ARTICLE IN PRESS

Review

Obesity and mortality of COVID-19. Meta-analysis

Abdulzahra Hussain [a,*], Kamal Mahawar [b], Zefeng Xia [c], Wah Yang [d], Shamsi EL-Hasani [e]

[a] Doncaster and Bassetlaw Teaching Hospitals, Doncaster, UK,Honorary Lecturer at Sheffield University.Sheffield.UK
[b] Bariatric Unit, Department of General Surgery, Sunderland Royal Hospital, Sunderland, UK
[c] Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Avenue, Wuhan, Hubei Province, China
[d] The First Affiliated Hospital of Jinan University, 613 Huangpu Avenue West, Guangzhou, Guangdong Province, China
[e] Bariatric Unit, Princess Royal University Hospital, King's College Hospitals NHS Foundation Trust, London, UK

ARTICLE INFO

ABSTRACT

Background: Obesity is a global disease with at least 2.8 million people dying each year as a result of being overweight or obese according to the world health organization figures. This paper aims to explore the links between obesity and mortality in COVID-19.
Methods: Electronic search was made for the papers studying obesity as a risk factor for mortality following COVID-19 infection. Three authors independently selected the papers and agreed for final inclusion. The outcomes were the age, gender, body mass index, severe comorbidities, respiratory support and the critical illness related mortality in COVID-19. 572 publications were identified and 42 studies were selected including one unpublished study data. Only 14 studies were selected for quantitative analysis.
Results: All the primary points but the gender are significantly associated with COVID-19 mortality. The age >70, [odd ratio (OR): 0.17, CI; 95%, P-value: <0.00001], gender [OR: 0.89; CI: 95%, P-value: 0.32], BMI > 25 kg/m^2 [OR: 3.68, CI: 95%, P-value: <0.003], severe comorbidities [OR: 1.84, CI:95%, P-value: <0.00001], advanced respiratory support [OR: 6.98, CI: 95%, P-value: <0.00001], and critical illness [OR: 2.03, CI: 95%, P-value: <0.00001].
Conclusions: Patients with obesity are at high risk of mortality from COVID-19 infection.

Contents

* Corresponding author.
    E-mail address: abdulzahra.hussain@nhs.net (A. Hussain).

Introduction

An increasing body of data suggests that outcomes with Coronavirus Disease 2019 (COVID-19) are worse in those suffering from obesity and that a significant proportion of those needing intensive care suffers from overweight or obesity [1].

Obesity is affecting most of the physiological processes and modifying the functions of the system including the immune system [2]. It is crucial to understand the effect of obesity on the course of infection to prevent or mitigate the morbidities and mortality [3,4]. In the current COVID-19 era, bariatric teams are aware of the potential risks and thus stressing the extra caution and appropriate management of these patients [5]. Knowing the scale of the obesity problem in the world, we anticipate difficult times for this group of patients in Europe, America, Middle East and rest of the world with a high rate of obesity [6]. In 2009, a significant percentage of admissions to the hospitals and mortality because of H1N1 Influenza A virus infection was due to obesity, an estimated 151,700–575,400 total deaths was reported [7,8].

It might not be surprising to see a similar effect with novel COVID-19 infection. Using World Health Organization (WHO) data on the cumulative number of COVID-19 deaths, mortality rates would be 5.6% (95% CI 5.4–5.8) for China and 15.2% (12.5–17.9) outside of China [9] which is a gloomy prediction like previous pandemics. Multi strains of the virus are likely identified, but we do not know what impact on the virulence/pathogenesis would be [10,11]. Although the overall mortality for each country is expected to be different due to other factors such as comparability between healthcare systems, lockdown date, the population size, testing, the timing of the first confirmed case and the criteria of admissions to the hospital [12], the implications on the health systems in Europe and America are huge and expected to report the highest mortality in the world.

There are multiple risk factors associated with mortality in COVID-19 patients. Studies had shown diabetes, cardiovascular, cerebrovascular, pulmonary diseases, age and male factors are the predictors of mortality [13–17].

The vast majority of the COVID-19 studies didn't report obesity as a mortality risk factor due to the lack of the body mass index (BMI)/total body weight (TBW) data or unawareness of obesity risk. The primary endpoint of this research is to investigate obesity as a risk factor for COVID-19 mortality. The secondary endpoints are to assess age, gender, and critical illness, need for advanced respiratory support and associated comorbidities as risk factors for mortality in COVID-19 infection.

We conducted this study to investigate if patients with obesity are more likely to die from COVID-19 compared to non-obese individuals.

We investigated the entire English language scientific literature following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Methods

Studies reporting mortality with COVID-19 in patients with and without obesity were independently identified from the published scientific literature by searching PubMed, Embase, Google, Google Scholar, and Springer, Elsevier, the Lancet, AMJ, BMJ, and Oxford journals using keywords like Coronavirus, COVID-19, obesity, obesity mortality during COVID-19, clinical characteristics of COVID-19 patients. Three independent authors [AH, KM, WY] screened the titles and abstracts for eligibility. Last of these searches were carried on 1st May. References identified from database searches were exported to EndNote (Clarivate Analytics).

After removal of duplicates, full-text articles were included if their abstracts were considered to be eligible by any author. The full-text of each study was assessed independently, and disagreements were resolved by discussion (we reached 95% overall agreement [43 out of 45]. The studies that reported data on mortality during COVID-19 crisis were included.

We excluded studies that did not separately report on mortality with COVID-19 in patients suffering from overweight or obesity, studies that were small (less than 20 patients) and reports of poor quality data (not including the BMI for mortality, not including the critical illness, the need for invasive respiratory support, the comorbidities). A total of 14 studies were included in our final quantitative analysis. Fig. 1 gives a PRISMA flow chart [43] for article selection.

Our hypothesis is: Mortality in COVID-19 patients is high among patients with obesity due to large adipose tissue mass with high expression of ACE2 receptors.

The primary objective of this study was to find out the effect of overweight or obesity on patients suffering from COVID-19. Our secondary objectives were to investigate the effect of age, gender, and co-morbidities.

Review Manager (RM) 5.3 software was used for statistical analysis. The P-value of <0.05 was regarded as significant. For the assessment of the risk of bias in the included studies, the Newcastle–Ottawa system was used (Table 1).

The heterogeneity was reported in this meta-analysis, it ranges from 93 to 98%. Heterogeneity was due to the presence of one or more outlying studies with results that conflict with the rest of the studies. We have addressed this issue by repeating the analysis without outlying studies. Initial statistical analysis showed high heterogeneity among the study, I^2 was high >90%. Recalculation and analysis was performed after identifying the study that skewed the results and increased heterogeneity. As a result the I^2 was 0–61%.

The diagnosis of COVID-19 in the selected studies was made by rRT-PCR (apps.who.it), and also by chest computed tomography CT scan.

Results

A total of 14 studies[15–20,34–42] reported on mortality with COVID-19 in patients with and without obesity.

Age: >70 years old is significant factor for mortality. The included studies of 403,535 patients, 807 patients <70 year died compared to 881 mortality in 5895 patients >70 year old. Heterogeneity: Chi^2 = 90.84, df = 4 (P < 0.00001); I^2 = 96%. (Fig. 2). By repeating the analysis after removing outlying studies [39,42], heterogeneity: Chi^2 = 2.21, df = 2 (P = 0.33); I^2 = 9% and the test for overall effect: Z = 8.61 (P < 0.00001).

Gender: Male gender is not a significant factor for mortality in COVID-19. There were 4 studies included [18,35,37,42].

420 mortality among 1034 men and 182 mortality among 462 women. The odd ratio was 0.89 and the test for overall effect: Z = 1.00 (P = 0.32), Heterogeneity: Chi^2 = 42.39, df = 3 (P < 0.00001); I^2 = 93% (Fig. 3).

After repeating the test by removing outlying studies [37,35], the heterogeneity: Chi^2 = 1.73, df = 1 (P = 0.19); I^2 = 42% without major change at significant test of overall effect [test for overall effect: Z = 0.84 (P = 0.40)].

BMI: there have been 531 deaths among 2451 patients with BMI of >25 kg/m^2, while 1701 deaths among 24,056 patients with BMI < 25 (Fig. 4).

The data shows Body Mass Index (BMI) to be significantly associated with the mortality (P-value 0.005, OR 3.68, CI 95% (Fig. 4). Heterogeneity: Tau^2 = 0.87; Chi^2 = 104.32, df = 5 (P < 0.00001); I^2 = 95%. Test for overall effect: Z = 2.92 (P = 0.003).
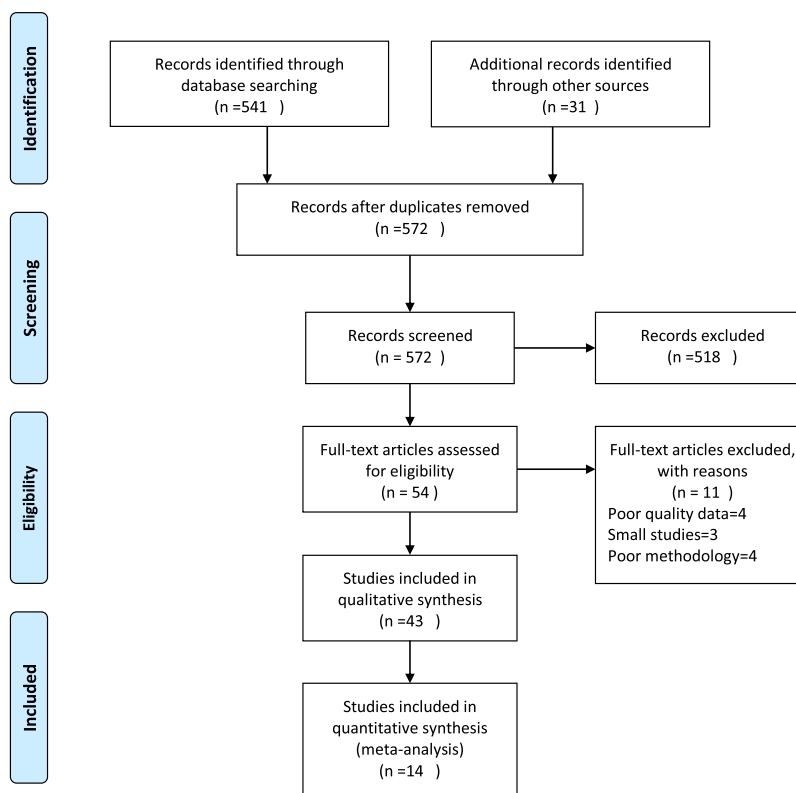
Fig. 1. Flow diagram.

Table 1
Newcastle–Ottawa quality of study assessment.

Study ID	Selection			Comparability	Outcome		Total
	Representation of the cohort	Selection of non exposed cohort	Ascertainment of the exposure		Assessment of the outcome	Adequacy of the outcome	
Arthur Simonnet 2020 [15]	★	–	★	–	★	★	★★★★
Bhatraju, 2020 [16]	★	–	★	–	★	★	★★★★
Caussy C 2020 [17]	★	–	–	–	★	★	★★★
Fei Zhou 2020 [18]	★	★	★	★	★	★	★★★★★
ICNARC 2020 [35]	★	★	★	★	★	★	★★★★★★
Jennifer Lighter 2020 [19]	★	–	★	–	★	★	★★★★
ldh.la.gov 2020 [36]	★	–	★	–	★	–	★★★
Luigi Palmieri, 2020 [37]	★	★	★	★	★	★	★★★★★★
Petrilli 2020 [38]	★	★	★	–	★	★	★★★★★
Robert Verity, 2020 [39]	★	–	★	–	★	★	★★★★
Xiang Bai 2020 [40]	★	–	★	–	★	★	★★★★
YD Peng 2020 [20]	★	–	★	–	★	★	★★★★
Xia Unpublished 2020 [41]	★	★	★	★	★	★	★★★★★★
Rong-Hui Du [42]	★	★	★	★	★	★	★★★★★★

By repeating the analysis after removing studies [16,35,35], heterogeneity is better : $Tau^2 = 0.23$; $Chi^2 = 5.16$, df = 2 (P = 0.0008); $I^2 = 61\%$,and the significance test almost the same [test for overall effect: Z = 1.76 (P = 0.0008)].

Advanced respiratory support: there have been 648 out of 867 patients with BMI < 25-needed advanced respiratory support compared to 183 patients with BMI > 25 of total 630 patients (Fig. 5). Patients with BMI > 25 kg/m^2 are significantly more likely to need advanced respiratory support (P-value 0.00001, OR 6.98, CI 95%) (Fig. 5). Heterogeneity: $Chi^2 = 16.72$, df = 3 (P = 0.0008); $I^2 = 82\%$ test for overall effect: Z = 14.54 (P < 0.00001).

By repeating the analysis without outlying one study data [41], heterogeneity: $Chi^2 = 1.35$, df = 2 (P = 0.51); $I^2 = 0\%$. Test for overall effect: Z = 12.89 (P < 0.00001).

Severe comorbidities: mortality among patients with severe comorbidities is significantly higher than no severe comorbidities, P-value <0.00001, OR 1.84, CI 955. (Fig. 6). Heterogeneity: $Chi^2 = 121.03$, df = 4 (P < 0.00001); $I^2 = 97\%$. Repeating analysis after removing the outlying studies [20,37,40], heterogeneity: $Chi^2 = 0.96$, df = 1 (P = 0.33); $I^2 = 0\%$. Test for overall effect: Z = 2.33 (P = 0.02).

Critical illness: 463 deaths among 1186 patients with BMI > 30 compared to 619 deaths among 3425 patients with BMI < 30. Obesity is a significant factor for critical illness during COVID-19, P-value <0.00001, OR 2.03, CI 95% (see Fig. 7).

By removing outlying one study [38], the heterogeneity: $Chi^2 = 0.14$, df = 1 (P = 0.71); $I^2 = 0\%$. Test for overall effect: Z = 15.39 (P < 0.00001).
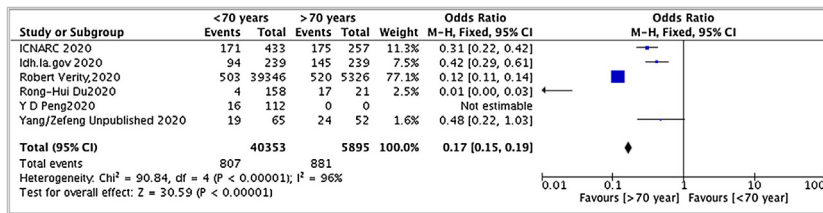
Fig. 2. Mortality among patients age >70 & <70 years.
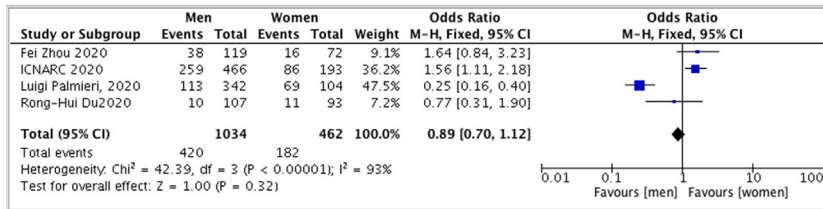
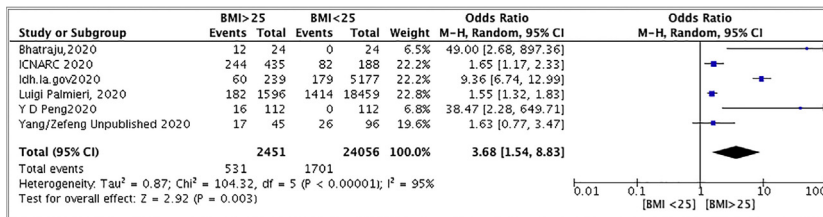**Fig. 3.** Mortality according to the gender.

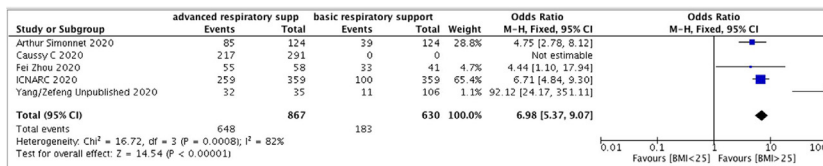**Fig. 4.** Mortality among patients with BMI > 25 kg/m^2 and <25 kg/m^2.

Fig. 5. Needs for advanced and basic respiratory support among patients with BMI > 25 kg/m^2 and <25 kg/m^2.
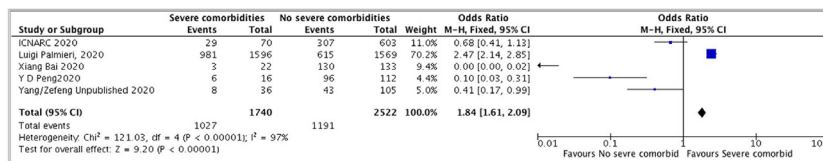

Fig. 6. Mortality among patients with and without severe comorbidities.

Discussion

The most important findings of this paper are obesity was an important associated factor for mortality in patients with COVID-19. This most likely because the patients in obesity were known to have a defective immune system that makes them vulnerable to a type of infection that specifically require a prompt cellular immunity response [18].

Obesity impairs immunity by altering the response of cytokines, resulting in a decrease in the cytotoxic cell response of immuno-competent cells which have a key anti-viral role in addition to disturb the balance of endocrine hormones, such as leptin, that
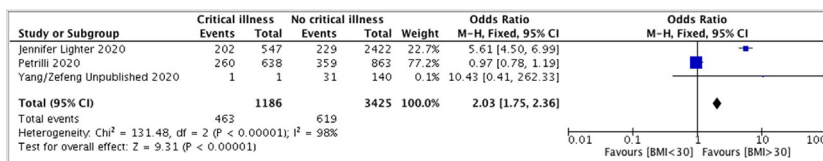

Fig. 7. Critical illness among patients with BMI > 25 kg/m^2 and <25 kg/m^2.

Table 2
Using the odd ratio (OR) of the available data to produce a scoring mortality model for COVID-19 infection.

Parameters	OR value	Age < 70	Female	BMI < 25	No severe comorbidities	No critical illness	No advanced respiratory support
Age > 70	0.17	0	Age < 70	Age < 70	Age < 70	Age < 70	Age < 70
Male	0.89	0.89	0	Female	Female	Female	Female
BMI > 25	3.68	3.68	3.68	0	MBI < 25	BMI < 25	BMI < 25
Severe comorbidities	1.84	1.84	1.84	1.84	0	No severe comorbidities	No severe comorbidities
Critical illness	2.03	2.03	2.03	2.03	2.03	0	No critical illness
Advanced respiratory support	6.98	6.98	6.98	6.98	6.98	6.98	0
Total	15.59	15.42	14.53	10.85	9.01	6.98	0

affect the interplay between metabolic and immune systems [19]. Obesity also leads to the involvement of adipose tissue-specific molecules (adipokines) in the generation of an environment that is favorable for diseases with an immune cause [20]. The dendritic cells (DCs) with crucial linking role between innate and adaptive immunity, produced twofold more of the immunosuppressive cytokine interleukin (Bello-Chavolla, #2)-10 than lean controls, and in turn stimulated fourfold more IL-4-production from allogeneic T cells. There are also negative impacts of the ability of DCs to mature and elicit appropriate T-cell responses to a general stimulus like viral infection [21].

Human angiotensin-converting enzyme 2 (ACE2) is the putative receptor for the entry of SARS-CoV2 into target cells with remarkably high affinity [22]. It is noteworthy that the level of expression of ACE2 in adipose tissue is reported to be higher than in lung tissue. The expression of ACE2 receptors is the same for adipose tissue in obese and non-obese patients but the difference is in the mass of the adipose tissues that made patients with obesity expressing high number of ACE2 receptors. This increment could explain why patients with obesity are showing severe form of the Covid-19 [23].

Chronic adipose tissue inflammation in obesity is influencing the activity of cells of innate and adaptive immunity [24]. Not only natural killer, macrophages, and neutrophils, but also underlying immune impairment in the responsiveness of lymphocytes is reported [25]. These changes are associated with an overall negative impact on chronic disease progression, immunity from infection, and vaccine efficacy in patients in obesity [26]. Statistical analysis of the patients who developed the severe disease and died in ITU suggested a significant association with obesity, and no surprise of the outcome if we understand the defective immune response highlighted above. The fact that obesity is usually a clustered of diseases leading to metabolic syndrome, making the previously confirmed mortality-predicting factors of diabetes, hypertension, cardiovascular diseases and other obesity-associated comorbidities as indirect evidence pointing to the obesity in well-conducted studies that did not include obesity data [14,17].

This study has confirmed patients above the age of 70 are likely to die from COVID-19, the same finding was confirmed in many other studies [16,27,28], which is expected outcome anyway. The other important results were mortality was not significantly different between men and women in general analysis, although it inclined towards men but does not reach statistical significance. This was also shown in the previous studies [14,27,29].

Patients in obesity are more likely to develop a critical illness than that of non-obesity [30–32]. It is crucial to note that patients with obesity not only suffer from their obesity but also from other metabolic disorders such as diabetes. This point should not be ignored because the cumulative risk of mortality increases with obesity-associated comorbidities. This indirectly refers to the metabolic syndrome and obesity-related comorbidities such as diabetes, hypertension, cardiac and cerebrovascular diseases. Several other studies had shown the same findings [29,33].

The other important outcome was the need for advanced respiratory support was significantly higher in patients in obesity. This is because of the detrimental effect of obesity on the lung volumes, functions and expansions in addition to the severity of the illness and magnitude of lung inflammation and damage in patients in obesity [29]. It goes without doubt that severe comorbidities are a risk factor for mortality in patients in obesity due to a defective immune system, under-functioning respiratory and cardiovascular systems, renal disease, diabetes, etc. This study has confirmed a significant association between comorbidities and mortality in patients in obesity.

Using the OR of the available data we were able to produce a scoring mortality model for patients in obesity with COVID-19 infection (see Table 2). This scoring system can be used to improve the care by identifying the high-risk patients.

Limitations of the study

This study included retrospective clinical reports suffer from some biases, the risk of biases was reported in methodology. There was a high grade of heterogeneity of the data. This was addressed by repeating the analysis after removing the outlying study data. There was no change in the overall test of significance, P-value remains <0.05. The heterogeneity reduced significantly and ranged from 0 to 61%. There was a lack of some data and were calculated indirectly from percentage and other provided parameters. There was one unpublished study data from China and the other 12 studies. Over two months period of search, we were aiming to include all available reports on mortality of obesity in COVID-19 infection, however, we may have missed some important studies that potentially affect the overall effects and conclusion from this meta-analysis. The populations studied differ in their comorbidities and severity. The definition of severe form is not consensual. The WHO defines overweight as BMI $\geq$ 25 kg/m^2 and obesity as BMI $\geq$ 30 kg/m^2. However, the Chinese-specific cut-off values for general adiposity define normal weight as BMI 18.5–23.9 kg/m^2, overweight as BMI 24.0–27.9 kg/m^2 and obesity as BMI $\geq$ 28 kg/m^2. COVID-19 mortality in children with obesity was not included and therefore not discussed.

Conclusions

Obesity is a risk factor for mortality in COVID-19. Age, critical illness, need for advanced respiratory support and severe comorbidities are also risk factors for mortality.

Conflict of interest

All authors confirm no conflict of interest or funding for this study.

CRediT authorship contribution statement

Abdulzahra Hussain: Conceptualization, Methodology, Software, Data curation, Writing - original draft. **Kamal Mahawar:** Conceptualization, Resources, Methodology, Writing - review & editing. **Zefeng Xia:** Resources, Writing - review & editing. **Wah Yang:** Resources, Writing - review & editing. **Shamsi EL-Hasani:**

Conceptualization, Resources, Methodology, Writing - review & editing, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - original draft.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.orcp.2020.07.002.

References

[1] Muscogiuri G, Pugliese G, Barrea L, Savastano S, Colao A. Commentary: Obesity: the "Achilles heel" for COVID-19? Metabolism 2020;108:154251.

[2] Fischer-Posovszky P, Moller P. The immune system of adipose tissue: obesity-associated inflammation. Pathologe 2020;41(May (3)):224–9, http://dx.doi.org/10.1007/s00292-020-00782-z.

[3] Houdek MT, Griffin AM, Ferguson PC, Wunder JS. Morbid obesity increases the risk of postoperative wound complications, infection, and repeat surgical procedures following upper extremity limb salvage surgery for Soft tissue sarcoma. Hand (N Y) 2019;14:114–20.

[4] Zhou X, Ye Y, Tang G, Zhou X. Obesity and infection, accompanying phenomenon or causal association? Clin Microbiol Infect 2018;24:668.

[5] Dietz W, Santos-Burgoa C. Obesity and its implications for COVID-19 mortality. Obesity (Silver Spring) 2020;28(June (6)):1005, http://dx.doi.org/10.1002/oby.22818. Epub 2020 Apr 18.

[6] Bluher M. Obesity: global epidemiology and pathogenesis. Nat Rev Endocrinol 2019;15:288–98.

[7] Louie JK, Acosta M, Samuel MC, et al. A novel risk factor for a novel virus: obesity and 2009 pandemic influenza A (H1N1). Clin Infect Dis 2011;52:301–12.

[8] Dawood FS, Iuliano AD, Reed C, et al. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study. Lancet Infect Dis 2012;12:687–95.

[9] Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, et al. Real estimates of mortality following COVID-19 infection. Lancet Infect Dis 2020;20(July (7)):773, http://dx.doi.org/10.1016/S1473-3099(20)30195-X.

[10] Mousavizadeh L, Ghasemi S. Genotype and phenotype of COVID-19: their roles in pathogenesis. J Microbiol Immunol Infect 2020;(March), http://dx.doi.org/10.1016/j.jmii.2020.03.022, pii: S1684-1182(20)30082-7.

[11] Cleemput S, Dumon W, Fonseca V, et al. Genome Detective Coronavirus Typing Tool for rapid identification and characterization of novel coronavirus genomes. Bioinformatics 2020;36(June (11)):3552–5, http://dx.doi.org/10.1093/bioinformatics/btaa145.

[12] Gaye B, Fanidi A, Jouven X. Denominator matters in estimating COVID-19 mortality rates. Eur Heart J 2020;(April), http://dx.doi.org/10.1093/eurheartj/ehaa282, pii: 5816893.

[13] Li X, Xu S, Yu M, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol 2020;146(July (1)):110–8, http://dx.doi.org/10.1016/j.jaci.2020.04.006.

[14] Du RH, Liang LR, Yang CQ, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J 2020;55(May (5)), http://dx.doi.org/10.1183/13993003.00524-2020, pii: 13993003.00524-2020.

[15] Kang YJ. Mortality rate of infection with COVID-19 in Korea from the perspective of underlying disease. Disaster Med Public Health Prep 2020:1–6.

[16] 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;46(June (6)):1294–7, http://dx.doi.org/10.1007/s00134-020-06028-z.

[17] Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA 2020;(April), http://dx.doi.org/10.1001/jama.2020.5394, pii: 2764365.

[18] Fortis A, Garcia-Macedo R, Maldonado-Bernal C, Alarcon-Aguilar F, Cruz M. The role of innate immunity in obesity. Salud Publica Mex 2012;54:171–7.

[19] Rojas-Osornio SA, Cruz-Hernandez TR, Drago-Serrano ME, Campos-Rodriguez R. Immunity to influenza: impact of obesity. Obes Res Clin Pract 2019;13:419–29.

[20] Karagiannides I, Pothoulakis C. Obesity, innate immunity and gut inflammation. Curr Opin Gastroenterol 2007;23:661–6.

[21] O'Shea D, Corrigan M, Dunne MR, et al. Changes in human dendritic cell number and function in severe obesity may contribute to increased susceptibility to viral infection. Int J Obes (Lond) 2013;37:1510–3.

[22] Kassir R. Risk of COVID-19 for patients with obesity. Obes Rev 2020;21:e13034.

[23] Li MY, Li L, Zhang Y, Wang XS. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infect Dis Poverty 2020;9:45.

[24] McLaughlin T, Ackerman SE, Shen L, Engleman E. Role of innate and adaptive immunity in obesity-associated metabolic disease. J Clin Invest 2017;127:5–13.

[25] Tanaka S, Inoue S, Isoda F, et al. Impaired immunity in obesity: suppressed but reversible lymphocyte responsiveness. Int J Obes Relat Metab Disord 1993;17:631–6.

[26] Andersen CJ, Murphy KE, Fernandez ML. Impact of obesity and metabolic syndrome on immunity. Adv Nutr 2016;7:66–75.

[27] Martins-Filho PR, Tavares CSS, Santos VS. Factors associated with mortality in patients with COVID-19. A quantitative evidence synthesis of clinical and laboratory data. Eur J Intern Med 2020;76:97–9, http://dx.doi.org/10.1016/j.ejim.2020.04.043. Epub 2020 Apr 23.

[28] Girgis CM, Clifton-Bligh RJ. Osteoporosis in the age of COVID-19. Osteoporos Int 2020;31(July (7)):1189–91, http://dx.doi.org/10.1007/s00198-020-05413-0.

[29] Huang JF, Wang XB, Zheng KI, et al. Obesity hypoventilation syndrome and severe COVID-19. Metabolism 2020:154249.

[30] Danziger J, Chen KP, Lee J, et al. Obesity, acute kidney injury, and mortality in critical illness. Crit Care Med 2016;44:328–34.

[31] Gharib M, Kaul S, LoCurto J, Perez M, Hajri T. The obesity factor in critical illness: between consensus and controversy. J Trauma Acute Care Surg 2015;78:866–73.

[32] Zheng KI, Gao F, Wang XB, et al. Obesity as a risk factor for greater severity of COVID-19 in patients with metabolic associated fatty liver disease. Metabolism 2020;108:154244.

[33] Sattar N, McInnes IB, McMurray JJV. Obesity a risk factor for severe COVID-19 infection: multiple potential mechanisms. Circulation 2020;142(July (1)):4–6, http://dx.doi.org/10.1161/CIRCULATIONAHA.120.047659.

[34] Walid MS, Robinson 3rd JS, Robinson ER, Brannick BB, Ajjan M, et al. Comparison of outpatient and inpatient spine surgery patients with regards to obesity, comorbidities and readmission for infection. J Clin Neurosci 2010;17:1497–8.

[35] ICNARC report on COVID-19 in critical care 04 April 20. Intensive Care National Audit and Research Centre. https://www.icnarc.org/About/Latest-News/2020/04/04/Report-On-2249-Patients-Critically-Ill-With-Covid-19. [Accessed 10 April 2020].

[36] http://ldh.la.gov/Coronavirus/. [Accessed 21 April 2020].

[37] Characteristics of SARS-CoV-2 patients dying in Italy Report based on available data on April 13th, 2020. https://www.epicentro.iss.it/en/coronavirus/bollettino/Report-COVID-2019_13_april_2020.pdf. [Accessed 24 April 2020].

[38] https://www.medrxiv.org/content/10.1101/2020.04.08.20057794v1. [Accessed 19 April 2020].

[39] https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30243-7/fulltext. [Accessed 22 April 2020].

[40] https://www.medrxiv.org/content/10.1101/2020.03.20.20037325v2. [Accessed 11 April 2020].

[41] Wah Yang, Zefeng Xia. Unpublished data. Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, The First Affiliated Hospital of Jinan University. China. Date of communication: 17/04/2020.

[42] Du Rong-Hui, Liang Li-Rong, Yang Cheng-Qing, Wang Wen, Cao Tan-Ze, Li Ming, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J 2020;55:2000524.

[43] Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Open Med 2009;334:e123–30.