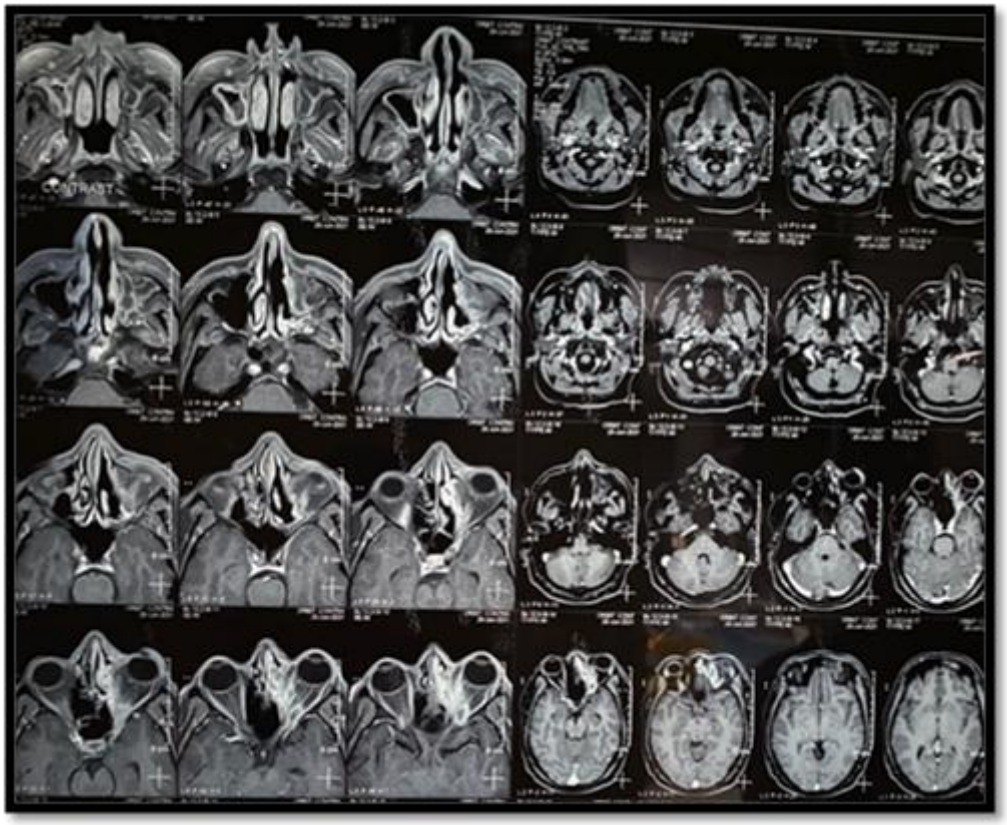

Fig 1: M/34 yrs, CECT: shows pansinusitis changes, with left preseptal and orbital cellulitis with extension into the left cavernous sinus region.

The tissue submitted for histopathological examination included FESS debridement, Maxillectomies-3 cases and orbital exenteration in 2cases.

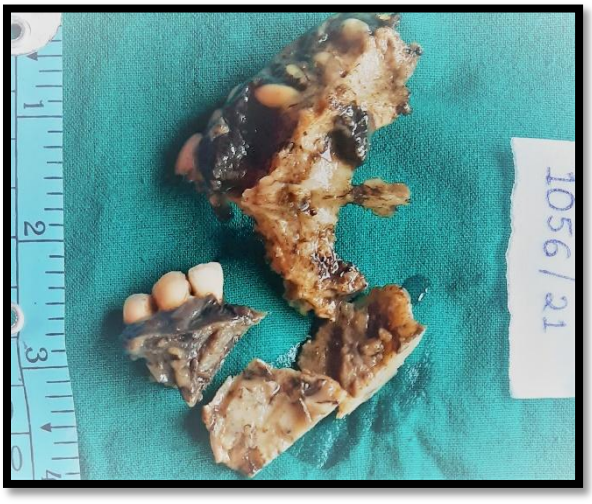

Fig 2: Maxillectomy specimen, showing gross osteomyelitis changes.

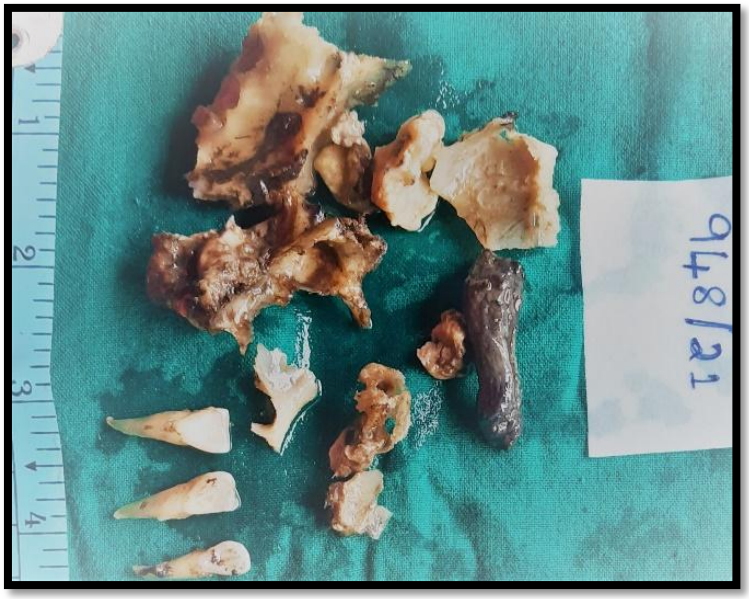

Fig 3: Maxillectomy specimen with gross osteomyelitis changes and dislodged teeth.

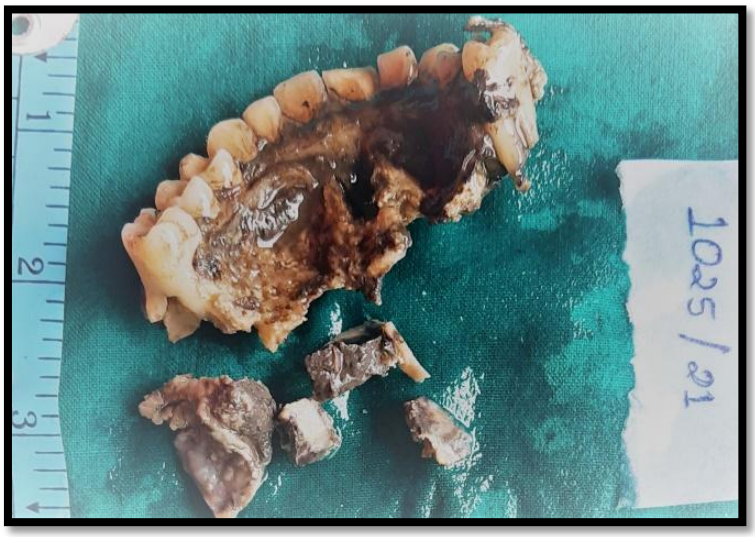

Fig 4: shows maxillectomy specimen, with gross bone and soft tissue destruction.

On microscopic examination, fungal morphology delineated with non-septate, broad and with near right angle branching were identified as Mucorales species, in 140 cases.

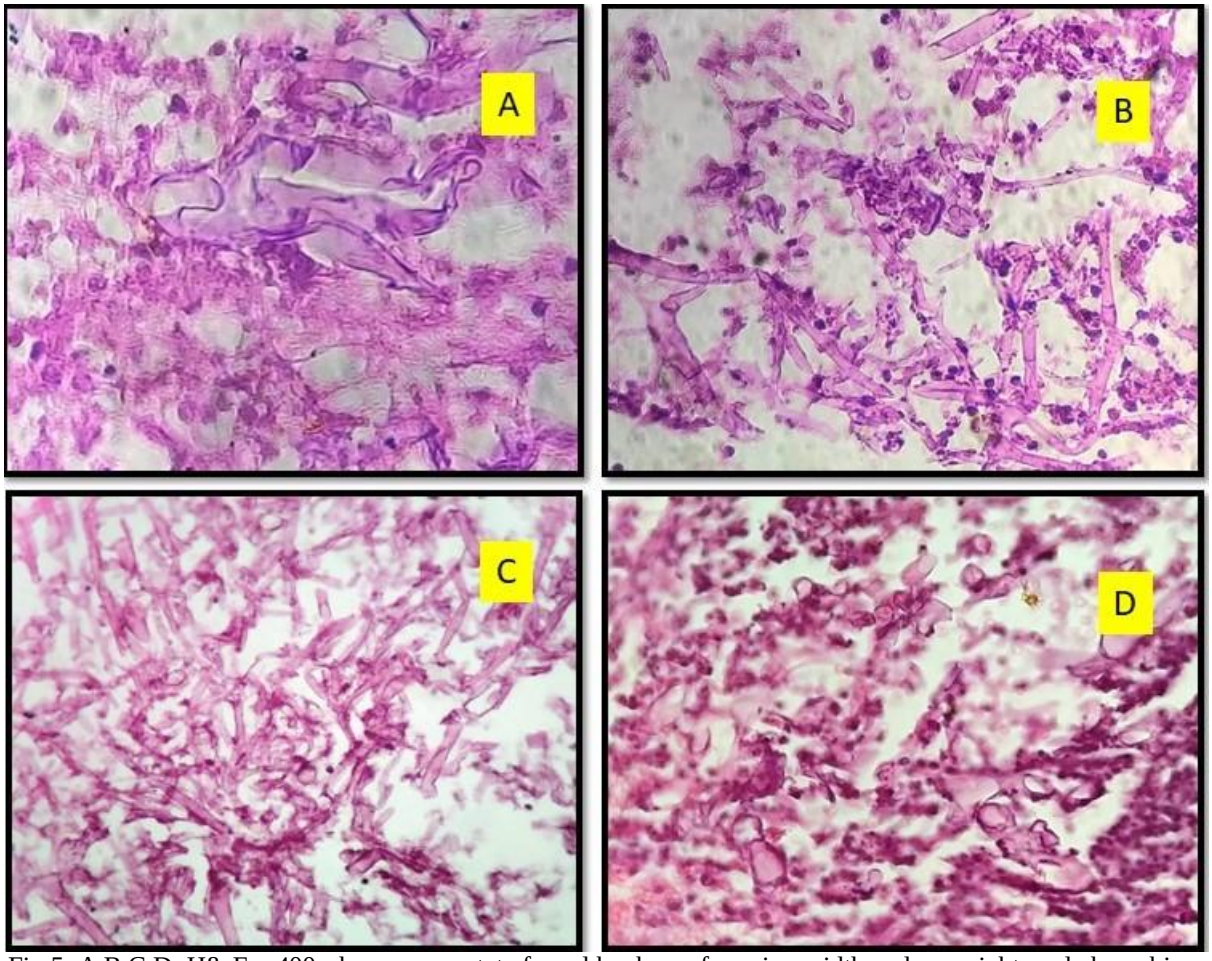

Fig 5: A,B,C,D: H& E, x400, show non-septate fungal hyphae, of varying width and near right angle branching, in a background of acute inflammation and necrosis.

Mixed fungal infections, including both mucor and aspergillus were identified in 4 cases.

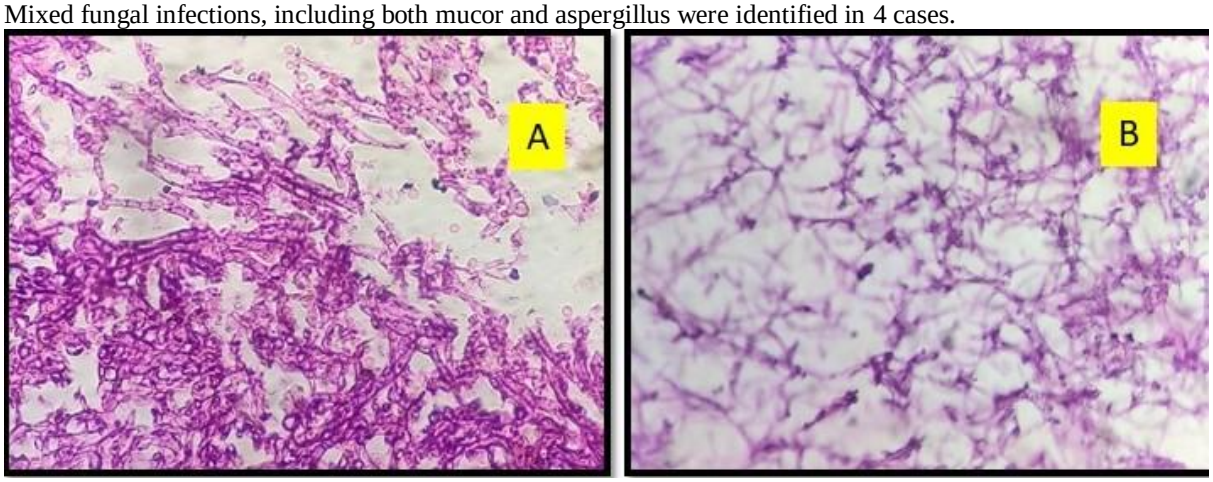

Fig 6: H&E, x400, A shows broad, non-septate fungal hyphae with right angle branching , morphologically resembling mucor and B- shows narrow , septate hyphae with acute angle branching, morphologically resembling aspergillus spp.

Only Aspergillus species were identified in 2cases

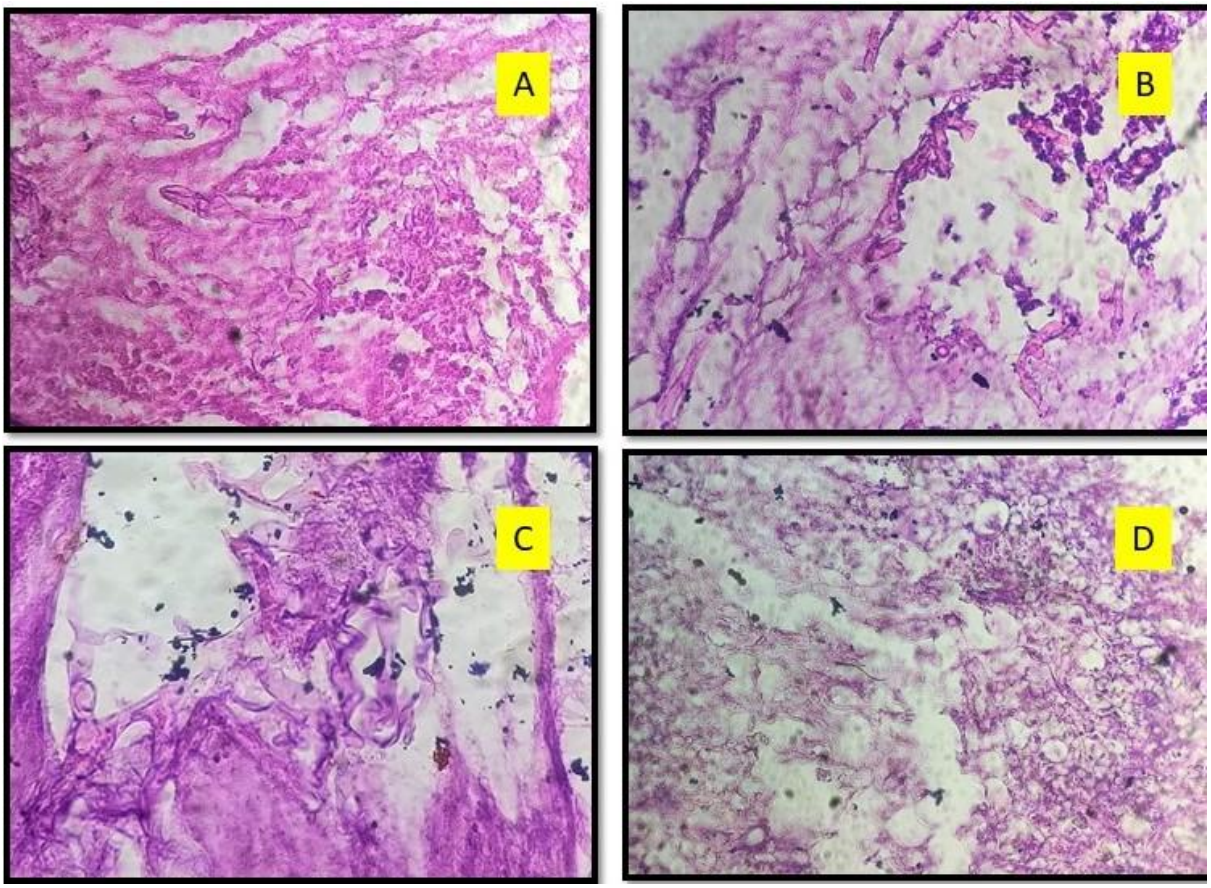

Fig 7: H & E, x400, A,B,C,D show broad, non-septate fungal hyphae invading into the adjacent soft tissue with acute inflammation and areas of infarction and necrosis.

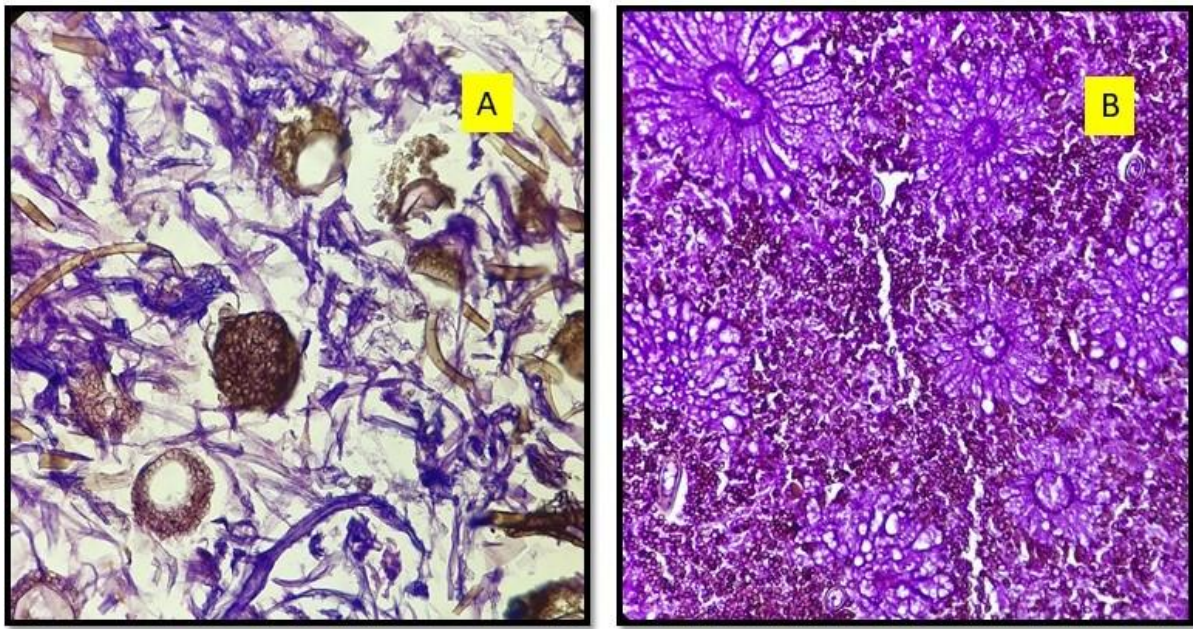

Fig 8: H & E, x400. A , B- show fruiting bodies along with the broad , non-septate fungal hyphae.

The associated histomorphological findings included dense suppurative inflammation (Fig10A), foreign body Granulomas (Fig 9 A,B), areas of infarction and necrosis, invasion into adjacent soft tissue, bone (Fig 10B) , angioinvasion (Fig 11) and perineural invasion were identified.

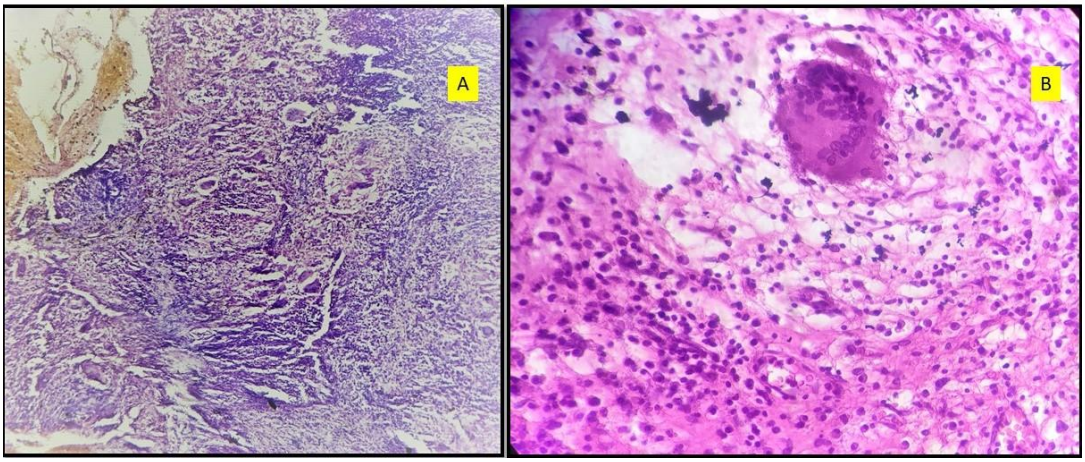

Fig 9, H & E, A-x100, B-x400, showing granulomatous reaction, with numerous foreign body type of giant cells.

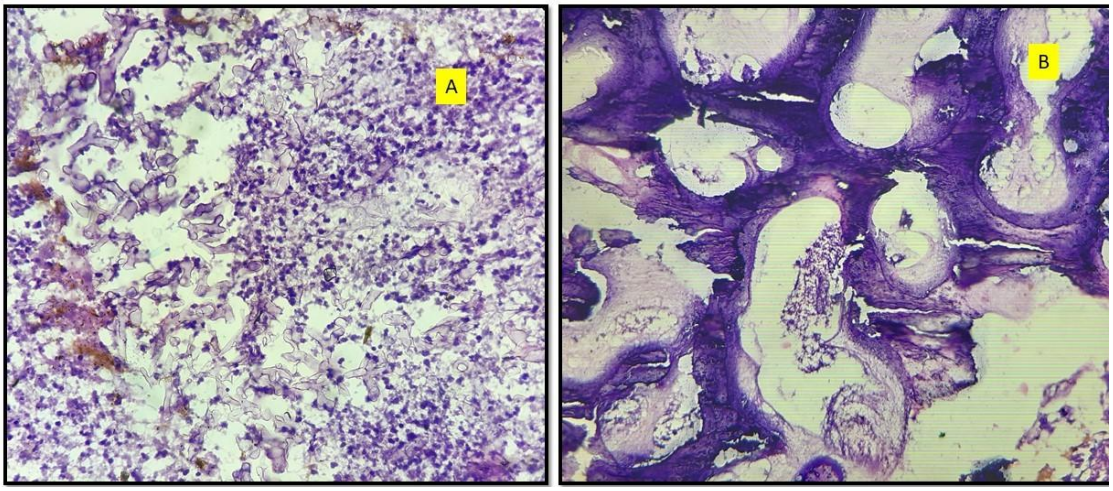

Fig 10: H & E, Ax100: acute suppurative inflammation. B-x100, invasion of mucor hyphae into bone.

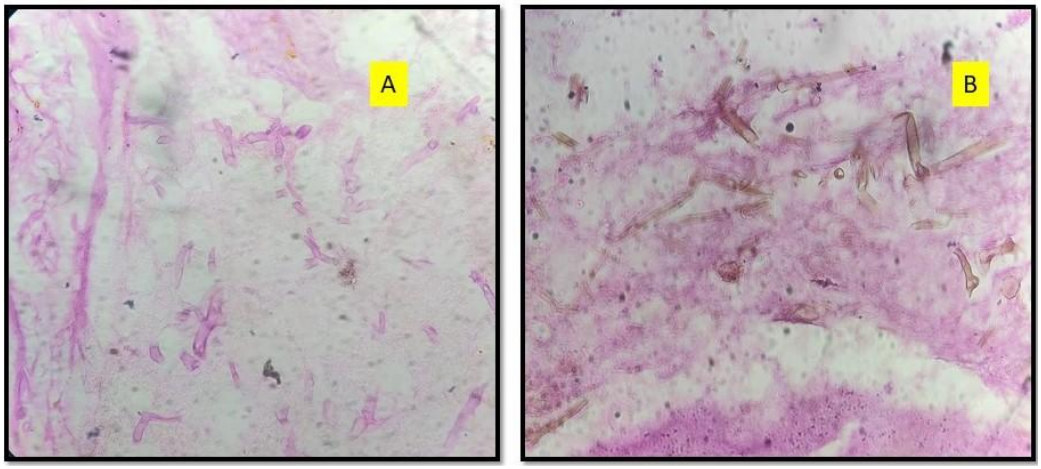

Fig 11: H&E,x100: areas of necrosis and infarction with numerous broad, non-septate fungal hyphae with near right angle branching- morphologically resembling mucor.

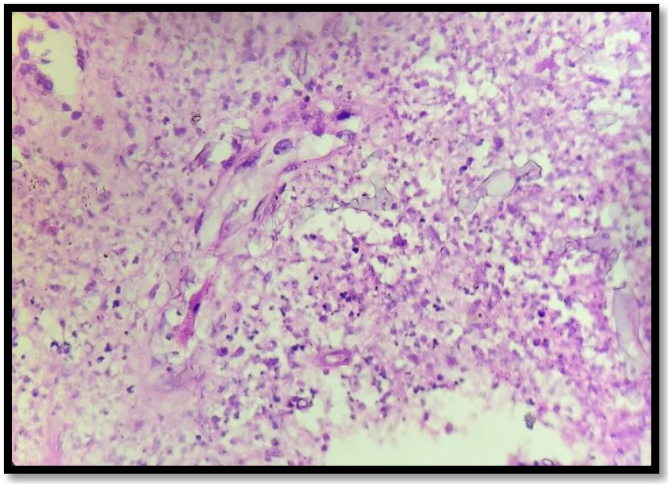

Fig 12: H & E, X100: Fungal hyphae invading the blood vessel wall- angioinvasion.

Perineural invasion was identified in 10 cases.Other Associated miscellaneous findings, included dilated congested blood vessels (Fig 13), ulcerated respiratory epithelium (Fig 14), increased mucus glands at some areas and dense inflammation consisting of lymphocytes and plasma cells.

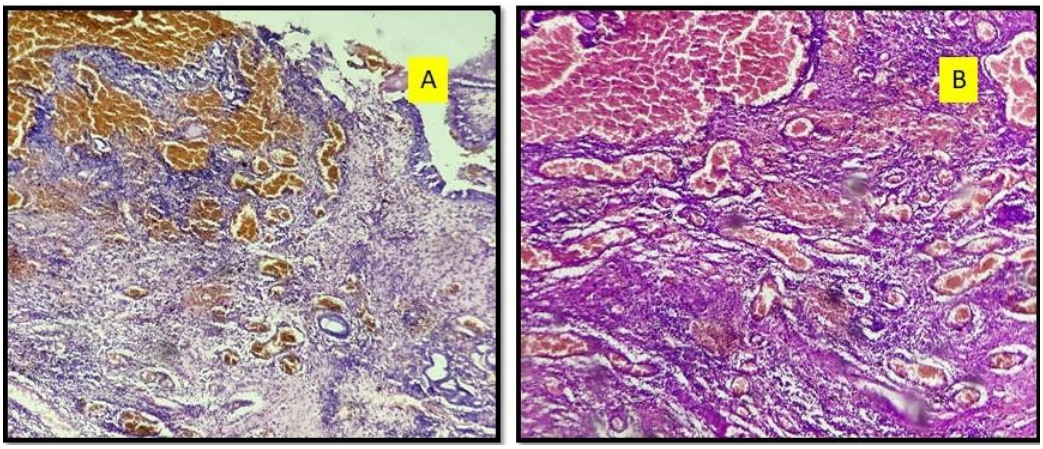

Fig 13: H& E: x100, A and B: shows numerous congested and dialed blood vessels.

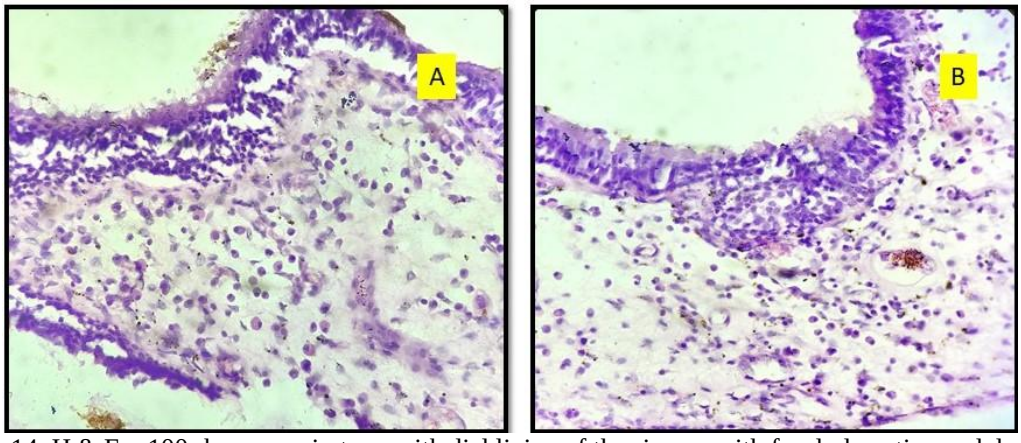

Fig 14: H & E, x100 shows respiratory epithelial lining of the sinuses with focal ulceration and dense inflammation in the subepithelium, consisting of lymphocytes and plasma cells.

IV. Discussion:

COVID-19 and mucormycosis share risk factors, such as presence of DM, which independently contribute to mortality, but have conflicting management principles. While immune suppression with steroids may be required in moderate to severe COVID-19, the use of steroids and the worsening glycemic control

provide an opportunity for mucor to become invasive. Mucor produces keto-reductase as a virulence factor enabling them to grow in the acidic and glucose-rich environment generated in ketoacidotic states [6,7].

Extensive angioinvasion with subsequent infarction of the surrounding tissues, necrosis, dense acute inflammation and granulomatous reaction were observed in majority of the cases, in our study.

Necrosis with or without infarction was seen in all the samples, studied by Sravani T et al [5]. Angioinvasion facilitates dissemination of the fungus from the site of infection to distant sites [8].

Hyphae of Mucorales species are broad, ribbon-like and aseptate or pauciseptate with wide angle bifurcation. The broad hyphae invade and occlude intermediate or large sized arteries or veins resulting in pale or hemorrhagic infarcts [9].

In the present study, the fungus was identified basing on the H & E and PAS stained tissue sections in all the cases. A co- infection was observed in 4 cases with Aspergillus species.

Sravani T et al reported co-infection by Candida species [5].

In our study, histological examination showed suppurative granulomas, dense neutrophilic infiltrate in majority of the cases, which is in concordance with the literature. In our study sparse or absent inflammation was noted in 10 cases.

Apart from angioinvasion in rhinocerebral mucormycosis, direct spread through cribriform plate into the anterior cranial fossa can occur, an it was suggested that this represents perineural spread [10] .

Cornley at al reported perineural invasion in 90% of biopsies that contained peripheral nerves [11].

In our series, perineural invasion was histologically identified in 10 samples and is associated with angioinvasion and extension into adjacent soft tissue and bone.

Availability of free iron in plasma and tissues in acidotic conditions leading to angioinvasion and neurotropism along with limited activity of antifugal agents are implicated in high mortality seen in mucormycosis .[8,12]

In conclusion, fungal rhino-sinusitis in post-covid patients is caused by Mucorales species, in the background of immunosuppression by uncontrolled diabetes and excessive steroid therapy. Early diagnosis and treatment is essential to minimize morbidity and mortality. Yield of organisms in culture is sub-optimal. Hence, histopathological examination plays a critical role in establishing the diagnosis and provides evidence of tissue invasion.

References:

[1]. .Farnoosh G, Alishiri G, Hosseini Zijoul SR, Dorostker R, Jalali Farahani A. Understanding the severe acute respiratory syndrome. J.Mil Med.2020,22:1-11.
[2]. A.M.Sagar.MUcormycosis. Clin.Infect.Dis; 14(1992) PP.S-126-S129.
[3]. A Werthman-hrenreidi. Mucormycosis with orbital compartment syndrome in a patient with COVID-19. Am.J.Emrg.Med;42 (2021),PP 264 e5-264e8.
[4]. P.G.Deutsch, J.Whittaker, S.Prasad. Invasive and non-invasive fungal rhinosinusitis -a review and update of the evidence.
[5]. Sravani T, Uppin SG, Uppin MS, Sundaram C. Rhinocerebral mucormycosis: Pathology revisited with emphasis on perineural spread. Neurol India 2014: 62: 383-6.
[6]. Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. Mycopathologica 2020; 185:599-606.
[7]. Chen X, Liao B.Cheng L et al. The microbial co infection in COVID-19. Appl Microbiol Biotechnol 2020; 104:7777-85.
[8]. Spellberg B, Edwards J Jr, Ibrhahim A. Novel perspectives on mucormycosis; Pathophysiology, presentation and management. Clin Microbiol Rev 2005; 18: 556-69.
[9]. Morace G, Borghi E. Invasive mold infections: Virulence and pathogenesis of Mucorales. Int J Microbiol 2012; 2012:349278.
[10]. Bowen BC, Post MJ. Intracranial infection. In: Atlas SW, editor. Magnetic Resonance Imaging of the Brain and Spine. New York: Raven Press; 1991.p501-308.
[11]. Cornley OA, Arikan-Akdagli A, Dannaoui E, groll Ah, lagran K, Chkrabarthi A et al. ESCMID and ECMM joint clinical guidelines for the diagnosis and management of mucormycosis 2013. Clin Microbiol infect 2014; 20 Suppl 3: 5-26.
[12]. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL et al. Epidemiology and outcome of mucormycosis: A review of 929 reported cases. Clin infect Dis 2005; 41: 634-53.

Dr.P.RamanaKumari, et. al. "A clinico-pathological study of fungal rhinosinusitis, in post-covid patients, at a tertiary care hospital, in coastal districts of Andhra Pradesh, India." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(01), 2022, pp. 23-31.