



Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Clinical considerations for patients with diabetes in times of COVID-19 epidemic

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1. Background and epidemiology

COVID-19 (Coronavirus Disease-2019), a disease caused by the coronavirus SARS-CoV-2 (Severe Acute Respiratory Syndrome-Coronavirus-2), has emerged as a rapidly spreading communicable disease affecting more than 100 countries across the globe at present. The disease is primarily spread through large respiratory droplets, though the possibility of other routes of transmission cannot be ruled out, as the virus has been found in stool and urine of affected individuals [1]. The disease severity has varied from mild self-limiting flu-like illness to fulminant pneumonia, respiratory failure and death. There are regional variations in the mortality rates and these estimates are rapidly changing as more data are becoming available. There were 95,333 confirmed cases of COVID-19 worldwide with a mortality rate of 3.4% according to the situation report of World Health Organisation on March 5, 2020 [2]. However, a much lower mortality of 1.4% has been reported in analysis of data of 1099 patients with laboratory-confirmed COVID-19 from 552 hospitals in mainland China [3]. Considering that the number of unreported and unconfirmed cases is likely to be much higher than the reported cases, the actual mortality may be less than 1%, which is similar to that of severe seasonal influenza [4]. India has 39 confirmed cases till 10th March, 2020 and contact surveillance of these cases is going on. The understanding of epidemiological characteristics of this infection is evolving on a daily basis as the disease is spreading to different parts of the globe.

2. Diabetes, respiratory infections and COVID19

Individuals with diabetes are at risk of infections, especially influenza and pneumonia. This risk can be reduced, though not completely eliminated, by good glycaemic control. All people with diabetes (above 2 years of age) are recommended pneumococcal and annual influenza vaccinations. Not only this, patients with diabetes have a severe disease when infected with respiratory viruses. Indeed, diabetes was seen as an important risk factor for

mortality in patients infected with Pandemic Influenza A 2009 (H1N1), Severe Acute Respiratory Syndrome (SARS) coronavirus and Middle East Respiratory Syndrome-related coronavirus (MERS-CoV) [5–7].

Data about COVID-19 in patients with diabetes is limited at present. Diabetes was present in 42.3% of 26 fatalities due to COVID-19 in Wuhan, China [8]. In a study in 140 patients with COVID-19 in Wuhan, China, diabetes was not a risk factor for severe disease course [9]. However, another study in 150 patients (68 deaths and 82 recovered patients) in Wuhan showed that the number of co-morbidities to be a significant predictor of mortality [10]. Analysis of 11 studies regarding laboratory abnormalities in patients with COVID-19 did not mention raised blood glucose or diabetes as predictor of severe disease [11]. Notwithstanding these small series, a report of 72,314 cases of COVID-19 published by Chinese Centre for Disease Control and Prevention showed increased mortality in people with diabetes (2.3%, overall and 7.3%, patients with diabetes) [12].

3. Measures to prevent COVID-19

Our knowledge about the prevalence of COVID-19 and disease course in people with diabetes will evolve as more detailed analyses are carried out. For now, it is reasonable to assume that people with diabetes are at increased risk of developing infection with SARS-CoV-2. Coexisting heart disease, kidney disease, advanced age and frailty are likely to have further increase in the severity of disease.

Following measures are suggested for prevention of this disease in patients with diabetes:

A. Specific Measures in Patients with Diabetes:

- a. It is important that people with diabetes maintain a good glycaemic control, as it might help in reducing the risk of infection and also the severity. More frequent monitoring of blood glucose levels (with use of self-monitoring blood glucose) is required. Good glycemic control may lessen chances of superadded bacterial pneumonia as well.

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- b. Patients with diabetes and co-existing heart disease or kidney disease need special care and attempts should be made to stabilise their cardiac/renal status.
 - c. Attention to nutrition and adequate protein intake is important. Any deficiencies of minerals and vitamins need to be taken care of.
 - d. Exercise has been shown to improve immunity, though it might be prudent to be careful and avoid crowded places like gymnasias or swimming pools.
 - e. It is important to take influenza and pneumonia vaccinations. The latter may decrease chances of secondary bacterial pneumonia after respiratory viral infection, however, data in present viral epidemic is not available.
- B. General Preventive Measures**
- a. Thorough handwashing with soap and water should be encouraged since it kills the virus. Use of alcohol-based hand rubs is also useful.
 - b. There is a need to practise proper respiratory hygiene with covering of mouth and nose with bent elbow or tissue when coughing or sneezing. Touching of mouth, nose and eyes should be avoided.
 - c. Contact with an affected person needs to be minimised. Use of recommended face masks is advised if there is a contact with someone with respiratory symptoms.
 - d. Non-essential travel to major affected areas should be avoided in order to restrict the spread of infection.

4. Measures in Patients of diabetes with COVID 19 infection

- a. In case a person with diabetes develops fever, cough, running nose or dyspnoea, the appropriate health authority needs to be notified as testing for this disease is available at selected places only.
- b. The affected person needs to be isolated for 14 days or till the symptoms resolve (whichever is longer). Country-specific guidelines need to be followed.
- c. Majority of patients have a mild disease and can be managed at home. Hydration should be maintained and symptomatic treatment with acetaminophen, steam inhalation etc. can be given.
- d. Patients with type 1 diabetes should measure blood glucose and urinary ketones frequently if fever with hyperglycemia occurs. Frequent changes in dosage and correctional bolus may be required to maintain normoglycemia.
- e. Anti-hyperglycemic agents that can cause volume depletion or hypoglycemia should be avoided. Dosage of oral anti-diabetic drugs may need to be reduced. Patients should follow sick day guidelines and may need more frequent monitoring of blood glucose and drug adjustment.
- f. Hospitalised patients with severe disease need frequent blood glucose monitoring. Oral agents especially metformin and sodium glucose cotransporter-2 inhibitors need to be stopped.
- g. Insulin is the preferred agent for control of hyperglycemia in hospitalised sick patients.

5. Unproven therapies and future directions

In the absence of a specific antiviral drug, anecdotal use of drugs like lopinavir, ritonavir, interferon-1 β , RNA polymerase inhibitor

remdesivir, and chloroquine has been reported. 2019-nCoV receptor binding site has a strong affinity with angiotensin converting enzyme 2 (ACE2) and inhibitors of the rennin angiotensin system may have a role in treating severe respiratory disease [13,14]. Zinc nanoparticles were shown to have inhibitory effects on H1N1 viral load, though their effect in COVID-19 is unknown and untested [15]. Vitamin C supplementation has some role in prevention of pneumonia and its effect on COVID-19 needs evaluation [16]. Efforts to develop a vaccine are underway, which will be a major tool to contain this epidemic [17].

References

- [1] Del Rio C, Malani PN. COVID-19-New insights on a rapidly changing epidemic. *J Am Med Assoc* 2020 Feb 28. <https://doi.org/10.1001/jama.2020.3072>.
- [2] Coronavirus disease 2019 (COVID-19) situation report – 45. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200305-sitrep-45-covid-19.pdf?sfvrsn=ed2ba78b_2.
- [3] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS. China medical treatment expert group for covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020 Feb 28. <https://doi.org/10.1056/NEJMoa2002032>.
- [4] Fauci AS, Lane HC, Redfield RR. Covid-19 - navigating the uncharted. *N Engl J Med* 2020 Feb 28. <https://doi.org/10.1056/NEJMe2002387>.
- [5] Yang JK, Feng Y, Yuan MY, Yuan SY, Fu HJ, Wu BY, Sun GZ, Yang GR, Zhang XL, Wang L, Xu X, Xu XP, Chan JC. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. *Diabet Med* 2006 Jun;23(6):623–8.
- [6] Schoen K, Horvat N, Guerreiro NFC, de Castro I, de GiassiKS. Spectrum of clinical and radiographic findings in patients with diagnosis of H1N1 and correlation with clinical severity. *BMC Infect Dis* 2019 Nov 12;19(1):964. <https://doi.org/10.1186/s12879-019-4592-0>.
- [7] Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, Zhu H, Zhao W, Han Y, Qin C. From SARS to MERS, thrusting coronaviruses into the spotlight. *Viruses* 2019 Jan 14;(1):11. E59.
- [8] Deng SQ, Peng HJ. Characteristics of and public health responses to the coronavirus disease 2019 outbreak in China. *J Clin Med* 2020 Feb 20;(2):9. <https://doi.org/10.3390/jcm9020575>. E575.
- [9] Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, Akdis CA, Gao YD. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy* 2020 Feb 19. <https://doi.org/10.1111/all.14238>.
- [10] Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med* 2020 Mar 3. <https://doi.org/10.1007/s00134-020-05991-x>.
- [11] Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. *Clin Chem Lab Med* 2020 Mar 3. <https://doi.org/10.1515/cclm-2020-0198>. pii://cclm.ahead-of-print/cclm-2020-0198/cclm-2020-0198.xml.
- [12] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention. *J Am Med Assoc* 2020 Feb 24. <https://doi.org/10.1001/jama.2020.2648>.
- [13] Sun ML, Yang JM, Sun YP, Su GH. Inhibitors of RAS might Be a good choice for the therapy of COVID-19 pneumonia. *Zhonghua Jiehe He Huxi Zazhi* 2020 Feb 16;43:E014. <https://doi.org/10.3760/cma.j.issn.1001-0939.2020.0014.0>.
- [14] Phadke M, Saunik S. Use of angiotensin receptor blockers such as Telmisartan, Losartan in nCoV Wuhan Corona Virus infections – novel mode of treatment. *BMJ* 2020;368. m406.
- [15] Ghaffari H, Tavakoli A, Moradi A, Tabarraei A, Bokharaei-Salim F, Zahmatkeshan M, Farahmand M, Javanmard D, Kiani SJ, Esghaei M, Pirhajati-Mahabadi V, Monavari SH, Ataei-Pirkooh A. Inhibition of H1N1 influenza virus infection by zinc oxide nanoparticles: another emerging application of nanomedicine. *J Biomed Sci* 2019;26(1):70.
- [16] Hemilä H. Vitamin C intake and susceptibility to pneumonia. *Pediatr Infect Dis J* 1997 Sep;16(9):836–7.
- [17] DRAFT landscape of COVID-19 candidate vaccines – 18 february 2020. Geneva: World health organization. <https://www.who.int/blueprint/priority-diseases/key-action/list-of-candidate-vaccines-developed-against-ncov.pdf>. opens in new tab.