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Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14 (2020) 963–964

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

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

COVID 19 could trigger global diabetes burden – A hypothesis

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ARTICLE INFO

Article history:
Received 14 June 2020
Received in revised form
21 June 2020
Accepted 24 June 2020

Keywords:
SARS-CoV-2
Diabetes mellitus
COVID-19
Pancreatic islets

The pandemic corona virus disease 2019 (COVID-19) caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) has threateningly jeopardized the life of each and every people around the world. According to earlier report, development of diabetes mellitus has strong temporal and geographical association with many viruses like Epstein–Barr, Coxsackie B virus, rubella, mumps, cytomegalovirus, enteroviruses, retroviruses, and varicella zoster virus [1]. Few cases of diagnosed diabetes are also presented with serological evidences of infection and isolation of viruses from the pancreas [1]. Thus, considering huge geographical spread, size of the population affected and strong association of viral infections with diabetes, SARS-CoV-2 pandemic necessitates surveillance for the long term impact on endocrine pancreas of COVID-19 survivors.

SARS-CoV-2 depends on two processes for its cellular entry – (i) viral spike (S) proteins (present on the surface of the virus) binds with angiotensin-converting enzyme 2 (ACE-2) present in the human cells (host cells) and (ii) priming of these S proteins by the host cell serine protease, furin and TMPRSS2 [2,3]. Expression of SARS-CoV receptor – ACE-2 proteins has been studied earlier in different human tissues like respiratory, cardiovascular, renal, and gastrointestinal, and pancreas [1] which demonstrated multi-system nature of SARS infection. In particular, clinical studies of human pancreatic islets showed strong immunostaining for ACE-2 proteins and TMPRSS2 [1,4]. Now it is an apparent question whether SARS-CoV-2 can enter the pancreatic islet cells. In this context, earlier studies presented evidence in favor of the entry of SARS-CoV into pancreas of infected patients [1,5] though the co-morbidities like diabetes mellitus or hypertension in these SARS infected patients were not elucidated.

Considering the structural and syndromic resemblance between SARS-CoV-2 and SARS-CoV, it is worthy to use previous knowledge of SARS-CoV infection during 2002–2003. A follow up study on SARS-CoV survivors has suggested that SARS-CoV may damage pancreatic islets and cause acute insulin dependent diabetes mellitus [1]. Further, glucose metabolic disorders including hyperglycemia, hyperinsulinemia, insulin resistance and type I or II diabetes were also reported in a large proportion of the recovered SARS patients [6]. Disturbed lipid metabolism and its associated disorders like hyperlipidemia, abnormal glucose metabolism, and cardiovascular abnormality were also reported in SARS survivors even after twelve years of infection [6].

Moreover, accumulating evidence suggest that perturbation in intracellular signaling cascades due to metabolic dysfunction is severely affected by SARS infection [7]. For instance, infection with both viral and bacterial pathogens is known to modulate ceramide (a shpingolipid) which antagonizes insulin signaling and abrogates glucose homeostasis. More importantly, it is evident from extensive clinical dataset that both acute and chronic infection favors insulin resistance and hence a risk factor for individuals with pre-diabetes to develop type II diabetes mellitus [7]. Although epidemiological studies showcased the impact of acute or chronic infection on development of type II diabetes mellitus so far, but these molecular

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https://doi.org/10.1016/j.dsx.2020.06.049

evidences are indicative of strong causal relationship between infection and diabetes development. Further, Ghosal et al. (2020) very recently reported that weight gain during 49 days lockdown due to COVID-19 pandemic in India may increase the risk of development of type 2 diabetes mellitus [8].

Cytokines play pivotal role in every facet of inflammation, immunity and development of diabetes mellitus. Thus, mild or severe cytokine storms (interferons, interleukins, chemokines, colony-stimulating factors and tumor necrosis factor) and virally driven hyperinflammation in COVID-19 patients [9] could be potential players directing negative impacts on the pancreatic islet cells in recovered COVID-19 patients. Also, these cytokines might have indirect effect on pancreatic islets secondary to severe lung infection in COVID-19 patients. Diabetes mellitus is one of the most important extrapulmonary comorbidities in individuals with chronic obstructive pulmonary disease, asthma, and interstitial lung diseases [10]. Thus, we presume that initial damages in lungs resulting from COVID-19 might have direct or indirect impact to cause metabolic dysfunction and diabetes mellitus in particular.

Taken together, it is noteworthy to speculate that SARS-CoV-2 might enter islets, and cause acute β-cell dysfunction followed by hyperglycemia and transient type II diabetes mellitus. Taken together, we anticipate that SARS-CoV-2 pandemic has touched off the need for follow up study to delineate the possible development of another stealthy public health crisis - diabetes mellitus in COVID-19 survivors.

Author contribution statement

SM and BKM drafted the manuscript; OB and SS did literature survey. All authors were involved in manuscript editing and approved the version submitted for publication.

Declaration of competing interest

All authors declare no conflict of interest.

References

[1] Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. Acta Diabetol 2010;47:193–9. https://doi:10.1007/s00592-009-0109-4.
[2] Hoffmann O, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 2020;181:1–10. https://doi.org/10.1016/j.cell.2020.02.052.
[3] Rizzo P, Sega FVD, Fortini F, Marracino L, Rapezzi C, Ferrari R. COVID-19 in the heart and the lungs: could we "Notch" the inflammatory storm? Basic Res Cardiol 2020;115:31. https://doi:10.1007/s00395-020-0791-5.
[4] Afar DE, Vivanco I, Hubert RS, Kuo J, Chen E, Saffran DC, et al. Catalytic cleavage of the androgen-regulated TMPRSS2 protease results in its secretion by prostate and prostate cancer epithelia. Canc Res 2001;61:1686–92.
[5] Ding Y, He L, Zhang Q, Huang Z, Che X, Hou J, et al. Organ distribution of severe acute respiratory syndrome (SARS) associated coronavirus (SARS-CoV) in SARS patients: implications for pathogenesis and virus transmission pathways. J Pathol 2004;203:622–30. https://doi:10.1002/path.1560.
[6] Wu Q, Zhou L, Sun X, Yan Z, Hu C, Wu J, et al. Altered Lipid Metabolism in recovered SARS patients twelve years after infection. Sci Rep 2017;7:9110. https://doi.org/10.1038/s41598-017-09536-z.
[7] Wensveen FM, Šestan M, Wensveen TT, Polić B. 'Beauty and the beast' in infection: how immune–endocrine interactions regulate systemic metabolism in the context of infection. Eur J Immunol 2019;49:982–95. https://doi:10.1002/eji.201847895.
[8] Ghosal S, Arora B, Dutta K, Ghosh A, Sinha B, Misra A. Increase in the risk of type 2 diabetes during lockdown for the COVID19 pandemic in India: a cohort analysis. Diabetes Metabol Syndr Clin Res Rev 2020. https://doi.org/10.1016/j.dsx.2020.06.020 (In Press).
[9] Zhang C, Wu Z, Li JW, Zhao H, Wang GQ. The cytokine release syndrome (CRS) of severe COVID-19 and Interleukin-6 receptor (IL-6R) antagonist Tocilizumab may be the key to reduce the mortality. Int J Antimicrob Agents 2020. 105954, https://doi:10.1016/j.ijantimicag.2020.105954.
[10] Papaioannou O, Karampitsakos T, Barbayianni I, Chrysikos S, Xylourgidis N, Tzilas V, et al. Metabolic disorders in chronic lung diseases. Front Med 2018;4:246. https://doi:10.3389/fmed.2017.00246.