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.

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Case Report

Obesity and COVID-19: The clash of two pandemics

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Background

The world is currently battling Coronavirus Disease 2019 (COVID-19), a disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). From the first reported cases in Wuhan in December 2019, the disease has spread so rapidly over the world that it was declared a pandemic by the World Health Organization in March 2020.

All this while, another pandemic, which is no less lethal, lurks in the background. Obesity, a silent killer which is increasingly prevalent globally, should not be forgotten.

Is there an association between obesity and COVID-19? What are the underlying mechanisms? Most importantly, what are the implications?

We present two cases for illustration and discussion.

Case reports

Case #1

A 19-year-old male with no past medical history presented with a four-day history of fever, sore throat and myalgia. He had no cough, breathlessness or anosmia. Prior to illness, he had travelled to the United Kingdom, but had no sick contact.

On initial assessment, the patient was febrile (temperature 39.6 °C), hypertensive (blood pressure 152/89 mm Hg) and tachycardic (heart rate 102 beats per minute). Oxygen saturation was 100% on ambient air. He was obese (body weight 152 kilograms [kg], height 1.9 metres [m], body mass index (BMI) 44 kg/m^2). Physical examination was unremarkable. Investigations revealed normal white cell count, absolute lymphocyte count and lactate dehydrogenase (LDH) (Table 1). Chest X-ray (CXR) showed right midzone consolidation. Oropharyngeal swab was positive for SARS-CoV-2 by real-time polymerase chain reaction (RT-PCR).

Table 1
Initial investigations, Case #1.

Investigation	Results	Reference range	Remarks
Full blood count			
Haemoglobin (g/dL)	14.9	14.0–18.0	Normal
White blood cells (10$\hat{9}$/L)	6.22	4.00–10.00	Normal
Absolute neutrophil count (10$\hat{9}$/L)	4.55	2.00–7.50	Normal
Absolute lymphocyte count (10$\hat{9}$/L)	1.02	1.00–3.00	Normal
Platelets (10$\hat{9}$/L)	200	140–440	Normal
Electrolytes			
Sodium (mmol/L)	138	136–146	Normal
Potassium (mmol/L)	4.2	3.5–5.1	Normal
Urea (mmol/L)	4.7	2.0–6.9	Normal
Creatinine (umol/L)	96	59–104	Normal
Liver function			
Albumin (g/L)	40	40–51	Normal
Total bilirubin (umol/L)	5	7–32	Normal
Alanine transaminase (U/L)	21	6–66	Normal
Aspartate transaminase (U/L)	24	12–42	Normal
Alkaline phosphatase (U/L)	77	39–99	Normal
Lactate dehydrogenase (mmol/L)	301	135–350	Normal
Inflammatory markers			
C-reactive protein (mg/L)	16.2	0.2–9.1	Normal
Procalcitonin (ug/L)	0.07	≤0.49	Normal

The patient's clinical course was stormy. On his fourth hospitalization day, repeat CXR showed worsening bilateral opacities. Supplemental oxygen was required, and he was commenced on lopinavir–ritonavir. On the eighth hospitalization day, the patient had worsening type 1 respiratory failure and was transferred to the intensive care unit (ICU). He improved with high-flow nasal oxygen, without need for mechanical ventilation. The duration of ICU and hospital stay was five and eighteen days respectively.

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Table 2
Initial investigations, Case #2.

Investigation	Results	Reference range	Remarks
Full blood count			
Haemoglobin (g/dL)	16.1	14.0–18.0	Normal
White blood cells (10^9/L)	5.48	4.00–10.00	Normal
Absolute neutrophil count (10^9/L)	3.35	2.00–7.50	Normal
Absolute lymphocyte count (10^9/L)	1.46	1.00–3.00	Normal
Platelets (10^9/L)	227	140–440	Normal
Electrolytes			
Sodium (mmol/L)	138	136–146	Normal
Potassium (mmol/L)	3.9	3.5–5.1	Normal
Urea (mmol/L)	3.3	2.0–6.9	Normal
Creatinine (umol/L)	67	59–104	Normal
Liver function			
Albumin (g/L)	49	40–51	Normal
Alanine transaminase (U/L)	18	6–66	Normal
Aspartate transaminase (U/L)	20	12–42	Normal
Alkaline phosphatase (U/L)	46	39–99	Normal
Lactate dehydrogenase (mmol/L)	214	135–350	Normal
Inflammatory markers			
C-reactive protein (mg/L)	**16.3**	0.2–9.1	**Elevated**
Procalcitonin (ug/L)	0.07	≤0.49	Normal

Case #2

An 18-year-old male with no past medical history presented with a one-week history of fever and dry cough. He had no recent contact or travel history. On initial assessment, the patient was afebrile (temperature 37.0 °C). Blood pressure was 129/77 mm Hg, heart rate was 96 beats per minute and oxygen saturation on ambient air was 98%. He was obese (body weight 88.7 kg, height 1.73 m, BMI 30.7 kg/m^2). Physical examination was significant for right basal lung crepitations.

Investigations revealed normal white cell count, absolute lymphocyte count and LDH with mildly elevated C-reactive protein (Table 2), while CXR showed bilateral consolidation. Oropharyngeal swab was positive for SARS-CoV-2 by RT-PCR.

The patient remained clinically stable during his 7-day hospital stay.

Discussion

Older age (>60 years old) and comorbidities such as diabetes mellitus (DM), hypertension, cardiovascular disease and chronic respiratory disease are well-established risk factors for severe COVID-19 [1,2]. Our cases depict young patients with obesity and no other risk factors, who developed COVID-19 of at least moderate intensity [3].

Obesity was a risk factor for hospitalization and death during the 2009 H1N1 influenza pandemic [4]. Similarly, obesity is an increasingly recognized risk factor for severe COVID-19 and death, including in young patients [5–9].

According to the COVID-NET database in the United States of America, obesity is the second most common underlying condition amongst patients hospitalized with COVID-19, occurring in 59% of those 18–49 years old [5]. In fact, it was more common than other described risk factors [1] such as DM (28.3%) and cardiovascular disease (27.8%) [5]. In a retrospective study of 3615 patients in New York, patients aged <60 years with a BMI 30–34.9 kg/m^2 and ≥35 kg/m^2 were 1.8 times and 3.6 times more likely to be admitted into critical care, compared to patients with BMI < 30 kg/m^2 [6]. In another study by Simonnet et al., patients with BMI > 35 kg/m^2 were 7.36 times more likely to receive invasive mechanical ventilation compared to those with BMI < 25 kg/m^2 [7]. These suggest a strong association between obesity and severe COVID-19.

In the Asian context where the initial epicentre of the outbreak occurred, obesity has also been shown to be an important risk factor for severe COVID-19. In a study of 112 patients in Wuhan, China, the BMI of the patients admitted to ICU (25.5 kg/m^2) was significantly higher than those admitted to the general hospital (22.0 kg/m^2). The patients in this study were further divided into a non-survivor and survivor group. The percentage of patients with BMI > 25 kg/m^2 was significantly higher in the non-survivor group (88.2%) compared to the survivor group (18.9%) [8]. Another study of 280 patients in Jiangsu, China, showed that patients with severe COVID-19 had significantly higher mean BMI (25.8 kg/m^2) than those with mild disease (23.6 kg/m^2) [9]. These BMI values, significantly lower than in the aforementioned studies in Caucasian patients, are consistent with the lower BMI cut-off points for obesity in Asians. Further studies are required in Asian populations to evaluate the correlation between BMI and severity of COVID-19, as well as determine the BMI cut-offs which predict severe disease.

There are several possible reasons for the link between obesity and COVID-19.

Obesity is closely linked to DM, hypertension and cardiovascular disease, aforementioned risk factors for severe COVID-19 [1,2]. Physical inactivity, common in obesity, may lead to impaired immune response [10]. The altered dynamics of pulmonary ventilation with reduced diaphragmatic excursion and a relative increase in anatomical dead space may account for the increased incidence of severe COVID-19 in patients with obesity [10].

The presence of a pro-inflammatory state in obesity may impair immune response and pulmonary function [11]. Of particular interest is leptin, which is involved in weight regulation by decreasing energy intake and increasing energy expenditure; as well as modulation of the innate and adaptive immune function through activation of neutrophils, macrophages and T lymphocytes [11,12]. Leptin-deficient mice developed severe obesity and appeared to have increased susceptibility to infections [11]. Compared to mice of normal weight, obese mice with H1N1 influenza infection had higher leptin levels, increased interleukin-6 (IL-6), increased pulmonary viral titers and increased mortality; while administration of anti-leptin antibodies led to improved survival [13]. In humans, the rare condition of congenital leptin deficiency notwithstanding, obesity is typically characterized by hyperleptinemia and leptin resistance [12]. Indeed, the authors proposed that leptin was a co-factor for the 2009 H1N1 pandemic [13], which leads to the intriguing question of the role of leptin in the current COVID-19 pandemic. On the other hand, examining the reverse association between obesity and viral infection, one of the possible mechanisms by which Adenovirus 36 causes obesity is through down-regulation of leptin expression [10]. It remains to be seen whether SARS-CoV-2 could have this effect.

An interesting observation is the association of obesity with lower Vitamin D serum levels [14]. As Vitamin D reduces the risk of viral infections through enhancing both innate and adaptive immunity [15], this might contribute to increased risk of COVID-19 in people with obesity. Interestingly, Vitamin D also modulates the expression of angiotensin converting enzyme 2 (ACE-2), which is the putative co-receptor for cellular SARS-CoV-2 entry [16]. Increased adipose tissue in obesity could lead to increased ACE-2 expression and risk of infection [17], although the link between ACE-2 and COVID-19 is currently unclear.

The clash of these two pandemics carries significant implications.

Obesity plays an important role in virus transmission. Adipose tissue may become a reservoir for SARS-CoV-2, leading to pro-

longed viral shedding, which has also been observed with other viruses including H1N1 influenza [10]. Obesity leads to poorer vaccination success and emergence of more virulent virus strains, due to blunted cytokine and interferon production [10]. In addition, people with obesity carry more infectious virus in exhaled breath due to higher ventilation volumes [10]. For these reasons, a consideration is prolonged quarantine in obese patients with COVID-19 [10], although this should be balanced with the potentially deleterious effects of social isolation.

Practical management issues include the need for bariatric hospital beds and equipment, difficulty with transport and shifting of patients, as well as constraints with imaging which might lead to delayed diagnosis. People with obesity who turn critically ill present more challenging intubations, difficulty with prone positioning and the risk of prolonged mechanical ventilation [18]. Due to changes in pharmacokinetics and pharmacokinetics in obesity, choosing the correct dosage of anti-microbials if often difficult, and under-dosing is common [19]. Furthermore, novel agents investigated in clinical trials may require additional dose-optimizing studies in obese patients.

The impact of COVID-19 extends beyond infected patients. Stay-at-home rules lead to increased sedentariness and consumption of processed, caloric-dense food. A major consequence is social isolation, which when added to social stigmatization due to obesity and pandemic-related stress, may increase psychosocial distress and maladaptive eating behaviours [20]. Virtual health tools such as telemedicine may be useful to reach out to this vulnerable group [20].

In summary, physicians should be aware of the far-reaching impact of the collision of the dual pandemics — obesity and COVID-19 [18].

Conflict of interest

We confirm that none of the authors have a conflict of interest.

Author agreement

We confirm that all authors had access to the data and participated in the preparation of this manuscript.

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We confirm that the work described has not been published previously, that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder.

Ethical statement

We have read and have abided by the statement of ethical standards for this manuscript which is submitted to the Obesity Research & Clinical Practice.

References

[1] 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. JAMA 2020;323(13):1239–42, http://dx.doi.org/10.1001/jama.2020.2648.
[2] Zhou F, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet (Lond Engl) 2020;395:1054–62.
[3] Gandhi RT, Lynch JB, del Rio C. Mild or moderate Covid-19. N Engl J Med 2020, http://dx.doi.org/10.1056/NEJMcp2009249. NEJMcp2009249, [In press].
[4] Morgan OW, et al. Morbid obesity as a risk factor for hospitalization and death due to 2009 pandemic influenza A(H1N1) disease. PLoS One 2010;5(3):e9694.
[5] Garg S, et al. Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019 — COVID-NET, 14 states, March 1–30, 2020. MMWR Morb Mortal Wkly Rep 2020;69(15):458–64.
[6] Lighter J, et al. Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission. Clin Infect Dis 2020, http://dx.doi.org/10.1093/cid/ciaa415. In press.
[7] Simonnet A, et al. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Obesity (Silver Spring) 2020;28(7):1195–9, http://dx.doi.org/10.1002/oby.22831.
[8] Peng YD, et al. Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-nCoV. Zhonghua Xin Xue Guan Bing Za Zhi 2020;48:E004. In press.
[9] Wu J, et al. Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19). J Intern Med 2020;288(1):128–38, http://dx.doi.org/10.1111/joim.13063.
[10] Luzi L, Radaelli MG. Influenza and obesity: its odd relationship and the lessons for COVID-19 pandemic. Acta Diabetol 2020;57:759–64.
[11] Mancuso P. Obesity and respiratory infections: does excess adiposity weigh down host defense? Pulm Pharmacol Ther 2013;26:412–9.
[12] Farr OM, Gavrieli A, Mantzoros CS. Leptin applications in 2015: what have we learned about leptin and obesity? Curr Opin Endocrinol Diabetes Obes 2015;22:353–9.
[13] Zhang AJX, et al. Leptin mediates the pathogenesis of severe 2009 pandemic influenza A(H1N1) infection associated with cytokine dysregulation in mice with diet-induced obesity. J Infect Dis 2013;207:1270–80.
[14] Walsh JS, Bowles S, Evans AL. Vitamin D in obesity. Curr Opin Endocrinol Diabetes Obes 2017;24:389–94.
[15] Grant WB, et al. Evidence that vitamin d supplementation could reduce risk of influenza and COVID-19 infections and deaths. Nutrients 2020;12(4):988.
[16] Carter SJ, Baranauskas MN, Fly AD. Considerations for obesity, vitamin D, and physical activity amidst the COVID-19 pandemic. Obesity (Silver Spring) 2020;28(7):1176–7, http://dx.doi.org/10.1002/oby.22838.
[17] Kassir R. Risk of COVID-19 for patients with obesity. Obes Rev 2020;21(6):e13034, http://dx.doi.org/10.1111/obr.13034.
[18] Ryan DH, Ravussin E, Heymsfield S. COVID 19 and the patient with obesity — the editors speak out. Obesity (Silver Spring) 2020;28(5):847.
[19] Huttunen R, Syrjänen J. Obesity and the risk and outcome of infection. Int J Obes 2005 2013;37(3):333–40.
[20] Sockalingam S, Leung SE, Cassin SE. The impact of COVID-19 on bariatric surgery: re-defining psychosocial care. Obesity (Silver Spring) 2020;28(6):1010–2, http://dx.doi.org/10.1002/oby.22836.