



THE RELATIONSHIP BETWEEN DIABETES AND COVID-19

Current status of the COVID-19 pandemic-

The COVID-19 pandemic caused by the SARS-CoV-2 virus has resulted in over 6 million deaths worldwide, including almost 1 million in the US. Although effective vaccines and new treatments have been developed, COVID-19 will remain a public health emergency for the foreseeable future due to vaccine hesitancy, the emergence of new variants of concern that may escape the effects of current vaccines, and the increasing evidence for long-term effects of COVID-19 (“long COVID”). Importantly, long COVID is common even in people who were not sick enough to be hospitalized, and long COVID may become a bigger problem than acute COVID-19 disease. Unfortunately, the COVID-19 pandemic is occurring during the ongoing global obesity/diabetes pandemic. The high proportion of obesity and prediabetes in the population exposed to the SARS-CoV-2 virus increases the chances of having severe acute COVID-19 and the risk of metabolic disease associated with long COVID, as described below.

Diabetes increases the severity of COVID-19-

It is now clear that COVID-19 severity is increased by several pre-existing conditions that are widespread in the US population. These include obesity and diabetes, heart disease, and high blood pressure (hypertension). People with type-1 or type-2 diabetes in particular are at risk for severe COVID-19, and have a much greater risk for hospitalization, ventilator support, and death. It is thought that the high blood glucose levels in type-1 diabetes and the chronic inflammation found in type-2 diabetes (usually in connection with obesity) contribute to the greater risk for severe COVID-19. Obesity, which is a major risk factor for prediabetes and type-2 diabetes, increases the chance for more severe respiratory diseases in general, and this is also true for COVID-19.

COVID-19 increases the risk of developing diabetes-

While diabetes makes it more likely that a person with diabetes will experience more severe COVID-19, the converse is also true- having COVID-19 can increase the risk of diabetes in people not previously diagnosed with diabetes. In some cases, this may be because the stress of acute COVID-19 makes previously mild symptoms of pre-existing diabetes more obvious so that diabetes becomes clinically evident. In other cases, the diabetes in long COVID may be truly new-onset (not present at all before). This is likely the result of the ability of the SARS-CoV-2 virus to infect the pancreatic islets that produce insulin as well as the fat tissue that helps control blood glucose levels. Although both type-1 and type-2 diabetes are risk factors for more severe acute COVID-19 infection, the exact type of diabetes seen in long COVID is still unclear.

The need for diabetes screening in people at risk for COVID-19 and in COVID-19 survivors-

These data suggest that screening for diabetes in people already at risk for severe COVID-19 because of age, immunocompromised status, or other metabolic disease will allow better monitoring of these individuals for COVID-19 exposure and indicate more aggressive treatment upon if they become infected. Conversely, diabetes screening of all people with previous COVID-19 would identify cases of long COVID in which previously undiagnosed diabetes is now more advanced, as well as cases in which new-onset diabetes is present, which will allow appropriate diabetes therapy to be started. **Diabetomics’ Glucema™ non-invasive, point-of-care diabetes screening test** that uses oral fluid to determine short-term average blood glucose levels can be an effective tool for assessing risk for severe COVID-19 and identifying COVID-19 survivors that have long COVID-linked diabetes.



REFERENCES

Effect of pre-existing diabetes on COVID-19 severity-

Feldman, EL, Savelieff, MG, Hayek, SS, Pennathur, S, Kretzler, M, et al. Covid-19 and Diabetes: A Collision and Collusion of Two Diseases. *Diabetes* 2020;69:pg2549-2565.PMC7679769

Muniangi-Muhitu, H, Akalestou, E, Salem, V, Misra, S, Oliver, NS, et al. Covid-19 and Diabetes: A Complex Bidirectional Relationship. *Front Endocrinol (Lausanne)* 2020;11:pg582936.PMC7578412

Drucker, DJ. Coronavirus Infections and Type 2 Diabetes-Shared Pathways with Therapeutic Implications. *Endocr Rev* 2020;41:pg457-470.PMC7184382

Marazuela, M, Giustina, A, Puig-Domingo, M. Endocrine and Metabolic Aspects of the Covid-19 Pandemic. *Rev Endocr Metab Disord* 2020;21:pg495-507.PMC7343578

Bornstein, SR, Dalan, R, Hopkins, D, Mingrone, G, Boehm, BO. Endocrine and Metabolic Link to Coronavirus Infection. *Nat Rev Endocrinol* 2020;16:pg297-298.PMC7113912

Barron, E, Bakhai, C, Kar, P, Weaver, A, Bradley, D, et al. Associations of Type 1 and Type 2 Diabetes with Covid-19-Related Mortality in England: A Whole-Population Study. *Lancet Diabetes Endocrinol* 2020;8:pg813-822.PMC7426088

Holman, N, Knighton, P, Kar, P, O'keefe, J, Curley, M, et al. Risk Factors for Covid-19-Related Mortality in People with Type 1 and Type 2 Diabetes in England: A Population-Based Cohort Study. *Lancet Diabetes Endocrinol* 2020;8:pg823-833.PMC7426091

Lim, S, Bae, JH, Kwon, HS, Nauck, MA. Covid-19 and Diabetes Mellitus: From Pathophysiology to Clinical Management. *Nat Rev Endocrinol* 2021;17:pg11-30.PMC7664589

Li, H, Tian, S, Chen, T, Cui, Z, Shi, N, et al. Newly Diagnosed Diabetes Is Associated with a Higher Risk of Mortality Than Known Diabetes in Hospitalized Patients with Covid-19. *Diabetes Obes Metab* 2020;22:pg1897-1906.PMC7283710

Papadokostaki, E, Tentolouris, N, Liberopoulos, E. Covid-19 and Diabetes: What Does the Clinician Need to Know? *Prim Care Diabetes* 2020;14:pg558-563.PMC7332931

McGurnaghan, SJ, Weir, A, Bishop, J, Kennedy, S, Blackburn, LAK, et al. Risks of and Risk Factors for Covid-19 Disease in People with Diabetes: A Cohort Study of the Total Population of Scotland. *Lancet Diabetes Endocrinol* 2021;9:pg82-93.PMC7832778

Kothandaraman, N, Rengaraj, A, Xue, B, Yew, WS, Velan, SS, et al. Covid-19 Endocrinopathy with Hindsight from Sars. *Am J Physiol Endocrinol Metab* 2021;320:pgE139-E150.PMC7816429

Singh, AK, Singh, R. Hyperglycemia without Diabetes and New-Onset Diabetes Are Both Associated with Poorer Outcomes in Covid-19. *Diabetes Res Clin Pract* 2020;167:pg108382.PMC7445123

Ebekozien, OA, Noor, N, Gallagher, MP, Alonso, GT. Type 1 Diabetes and Covid-19: Preliminary Findings from a Multicenter Surveillance Study in the U.S. *Diabetes Care* 2020;43:pg83-e85.PMC7372041

Liang, X, Xu, J, Xiao, W, Shi, L, Yang, H. The Association of Diabetes with Covid-19 Disease Severity: Evidence from Adjusted Effect Estimates. *Hormones (Athens)* 2021;20:pg409-414.PMC7685958



Smith, SM, Boppana, A, Traupman, JA, Unson, E, Maddock, DA, et al. Impaired Glucose Metabolism in Patients with Diabetes, Prediabetes, and Obesity Is Associated with Severe Covid-19. *J Med Virol* 2021;93:pg409-415.PMC7361926

Effect of COVID-19 on new-onset diabetes-

Hollstein, T, Schulte, DM, Schulz, J, Gluck, A, Ziegler, AG, et al. Autoantibody-Negative Insulin-Dependent Diabetes Mellitus after Sars-Cov-2 Infection: A Case Report. *Nat Metab* 2020;2:pg1021-1024, doi.10.1038/s42255-020-00281-8

Hayden, MR. An Immediate and Long-Term Complication of Covid-19 May Be Type 2 Diabetes Mellitus: The Central Role of Beta-Cell Dysfunction, Apoptosis and Exploration of Possible Mechanisms. *Cells* 2020;9.PMC7697826

Khunti, K, Del Prato, S, Mathieu, C, Kahn, SE, Gabbay, RA, et al. Covid-19, Hyperglycemia, and New-Onset Diabetes. *Diabetes Care* 2021;44:pg2645-2655, doi.10.2337/dc21-1318

Al-Aly, Z, Xie, Y, Bowe, B. High-Dimensional Characterization of Post-Acute Sequelae of Covid-19. *Nature* 2021;594:pg259-264, doi.10.1038/s41586-021-03553-9

Li, J, Wang, X, Chen, J, Zuo, X, Zhang, H, et al. Covid-19 Infection May Cause Ketosis and Ketoacidosis. *Diabetes Obes Metab* 2020;22:pg1935-1941.PMC7264681

Chee, YJ, Ng, SJH, Yeoh, E. Diabetic Ketoacidosis Precipitated by Covid-19 in a Patient with Newly Diagnosed Diabetes Mellitus. *Diabetes Res Clin Pract* 2020;164:pg108166.PMC7194589

Heaney, AI, Griffin, GD, Simon, EL. Newly Diagnosed Diabetes and Diabetic Ketoacidosis Precipitated by Covid-19 Infection. *Am J Emerg Med* 2020;38:pg2491 e2493-2491 e2494.PMC7274947

Suwanwongse, K, Shabarek, N. Newly Diagnosed Diabetes Mellitus, DKA, and Covid-19: Causality or Coincidence? A Report of Three Cases. *J Med Virol* 2021;93:pg1150-1153.PMC7404645

Reddy, PK, Kuchay, MS, Mehta, Y, Mishra, SK. Diabetic Ketoacidosis Precipitated by Covid-19: A Report of Two Cases and Review of Literature. *Diabetes Metab Syndr* 2020;14:pg1459-1462.PMC7395228

Alsadhan, I, Alruwashid, S, Alhamad, M, Alajmi, S, Alshehri, S, et al. Diabetic Ketoacidosis Precipitated by Coronavirus Disease 2019 Infection: Case Series. *Curr Ther Res Clin Exp* 2020;93:pg100609.PMC7590633

Naguib, MN, Raymond, JK, Vidmar, AP. New Onset Diabetes with Diabetic Ketoacidosis in a Child with Multisystem Inflammatory Syndrome Due to Covid-19. *J Pediatr Endocrinol Metab* 2021;34:pg147-150, doi.10.1515/jpem-2020-0426

Soliman, AT, Al-Amri, M, Alleethy, K, Alaaraj, N, Hamed, N, et al. Newly-Onset Type 1 Diabetes Mellitus Precipitated by Covid-19 in an 8-Month-Old Infant. *Acta Biomed* 2020;91:pgahead of print.PMC7717024

Unsworth, R, Wallace, S, Oliver, NS, Yeung, S, Kshirsagar, A, et al. New-Onset Type 1 Diabetes in Children During Covid-19: Multicenter Regional Findings in the U.K. *Diabetes Care* 2020;43:pg170-e171, doi.10.2337/dc20-1551

Sathish, T, Kapoor, N, Cao, Y, Tapp, RJ, Zimmet, P. Proportion of Newly Diagnosed Diabetes in Covid-19 Patients: A Systematic Review and Meta-Analysis. *Diabetes, Obesity and Metabolism* 2021;23:pg870-874, doi.<https://doi.org/10.1111/dom.14269>





Barrett CE, Koyama, AK, Alvarez P, Chow, W, Lundeen, EA, et al. Risk for Newly Diagnosed Diabetes >30 Days after Sars-Cov-2 Infection among Persons Aged <18 Years — United States, March 1, 2020–June 28, 2021. *MMWR Morb Mortal Wkly Rep* 2022, doi:<http://dx.doi.org/10.15585/mmwr.mm7102e2>

Sá-Ferreira, COD, Costa, CHMD, Guimarães, JCW, Sampaio, NS, Silva, LDML, et al. Diabetic Ketoacidosis and Covid-19: What Have We Learned So Far? *American Journal of Physiology-Endocrinology and Metabolism* 2022;322:pgE44-E53, doi.10.1152/ajpendo.00244.2021

Wander, PL, Lowy, E, Beste, LA, Tulloch-Palomino, L, Korpak, A, et al. The Incidence of Diabetes among 2,777,768 Veterans with and without Recent Sars-Cov-2 Infection. *Diabetes Care* 2022, doi.10.2337/dc21-1686

Rubino, F, Amiel, SA, Zimmet, P, Alberti, G, Bornstein, S, et al. New-Onset Diabetes in Covid-19. *N Engl J Med* 2020;383:pg789-790.PMC7304415

Atkinson, MA, Powers, AC. Distinguishing the Real from the Hyperglycaemia: Does Covid-19 Induce Diabetes? *The Lancet Diabetes & Endocrinology* 2021;9:pg328-329, doi:[https://doi.org/10.1016/S2213-8587\(21\)00087-5](https://doi.org/10.1016/S2213-8587(21)00087-5)

Unnikrishnan, R, Misra, A. Diabetes and Covid19: A Bidirectional Relationship. *Nutrition & Diabetes* 2021;11:pg21, doi.10.1038/s41387-021-00163-2

Papachristou, S, Stamatiou, I, Stoian, AP, Papanas, N. New-Onset Diabetes in Covid-19: Time to Frame Its Fearful Symmetry. *Diabetes Therapy* 2021;12:pg461-464, doi.10.1007/s13300-020-00988-7

Steenblock, C, Schwarz, PEH, Ludwig, B, Linkermann, A, Zimmet, P, et al. Covid-19 and Metabolic Disease: Mechanisms and Clinical Management. *The Lancet Diabetes & Endocrinology* 2021;9:pg786-798, doi:[https://doi.org/10.1016/S2213-8587\(21\)00244-8](https://doi.org/10.1016/S2213-8587(21)00244-8)

Clarke, SA, Abbara, A, Dhillon, WS. Impact of Covid-19 on the Endocrine System: A Mini-Review. *Endocrinology* 2021;163, doi.10.1210/endo/bqab203

Montefusco, L, Ben Nasr, M, D'Addio, F, Loretelli, C, Rossi, A, et al. Acute and Long-Term Disruption of Glycometabolic Control after Sars-Cov-2 Infection. *Nature Metabolism* 2021;3:pg774-785, doi.10.1038/s42255-021-00407-6

Cromer, SJ, Colling, C, Schatoff, D, Leary, M, Stamou, MI, et al. Newly diagnosed diabetes vs. pre-existing diabetes upon admission for COVID-19: Associated factors, short-term outcomes, and long-term glycemic phenotypes. *J Diabet Complications* <https://doi.org/10.1016/j.jdiacomp.2022.108145>

Rathman, W, Kuss, O, Kostev, K. Incidence of newly diagnosed diabetes after COVID-19. *Diabetologia* 2022, <https://doi.org/10.1007/s00125-022-05670-0>

Xie Y, Al-Aly Z. Risks and burdens of incident diabetes in long COVID: a cohort study. *Lancet Diabet Endo* 2022, [https://doi.org/10.1016/S2213-8587\(22\)00044-4](https://doi.org/10.1016/S2213-8587(22)00044-4)

