

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to the Editor

Normal weight obesity and COVID-19 severity: A poorly recognized link



People with obesity (those with high body mass index (BMI)) and coronavirus disease 2019 (COVID-19) are at increased risk of requiring intensive care unit admission and mechanical ventilation, and death [1]. Although BMI is a commonly used measure of obesity in clinical settings, it cannot delineate fat-free mass from adipose tissue [2]. Thus, people with normal weight on the BMI scale can have elevated body fat percent, particularly in the visceral area, an entity called normal weight obesity (NWO) [2,3]. Indeed, emerging evidence shows that visceral adiposity, independent of BMI, is associated with high risk of critical illness in patients with COVID-19 [4,5]. Identifying NWO individuals, who are at high risk for metabolic dysregulation and cardiometabolic disorders [3,6], is often and easily overlooked in clinical practice, where screening for obesity is based solely on BMI [3].

Reports from the USA and the UK show that South Asians, blacks, and other ethnic minorities are more likely to contract COVID-19 and experience severe forms of illness compared with whites [7,8]. While these could be due to differences in socioeconomic, cultural, or lifestyle factors [8], the role of excess body fat cannot be ignored. South Asians and blacks generally have a higher body fat percent than whites for a given level of BMI [9,10]. Several potential mechanisms for poor COVID-19 outcomes in obese people, including endothelial dysfunction, insulin resistance, immune dysfunction, and chronic inflammation [11], are directly related to excess amounts of body fat [3]. Moreover, certain key cytokines involved in the pathogenesis and disease progression of COVID-19, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha) [12], are also synthesized in adipose tissue [13]. These cytokines are usually elevated in individuals with increased body fat, irrespective of their BMI [3]. Thus, adipose tissue can act as a reservoir for the virus, leading to increased and prolonged viral shedding [11].

The use of the sagittal image of chest computed tomography (done routinely to diagnose COVID-19 pneumonia) to assess visceral adiposity [4,5], along with BMI, is a promising strategy to identify NWO individuals in clinical settings. Understanding the association between NWO and COVID-19 disease severity could inform better risk stratification and management of COVID-19 patients, especially those of South Asian and African origins.

Funding

None.

Author contributions

TS conceived the idea, conducted the literature search, and draft the first version of the manuscript. NK reviewed and edited the manuscript. Both authors approved the submission of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

- [1] de Siqueira JVV, Almeida LG, Zica BO, Brum IB, Barceló A, de Siqueira Galil AG. Impact of obesity on hospitalizations and mortality, due to COVID-19: a systematic review. Obes Res Clin Pract 2020. <u>https://doi.org/10.1016/j.orcp.2020.07.005</u>.
- [2] Kapoor N, Furler J, Paul TV, Thomas N, Oldenburg B. Normal weight obesity: an underrecognized problem in individuals of South Asian descent. Clin Therap 2019;41:1638–42.
- [3] Franco LP, Morais CC, Cominetti C. Normal-weight obesity syndrome: diagnosis, prevalence, and clinical implications. Nutr Rev 2016;74:558–70.
- [4] Battisti S, Pedone C, Napoli N, Russo E, Agnoletti V, Nigra SG, et al. Computed tomography highlights increased visceral adiposity associated with critical illness in COVID-19. Diabetes Care 2020;43:e129–30.
- [5] Petersen A, Bressem K, Albrecht J, Thieß H-M, Vahldiek J, Hamm B, et al. The role of visceral adiposity in the severity of COVID-19: highlights from a unicenter cross-sectional pilot study in Germany. Metabolism 2020;110. <u>https://doi.org/</u> 10.1016/j.metabol.2020.154317.

- [6] Kapoor N, Lotfaliany M, Sathish T, Thankappan KR, Thomas N, Furler J, et al. Prevalence of normal weight obesity and its associated cardio-metabolic risk factors - results from the baseline data of the Kerala Diabetes Prevention Program (KDPP). PLoS One 2020;15. <u>https://doi.org/10.1371/journal. pone.0237974</u>.
- [7] Pan D, Sze S, Minhas JS, Bangash MN, Pareek N, Divall P, et al. The impact of ethnicity on clinical outcomes in COVID-19: a systematic review. EClinicalMedicine 2020;23. <u>https://doi.org/ 10.1016/j.eclinm.2020.100404</u>.
- [8] Khunti K, Singh AK, Pareek M, Hanif W. Is ethnicity linked to incidence or outcomes of covid-19?. BMJ 2020;369. <u>https://doi.org/10.1136/bmj.m548</u>.
- [9] Deurenberg P, Deurenberg-Yap M, Guricci S. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. Obes Rev 2002;3:141–6.
- [10] Heymsfield SB, Peterson CM, Thomas DM, Heo M, Schuna Jr JM. Why are there race/ethnic differences in adult body mass index-adiposity relationships? A quantitative critical review. Obes Rev 2016;17:262–75.
- [11] Sattar N, McInnes IB, McMurray JJV. Obesity is a risk factor for severe COVID-19 infection: multiple potential mechanisms. Circulation 2020;142:4–6.
- [12] Sinha P, Matthay MA, Calfee CS. Is a "cytokine storm" relevant to COVID-19?. JAMA Intern Med 2020;180. <u>https:// doi.org/10.1001/jamainternmed.2020.3313</u>.
- [13] Maximus PS, Al Achkar Z, Hamid PF, Hasnain SS, Peralta CA. Adipocytokines: are they the theory of everything?. Cytokine 2020;133 155144.

Thirunavukkarasu Sathish^{*} Population Health Research Institute (PHRI), McMaster University, Hamilton, ON L8L 2X2, Canada ^{*} Corresponding author. E-mail address: speaktosat@gmail.com

Nitin Kapoor

Department of Endocrinology, Diabetes and Metabolism, Christian Medical College, Vellore 632004, Tamil Nadu, India Non Communicable Disease Unit, Melbourne School of Population and Global Health, University of Melbourne, VIC 3053, Australia

Available online xxxx