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A STUDY ON EPIDEMIOLOGY AND BIOCHEMICAL PARAMETERS IN PATIENTS OF COVID-19 ASSOCIATED MUCORMYCOSIS(CAM) ADMITTED IN A TERTIARY LEVEL DEDICATED COVID HOSPITAL IN EASTERN INDIA

Medicine

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ABSTRACT

Background: As the pandemic progresses mucormycosis cases have increased over time in active COVID or in recent (<6 weeks) COVID infected patients. Prompted by these observations we aimed to analyse COVID associated mucormycosis cases in respect to demography, clinical, laboratory parameters.

Materials And Methods: This study was conducted in a retrospective descriptive way. All COVID-19 associated mucormycosis (CAM) cases admitted in IPD of Medical College & Hospital, Kolkata in the year 2021 were enrolled and were assessed on clinical, laboratory parameters. Nineteen eligible patients were analysed after selecting according to inclusion & exclusion criteria.

Results: This study found that mean age of the mucormycosis patients were 49.79 ± 12.30 years. Majority of the patients (73.68%) were male. 21.05% of patients were from urban areas and 52.63% were smoker. Diabetes was leading (84.21%) amongst co-morbidities. Active COVID infection was present in 36.84% of patients and 57.89% of patients were COVID-recovered. History of prior/concomitant steroid used noted in 63.16% of patients. Lesions of mucormycosis were more on left side (63.16%). Rhino-orbital involvement was present in majority (71.43%). 36.84% of patients succumbed to death. Age related mortality was not found to be statistically significant (p=0.282). Mean of hospital stay were significantly more in cured (p=0.000). Surgery was found to be statistically beneficial in terms of mortality amongst mucormycosis cases (p=0.000) when done along with antifungal. Active COVID infection with mucormycosis increases the risk of mortality (p=0.001). Surprisingly prior steroid use was not found to be associated with increased mortality (p=0.678). Severe COVID infection was associated with significantly increased mortality (p=0.002). Mean of haemoglobin was found to be significantly lower in deceased patients (p=0.006). Also, mean of D-dimer was significantly higher in deceased subjects (p=0.029).

Conclusion: So, COVID and mucormycosis co-infection poses significant morbidity and mortality and several factors play important role in co-infected patients.

KEYWORDS

Mucormycosis; CAM; COVID-19; co-morbidity

INTRODUCTION

During the past two decades, mucormycosis has been an emerging fungal infection with high mortality rates. These are caused by fungi of the class Zygomycetes (consisting of the orders Mucorales and Entomophthorales). The majority of human infections are due to Mucorales fungi. So, the terms mucormycosis and zygomycosis are used interchangeably [1,2]. Usual these infections occur in immunocompromised subjects and progress locally via direct extension into adjacent tissues but not commonly are angio-invasive or become disseminated [2,3–5]. Mucorales species are angio-invasive, causing infarctions in affected tissues, and the mucormycosis disease spectrum ranges from cutaneous, rhino-cerebral, and pulmonary to disseminated and frequently fatal infections, especially in immunocompromised hosts [6,7]. The pandemic coronavirus disease 2019 (COVID-19) continues to be a significant problem worldwide since 2020.While several treatment options have been tried, none except systemic glucocorticoids have been shown to improve survival in COVID-19. Invasive pulmonary aspergillosis also complicates the course of COVID-19. [8] Glucocorticoids are inexpensive, easily available, and have been shown to reduce mortality in hypoxemic patients with COVID-19.[9] Recently, several cases of mucormycosis in people with COVID-19 have been increasingly seen world-wide, in particular from eastern India. India has highest cases of the mucormycosis in the world as per data [10,11]. So, in COVID-19 pandemic era studying demography amongst mucormycosis infected patients has become important to predicting outcome and determining future treatment options in COVID-19 and mucormycosis. This study was conducted aimed to analyse of epidemiology, predisposing factors, biochemical parameters in patients of COVID-19 associated mucormycosis (CAM) admitted in IPD of Medical College & Hospital, Kolkata in the year 2021.

MATERIAL AND METHODS

Study design, Subjects and Settings: This study was conducted in a retrospective descriptive way. All COVID-19 associated mucormycosis (CAM) cases admitted in IPD of Medical College & Hospital, Kolkata in the year 2021 were enrolled according to exclusion and inclusion criteria and were assessed on clinical, laboratory parameters.

Human Subjects Protection: The study was approved by the Institutional Ethics Committee (IEC), Medical College, Kolkata (Ref No: MC/KOL/IEC/NON-SPON/1102/06/2021dated:09/06/2021).

DATA COLLECTION: 19 eligible patients were enrolled after selecting according to inclusion & exclusion criteria. Their IPD treatment records were analysed for clinical, laboratory parameters. They were managed and followed up according to current COVID-19 and mucormycosis management protocol in India [12].

STUDY POPULATION: All COVID-19 associated mucormycosis (CAM) cases admitted in IPD of Medical College & Hospital, Kolkata in the year 2021 were enrolled.

INCLUSION CRITERIA:

1. COVID-19 RT-PCR / Rapid Antigen Test (RAT)- positive within 6 weeks of diagnosis of mucormycosis
2. Microscopically (smear or culture)/ histo-pathologically proven mucormycosis
3. Patients >12 years of age

EXCLUSION CRITERIA:

1. Pregnant women
2. Lactating women
3. Paediatric patients (<12 years of age)
4. Other co-existing infections (except COVID-19 & mucormycosis)

STUDY DEFINITIONS:

Covid-19 infection: A patient hospitalized with a positive SARS-COV-2 reverse transcriptase polymerase chain reaction (RT-PCR) or rapid antigen test (RAT) from a nasopharyngeal swab or other respiratory sample.

Mucormycosis infection: A patient with symptoms and radiological signs suggestive of mucormycosis with a tissue biopsy with evidence of mucormycosis under a microscope or in a fungal culture

CAM (COVID associated Mucormycosis): COVID19 and Mucormycosis co-infection where mucor infection should be within 6 weeks of COVID diagnosis.

Clinical, Laboratory, radiology and other parameters monitored: Clinical history [with special reference to demography, steroid use, co-morbidities, use of immunosuppressants, previous COVID-19 infection, glycaemic control (HbA1C) before hospital admission] and examination details from medical records were analysed. Laboratory records those were analysed- Haematology data (White blood cell count, neutrophil, lymphocyte and platelet count and erythrocyte sedimentation rate [ESR]); Immunological and Biochemical inflammatory markers (C-reactive protein), D-dimer, blood urea, creatinine, LFT, P-Time/INR, serum electrolytes; Radiology data- Chest X-ray, HRCT Thorax- CT severity index, CT PNS, CT scan of brain, MRI of brain; Histopathological parameters- KOH smear, fungal Culture & sensitivity results

DATA ANALYSIS: Data were tabulated and were analysed according to appropriate statistical methods.

RESULT

We analysed medical records of 19 patients with COVID associated Mucormycosis (CAM) admitted in in-patient- department (IPD) of Medical College, Kolkata in the year 2021. We found that mean age of the patients were 49.79 ± 12.30 years. There were differences in means of ages in male and female cases but this was not statistically significant (p=0.451) [Table 1]. Majority of the patients (73.68%) were male [Table 1]. 21.05% of patients were from urban areas and 52.63% were smoker [Table 1]. Diabetes was leading (84.21%) amongst co-morbidities followed by hypertension (10.53%) and chronic kidney disease (10.53%) [Table 1]. In diabetic patients 84.21% were receiving oral hypoglycaemics (OHA) & Insulin + OHA requiring patients were 47.37% [Table 1]. Active Covid infection was present in 36.84% of patients and 57.89% of patients were COVID-recovered; but were within 6 weeks of COVID infection [Table 1]. Amongst COVID recovered patients mean time from COVID recovery to mucor diagnosis was 17.32 ± 20.02 days [Table 1]. Only 21.05% of patients received at least one dose of COVID vaccine [Table 1]. On analysis of COVID severity status; mild and severe cases were 26.32% each and severe cases were seen in 42.11% of patients [Table 1]. History of prior/concomitant steroid used noted in 63.16% of patients [Table 1]. Duration of symptoms/lesions compatible with mucormycosis was mean of 15.05 ± 18.01 days [Table 1].

Table 1: Demography and History of Mucormycosis cases (n=19)

Attributes	Division	Total (n=19)	P value*
Age, in years mean ± SD	Total	49.79 ± 12.30	
	Male	47.36 ± 12.40	0.451
	Female	56.60 ± 10.11	
Male, number (%)		14 (73.68%)	
Co-morbid conditions	Diabetes Mellitus	16 (84.21%)	
	Hypertension	02 (10.53%)	
	Chronic Kidney Disease	02 (10.53%)	
COVID-19 status	History of COVID	11 (57.89%)	
	Active COVID	07 (36.84%)	
	No History of COVID	01 (05.26%)	
Time since COVID recovery, in days mean ± SD (n=11)		17.32 ± 20.02	
At least one dose of COVID vaccine		04 (21.05%)	
Severity of COVID	Mild	05 (26.32%)	
	Moderate	08 (42.11%)	
	Severe	05 (26.32%)	
Prior/concomitant steroid use		12 (63.16%)	
Prior treatment in diabetic group	OHA	16 (84.21%)	
	Insulin + OHA	09 (47.37%)	
Urban		04 (21.05%)	
Smoking		10 (52.63%)	
Duration of symptoms/lesions, in days mean ± SD		15.05 ± 18.01	

*t-test

Lesions of mucormycosis were more on left side (63.16%) followed by right (31.58%) and bilateral (05.26%) [Table 2]. Rhino-orbital involvement was present in majority (71.43%) [Table 2]. We analysed factors related to outcome of mucormycosis cases. Amongst our cases seven (36.84%) patients succumbed to death. Age related mortality was not found to be statistically significant (p=0.282) though mean age amongst deceased was slightly lower than the cured patients [Table 2]. There was not any statistically significant difference in male and female patients in terms of mortality [Table 2]. Mean of hospital stay amongst cured were 30.75 ± 4.20 days whereas in deceased it was 16.86 ± 5.08 days; these differences were found to be significant (p=0.000) [Table 2]. All subjects received Amphotericin B but surgery was found to be statistically beneficial in terms of mortality amongst mucormycosis cases (p=0.000) when done along with antifungal [Table 2]. Active COVID infection with mucormycosis increases the risk of poor outcome (p=0.001) [Table 2]. Surprisingly prior steroid use was not found to be associated with increased mortality (p-0.678) [Table 2]. Also, history of smoking did not contribute to increased mortality (p=0.515) [Table 2]. Duration of symptoms or lesions related to mucormycosis did not contribute to mortality (p=0.725) [Table 2]. Amongst mucor patients COVID disease with severe grade associated with significantly increased mortality (p=0.002) [Table 2]. Mean of haemoglobin was found to lower in deceased patients and these differences were statistically significant (p=0.006) [Table 2]. Also, mean of D-dimer was higher in deceased subjects and these differences were statistically significant (p=0.029) [Table 2].

Table 2: Clinical, biochemical, treatment and outcome profile of Mucormycosis cases

Attributes	Division	Total (n=19)	P value*
Age related mortality years, mean ± SD	Cured	52.17 ± 13.22	0.282
	Deceased	45.71 ± 10.14	
Sex related mortality	Male (n=14)	05 (35.71%)	0.865
	Female (n=5)	02 (40.00%)	
Side of the lesions	Left	12 (63.16%)	
	Right	06 (31.58%)	
	Bilateral	01 (05.26%)	
Mucor involvement	Rhino-orbito-cerebral	04 (21.05%)	
	Rhino-orbital	15 (71.43%)	
Duration of hospital stay	Total	25.63 ± 8.17	
	Cured	30.75 ± 4.20	0.000
	Deceased	16.86 ± 5.08	
Surgery	Total	13 (68.42%)	
	Cured	12	0.000
	Deceased	01	
COVID-19 status and mortality	History of COVID (n=11)	01 (09.09%)	0.003
	Active COVID (n=07)	06 (85.71%)	0.001
Prior steroid use and mortality (n=12)	Cured	08 (66.67%)	0.678
	Deceased	04 (33.33%)	
Smoking related mortality (n=10)	Cured	07 (70.00%)	0.515
	Deceased	03 (30.00%)	
Mortality and duration of symptoms/lesions, in days mean ± SD	Cured	15.25 ± 23.51	0.725
	Deceased	13.00 ± 4.24	
Mortality and severity of COVID	Mild (n=05)	00 (00.00%)	0.002
	Moderate (09)	02 (22.22%)	
	Severe (n=05)	05 (100%)	
Haemoglobin and mortality, mean g/dl ± SD	Cured	11.52 ± 01.74	0.006
	Deceased	09.04 ± 01.50	
D-dimer and mortality, mean ng/ml ± SD	Cured	927.00 ± 951.90	0.029
	Deceased	1907.14 ± 680.56	

*t-test, Chi-square test

DISCUSSION

This study found that mean age of the mucormycosis patients were 49.79 ± 12.30 years. There were statistically non-significant differences in means of ages in male and female. Majority of the

patients (73.68%) were male. 21.05% of patients were from urban areas and 52.63% were smoker. Bala et al[13] showed that the mean age of the patients was 40.43 years, with 72% male. Diabetes was leading (84.21%) amongst co-morbidities. In diabetic subjects majority (84.21%) were receiving oral hypoglycaemics (OHA). Chakrabarti et al. [14] found also that diabetes mellitus is the commonest risk factor associated with mucormycosis in India. Active COVID infection was present in 36.84% of patients and 57.89% of patients were COVID-recovered; Only 21.05% of patients received at least one dose of COVID vaccine. On analysis of COVID severity status; mild and severe cases were 26.32% each and moderate cases were seen in 42.11% of patients. History of prior/concomitant steroid used noted in 63.16% of patients. Involvement of mucormycosis were more on left side (63.16%). Rhino-orbital involvement was present in majority (71.43%). Nithyanandam et. al[15] found that 88% of rhino-cerebral mucormycosis (ROCM) patients were diabetic. Amongst our cases seven (36.84%) patients succumbed to death. Age related mortality was not found to be statistically significant (p=0.282). There were not any statistically significant gender differences in terms of mortality. Mean of hospital stay were more in cured and this was found to be significant (p=0.000). All patients received Amphotericin B but Surgery was found to be statistically beneficial in terms of mortality amongst mucormycosis cases (p=0.000) when done along antifungal. Roden MM et. al[16] also found similar benefit of surgery alongside antifungals. Active COVID infection with mucormycosis increases the risk of mortality (p=0.001). Surprisingly prior steroid use was not found to be associated with increased mortality (p=0.678). Also, history of smoking and duration of symptoms or lesions related to mucormycosis did not contribute to increased mortality (p=0.515). Severe COVID infection was associated with significantly increased mortality (p=0.002). Mean of haemoglobin was found to lower in deceased patients (p=0.006). Also, mean of D-dimer was higher in deceased subjects (p=0.029). No study has done such extensive analysis of outcome predictors in mucormycosis cases so far.

CONCLUSION

In conclusion, this study found that demography, steroid use, hospital course, laboratory parameters play an important role in determining the outcome and treatment modalities. Also, some patients with COVID infection seemed to more vulnerable for acquiring mucor infection. Further study with larger number of patients may yield more information related to these.

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