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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Muthu V, Agarwal R, Patel A, et al. Definition, diagnosis, and management of COVID-19-associated pulmonary mucormycosis: Delphi consensus statement from the Fungal Infection Study Forum and Academy of Pulmonary Sciences, India. *Lancet Infect Dis* 2022; published online April 4. https://doi.org/10.1016/S1473-3099(22)00124-4.

Supplementary appendix:

Article title: Definition, diagnosis, and management of COVID-19-associated pulmonary mucormycosis: Delphi consensus statement from the Fungal Infection Study Forum and Academy of Pulmonary Sciences (FISF-APS), India.

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Supplemental tables:

Table S1: Prevalence of COVID-19-associated mucormycosis (CAM) and COVID-19-associated pulmonary mucormycosis (CAPM) from the published literature

Country	Reference	Prevalence of CAM	Prevalence of CAPM
India	Patel et al(6)	0.27% of hospitalized COVID-19 1.6% of COVID-19 patients in ICU	0.15% of hospitalized COVID-19
India	Ramaswami et al(14)	4.3% (70/1,647) ED admission	
India	Selarka et al(15)	1.8% of hospitalized COVID-19	NA
Chile	Rabagliati et al(19)	-	0.12% of hospitalized COVID-19
Germany	Seidel et al(16)	0.15% to 0.67% of hospitalized COVID-19 In COVID-19 ICU patients, 1.47% to 1.68%	- -
Mexico	Guzmán-Castro et al(13)	0.04% of COVID-19 diagnosed during the study period (both hospitalized and non-hospitalized)	0.007% of COVID-19 (both hospitalized and non-hospitalized) during the study period
France	Danion et al(18)	0.004% of COVID-19 hospitalized in France during the study period	0.004% of COVID-19 hospitalized in France during the study period
Turkey	Bayram et al(17)	0.03% of hospitalized COVID-19	NA
France	Gangneux et al(12)		1% of mechanically ventilated subjects COVID-19

COVID-19 – coronavirus disease; ED – emergency department; ICU -intensive care unit

Table S2: Computed tomography findings of COVID-19-associated pulmonary mucormycosis (CAPM) versus COVID-19-associated pulmonary aspergillosis (CAPA)

Highly suggestive	**CAPM**	**CAPA***
Thick-walled cavity	+++	++
Reversed halo sign	+++	+
Large consolidation or necrotizing pneumonia	+++	++
Mycotic aneurysm	+++	+
Bird's nest sign	+++	+
Multiple large nodules (nodules >1cm)	+++	++
Halo sign	+	+++
Air crescent sign	+	+++
Suggestive		
Pleural effusion	+++	+
Non-specific		
Pneumothorax	++	++
Centrilobular nodules or tree-in-bud appearance	-	+++

*or dual infections

Table S3: Diagnosis of dual infections, COVID-19-associated pulmonary mucormycosis (CAPM) versus COVID-19-associated pulmonary aspergillosis (CAPA) in different categories

Category	**Diagnostic features**
Proven CAPM with Proven CAPA	Lung aspirate/biopsy/pleural fluid with: 1. Aseptate and septate hyphae seen on histopathology/direct microscopy 2. Aseptate hyphae on microscopy with *Aspergillus* growing in culture 3. Septate hyphae on microscopy with Mucorales growing in culture 4. Growth of both *Aspergillus* and Mucorales in culture Culture positivity should prompt a search for corresponding hyphal morphology in the original specimen
Proven CAPM with probable CAPA	Lung aspirate/biopsy/pleural fluid with aseptate hyphae or Mucorales grown in culture AND BAL fluid showing septate hyphae or BAL growing *Aspergillus* or serum GM ODI >0.5 or BAL GM ODI >1
Proven CAPM with possible CAPA	Lung aspirate/biopsy/pleural fluid with aseptate hyphae or growth of Mucorales AND Non-BAL LRT sample showing septate hyphae/growth of *Aspergillus* or non-BAL GM ODI >4.5 or non-BAL GM ODI >1.2 on at least two occasions
Probable CAPM with proven CAPA	Lung aspirate/biopsy/pleural fluid with septate hyphae or *Aspergillus* grown in culture AND Aseptate hyphae on cytology or direct microscopy or growth of Mucorales in BAL fluid
Probable CAPM with probable CAPA	Clinical and radiological features consistent with CAPM/CAPA with: 1. Aseptate hyphae on cytology or direct microscopy or growth of Mucorales in BAL fluid AND 2. BAL fluid showing septate hyphae or growth of *Aspergillus* or serum GM ODI >0.5 or BAL GM ODI >1
Probable CAPM with possible CAPA	Clinical and radiological features consistent with CAPM/CAPA with: 1. Aseptate hyphae on cytology/direct microscopy or growth of Mucorales in BAL fluid AND 2. Non-BAL LRT sample showing septate hyphae or growth of *Aspergillus* or non-BAL GM >4.5 or non-BAL GM>1.2 on at least two occasions

BAL: bronchoalveolar lavage; GM: galactomannan; LRT: Lower respiratory tract; Non-BAL: non-bronchoscopic specimens like mini-BAL or bronchial wash or endotracheal aspirates; ODI: optical density index

Supplemental figures:

Figure S1: The Delphi methodology followed in the development of consensus opinion for defining, diagnosing, and managing COVID-19-associated pulmonary mucormycosis (CAPM)

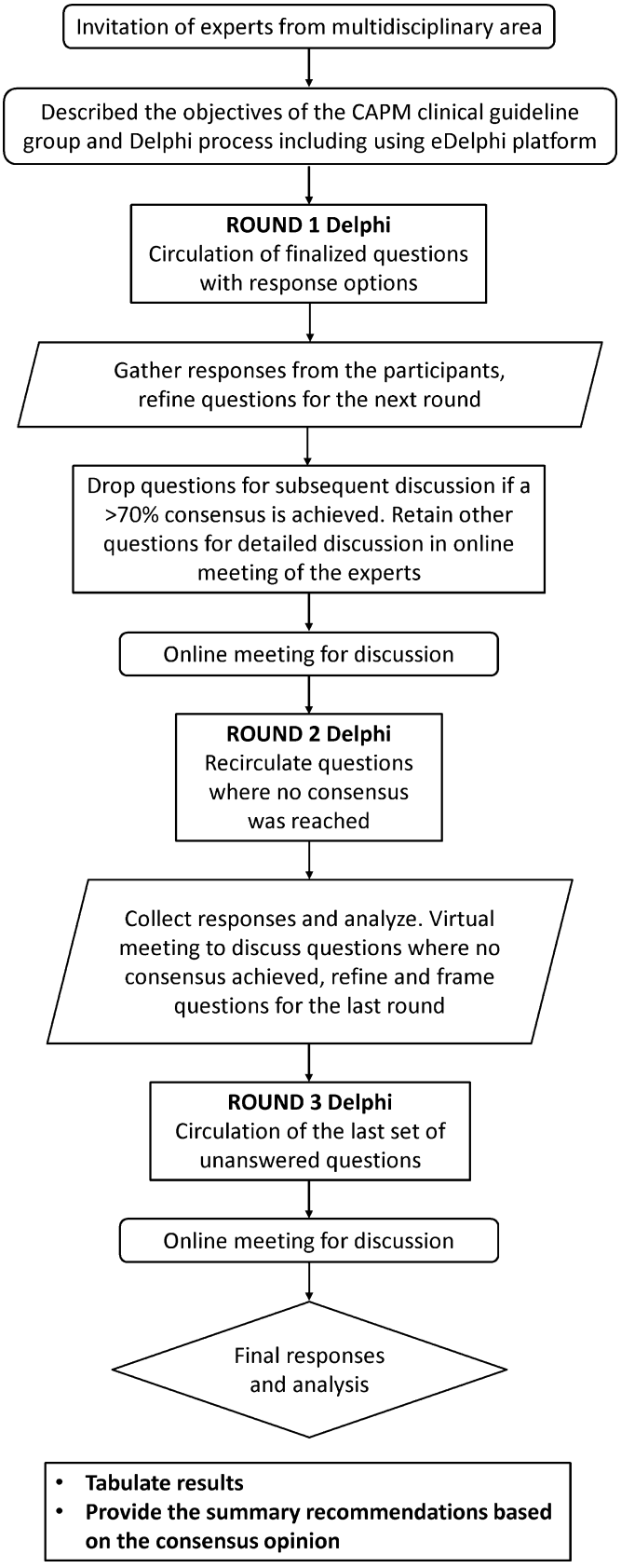


Figure S2: Forest plot showing the prevalence of COVID-19-associated pulmonary mucormycosis (CAPM) among hospitalized COVID-19 patients. Each square represents the proportion of patients with CAPM, and the horizontal line represents the corresponding 95% confidence interval. The pooled proportion of CAPM among subjects hospitalized with COVID-19 is presented as a diamond.

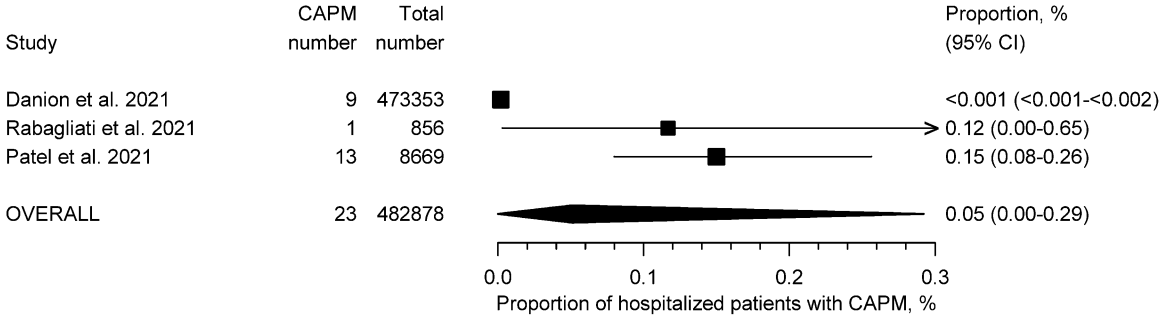


Figure S3: Computed tomography findings in patients with microbiologically confirmed COVID-19-associated pulmonary mucormycosis (CAPM): (A) reversed halo sign evolving into a cavity (white arrow) on the left side along with mild pleural effusion (black arrowhead), also seen are intralobular septal thickening on the contralateral lung (white arrowhead). (B) Imaging from another CAPM patient demonstrating a cavity (black arrow) on the left side with intracavity contents and internal septations. (C) Mediastinal window of a patient with proven CAPM showing abscess in the right lower lobe with mycotic aneurysm (white arrow) and minimal pleural effusion.

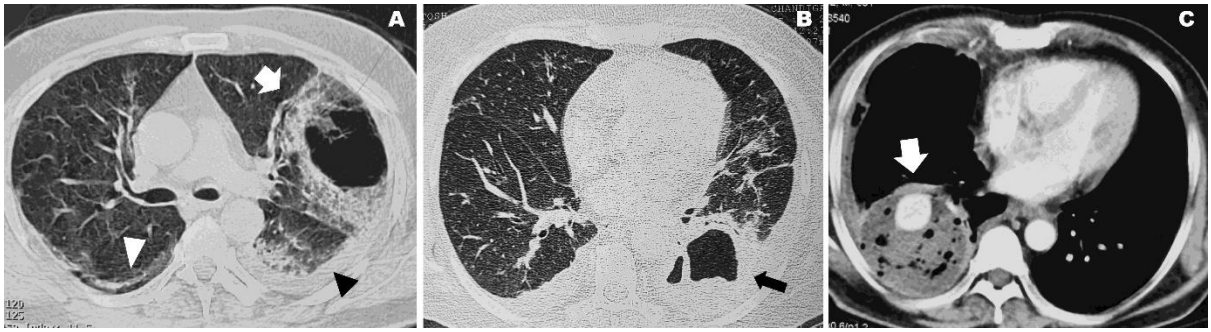
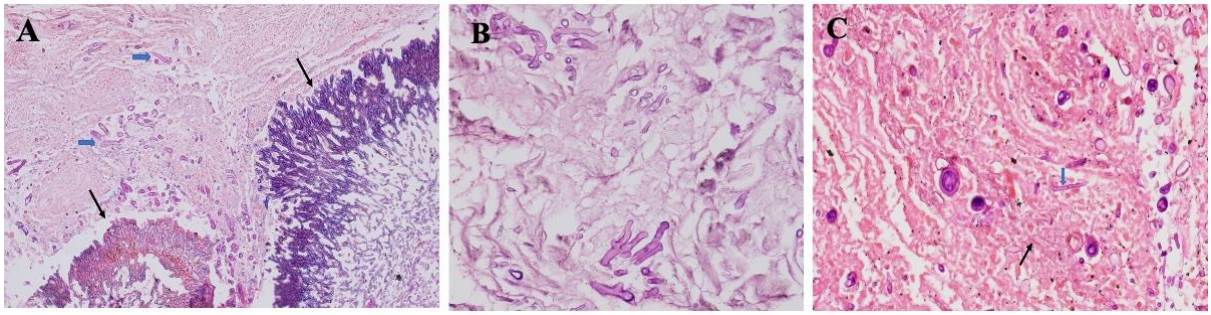


Figure S4: Panel A shows the photomicrograph of a cavity colonized by entangled mass of fungal hyphae conforming to the morphology of *Aspergillus* (black arrows) and the periphery showing infarcted lung parenchyma with fungal hyphae suggestive of mucormycosis. Panel B demonstrates the morphology of fungi conforming to mucormycosis that is better appreciated in this photomicrograph obtained from a site away from the cavity wall. Panel C shows the photomicrograph of bland necrosis with numerous fungal hyphae; some with thin wall and foldable consistent with Mucormycosis (black arrow) and some with septate hyphae conforming to the morphology of *Aspergillus* (blue arrow).



Methodology of systematic review:

We performed a systematic review (Figure) of the PubMed and Embase databases (till 25th September 2021), using the following free text search terms: ("COVID" OR "SARS-CoV" OR "coronavirus") AND (mucor* OR "zygomycosis"). The references obtained from the search were imported to a commercially available reference manager software (Endnote). After excluding duplicate citations and unrelated articles, we reviewed 236 articles in detail. We reviewed the articles reporting cases of COVID-19-associated pulmonary mucormycosis (CAPM), relevant review articles and large series of COVID-19-associated mucormycosis (CAM) to identify the questions to be addressed. Three authors (VM, RA, and AC) formulated the initial set of questions based on the literature review. The questions were further refined by incorporating the comments received from the CAPM guideline group.

Citations reviewed for formulating the questions for Delphi consensus are provided below:

Article describing cases of CAPM: (n=25)[1-25]

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