COVID-19 AND RHINO-ORBITAL MUCORMYCOSIS: WHAT'S THE LINK?

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ABSTRACT:

Background: *COVID-19 associated mucormycosis (CAM) is an emerging disfiguring and fatal problem, which affects particularly patients with uncontrolled diabetes. The complex relationship between COVID-19 and mucormycosis is still mostly unknown.*

Aim of work: *The aim of this study is to find the incidence and risk factors of orbital mucormycosis among covid and post covid patients in one year at Ain Shams University Hospitals (ASUH).*

Patients and Methods: *This descriptive retrospective cohort study was conducted at the Ophthalmology Outpatient Clinic, Ophthalmology Department, Ain Shams University hospitals in the period from 1 January 2021 until 31 December 2021. All the enrolled patients underwent detailed history, ophthalmic examination and imaging.*

Results: *Our study results revealed ROCM cases in 2021 at ASUH were much higher than the numbers presenting during equivalent intervals before COVID-19 pandemic, and among 92 cases of rhino-orbital mucormycosis within one year, 93.5% was during or within 2 weeks of COVID-19 infection. The rate of these cases varied prospectively with number of new COVID-19 cases in Egypt within the same period. COVID-19, diabetes mellitus, frequent oxygen support and corticosteroid for COVID-19 management use were the dominant predisposing factors for ROCM. Older age >50 years, admission to an ICU, Haematological malignancy and brain involvement were independently associated with a higher risk for death.*

Conclusion: *Clinicians should be vigilant about the appropriate use of steroids for COVID-19 management and ensure the use of aseptic precautions during oxygen support to minimize risk for mucormycosis following COVID-19 treatment.*

Keywords: *COVID-19, Mucormycosis, COVID-19 associated mucormycosis, Debridement, Amphotericin B, Fungal infection, Opportunistic infection.*

INTRODUCTION:

COVID-19 is a novel disease with unclear pathophysiology. However, every moment clinicians find and learn about it. Ophthalmologists noticed that orbital infections especially mucormycosis are related to covid infections.[1] So, we aim in this study to find this relationship and measure the incidence and risk factors of mucormycosis among these patients.

The acute respiratory corona virus disease (COVID-19) is a new and not well-known pandemic which is caused by the coronavirus strain SARS-CoV-2.[1] Every day

we try to learn more about it and its pathophysiology and its ophthalmological implications.[2] In ophthalmological practice, several cases of orbital mucormycosis in covid and post-covid patients was noticed recently that required scientific study of the incidence of that and to search for the risk factors affecting it.[3]

Orbital infections are frequent and very serious.[4] The source of infections may be through direct inoculation, hematogenous spread and by extension from nearby structures. Direct inoculation may be secondary to surgery, trauma and or intra orbital foreign bodies.[5] Hematogenous spread may be due to systemic sepsis or bacterial endocarditis. The orbital infections can extend to the orbit from dacryocystitis, preseptal cellulitis, periorbital cellulitis, facial skin infections, otitis media, pharyngitis and in sixty percent of patients from sinusitis, most commonly the ethmoid sinus due to its thin weak wall.[6]

Rhinocerebral-orbital type of mucormycosis is a serious opportunistic fungal infection.[7] The fungus can spread directly to the orbital cavity and to the brain after invading the mucosa of the paranasal sinuses.[3] This type of infection which is rapidly progressive and fatal with a high mortality rate, affects specific type of patients.[8] Type 2 Diabetes Mellitus with a history of diabetic ketoacidosis, history of steroids and immunosuppressive drugs intake, neutropenia, organ transplantation, blood transfusion and malignancies are major predisposing factors.[7]

Viral infections such as COVID-19 have severe clinical course and worse complications in patients with chronic medical disorders, older people or those with weak immune system.[9] Viral infections in diabetic patients are difficult in management with the possibility of appearance of diabetic complications as the blood glucose levels are fluctuating, so the virus can live and manifest in elevated blood glucose environment. Also, a compromised immune system to fight the virus in diabetic patient is another reason.[10]

Mucormycosis usually affects diabetic patients with uncontrolled blood glucose levels or with diabetic complications but the development of orbital mucormycosis in diabetic patients during COVID-19 infection or post-COVID-19 infection must be studied.

AIM OF THE WORK:

The aim of this study is to find the incidence and risk factors of orbital mucormycosis among COVID and post-COVID patients in one year at Ain Shams University Hospitals.

PATIENTS AND METHODS:

This descriptive retrospective cohort study was conducted at the Ophthalmology Outpatient Clinic, Ophthalmology Department, Ain Shams University hospitals in the period from 1 January 2021 until 31 December 2021. It was conducted in accordance with the ethical standards stated by the Ethical Committee of Ain Shams University Hospitals with informed consents obtained from all participants.

Inclusion Criteria includes patients who presented with PCR positive Covid-19 within less than 3 months and had orbital mucormycosis diagnosed clinically and by CT brain and orbit in less than 3 months after PCR positive COVID-19. While exclusion Criteria include patients who were not diagnosed with COVID-19 in the last 3 months, had other orbital pathologies, or had orbital mucormycosis caused by direct inoculation.

All the enrolled patients underwent detailed history which included demographic data (age and gender), duration of mucormycosis disease, the medical events prior to disease presentation, the date of last Covid-19 PCR and the history of Covid-19

vaccination, mucormycosis management (debridement, exenteration, ICU admission ...etc.), Covid-19 management (Home isolation, hospital administration or ICU administration), past ophthalmic history including previously performed surgeries, previous ocular traumas, or chronic use of eye drops, Diabetes Mellitus (newly diagnosed during mucormycosis presentation or known diabetic, duration of DM if known diabetic, on insulin or not, and HbA1C level during mucormycosis presentation), and past medical history.

Ophthalmic Examination of the enrolled cases included visual acuity, pupil, ocular motility, complete external examination, complete slit lamp biomicroscopy examination. CT brain and orbit, and contrast-enhanced magnetic resonance imaging (MRI) was used in imaging of them.

Statistical Analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric and median, interquartile range (IQR) when data found non-parametric.

Also, qualitative variables were presented as number and percentages. Consequently, inferential statistics using a chi-squared test ($\chi 2$), Fisher's exact test, Shapiro–Wilk test, Mann–Whitney (U) test, and Kruskal–Wallis (H) test, and binary logistic regression test were all carried out to evaluate the association between mucormycosis incidence and outcomes and its demographic and medical risk factors. All inferential tests were performed with the assumptions of confidence interval (CI) 95% and significance level (Sig.) <0.05.

RESULTS:

This descriptive retrospective cohort study included 92 patients within one year starting from 1 January 2021 until 31 December 2021. Age ranged from 19 to 86 yrs. (53.08±14.26). Regarding the gender of the patients, 49 of the enrolled patients who had rhino-orbital mucormycosis were females (53.30%) while 43 (46.70%) were males.

Table 1 details the different precipitating factors for rhino-orbital mucormycosis that were diagnosed in the enrolled patients. As the table illustrates, within 2 weeks after recovery from covid disease constituted the highest percentage of patients (69.6%).

Table (1): Incidence of the various precipitating factors for ROCM in the enrolled group

Time of mucormycosis presentation	**No.= 92**
Within 2 weeks after recovery from covid disease	64 (69.6%)
During covid disease	20 (21.7%)
During covid disease **and** within four days after upper teeth extraction	1 (1.1%)
Within 2 weeks after recovery from covid disease **and** within four days after upper teeth extraction	1 (1.1%)
Within four days after upper teeth extraction	4 (4.3%)
Within 1 month after covid-19 vaccination	1 (1.1%)
None of the above	1 (1.1%)

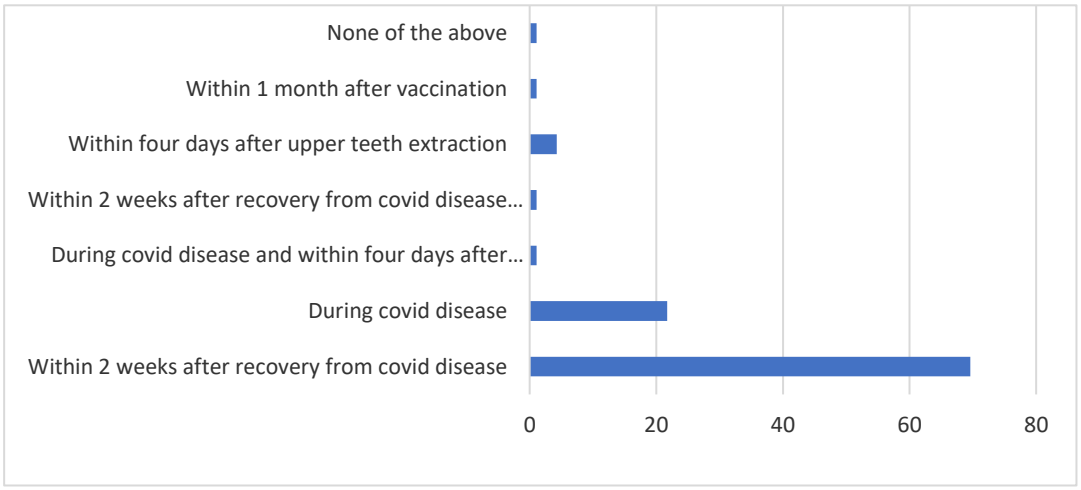

Diagram (1): Incidence of the various precipitating factors for rhino-orbital mucormycosis.

The positive group of this study is the group of patients who had covid-19 associated mucormycosis (CAM), so the first four rows in Table 1 represent the positive group of this study which are 86 cases (93.48%). The last three rows of Table 1 show mucormycosis cases not following COVID-19 infection and resemble the negative group of this study which contains 6 cases (6.52%).

In this study there was no significant association between CAM and gender (P-value:0.496), age (P-value:0.325), cerebral involvement (P-value:0.893), month of rhino-orbital mucormycosis (ROM) disease presentation, management and outcome of mucormycosis, and general medical condition as shown in the below table.

Table (2): Relation between CAM and different parameters

		Negative group (non-CAM)	Positive group CAM	Test value	P-value
		No.= 6	No.= 86		
Gender	Female	4 (66.7%)	45 (52.3%)	0.463*	0.496
	Male	2 (33.3%)	41 (47.7%)		
Age	Mean±SD	47.50 ± 8.73	53.47 ± 14.52	-0.990•	0.325
	Range	36 – 56	19 – 86		
Cerebral involvement	Rhino orbital	4 (66.7%)	55 (64.0%)	0.018*	0.893
	Rhino orbital cerebral	2 (33.3%)	31 (36.0%)		
Month of ROM disease presentation	January	0 (0.0%)	7 (8.1%)	0.529	0.467
	February	0 (0.0%)	2 (2.3%)	0.143	0.705
	March	0 (0.0%)	5 (5.8%)	0.369	0.543
	April	0 (0.0%)	4 (4.7%)	0.292	0.588
	May	0 (0.0%)	12 (14.0%)	0.963	0.326
	June	0 (0.0%)	10 (11.6%)	0.783	0.376
	July	4 (66.7%)	5 (5.8%)	23.533	0.000
	August	0 (0.0%)	6 (7.0%)	0.448	0.503
	September	0 (0.0%)	3 (3.5%)	0.216	0.642
	October	0 (0.0%)	12 (14.0%)	0.963	0.326
	November	1 (16.7%)	8 (9.3%)	0.345	0.556
	December	1 (16.7%)	12 (14.0%)	0.034	0.853

Mucormycosis management				
Conservative management (no surgical intervention)	1 (16.7%)	10 (11.6%)	0.135*	0.713
Debridement	5 (83.3%)	76 (88.4%)	0.135*	0.713
Exenteration	0 (0.0%)	7 (8.1%)	0.529*	0.467
ICU admission	3 (50.0%)	52 (60.5%)	0.255*	0.613

Mucormycosis outcome					
Disfigurement		4 (66.7%)	65 (75.6%)	0.395*	0.941
Complete loss of vision (one eye or both eyes)		3 (50.0%)	44 (51.2%)	0.003*	0.956
Death		2 (33.3%)	29 (33.7%)	0.000*	0.985
Time of death after hospital presentation (days)	Median (IQ)	2 (1 – 3)	10 (5 – 16)	-1.974≠	0.048
	Range	1 – 3	1 – 60		
General medical condition					
Medically free		0 (0.0%)	2 (2.3%)	0.143*	0.706
Newly diagnosed DM		2 (33.3%)	16 (18.6%)	0.773	0.379
Known DM		4 (66.7%)	64 (74.4%)	0.175	0.676
DM duration	Median (IQ)	8.5 (2 – 15)	12.5 (6.5 – 20)	-1.072≠	0.284
	Range	2 – 15	1 – 30		
Insulin		3 (75.0%)	41 (64.1%)	0.012*	0.912
OHGs only		1 (25.0%)	23 (35.9%)	0.295*	0.587
HTN		3 (50.0%)	31 (36.0%)	0.469*	0.494
Haematological malignancy		0 (0.0%)	2 (2.3%)	0.143*	0.706
Cardiac		0 (0.0%)	8 (9.3%)	0.611*	0.434
On long term steroids		2 (33.3%)	2 (2.3%)	12.967*	0.000
Hepatic disease		0 (0.0%)	3 (3.5%)	0.216*	0.642
Renal disease		0 (0.0%)	1 (1.2%)	0.071*	0.790
Hypothyroid		0 (0.0%)	1 (1.2%)	0.071*	0.790
Patients have comorbidities otherwise DM and HTN		2 (33.3%)	12 (14%)	1.633*	0.201

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
*: Chi-square test; ≠: Mann-Whitney test

As regards the different lines of management of covid-19, Table (3) and diagram (2) shows that oxygen inhalation was the most prevalent line of management while Actemra medication was the least detected.

Table (3): Prevalence of different lines of management of COVID-19

COVID-19 management	
Conservative with home isolation	26 (30.2%)
Oxygen support	70 (81.4%)
Hospital isolation	21 (24.4%)
Steroids tablets	44 (51.2%)
Steroid's injection	60 (69.8%)
Steroids in general	67 (77.9%))
Actemra	13 (15.1%)
ICU admission	19 (22.1%)

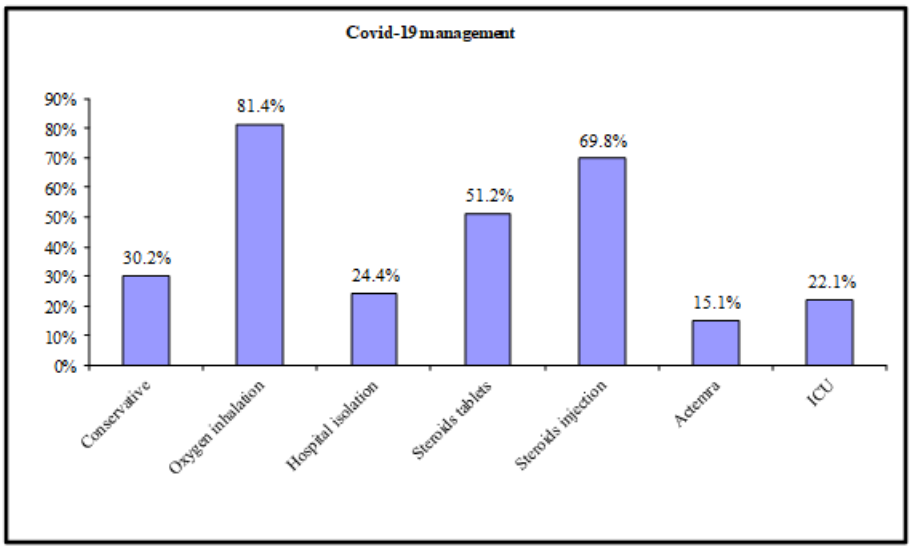

Diagram (2): Prevalence of different lines of management of COVID-19.

Regarding the incidence of CAM and its complications according to the age subgrouping, it was evident that CAM was more prevalent in the older age subgroups, where the highest prevalence was among the oldest age subgroup (50-69 years old). The percentage of loss of vision was more prevalent in >80 years old while the percentage of dead cases increased in ascending order with age.

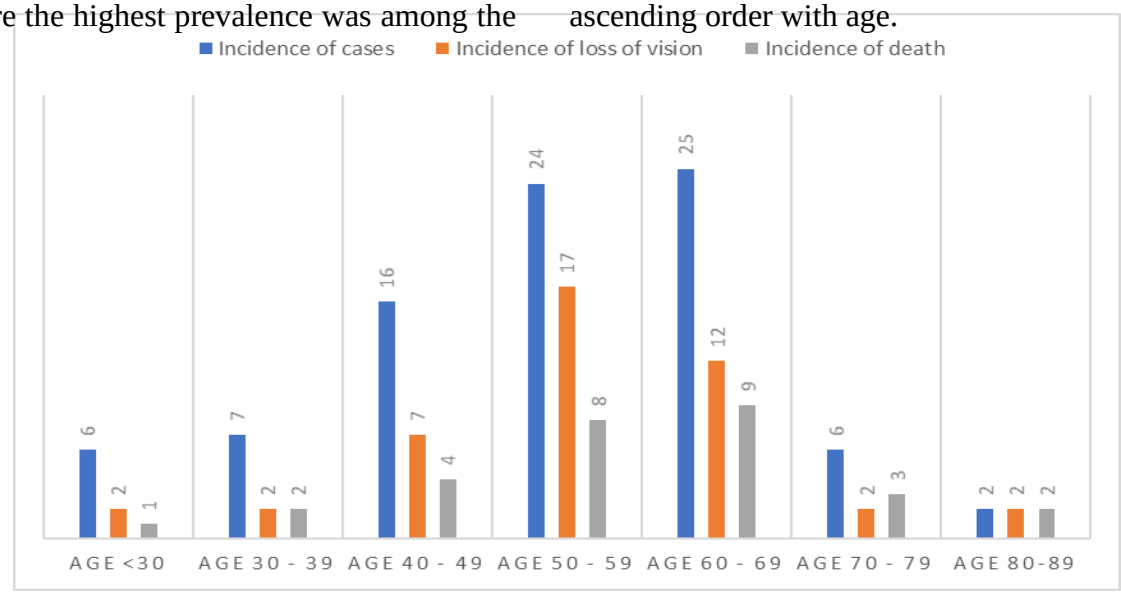

Diagram (3): Incidence of cases and complications according to age subgrouping**.**

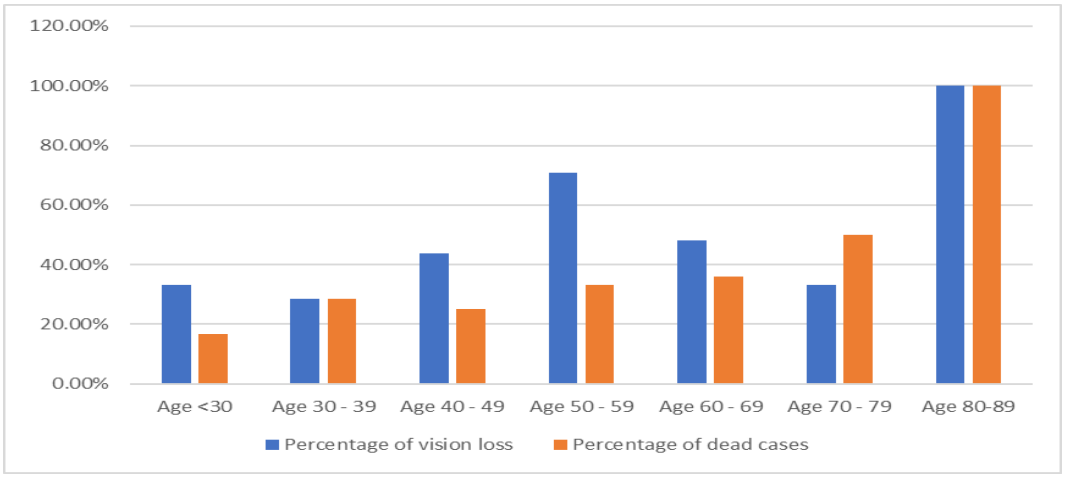

Diagram (4): Percentage of complications according to age subgrouping.

According to the months that had the most prevalent cases, 14% of cases were detected in the months of May, October, and December.

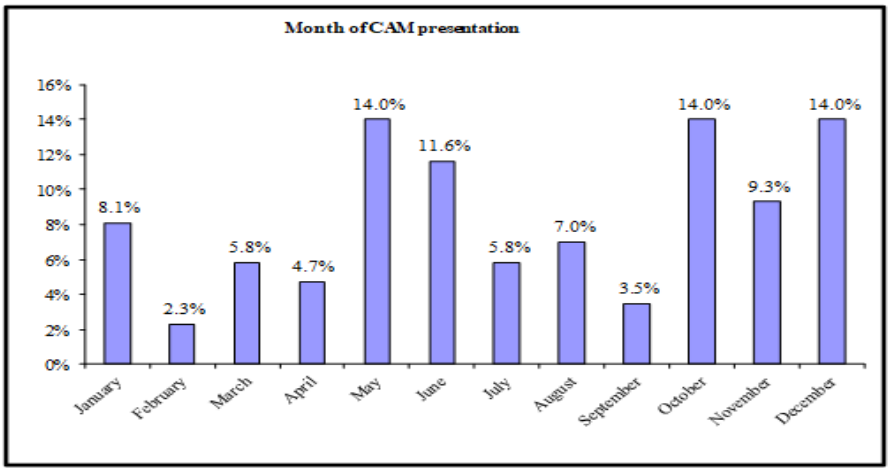

Diagram (5): Incidence of new CAM cases according to months.

A further analysis for the death and alive cases showed that cerebral involvement and haematological malignancy had significant association with mortality. Also, ICU admission and conservative management were associated with death cases. However, debridement was significantly associated with decreased mortality.

Table (4): Comparison between dead and alive cases of CAM disease

		Dead or alive		Test value	P- value
		Alive	Dead		
		No.= 57 (66.3%)	No.= 29 (33.7%)		
Gender	Female	29 (50.9%)	16 (55.2%)	0.142*	0.706
	Male	28 (49.1%)	13 (44.8%)		
Age	Mean±SD	51.49 ± 14.27	57.34 ± 14.48	-1.790•	0.077
	Range	19 – 77	19 – 86		
Cerebral involvement	Rhino orbital	54 (94.7%)	1 (3.4%)	69.483*	<0.001
	Rhino orbital cerebral	3 (5.3%)	28 (96.6%)		
Month of ROM disease presentation	January	5 (8.8%)	2 (6.9%)	0.090*	0.764
	February	2 (3.5%)	0 (0.0%)	1.042*	0.307
	March	3 (5.3%)	2 (6.9%)	0.094*	0.759

	April	3 (5.3%)	1 (3.4%)	0.143*	0.705
	May	5 (8.8%)	7 (24.1%)	3.780*	0.052
	June	8 (14.0%)	2 (6.9%)	0.953*	0.329
	July	5 (8.8%)	0 (0.0%)	2.701*	0.100
	August	5 (8.8%)	1 (3.4%)	0.839*	0.360
	September	1 (1.8%)	2 (6.9%)	1.510*	0.219
	October	9 (15.8%)	3 (10.3%)	0.475*	0.491
	November	3 (5.3%)	5 (17.2%)	3.269*	0.071
	December	8 (14.0%)	4 (13.8%)	0.001*	0.975
Time of mucormycosis presentation					
During covid disease		11 (19.3%)	10 (34.5%)	2.401*	0.121
Within four days after upper teeth extraction		2 (3.5%)	0 (0.0%)	1.042*	0.307
Within 2 weeks after recovery from covid disease		46 (80.7%)	19 (65.5%)	2.401*	0.121
Mucormycosis Management					
Conservative management (no surgical intervention)		0 (0.0%)	10 (34.5%)	22.241*	<0.001
Debridement		57 (100.0%)	19 (65.5%)	22.241*	<0.001
Exenteration		3 (5.3%)	4 (13.8%)	1.870*	0.171
ICU admission		25 (43.9%)	27 (93.1%)	19.498*	<0.001
Mucormycosis Outcome					
Disfigurement		37 (64.9%)	28 (96.6%)	12.842*	0.005
Complete loss of vision (one eye or both eyes)		26 (45.6%)	18 (62.1%)	2.083*	0.149
Covid-19 management					
Conservative with home isolation		15 (26.3%)	11 (37.9%)	1.229*	0.268
Oxygen support		44 (77.2%)	26 (89.7%)	1.971*	0.160
Hospital isolation		4 (7.0%)	5 (17.2%)	2.144*	0.143
Steroids tablets		27 (47.4%)	16 (55.2%)	0.468*	0.494
Steroids injection		40 (70.2%)	19 (65.5%)	0.194*	0.660
Actemra		7 (12.3%)	6 (20.7%)	1.059*	0.303
ICU admission		10 (17.5%)	9 (31.0%)	2.032*	0.154
General medical condition					
Medically free		2 (3.5%)	0 (0.0%)	1.042*	0.307
Newly diagnosed DM		13 (22.8%)	3 (10.3%)	1.971*	0.160
Known DM		41 (71.9%)	23 (79.3%)	0.550*	0.458
DM duration	Median (IQ)	10 (6 – 18)	14 (7 – 22)	-0.512≠	0.609
	Range	1 – 30	1 – 30		
Insulin		24 (58.5%)	17 (73.9%)	2.102*	0.147
OHGs only		17 (41.5%)	6 (26.1%)	0.819*	0.366
HTN		18 (31.6%)	13 (44.8%)	1.463*	0.226
Haematological malignancy		0 (0.0%)	2 (6.9%)	4.025*	0.045
Cardiac		4 (7.0%)	4 (13.8%)	1.046	0.306
On long term steroids		1 (1.8%)	1 (3.4%)	0.243*	0.622
Hepatic disease		1 (1.8%)	2 (6.9%)	1.510*	0.219
Renal disease		0 (0.0%)	1 (3.4%)	1.989*	0.158
Hypothyroid		0 (0.0%)	1 (3.4%)	1.989*	0.158
Patients have comorbidities otherwise DM and HTN		5 (8.8%)	7 (24.1%)	3.780	0.052

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

*: Chi-square test; •: Independent t-test, ≠: Mann-Whitney test

DISCUSSION:

Rhino-orbital-cerebral mucormycosis outbreak was arising among patients who were undergoing treatment for COVID-19 with subsequent morbidity and mortality.[11] Our study in Ain shams university Hospitals (ASUH), a tertiary care teaching hospital, found that the prevalence of CAM was 93.5% in ROCM patients managed in hospital wards and ICUs within 2021. We found a 7.7-fold increase in ROCM cases during 2021 than 2019; we attribute the increase to COVID-19.

Most CAM cases were diagnosed approximately within 2 weeks after COVID-19 diagnoses requiring steroids and oxygenation support. Hypoxemia due to COVID-19 and inappropriate use of glucocorticoid drugs were independently associated with development of CAM.[12] The mortality rate for CAM patients was high (33.7%) but was comparable to rates for non-CAM patients (33.3%). The mortality rate of cases reported from India (36.5%) was also less than the globally reported cases (61.9%).[13] Older age >50 years, admission to an ICU, Haematological malignancy and brain involvement were independently associated with a higher risk for death in this study, similarly studies and systematic reviews globally.[11,12,13,14,15,16,17]

Approximately 93% of CAM patients had either previously or newly diagnosed diabetes, which is known to increase the risk for mucormycosis 2.5-fold.[7] Furthermore, 80% of the patients with diabetes received steroids for COVID-19 management. Taken together, the underlying illnesses and medications needed to manage COVID-19 created an ideal setting for the outbreak of mucormycosis.[17]

In our study, 52.3% of CAM patients were women as Western India study[18], unlike most of previous studies which found that male gender represented the majority of cases.[13,19,20] Although, we found diabetes mellitus was the most common underlying disease for both CAM and non-CAM patients, 7% of CAM were non-diabetic. One third of the non-diabetic cases had hematological malignancies, which is known to increase the risk for mucormycosis 3.9-fold.[7]

SARS-CoV-2 has been shown to affect the beta cells of the pancreas, resulting in metabolic derangement, possibly causing diabetes mellitus.[21,22] Whether more frequent new diagnosis (18.6%) of diabetes mellitus during the evaluation for CAM is related to SARS-CoV-2 infection, glucocorticoid therapy, or a chance occurrence remains unclear. Unfortunately, we do not have glycated hemoglobin values taken at admission for all newly detected diabetes cases in our study, so we cannot determine if these patients had diabetes mellitus before CAM developed.

Among 86 CAM cases, 2 (2.3%) had COVID-19 as the only underlying disease; they were treated with glucocorticoid therapies. Whether COVID-19 itself causes immune dysregulation and predisposes patients to invasive mucormycosis remains an unproven possibility. The persisting immune dysregulation during the recovery phase of COVID-19 infection also confers additional risk,[23] 75.6% of CAM patients developed ROCM within two weeks after recovery from COVID-19, while the rest of patients had ROCM during being PCR positive of COVID-19.

Tocilizumab, sold under the brand name Actemra and manufactured by Genentech, use in COVID-19 has been reported as a risk factor for invasive candidiasis.[24] However, only 15.1% of the CAM patients in this study received tocilizumab.

Potential reasons for the outbreak of mucormycosis during the COVID-19 pandemic need further exploration. Egypt's 18.4% diabetes rate among the national

population is among the world's highest. Steroid use for moderate to severe COVID-19 and even for mild COVID-19 may have resulted in uncontrolled diabetes or development of new diabetes, a known risk factor for mucormycosis.[7]

Contaminated ventilation systems, air conditioners, and ongoing construction in hospitals have been reported to cause outbreaks of mucormycosis in the past.[25] Oxygen support represented 81.4% of COVID-19 management in CAM cases and 89.7% of dead cases among CAM cases. However, we did not estimate the burden of Mucormycetes spores in the hospital environment or the oxygen supply at home isolation.[26]

Thus, the widespread presence of Mucorales fungi in community and hospital settings could become a source of infection in susceptible populations.[26] Bhatia[27] speculated that oxygenation via facemask or nasal cannula may have inoculated the fungi in the upper respiratory tract when a contaminated water humidifier was used, but further exploration is needed .

The high mortality rate for CAM is a major concern.[11] Patients with CAM were older (53.5 years) than non-CAM patients (47.5 years). Furthermore, (50-69 years) age subgroup cases represented 57% of CAM cases, with average of death after 10 days of hospital presentation for all CAM patients .

Evidence suggests that older age imparts increased risk for hospitalization, respiratory failure, ICU admission, and attendant glucocorticoid therapy in COVID-19.[28,29] Thus, age >50 years also was associated with an increased risk for death among our study. However, we saw no difference in mortality rates between CAM and non-CAM patients. Of course, increased risk for death due to COVID-19 itself cannot be ruled out for these CAM patients. The early diagnosis of ROCM, combination of surgery and antifungal therapy was significantly associated with better survival in the ROM patients in this study, conforming with previous experiences.[19]

Disfigurement and loss of vision represented major morbidity among ROCM patients. While Disfigurement was found in 75.6% of CAM patients, 51.2% of CAM patients had loss of vision in one or both eyes which affects quality of life and (50-59 years) age subgroup had the most cases. Moreover, 8.1% of CAM cases had orbital exenteration surgery besides the debridement.

Incidence of new CAM cases in our study according to months in 2021 in Egypt showed similarity with incidence of new COVID-19 in the same period in Egypt. According to WHO and worldometer records[30,31], In the end of December 2020, level of new COVID-19 cases reached its peak at 1400 new cases, and from the beginning of January 2021 till the beginning of February 2021, it started to decrease gradually .

After that the level reached plateau till the beginning of April when it started to increase till its highest peak on mid-May since it reached 1200 new cases. However, this level started to decrease rapidly till reaching the lowest point in July and August. Since that, it started to increase again at the beginning of September till mid-October to reach the plateau level around 900 new cases till the end of the year. The last increase and decrease in level of new COVID-19 new cases resemble rate and form of new CAM cases in the following months in our study.

Like that, the incidence of death cases of COVID-19 in Egypt and CAM cases in our study according to months of 2021 have similarity to some extent where, May and November had the highest incident cases .

Around ten studies were published discussing CAM outbreak in Egypt, but the period of study ranged from two to six months and. These studies had relatively inadequate number of cases, since the number

of cases ranged from one to twenty-six CAM patients. They reported that the number of CAM patients were much higher than the numbers presenting in the prior 3 years during equivalent intervals (range, one to two cases), and were much higher than those reported in the literature in different settings in the pre-pandemic era.[32,33,34,35,36]

Abdel-Aziz M et al., 2022 reported 16 new CAM cases in Cairo University Hospitals during the first six months in 2021 which were double the number seen in the same period of the previous year. It showed that all of them were recovered COVID-19 diabetic patients, and corticosteroids were included in their treatment protocol.[37]

Strengths and limitations:

The first limitation of our study is that, because of its retrospective nature, some data were missing because of a gap in the documentation. Missing data included information on whether the oral steroids were administered in outpatient or inpatient settings for COVID-19, as well as data on status of glycemic control of diabetes. We also do not have data on the timing of amphotericin B use, timing of surgery, or duration of sequential antifungal therapy, which are critical factors that have a bearing on mucormycosis outcomes; hence, we could not analyze these factors .

Other unexplored factors, including genetic predisposition, might explain the high prevalence of CAM patients. Thus, prospective studies from the rest of the world, especially those severely affected by the COVID-19 pandemic, would be needed to ascertain the epidemiology of CAM. Finally, whether dissemination of mucormycosis took place beyond the rhino-sino-orbital and cerebral regions was not documented. Considering the lower mortality rate, however, dissemination of the disease beyond these regions is unlikely. The strength of our study is the large number of patients, which lends credibility to our observations. As well, the one-year duration, which gave an idea on the different rates of CAM cases in different months which differed according to severity of waves of the pandemic COVID-19.

Conclusion

Our study results showed that ROM cases in 2021 at ASUH were much higher than the numbers presenting during equivalent intervals before COVID-19 pandemic, and the rate of these cases varied prospectively with number of new COVID-19 cases in Egypt within the same period. COVID-19, diabetes mellitus, frequent oxygen support and corticosteroid for COVID-19 management use were the dominant predisposing factors for ROCM. Older age >50 years, admission to an ICU, haematological malignancy and brain involvement were independently associated with a higher risk for death .

Clinicians should be vigilant about the appropriate use of steroids for COVID-19 management and ensure the use of aseptic precautions during oxygen support to minimize risk for mucormycosis following COVID-19 treatment. Physicians should ensure they use appropriate drugs and doses in treating COVID-19 patients. ROCM should be considered among patients treated for COVID-19 who experience face pain, nasal blockage, and headache with or without nose eschar, particularly among those with diabetes and those who have received steroids.

Conflicts of Interest: The authors state that the publishing of this paper is free of any conflicts of interest.

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داء الكوفيد١٩ والالتهاب الفطري العفني الخبيث بمحجر العين والجيوب الأنفية: ما الرابط بينهما؟

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الخلفية: إن داء الالتهاب الفطري العفني الخبيث المرتبط بداء كوفيد١٩ مشكلة بدأت في الظهور مهددة بالتشوهات والوفاة خصوصاً لمرضى داء السكري الغير متحكم فيه. العلاقة المعقدة بين داء الإلتهاب الفطري العفني الخبيث وبين داء كوفيد ١٩ مازالت غير معروفة بدرجة كبيرة.

الهدف: هذه الدراسة تهدف إلى معرفة مدى حدوث داء الفطر العفني الخبيث بمحجر العين بين المرضى أثناء و بعد إصابتهم بمرض كوفيد١٩ خلال عام و ذلك في مستشفيات جامعة عين شمس.

الطرق: أقيمت هذه الدراسة الجماعية الإستعادية للأحداث في عيادات الرمد الخارجية و قسم الرمد بمستشفيات جامعة عين شمس خلال الفترة من ١ يناير ٢٠٢١ إلى ٣١ ديسمبر ٢٠٢١، وقد تم أخذ تاريخ مرضي مفصل و تم عمل فحص للعين و محجر العين و الفحوصات التصويرية لجميع المرضى

النتائج: أوضحت هذه الدراسة أن حالات الفطر العفني بمحجر العين في عام ٢٠٢١ كانت أعلى بدرجة كبيرة من أعداد الحالات التي ظهرت في مثل هذه الفترة قبل ظهور وباء كوفيد١٩، كما أنه من بين ٩٢ من مرضى داء الفطر العفني الخبيث بمحجر العين وبالجيوب الأنفية خلال عام واحد ظهر أنه ٩٣,٥ ٪ منهم أصيب بالمرض أثناء أو خلال أسبوعين من الإصابة بداء كوفيد١٩ كما ظهر أن معدل هذه الحالات تغير بصورة طردية مع أعداد حالات كوفيد في مصر في نفس الفترة، لقد كان داء كوفيد١٩ و داء السكري بالإضافة إلى علاج كوفيد١٩ بالكورتيزون و إمدادات الأكسجين المتكررة هم العوامل الموطئة المهيمنة لداء الفطر العفني بمحجر العين و المخ و الجيوب الأنفية. كما كان من الواضح أيضاً أن أعمار المرضى فوق الخمسين و احتياج المرضى دخول أقسام الرعاية المركزة و المعاناة من أمراض سرطانات الدم و توغل الفطر إلى المخ هم أعلى العوامل الخطرة التي قد تزيد إحتمالية حدوث الوفاة نتيجة داء الفطر العفني بمحجر العين و المخ و الجيوب الأنفية

الخاتمه: على الأطباء توخي الحذر عند إستخدام الكورتيزون في علاج حالات كوفيد١٩ كما ينبغي التأكد من وجود بيئة معقمة و إنخاذ إجراءات التعقيم أثناء إمداد المرضى بالأكسجين و ذلك لتقليل فرصة الإصابة بداء الفطري العفني الخبيث بعد داء كوفيد١٩