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Original Article

Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India

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ABSTRACT

Background and aims: There are increasing case reports of rhino-orbital mucormycosis in people with coronavirus disease 2019 (COVID-19), especially from India. Diabetes mellitus (DM) is an independent risk factor for both severe COVID-19 and mucormycosis. We aim to conduct a systematic review of literature to find out the patient's characteristics having mucormycosis and COVID-19.

Methods: We searched the electronic database of PubMed and Google Scholar from inception until May 13, 2021 using keywords. We retrieved all the granular details of case reports/series of patients with mucormycosis, and COVID-19 reported world-wide. Subsequently we analyzed the patient characteristics, associated comorbidities, location of mucormycosis, use of steroids and its outcome in people with COVID-19.

Results: Overall, 101 cases of mucormycosis in people with COVID-19 have been reported, of which 82 cases were from India and 19 from the rest of the world. Mucormycosis was predominantly seen in males (78.9%), both in people who were active (59.4%) or recovered (40.6%) from COVID-19. Pre-existing diabetes mellitus (DM) was present in 80% of cases, while concomitant diabetic ketoacidosis (DKA) was present in 14.9%. Corticosteroid intake for the treatment of COVID-19 was recorded in 76.3% of cases. Mucormycosis involving nose and sinuses (88.9%) was most common followed by rhino-orbital (56.7%). Mortality was noted in 30.7% of the cases.

Conclusion: An unholy trinity of diabetes, rampant use of corticosteroid in a background of COVID-19 appears to increase mucormycosis. All efforts should be made to maintain optimal glucose and only judicious use of corticosteroids in patients with COVID-19.

1. Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with a wide range of opportunistic bacterial and fungal infections [1]. Both *Aspergillus* and *Candida* have been reported as the main fungal pathogens for co-infection in people with COVID-19 [2]. Recently, several cases of mucormycosis in people with COVID-19 have been increasingly reported world-wide, in particular from India. The primary reason that appears to be facilitating Mucorales spores to germinate in people with COVID-19 is an ideal environment of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycemia, steroid-induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels (increased ferritins) and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated or background comorbidities) coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators.

Phycomycosis or zygomycosis was first described in 1885 by Paltauf [3] and later coined as Mucormycosis in 1957 by Baker [4] an American pathologist for an aggressive infection caused by *Rhizopus*. Mucormycosis is an uncommon but a fatal fungal infection that usually affects patients with altered immunity. Mucormycosis is an angioinvasive disease caused by mold fungi of the

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genus *Rhizopus*, *Mucor*, *Rhizomucor, Cunninghamella* and *Absidia* of Order- Mucorales, Class- Zygomycetes [5]. The *Rhizopus Oryzae* is most common type and responsible for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the Rhino-orbital-cerebral (ROCM) form [6]. Mode of contamination occurs through the inhalation of fungal spores.

Globally, the prevalence of mucormycosis varied from 0.005 to 1.7 per million population, while its prevalence is nearly 80 times higher (0.14 per 1000) in India compared to developed countries, in a recent estimate of year 2019–2020 [7–9]. In other words, India has highest cases of the mucormycosis in the world. Notwithstanding, India is already having second largest population with diabetes mellitus (DM) and was the diabetes capital of the world, until recently [10]. Importantly, DM has been the most common risk factor linked with mucormycosis in India, although hematological malignancies and organ transplant takes the lead in Europe and the USA [9]. Nevertheless, DM remains the leading risk factor associated with mucormycosis globally, with an overall mortality of 46% [11]. Indeed, presence of DM was an independent risk factor (Odds ratio [OR] 2.69; 95% Confidence Interval 1.77–3.54; $P < 0.001$) in a large 2018 meta-analysis of 851 cases of rarely occurring mucormycosis, and the most common species isolated was *Rhizopus* (48%) [11]. While long term use of corticosteroids have often been associated with several opportunistic fungal infection including aspergillosis and mucormycosis, even a short course of corticosteroids has recently been reported to link with mucormycosis especially in people with DM. A cumulative prednisone dose of greater than 600 mg or a total methyl prednisone dose of 2–7 g given during the month before, predisposes immunocompromised people to mucormycosis [12]. There are few case reports of mucormycosis resulting from even a short course (5–14 days) of steroid therapy, especially in people with DM [13]. Surprisingly, 46% of the patients had received corticosteroids within the month before the diagnosis of mucormycosis in the European Confederation of Medical Mycology study [14].

These findings need a relook in the context of COVID-19 pandemic where corticosteroids are often being used. There has been a steep rise in case reports/series of mucormycosis in people with COVID-19 especially from India. Similarly, many cases are being reported from other parts of globe. Several anecdotal cases are also being reported in grey literature such as the print and electronic media. These finding are unprecedented and carry an immense public health importance, primarily because fatality rate with mucormycosis is pretty high. Especially the intracranial involvement of mucormycosis increases the fatality rate to as high as 90% [15]. Moreover, rapidity of dissemination of mucormycosis is an extraordinary phenomenon and even a delay of 12 h in the diagnosis could be fatal, the reason 50% of cases of mucormycosis have been historically diagnosed only in the post-mortem autopsy series [16]. This prompted us to conduct a systematic review of published case reports/series of mucormycosis in people with COVID-19, to know its temporal associations in relation to comorbidities, association with drugs being used in COVID-19 and overall characteristics of patients with its outcome. We additionally postulated a mechanistic explanation as to why mucormycosis could be increasingly linked to COVID-19 and is being reported increasingly from India.

2. Methods

A systematic literature search was conducted in the electronic database of PubMed and Google Scholar from inception until May 13, 2021 using keyword “COVID-19”, “SARS CoV-2”, AND “Mucormycosis”, “Zygomycosis”, “Phycomycosis, “Mucorales”, “Mucor”, “Rhizopus”, “Rhizomucor”, “Cunninghamella”, and “Absidia”. Details of all the cases that reported mucormycosis (both confirmed and suspected) in people with COVID-19 so far, were retrieved. Characteristics of each patient was collected on excel sheet and analyzed on various endpoints and outcomes. Two authors independently checked the veracity of data.

3. Results

Overall, 28 articles were found to report the original case(s) from the database of PubMed (24/28) and Google Scholar (4/28) [17–44]. A total of 101 cases of mucormycosis (including confirmed [95/101] and suspected [6/101]) in people with confirmed (RT-PCR diagnosis) COVID-19 were retrieved (Table 1). Largely, 82 cases (81.2%) of mucormycosis in patients with COVID-19 were reported from India, followed by 9 cases (8.9%) from USA and 3 cases (3.1%) from Iran. Only 19 (18.8%) cases as of now were reported from other parts of the world. One study by Satish et al. [25] that reported 11 case-series of mucormycosis in people with COVID-19 from India lacked granular detail of every patient and therefore excluded from some of the analysis. Pooled data from this study showed mucormycosis was predominantly seen in males (78.9%), both in people who were active (59.4%) or recovered (40.6%) from COVID-19. Recovered COVID-19 was defined as those who were either discharged from hospital or in-hospital but 2-weeks had passed post-detection, although there was evident overlap across the cases. Hyperglycemia at presentation (due to pre-existing DM or new-onset hyperglycemia or new-onset diabetes or diabetic ketoacidosis [DKA]) was the single most important risk factor observed in majority of cases (83.3%) of mucormycosis in people with COVID-19, followed by cancer (3.0%). Pre-existing DM accounted for 80% of cases, while concomitant DKA was present in nearly 15% of people with mucormycosis and COVID-19. History of corticosteroid intake for the treatment of COVID-19 was present in 76.3% of cases, followed by remdesivir (20.6%) and tocilizumab (4.1%). Commonest organ involved with mucormycosis was nose and sinus (88.9%), followed by rhino-orbital (56.7%) and ROCM type (22.2%). Overall mortality was noted in 30.7% of the cases. Table 2 summarizes the findings from 101 cases of mucormycosis in people with COVID-19.

4. Discussion

Although mucormycosis is an extremely rare in healthy individuals but several immunocompromised conditions predispose it. This includes uncontrolled DM with or without DKA, hematological and other malignancies, organ transplantation, prolonged neutropenia, immunosuppressive and corticosteroid therapy, iron overload or hemochromatosis, deferoxamine or desferrioxamine therapy, voriconazole prohylaxis for transplant recipients, severe burns, acquired immunodeficiency syndrome (AIDS), intravenous drug abusers, malnutrition and open wound following trauma [45]. Mucormycosis can involve nose, sinuses, orbit, central nervous system (CNS), lung (pulmonary), gastrointestinal tract (GIT), skin, jaw bones, joints, heart, kidney, and mediastinum (invasive type), but ROCM is the commonest variety seen in clinical practice worldwide [45]. It should be noted that term ROCM refers to the entire spectrum ranging from limited sino-nasal disease (sino-nasal tissue invasion), limited rhino-orbital disease (progression to orbits) to rhino-orbital-cerebral disease (CNS involvement) [46]. The area of involvement may differ due to underlying condition. For example, ROCM is frequently observed in association with uncontrolled diabetes and DKA, whereas pulmonary involvement is often observed in patients having neutropenia, bone marrow and organ transplant, and hematological malignancies, while GIT gets involved more in malnourished individuals. Giant cell invasion, thrombosis and eosinophilic necrosis of the underlying tissue is the

Table 1
Mucormycosis in COVID-19 – Summary of 101 cases reported world-wide till May' 2021.

First author	Place (of report)	N	Age, range, M/F	Comorbidities		Confirmed/ Suspected COVID-19 (Active/Recovered)	Treatment received for COVID-19			Confirmed/Suspected Mucor	Location of mucormycosis						Outcome
				DM	Cancer		Steroid	Tocilizumab	Remdesivir		Nasal/ Sinus	Orbit	CNS	Bone	Lung	GIT	
Case report/series from India																	
Mehta et al.[17]	Mumbai	1	60, M	Y	N	Confirm, A	Y	Y	N	Confirm	Y	Y	N	N	N	N	Death
Garg et al.[18]	Chandigarh	1	55, M	Y	N	Confirm, A	Y	N	Y	Confirm	N	N	N	N	Y	N	Improving
Maini et al.[19]	Mumbai	1	38, M	N	N	Confirm, R	Y	N	Y	Confirm	Y	Y	N	N	N	N	Improved
Saldanha et al.[20]	Mangalore	1	32, F	Y	N	Confirm, A	NR	NR	NR	Confirm	Y	Y	N	N	N	N	Improved
Revannavar et al.[21]	Mangalore	1	Middle age, F	Y, NDD	N	Confirm, A	N	N	N	Confirm	Y	Y	Y	N	N	N	Improving
Sen et al.[22]	Mumbai	6	46.2–73.9, M: 6	Y: All	N	Confirm, A: 1 R: 5	Y: 5 N: 1	N	N	Confirm: 5, Suspect: 1	Y: All	Y: All	Y: 5 N: 1	N	N	N	Improving
Sarkar et al.[23]	Puducherry	10	27-67, M: 8 F: 2	Y: All, DKA: 9	N	Confirm, A: 10	Y: 10	N	Y: 5 N: 5	Confirm: 6, Suspect: 4	Y: All	Y: All	Y: 1	N	N	N	Death: 4, Improved: 2, Unchanged: 4
Mishra et al.[24]	Bangalore	10	37-78, M: 9 F: 1	Y: 8 N: 2	N	Confirm, A: 10	Y: 6 N: 4	Y: 1 N: 9	Y: 6 N: 4	Confirm: All	Y: All	Y: 2	N	Y: 1	N	N	Death: 4 Improved: 5 LFU: 1
Satish et al.[25]	Bangalore	11	30-74, M: NR F: NR	Y: Majority	Y: 1 (Leukemia)	Confirm, A: 11	N	N	N	Confirm: All	Y: Majority	Y: Majority	Y: NR	N	N	N	Death: 2 LAMA: 5 Improving: 4
Moorthy et al.[26]	Bangalore	17	39-73, M: 15 F: 2	Y: 15 N: 2	N	Confirm, A: 4 R: 13	Y: 15 N: 2	N	N	Confirm: All	Y: All	Y: 11 N: 6	Y: 8 N: 9	Y: 14 N: 3	N	N	Death: 7 Alive: 9 LFU: 1
Sharma et al.[27]	Jaipur	23	NR M: 15 F: 8	Y: 21 N: 2	N	Confirm, A: 4 R: 19	Y: All	N	N	Confirm: All	Y: All	Y: 10	Y: 2	N	N	N	Death: 0 LFU: 2 Alive: 21
Case report/series from other parts of world																	
Hanley et al.[28]	UK	1	22, M	N	N	Confirm, A	NR	NR	NR	Confirm: Autopsy	N	N	N	N	Y	N	Autopsy report
Dallalzadeh et al.[29]	USA	2	36, M 48, M	Y:2 DKA: 2	N	Confirm, A: 2	Y:2	N	Y:2	Confirm: 1 Suspected: 1	Y	Y	Y	N	N	N	Death: 1 Unchanged: 1
Werthman-E et al.[30]	USA	1	33, F	N, DKA	N	Confirm, A	N	N	N	Confirm	Y	Y	N	N	N	N	Improving
Placik et al.[31]	USA	1	49, M	N	N	Confirm, A	Y	Y	Y	Confirm	N	N	N	N	Y	N	Death
Mekkonen et al.[32]	USA	1	60, M,	T1DM	N	Confirm, A	Y	N	Y	Confirm	Y	Y	N	N	N	N	Death
Alekseyev et al.[33]	USA	1	41, M	T1DM, DKA	N	Confirm, A	Y	N	N	Confirm	Y	N	Y	N	N	N	Recovered
Johnson et al.[34]	USA	1	79, M	Y	N	Confirm, A	Y	N	Y	Confirm, AF +	N	N	N	N	Y	N	Improving
Kanwar et al.[35]	USA	1	56, M	N	N	Confirm, A	Y	Y	N	Confirm	N	N	N	N	Y	N	Death
Khatri et al.[36]	USA	1	68, M	Y	N, (HT)	Confirm, R	Y	N	N	Confirm	N	N	N	N, Skin	N	N	Death
Monte Junior et al.[37]	Brazil	1	86, M	N	N	Confirm, A	N	N	N	Confirm	N	N	N	N	N	Y	Death
Pasero et al.[38]	Italy	1	66, M	N	N	Confirm, A	N	N	N	Confirm	Y	N	N	N	Y	N	Death
Bellanger et al.[39]	France	1	55, M	N	Y, (Lymphoma)	Confirm, A	N	N	N	Confirm, AF +	N	N	N	N	Y	N	Death
Karimi-G et al.[40]	Iran	1	61, M	N, NOD	N	Confirm, R	Y	N	Y	Confirm	Y	Y	N	N	N	N	Improving
Veisi et al.[41]	Iran	2	40, F:1; 54, M:1	N: 1 Y:1	N	Confirm, A: 2	Y: 2	N: 2	Y: 2	Confirm, All	Y: 2	Y: 2	Y: 1 N: 1	N	N	N	Death: 1 Recovered: 1

(*continued on next page*)

Table 1 (*continued*)

First author	Place (of report)	N	Age, range, M/F	Comorbidities		Confirmed/Suspected COVID-19 (Active/Recovered)	Treatment received for COVID-19			Confirmed/Suspected Mucor	Location of mucormycosis						Outcome
				DM	Cancer		Steroid	Tocilizumab	Remdesivir		Nasal/ Sinus	Orbit	CNS	Bone	Lung	GIT	
Sargin et al.[42]	Turkey	1	56, F	Y, DKA	N	Confirm, R	Y	N	N	Confirm	Y	Y	Y	N	N	N	Death
Waizel-H et al.[43]	Mexico	1	24, F	N, DKA	N	Confirm, A	N	N	N	Confirm	Y	Y	N	N	N	N	Death
Zurl et al.[44]	Austria	1	53, M	N	Y, (Leukemia)	Confirm, A	N	N	N	Confirm, Autopsy	N	N	N	N	Y	N	Death

DM: Diabetes mellitus, CNS: Central nervous system, GIT: Gastro-intestinal tract, M: Male, F: Female, T1DM: Type 1 diabetes mellitus, DKA: Diabetic ketoacidosis, NOD: New-onset diabetes, NDD: Newly detected diabetes, A: Active COVID-19, R: Recovered COVID-19, Y: Yes, N: No, HT: Heart transplant, AF: Aspergillosis fungi, LFU: Lost to follow-up, LAMA: Left against medical advice.

pathological hallmark of mucormycosis. Microbiological identification of the hyphae based on diameter, presence or absence of septa, branching angle (right or acute branching), and pigmentation, differentiates it from other fungal infections. The 1950 Smith and Krichner [47] criteria for the clinical diagnosis of mucormycosis are still considered to be gold standard and include:

(i) Black, necrotic turbinate's easily mistaken for dried, crusted blood,
(ii) Blood-tinged nasal discharge and facial pain, both on the same side,
(iii) Soft peri-orbital or peri-nasal swelling with discoloration and induration,
(iv) Ptosis of the eyelid, proptosis of the eyeball and complete ophthalmoplegia and, (*v*) Multiple cranial nerve palsies unrelated to documented lesions.

A 2019 nationwide multi-center study of 388 confirmed or suspected cases of mucormycosis in India prior to COVID-19, Prakash et al. found that 18% had DKA and 57% of patients had uncontrolled DM [48]. Similarly, in a data of 465 cases of mucormycosis without COVID-19 in India, Patel et al. [49] has shown that rhino-orbital presentation was the most common (67.7%), followed by pulmonary (13.3%) and cutaneous type (10.5%). The predisposing factors associated with mucormycosis in Indians include DM (73.5%), malignancy (9.0%) and organ transplantation (7.7%) [49]. Presence of DM significantly increases the odds of contracting ROCM by 7.5-fold (Odds ratio 7.55, $P = 0.001$) as shown in a prospective Indian study, prior to COVID-19 pandemic [50]. In a recent systematic review conducted until April 9, 2021 by John et al. [51] that reported the findings of 41 confirmed mucormycosis cases in people with COVID-19, DM was reported in 93% of cases, while 88% were receiving corticosteroids. These findings are consistent with our findings of even larger case series of 101 mucormycosis cases (95 confirmed and 6 suspected) in Covid-19, where 80% cases had DM, and more than two-third (76.3%) received a course of corticosteroids. Collectively, these findings suggest a familiar connection of mucormycosis, diabetes and steroid, in people with COVID-19.

Since there are no studies that compared patients of mucormycosis in non-diabetic COVID-19 who did not receive steroids versus COVID-19 patients who received steroids and developed mucormycosis, it is difficult to establish a causal effect relationship between COVID-19 and mucormycosis in relation to corticosteroids. Nonetheless, there appears to be a number of triggers that may precipitate mucormycosis in people with COVID-19 in relation to corticosteroids:

(i) Presence of DM with or without DKA increases the risk of contracting mucormycosis and DM is often associated with an increased severity of COVID-19,
(ii) Uncontrolled hyperglycemia and precipitation of DKA is often observed due to corticosteroid intake. Low pH due to acidosis is a fertile media for mucor spores to germinate. Moreover, steroid use reduces the phagocytic activity of WBC (both first line and second line defense mechanism), causes impairment of bronchoalveolar macrophages migration, ingestion, and phagolysosome fusion, making a diabetic patient exceptionally vulnerable to mucormycosis.
(iii) COVID-19 often causes endothelialitis, endothelial damage, thrombosis, lymphopenia, and reduction in $CD4^+$ and $CD8^+$ T-cell level and thus predisposes to secondary or opportunistic fungal infection,
(iv) Free available iron is an ideal resource for mucormycosis. Hyperglycemia causes glycosylation of transferrin and

Table 2
Characteristics of 101 patients of mucormycosis with COVID-19.

Confirmed mucormycosis, N = 101		n, (%)	Remarks and limitations
Country reported (Published)	India	82 (81.2)	Highest cases reported from India. ≈ denotes nearest rounded of value.
	USA	9 (8.9)	
	Iran	3 (≈3.0)	
	UK	1 (≈1.0)	
	France	1 (≈1.0)	
	Italy	1 (≈1.0)	
	Brazil	1 (≈1.0)	
	Turkey	1 (≈1.0)	
	Mexico	1 (≈1.0)	
	Austria	1 (≈1.0)	
Age (Years)		Range 22-86	–
Sex	Male	71/90 (78.9)	More commonly observed in males.
	Female	19/90 (21.1)	
COVID-19 status	Active	60/101 (59.4)	Exact definition of active and recovered cases of COVID-19 was different and not unanimous.
	Recovered	41/101 (40.6)	
Risk factors	Hyperglycemia at presentation	75/90 (83.3)	No unanimous definition of hyperglycemia.
	Malignancy	3/101 (3.0)	2 Leukemia, 1 Lymphoma
	Post-transplant	1/101 (1.0)	1 Heart transplant
Hyperglycemia at presentation	Pre-existing DM	72/90 (80.0)	Unless reported as insulin-dependent or type 1 diabetes, all cases were assumed as type 2 diabetes. Lack of baseline HbA1c data and duration of diabetes for majority of DM patients.
	Types of DM[#]	–	
	Type 2 diabetes	70/72 (97.2)	
	Type 1 diabetes	2/72 (2.8)	
	New-onset DM/hyperglycemia	2/90 (2.2)	
	Presented with DKA	15/101 (14.9)	
Treatment history of COVID-19	Steroid	74/97 (76.3)	Few cases were received all 3 drugs for COVID-19.
	Tocilizumab	4/97 (4.1)	
	Remdesivir	20/97 (20.6)	
Mucormycosis	Confirmed	95/101 (94.1)	Confirmed denotes microbiological or histopathological diagnosis.
	Suspected	6/101 (5.9)	
Location of mucormycosis	Nasal/Sinus	80/90 (88.9)	There appears to have an overlap between Nasal/Sinus only and Rhino-orbital variety.
	Rhino-orbital	51/90 (56.7)	
	Rhino-orbito-cerebral	20/90 (22.2)	
	Bone involvement	15/101 (14.9)	
	Pulmonary	8/101 (7.9)	
	Gastrointestinal	1/101 (1.0)	
	Cutaneous	1/101 (1.0)	
Outcomes	Alive (Improved/Improving)	56/101 (55.4)	Outcomes is difficult to assess considering that several cases were still under in-hospital treatment and their final outcome are not yet known.
	Unchanged	5/101 (5.0)	
	Death	31/101 (30.7)	
	Status unknown (LFU, LAMA)	9/101 (8.9)	

DM: Diabetes mellitus, DKA: Diabetic ketoacidosis, LFU: Lost to follow-up, LAMA: Left against medical advice.

ferritin, and reduces iron binding allowing increased free iron. Moreover, increase in cytokines in patients with COVID-19 especially interleukin-6, increases free iron by increasing ferritin levels due to increased synthesis and decreased iron transport. Furthermore, concomitant acidosis increases free iron by the same mechanism and additionally by reducing the ability of transferrin to chelate iron,

(v) High glucose, low pH, free iron, and ketones in presence of decreased phagocytic activity of WBC, enhances the growth of mucor. In addition, it enhances the expression of glucose-regulator protein 78 (GRP-78) of endothelium cells and fungal ligand spore coating homolog (CotH) protein, enabling angio-invasion, hematogenous dissemination and tissue necrosis [52].

Fig. 1 depicts the postulated mechanism of increased propensity of having mucormycosis infection in COVID-19 patients.

There are certain limitations to conduct this kind of systematic review based on case reports/series subject to publication biases and considerable heterogeneity in reporting cases. It is highly likely that reported cases of mucormycosis may be an underrepresentation of the real burden owing to difficulty in making a microbiological or histopathological diagnosis especially in a raging pandemic setting. While some case reports had every minute detail, other did not report important parameter, for example – duration of DM, lack of baseline HbA1c data in majority of cases. Secondly, the lack of a denominator value may not allow the true estimation of mucormycosis incidence in people with COVID-19 compounded by the lack of control. Thirdly, defining active and recovered COVID-19 and its relation to the onset of mucormycosis could be difficult considering the lower sensitivity of confirmatory RT-PCR. Finally, evaluating the outcomes in people with mucormycosis and COVID-19 could be difficult at the moment because these case reports have been published while many of these patients are still under treatment. Other minor limitations have been highlighted in Table 2.

5. Conclusions

Increase in mucormycosis in Indian context appears to be an unholy intersection of trinity of diabetes (high prevalence genetically), rampant use of corticosteroid (increases blood glucose and

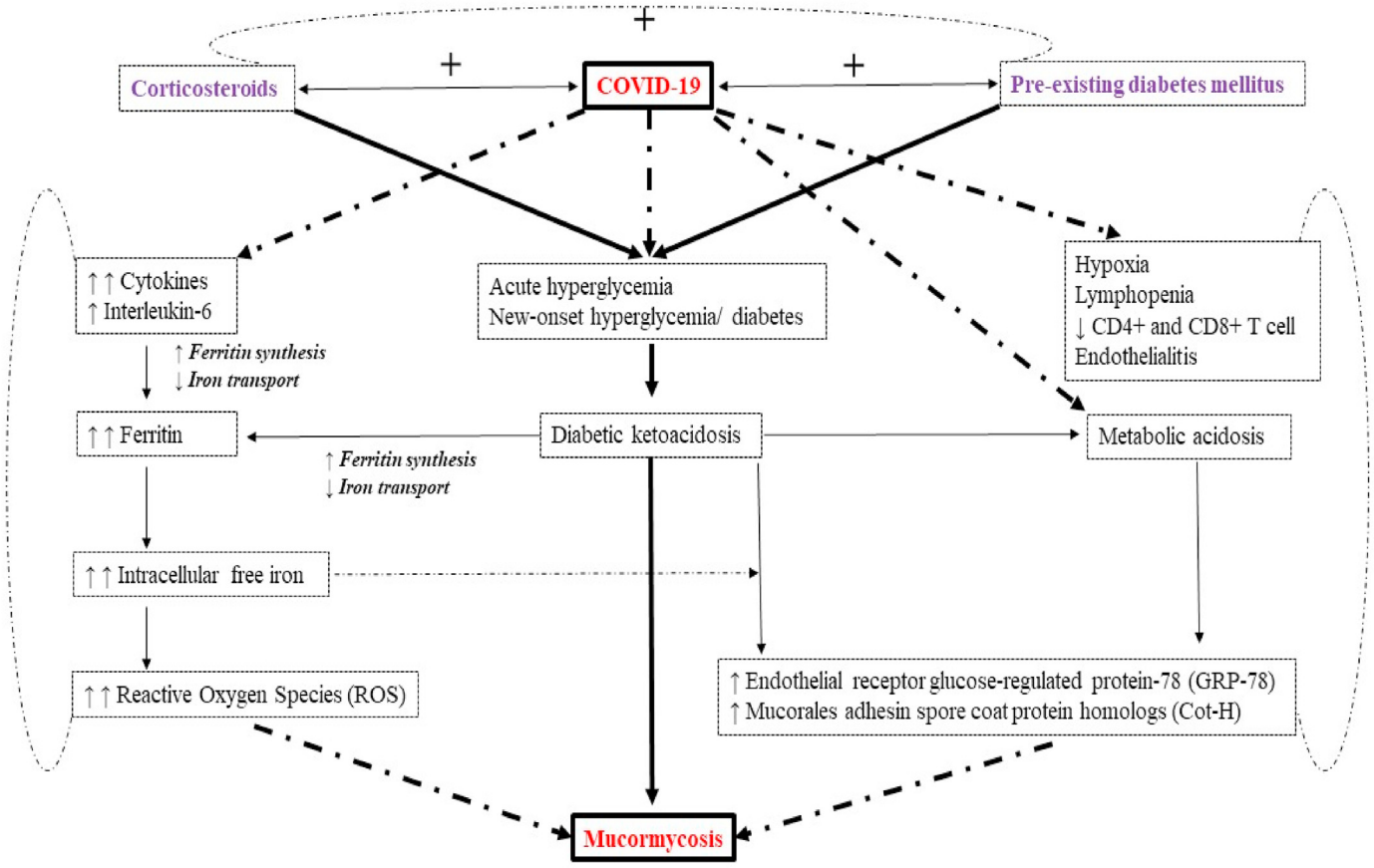

Fig. 1. Postulated interaction of diabetes, corticosteroid and COVID-19 with mucormycosis.

opportunistic fungal infection) and COVID-19 (cytokine storm, lymphopenia, endothelial damage). All efforts should be made to maintain optimal hyperglycemia and only judicious evidence-based use of corticosteroids in patients with COVID-19 is recommended in order to reduce the burden of fatal mucormycosis.

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Author's contribution

AKS conceptualized, searched the literature and wrote first draft; RS made the tables, analyzed the data and revised the first draft, SRJ and AM edited the final draft. All authors agreed mutually to submit for publication.

Authorship

All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship and take responsibility for the integrity of the work. They confirm that this paper will not be published elsewhere in the same form, in English or in any other language, including electronically.

Declaration of competing interest

We hereby declare that we have no conflict of interest, related to this article titled “Mucormycosis in COVID-19: A Systematic Review of Cases Reported Worldwide and in India”.

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