

## The Potential Role of the Multi-faceted Properties of Cholesterol Lowering Agents in the Management of the Dreaded Pandemic of Covid-19

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*#NITRD also functioned as Covid-19 Centre under the aegis of Ministry of Health and Family Welfare, Government of India, f. 01-05-2021 and allotted around 100 beds for exclusive management of Covid-19 patients.*

Humanity has rarely faced such a resilient and devastating adversary such as the current pandemic caused by the SARS-CoV2 Virus or simply Covid-19. It has wiped millions of people all around the Globe with relentless savagery. However, as always, we human beings are now learning more and more about this lethal enemy. A very great effort is being performed to find protection and cure and new drugs and vaccines are being discovered. Crucially we have been partly successful in repurposing the drugs for Covid-19 which were already being used for different purposes.

In this short review, we examine the anti-viral and anti-inflammatory properties of a drug that is used quite routinely in the management of Dyslipidaemias – Statins! It seems peculiar that the Covid-19 virus would be in any way susceptible to the effects of such a drug as the connection seems lacking. However, during the fatal Ebola Virus (EBOV) outbreak in West Africa, statins showed evidence of effectiveness in decreasing the infectivity by reduced processing of certain glycoproteins and they are subsequent entries in EBOV [1]. With the passage of time, there is accumulating evidence about the versatile properties of the Statins. The statins apart from their cholesterol-lowering effect also exhibit a multitude of Pleiotropic effects. Apart from being strong antioxidants, statins also exhibit several pleiotropic effects such as endothelial dysfunction improvement, increased nitric oxide bioavailability, anti-inflammatory action, and atherosclerotic plaque stability [2].

Much of the damage that occurs in Covid-19 Pneumonia is not by the virus per se but because of the strong inflammatory response of the body to it leading to a deluge of pro-inflammatory cytokines such as IL-1 $\beta$ , TNF- $\alpha$ , and IL-6, a process which is often described as the Cytokine storm [3]. With further progression, the organs start getting damaged, and ultimately death ensues. Hence it can be said that our

own saviors turn upon us to wreak havoc and death, instigated by our lethal enemy, the Covid-19 virus.

There is some evidence which suggests that Statins when administered to Hospitalized patients with Covid-19 infection may lead to a favourable outcome. But there is still a lack of robust data to endorse the routine use of Statins in Covid-19 patients. Apart from EBOV, there are other viral infections in which statins have shown beneficial effects such as Influenza. The ARDS pattern seen in Covid-19 infection is different from the usual ARDS. Though there is strong hypoxemia, there is somewhat preserved compliance of the lungs, something which is not typical of usual ARDS [4]. Hence, the respiratory distress may be disproportionately less as compared to the severity of hypoxemia. Moreover, a thrombo-embolic phenomenon because of hypercoagulability and dysfunctional endothelial response may be the chief cause of Covid related respiratory illness [5].

The protective role of statins in Covid-19 illness may also depend on the solubility of the drugs, whether hydrophilic (water-soluble) or lipophilic (fat-soluble). The target receptors through which the virus gains entry is present not only in the lungs but also in several other parts of the body such as adipose tissue and the central nervous system. Hence, in the case of lipophilic statins such as atorvastatin, the benefit may be more owing to their infiltration in the sites where hydrophilic Statins such as rosuvastatin may not be able to gain entry. This includes the blood-brain barrier and adipose tissue, the latter having a high number of ACE2 receptors [6].

Viral replication also depends a lot on lipid metabolism and the lipid-lowering properties of the Statins probably also play an important antiviral role in reducing the proliferation of the Virus. There is some concern about the adverse effects of Statins in hospitalized patients such as elevation of liver enzymes, dysglycemia, and myopathy. However, there is evidence to support the fact that this is not probably so and the potential benefit of statins in combating the illness may outweigh the risk of side effects [7].

## Conclusion

To conclude, in the fight against this dreadful pandemic, repurposed drugs are showing promising results, and in this brief review, an attempt has been made to highlight the potential role of Statins especially the lipophilic ones such as atorvastatin in the Global anti-Covid 19 crusade. The advantages of low cost and a decreased risk of

adverse effects further lends support to the utilization of this multifaceted class of agents for management of a dreadful disease. However, we need large, randomized trials to fully validate and endorse the role of the Statins in the Battle against Covid-19.

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