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## Original Article

## Diabetes mellitus and Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM): A wake-up call from Egypt



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## To the editor,

While the whole world started Coronavirus Disease 2019 (COVID-19) vaccine campaign aiming at ending the pandemic other areas of the world started to suffer from a devastating new complication of the disease. Increased cases of COVID-19 Associated Mucormycosis (CAM) has been noted [1–3]. We had observed this phenomenon in Egypt over the past few weeks similar to the situation in India.

All patients who had imaging findings of bone destruction and suspicion for fungal sinusitis following documented COVID-19 evaluated by authors from March 15th to May 15th 2021, were included. The patients' demographic data, comorbidities, host risk factors, microbiologic data and management were collected.

The study included 21 patients evaluated in 11 different

hospitals in metropolitan Cairo, Egypt (Patient characteristics in Table 1). Diabetes Mellitus was present in all patients on admission except two, 5/21 (23.8%) patients did not have prior history of diabetes and 3/21 (14.3%) presented with diabetic ketoacidosis, 10/21 (47.6%) had rhino-orbital disease, 5/21 (23.8%) had rhino-cerebral disease and one patient (4.7%) had pulmonary disease. 17/21 (81%) patients received amphotericin B either alone or in combination, 3 (14.3%) received itraconazole, and 2 (9.5%) received voriconazole. Mortality was 7/21 (33.3%), 5 of them (71.4%) had rhino-cerebral disease.

The aim of this study was to highlight the growing problem of CAM in Egypt and it was clear that younger patients had the best outcomes and older patients and patients with cerebral extension had the worse outcomes. Amphotericin B was the backbone of all our treatment regimens, diabetes was present in 90.5% of patients on admission. In the study of Singh et al. that included 101 CAM, most of them are from India, diabetes mellitus was present in 80% of cases and corticosteroid intake was administered by 76.3% of cases [2]. All our patients received corticosteroid therapy

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**Table 1**  
Characteristics of patients included in this report.

Age/Sex	Diabetes	Comorbidities	Presentation	Site	Treatment	Outcome	Surge	Microbiology	Notes
38/M	New onset	Sinusitis	- Nasal obstruction - Facial and orbital pain	Sinus	L-AmB then POS	Alive	Within 24h	Mucorales	<b>Pathology proven mucormycosis</b>
57/M	Yes	Hypertension	- Tooth pain and dysphagia - Headache	Sinus	L-AmB + POS then POS	Alive	Within 24h	No growth	<b>Pathology proven mucormycosis</b> <b>Palatal perforation on admission</b>
48/F	Yes	Morbid obesity	- Left eye ophthalmoplegia and ptosis - Right orbital Apex syndrome	Rhino- orbital	L-AmB then POS	Alive	Within 48h	Mucorales and Aspergillus fumigatus	<b>Pathology proven mucormycosis</b>
54/M	Yes	Hypertension Atrial Fibrillation Ischemic cardiomyopathy Chronic Kidney disease	- Left facial palsy - Headache	Rhino- orbital	L-AmB plus POS	Alive	Not done	Pseudomonas aeruginosa	<b>Pathology proven mucormycosis</b> <b>Palatal perforation on admission</b>
55/M	Yes	Hypertension	Headache	Sinus	L-AmB	Alive	Not done	NA	<b>Improved with medical treatment only</b>
65/F	Yes	Hypertension Hypothyroidism Dyslipidemia	Respiratory Distress	Pulmonary	AmB plus POS	Alive	Not done	- Culture grew Rhizopus, Aspergillus flavus and Aspergillus fumigatus - Has associated CAPA and Polymicrobial Carbapenem Resistant acinetobacter and klebsiella pneumonia	<b>- Received Tocilizumab</b>
49/F	Yes with DKA	Ischemic heart disease	Right eye ophthalmoplegia and proptosis	Rhino- orbital	AmB	Alive	Not done	Not done	<b>Lost to follow up</b>
32/M	None	None	- Rt Periorbital oedma - Facial swelling and headache	Rhino, orbital	ITC	Alive	Within 24h	Culture grew only <i>Acinetobacter Baumanni</i>	
56/M	Yes	Asthma Long Covid	- Left orbital edema - Ophthalmoplegia and vision loss	Rhino- orbital	AmB	Alive	Within 24h but later required orbital exentration	- Cultures grew only candida and aspergillus Sp	<b>- Received Tocilizumab</b> <b>- Developed postoperative ischemic stroke</b>
52/F	Yes	Ischemic heart disease Asthma	- Left orbital edema - Ophthalmoplegia with rapid deterioration of vision	Rhino- orbital	AmB then VRC	Alive	Within 48h but required orbital exentration	- Culture grew only <i>Acinetobacter Baumanii</i>	<b>- Received Tocilizumab</b>
61/M	Yes	Ischemic heart disease	- Left facial edema - Proptosis	Rhino- orbital	ITC	Alive	Within 72h	Negative cultures	
39/M	New onset	None	- Left sided pansinusitis - Severe headache with retroorbital pain	Sinus	ITC	Alive	Within 72h	negative culture	<b>Fungal mud with</b>
45/F	None	None	- Left sided sinusitis - Diminution of vision with mild proptosis	Rhino- orbital	AmB	Alive	Within 48h	- Negative cultures	<b>- Had periseptal and orbital abscess</b> <b>- Immediate postoperative improvement of vision</b>
69/M	Yes	None	- Pansinusitis - Blackish discoloration	Sinus	VRC	Alive	24h	- Culture failed to grow mucor and only reported Aspergillus	<b>- Received Tocilizumab</b> <b>- Had septal</b>

60/F	Yes	Asthma Hypertension Ischemic stroke	of the palate - Malignant otitis externa	Altered mental status	Rhino- orbital	L-AmB	Died (21D)	Not done	NA	<b>perforation</b> - <b>Required another endoscopic debridement after 2 weeks</b> - <b>L-AmB treatment interrupted due to AKI</b>
68/M	Yes	Hypertension Ischemic cardiomyopathy Peripheral arterial disease Morbid obesity	Ptosis and ophthalmoplegia Blackish discoloration of face		Rhino- cerebral	L-AmB plus POS plus AFG	Died (13D)	Within 48h	- Culture grew Mucorales - Culture grew CR KP	- <b>Confirmed by pathology</b> - <b>Course complicated by CR KP meningitis requiring intrathecal Colistin</b>
65/F	New onset with DKA	Hypertension Ischemic heart disease	- Altered mental status - Blackish discoloration of face		Rhino- cerebral	L-AmB plus POS plus Anidulafungin	Died (11D)	5D	NA	<b>CNS involvement with MCA occlusion on admission</b>
72/M	Yes	Ischemic heart disease Chronic Kidney disease	- Bilateral diminution of vision		Rhino- cerebral	AmB then VRC	Died (25D)	Not done	Not done	- <b>Patient had persistent positive COVID-19 swab that delayed surgery</b> - <b>Course complicated by massive ischemic stroke with central retinal artery occlusion</b>
65/M	Yes	Hypertension	- Left eye swelling and pain - Left facial edema		Rhino- cerebral	L-AmB	Died (27 D)	Within 48h	- NA	- <b>Received Tocilizumab</b> - <b>Left ICA occlusion with MCA infarction</b>
36/M	New onset	None	Right eye swelling and proptosis		Rhino-orbital	L-AmB	Died (7D)	4 days	NA	<b>Septic shock following surgery</b>
44/M	<b>New onset with DKA</b>	<b>Lumbar disk prolapse</b>	<b>Altered mental status</b> <b>Bilateral proptosis</b>		<b>Rhino-cerebral</b>	<b>AmB</b>	<b>Died (16 D)</b>	<b>Not done</b>	<b>Not done</b>	<b>Course complicated by cavernous sinus thrombosis and MCA occlusion</b>

AFG: Anidulafungin; AKI: acute kidney injury; AmB: conventional amphotericin B; CAPA: Covid Associated Pulmonary Aspergillosis; CNS: central nervous system; CR KP: Carbapenem resistant Klebsiella pneumonia; D: day; DKA: diabetic ketoacidosis; F: female; GNB: Gram negative bacilli; ICA: internal carotid artery; ITC: itraconazole; L-AmB: liposomal amphotericin B; M: male; MCA: middle cerebral artery; POS: Posaconazole; VRC: voriconazole.

**Table 2**  
Characteristics of the survived patients in comparison to the ones who died.

	Alive (14/21)	Deceased (7/21)
Sex	9 (64.3%) males 5 (35.7%) females	5 (71.4%) males 2 (28.6%) females
Age in years (mean $\pm$ SD)	50 $\pm$ 9.5	59.8 $\pm$ 12.9
Comorbidities and possible risk factors	12/14 (85.7%) Diabetes 14/14 (100%) corticosteroid intake 4/14 (28.6%) received Tocilizumab 4/14 (28.6%) Hypertension 4/14 (28.6%) Ischemic heart disease 1/14 (7.14%) Morbid obesity	7/7 (100%) Diabetes 7/7 (100%) corticosteroid intake 1/7 (14.2%) received Tocilizumab 4/7 (57.14%) Hypertension 3/7 (42.8%) Ischemic heart disease 1/7 (14.2%) Morbid obesity
Site	5/14 (35.7%) Sinus 8/14 (57.14%) Rhino-orbital 1/14 (7.14%) Pulmonary	2/7 (28.6%) Rhino-orbital 5/7 (71.4%) Rhino-cerebral
Treatment	1/14 (7.14) L-AmB 4/14 (28.6%) AmB 4/14 (28.6%) AmB and POS 3/14 (21.4%) ITC	3/7 (42.8%) L-AmB 2/7 (28.6%) L-AmB and POS 1/7 (14.3%) AmB
Surgical debridement	10/14 (%)	4/7 (57.14%)
Time of surgery	5/10 (50%) within 24 h 3/10 (30%) within 48 h 2/10 (20%) within 72 h	2/4 (50%) within 48 h ¼ (25%) after 4 days ¼ (25%) after 5 days

AmB: Conventional Amphotericin B; ITC: Itraconazole; L-AmB: Liposomal Amphotericin B; POS: Posaconazole.

irrespective of clinical staging of COVID-19 which is largely driven by social media promoting high dose steroids. It was clear that patients who had early surgical debridement had the best outcome without organ loss and vision was preserved but there is always a selection bias as milder cases have better chances at surgery while critically ill patients either are too unstable for surgery or family defer procedure (Table 2).

CAM is a life-threatening condition that adds fuel to the fire and public health authorities should encourage following guidelines in COVID-19 and avoid non-evidence-based therapies.

#### Declaration of competing interest

The authors have no conflict of interest.

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