

# A Deadly Combination- Coronavirus and Diabetes Mellitus: Where are we now?

Mayuri Mundhe

*Navsahyadri Institute of Pharmacy, Pune*

**Abstract - Individuals with diabetes are increased risk for bacterial, viral, and parasitic infections and one of the most common co-morbidity and correlated with higher mortality. Coronavirus attacked on 160 countries and spread through animals, human to human transmission also possible. COVID-19 highlights the importance of understanding shared disease potential mechanism through two coronavirus receptor protein angiotensin converting enzyme2 (ACE2) and dipeptidyl peptidase-4 (DPP-4) establish pathway regulating inflammation, we review the basic interaction between coronavirus and Diabetes, highlighting the gap in knowledge that require further studies pertinent to deadly combination of COVID-19 patients with Diabetes Mellitus. Old age was a significant risk factor for development of severe acute respiratory syndrome (SARS-CoV-2) and the progression from SARS-CoV-2 to death.**

**Index Terms - COVID-19, Co-morbidities, Diabetes mellitus, ACC-2, DPP-4, SARS-CoV-2.**

## 1. INTRODUCTION

At the end of 2019, recently known Coronavirus has promptly transfer through China and rest of the World. The disease caused by is was named Corona Virus Disease 2019 (COVID-19) by WHO. Coronavirus are wrapped virus with non-segmented, single-stranded and positive-sense RNA genome known to cause respiratory infection in human i.e Sever acute respiratory syndrome coronavirus (SARS-CoV-2) and Middle east respiratory syndrome (MERS-CoV). COVID-19 with Diabetes Mellitus Potentiate progress of (SARS-CoV-2) and Septic shock hence multiple organ failure particularly in elderly patients. Diabetes is second most prevalent co-morbidity after hypertension in peoples hospitalized with COVID-19. The surface receptor for (SARS-CoV-2) is Angiotensin Converting Enzyme 2 (ACE2). The link between COVID-19 and Diabetes is dipeptidyl peptidase-4 (DPP-4) enzyme which functional

receptor for human coronavirus-Erasmus Medical Center (hCoV-EMC), the virus responsible for (MERS-CoV).

Aim is to analyze the negative outcomes behind the combination of Coronavirus and Diabetes Mellitus with death rate and provide answers to caregivers and patients regarding the risk factor related to diabetes for COVID-19 prognosis. The mortality rate of COVID-19 with Diabetes Mellitus up to 7.3% higher than patients without any co-morbidities 0.9% and this overview explanation for Why COVID-19 patients died of multiple organ failure. Old age and diabetes are associated with an increased risk of Frailty (Multisystem Dysregulation Syndrome). In some cases, COVID-19 infection suggests increased prevalence of frailty. Found that pneumonia, release of tissue related enzymes, excessive uncontrolled inflammation responses and hypercoagulable state associated with dysregulation of metabolism, serum ferritin and coagulation index higher in diabetic patient more susceptible to coronavirus.

## 2. POTENTIAL MECHANISMS THAT INHANCE COVID-19 PATIENTS DEATH RATE WITH DIABETES

Angiotensin converting Enzyme 2 (ACE2) and Dipeptidyl Peptidase-4 (DPP-4) are protein receptors of corona virus. (ACE2) In various organ system including brain, intestine, kidney, pancreas, alveolar AT2 cells, myocardium, lungs and shows more expression in diabetic patient. ACE2 capable of binding set of coronavirus spike proteins, including SARS-Cov-2 spike protein. More cellular binding. Hypoglycemic agents, statins, antihypertensives, ACE inhibitor upregulate ACE2. COVID-19 reduces ACE2 expression inducing cellular damage, hyperinflammation and respiratory failure. ACE expression on pancreatic B-cell which directly effect

on B-cell function induce new onset diabetes. Greater for diabetes complication like diabetic ketoacidosis (DKA).

Second potential mechanism is related to DPP-4 enzyme which is bind to MERS-CoV undergoes proteolytic activation through the cellular serine protease TMPRSS2 which allows transmembrane unit, s2, of MERS-Cov S to fuse the viral membrane to cellular membrane. DPP4 cleaves wide range of peptide hormones, chemokines and bioactive immunomodulatory proteins. Increase DPP4 expression detects lungs disease, inducing COPD. Diabetes Mellitus inhibit the neutrophil, chemotaxis, lower secretion of cytokines, polymorphonuclear leukocytes, phagocytosis and intracellular killing of microbes so impairment in adaptive immunity.

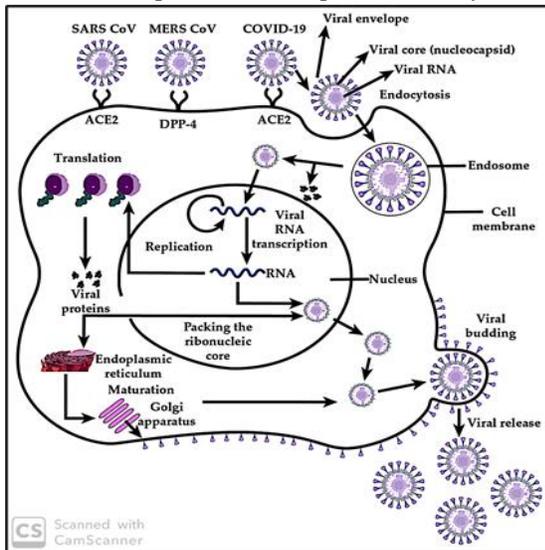


Fig. Pathogenesis of Coronavirus infection

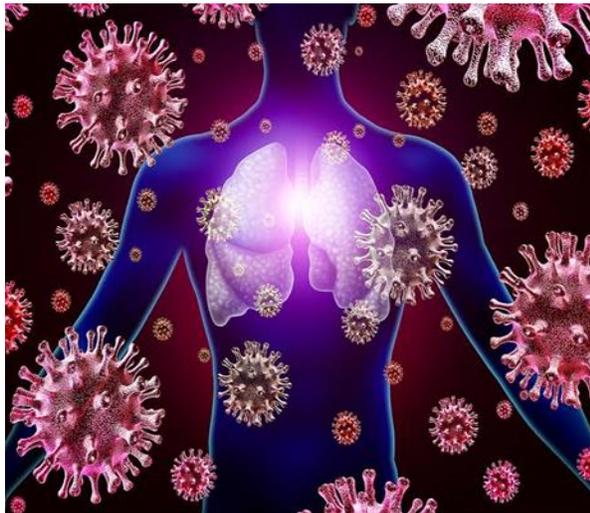


Fig. Infected Body by Coronavirus

### 3. METHODS

A precise search was performed on studies published from January 2020 to May 7, 2020, in web of science database. To identify missing studies, I checked the reference list for each search paper. According to the indices of the various databases, use the search term “2019 novel coronavirus and COVID-19” and “comorbidities, clinical characteristics, epidemiological” without any language restriction. Ratios are used to describe the risk of diabetes in severe patients compared with non-severe patient.

### 4.CONCLUSION

The available evidence shows Diabetes Mellitus is second important death factors impacting the clinical severity of coronavirus infection. ACE2 and DPP-4 this two are important physiological regulators of glucose homeostasis and the related pathways produce harm to the coronavirus infection. Patients with diabetes were older (65-99) had higher mortality but hand no significant difference in gender and other symptoms.

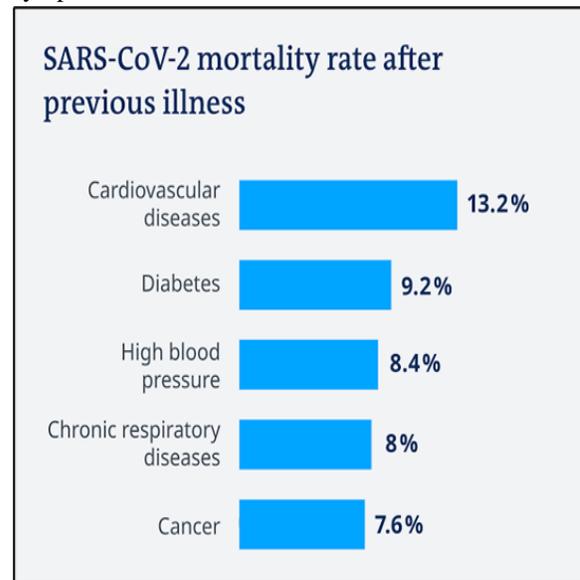


Fig. Mortality rate of COVID-19 patients with Diabetes

### REFERENCES

[1] Lei Fang, George Karakiulakis, and Michael Roth, “Are patients with hypertension and diabetes mellitus increased risk for COVID-19

- infection”, *Lancet Respir Med.* 2020 April; 8(4): e21.
- [2] Stefan R. Bornstein, Rinkoo Dalan, David Hopkins, Geltrude Mingrone and Bernhard O. Boehm, “Endocrine and metabolic link to coronavirus infection”, *Nature Reviews Endocrinology* (2020).
- [3] Ranganath Muniyappa and Sriram Gubbi, “COVID-19 pandemic, coronavirus, and diabetes mellitus”, *American Journal of Physiology Endocrinology and Metabolism*, 2020.
- [4] Jing Yang, Ya Zheng, Xi Gou, Ke Pu, Zhaofeng Chen, Qinghong Guo, Rui Ji, Haojia wang, Yuping Wang, Yongning Zhou, “Prevalence of comorbidities and its effect in patients infected with SARS-CoV-2: a systematic review and meta-analysis”, *International Journal of Infectious Disease* 94 (2020) 91-95.
- [5] Gianluca Lacobellis, “COVID-19 and diabetes; can DPP4 inhibition play a role?”, *DIABETES RESEARCH AND CLINICAL PRACTICE*: VOLUME 162, 108125, 2020.
- [6] Jun Zhou and Jie Tan, “Diabetes patients with COVID-19 need better blood glucose management in Wuhan, china”, *Metabolism*, 2020, 107:154216.
- [7] Aihong Wang, Weibo Zhao, Zhangrong Xu, Jianwen Gu, “Timely blood glucose management for the outbreak of 2019 novel coronavirus disease (COVID-19) is urgently needed”, *Diabetes Research and Clinical Practice*: VOLUME 162, 108118, 2020.
- [8] Weina Guo Mingyue Li Yalan Dong Haifeng Zhou Zili Zhang Chunxia Tian Renjie Qin Haijun Wang Yin Shen Keye Du Lei Zhao Heng Fan Shanshan Luo, Desheng Hu, “Diabetes is risk factor for the progression and prognosis of COVID-19”, *Diabetes / Metabolism Research and Reviews*, 2020.
- [9] Antonio Ceriello, Anca Pantea Stoian, Manfredi Rizzo, “COVID-19 and diabetes management: What should be considered?”, *Diabetes Research and Clinical Practice*: Volume 163, 2020, 108151.
- [10] A. J. Sinclair, A. H. Abdelhafiz, “Age frailty and diabetes- triple jeopardy for vulnerability to COVID-19 infection”, *EClinical Medicine* published by The Lancet, 2020, 100343.
- [11] Prof Stefan R Bornstein, MD; Prof Francesco Rubino, MD; Prof Kamlesh Khunti, MD; Prof Geltrude Mingrone, MD; David Hopkins, MD; Prof Andeas L Birkenfeld, et al, “Practical recommendations for the management of diabetes in patients with COVID-19”, *The Lancet Diabetes and Endocrinology*, 2020.
- [12] Daniel J Drucker, “Coronavirus Infection and Type 2 Diabetes- Shared Pathways with Therapeutic Implications”, *Endocrine Reviews: Volume 41, Issue 3*, 2020.
- [13] “Coronavirus and its impact on Diabetic Patients”, *Journl of Diabetes and Metabolism*, Issue 2155-6156.
- [14] Meredith Goodwin, MD. FAAFP, “How does COVID-19 affects people with diabetes?”, *Medical news*, 2020.
- [15] Hannah Kleine- Weber, Simon Schroeder, Markus Hoffmann, “Polymorphisms in dipeptidyl peptidase 4 reduce host cell entry of Middle East Respiratory Syndrome coronavirus”, *Emerging Microns and Infection*, 2020, 9(1): 155-168.

#### Important Links

1. <https://www.google.com/amp/s/www.endocrineweb.com/amp/62907>
2. <https://www.sciencemediacentre.org/expert-reaction-to-questions-about-high-blood-pressure-diabetes-and-ace-inhibitor-drugs-and-risk-of-covid-19-infection/>
3. <https://www.worldometers.info/coronavirus/coronavirus-age-sex-demographics>