Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letters to the Editor

Should statins be considered for the management of mucormycosis in COVID-19?

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Dear Editor

Mucormycosis has emerged as the newest threat among Coronavirus disease-2019 (COVID-19) patients [1]. Among 101 worldwide mucormycosis cases, 81.2% were from India alone during COVID-19 [2]. Hypoxia, hyperglycemia, acidosis, hyperferritinemia, and rampant steroid use create a fertile soil for Rhizopus to grow [2]. While diabetes and COVID-19 form unholy association since inception [3], advent of mucormycosis forms the deadly trinity (mortality rate ~30.7%) [2]. Hyperglycemia, found in 83.3% cases, is the single most important risk factor for developing mucormycosis among COVID-19 patients [2]. Prompt diagnosis, normoglycemia, tapering of glucocorticoids, anti-fungals and surgical debridement are the cornerstones of management [4].

While amphotericin-B is the drug of choice, posoconazole and isavucoanzoleare alternatives [5]. Due to upsurge of both COVID-19 and mucormycosis, scarcity of these drugs has raised concern [6]. Authorities have cautioned against the use of prophylactic antifungals to curb mucormycosis [7]. Thus, there is urgent requirement of alternative, cheaper medications. In this context we examine whether statins can be repurposed as potential *anti*-COVID-19-cum-*anti-Rhizopus* therapy to combat mucormycosis.

There is growing interest regarding statins to be deployed against COVID-19 because of their multifaceted pleiotropic effects [8,9]. Multiple studies and meta-analyses have shown improved

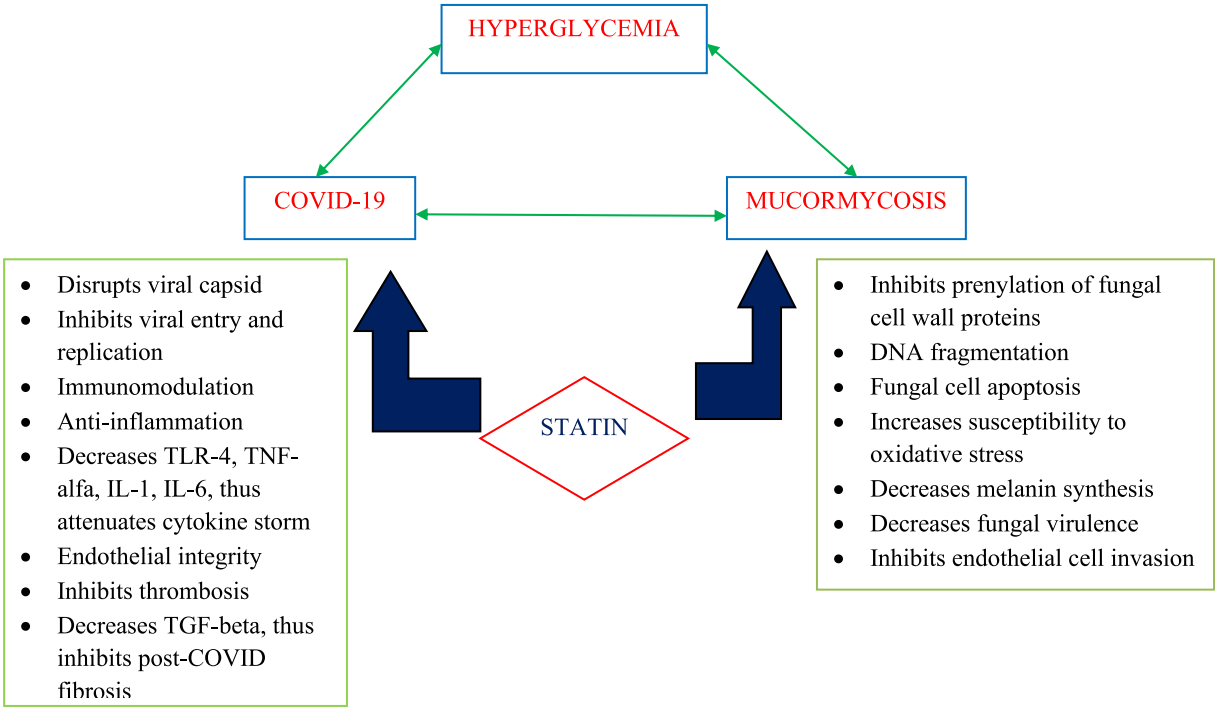

Fig. 1. Mechanisms by which statins act against deadly duo of COVID-19 and mucormycosis.
(TLR- Toll like receptor, TNF- Tumor necrosis factor, IL- Interleukin, TGF- Transforming growth factor).

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outcome among COVID-19 patients with history of taking statins [10–13]. Unfortunately, there is no randomized control trial available to explore the efficacy and benefits of statins in COVID-19 at present.Anti-fungal potential of statins is well-known and widespread use of statins is one of the reasons behind the lesser incidence of zygomycosis among diabetics since 1990s [14]. Lovastatin caused apoptosis of *Mucor racemosus* [15]. Amphotericin-B in combination with atorvastatin or lovastatin against *Rhizopus oryzae* was more effective than amphotericin-B alone [16]. Similar success has been noticed with fluvastatin and rosuvastatin against *Rhizomucor* and *Rhizopus* [17].I nvestigators showed statins impaired fungal morphogenesis by inhibiting isoprenylation of vital cell wall proteins, decreased germination, induced DNA fragmentation, increased susceptibility to oxidative stress, attenuated fungal virulence and prevented endothelial invasion (independent of GRP78/CotH interactions) [18]. Although these data from cell-basedand animal studies are encouraging, real world clinical data and human studies are needed to know whether statins reach enough tissue concentration to exert their antifungal activity when administered in usual therapeutic dosage (Fig. 1).

Diabetic patients, commonly being dyslipidemic should be screened for it and statins should be started without delay. Whether normolipdemic patients with diabetes on steroids are potential candidates for statin to prevent mucormycosis is to be explored. Although statins have been found to be safe among COVID-19 patients, their side effects and drug interactions with anti-fungals should be considered.

Authors' contribution

SC generated the concept, did the literature search and wrote the first draft which was then critically reviewed and modified by BV, DS, AM and UKO. All authors agreed upon the final form of the article.

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Declaration of competing interest

Nil.

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