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Survival analysis based on body mass index in patients with Covid-19 admitted to the intensive care unit of Amir Al-Momenin Hospital in Arak – 2021

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ABSTRACT

Introduction: The potential risk of obesity on the severity of COVID-19 has been proposed. The main purpose of this study was to investigate the effect of BMI on the survival rate of COVID-19 patients admitted to the ICU.

Methods & materials: Patients with COVID-19 admitted to ICU were included. Gender, height, weight, BMI, age, underlying disease status, prescribed drugs and nutritional supplements, and clinical and laboratory parameters at the beginning of admission were recorded. Death or discharge from the ICU and the days elapsed to these events were also reviewed and recorded. Data analysis was performed using the Cox regression model.

Results: assessing 193 patients showed that BMI was not related to the survival rate even after adjusting for other potential confounding variables. It was shown that arterial oxygen saturation and taking Famotidine were the significant factors determining the time to event in these patients.

Conclusion: The BMI at the time of ICU admission has no effect on survival rate and time to event in COVID-19 infected patients admitted to ICU.

1. Introduction

Coronavirus 2019 (COVID-19) or SARS-CoV-2, includes a range of diseases from asymptomatic infection (Mizumoto et al., 2020) to severe respiratory infection and inflammation in about twenty percent of patients (Wu and McGoogan, 2020). Identifying risk factors for the severe form of this disease and mortality is important for determining possible prevention approaches.

More recent studies have shown that diabetes mellitus (DM), cardiovascular disease (CVD), lung disease, age, and gender are well-known predictors of mortality in COVID-19 (Grasselli et al., 2020; Ruan et al., 2020; Kang, 2020; Emami et al., 2021; Shrestha et al., 2021). Understanding the impact of obesity on the COVID-19 severity is also important to prevent or reduce complications and mortality (Houdek et al., 2019; Chowdhury et al., 2021; Abbas et al., 2020). Obesity has been shown that disrupts the immune system and reduces the cytotoxic cell response of immune cells (Rojas-Osorno et al., 2019; Sureshchandra et al., 2019). It involves specific molecules of adipokines that have adverse effects on normal immune function (Andersen et al., 2016). Obesity also has disruptive effects on the dendritic cell’s ability to induce T cell response to a stimulus such as viral infection (O’Shea et al., 2005; Sartaj Sohrab et al., 2017; Almond et al., 2013).

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Currently, the potential risk of obesity on the severity of COVID-19 has been proposed (Almond et al., 2013). In 2009, it was estimated that a significant percentage of hospital admissions and deaths due to H1N1 influenza virus infection were due to obesity (Louie et al., 2011). Studies show that the outcome of COVID-19 is worse in obese patients, and a significant proportion of people who need intensive care suffer from overweight or obesity (Muscogiuri et al., 2020; Hussain et al., 2020). Angioteins-converting enzyme (ACE2), a receptor known for the entry of SARS-CoV2 into target cells, has been reported to have higher expression in adipose tissue (AT) than lung tissue. ACE2 receptors expression for AT is the same in obese and non-obese patients, but it is the difference in AT mass that causes obese patients to express larger amounts of ACE2 receptors, which in turn may cause severe forms of COVID-19 (Li et al., 2020). In other words, it seems that obese patients are more likely than other patients to have a critical condition in COVID-19 (Li et al., 2020).

It is important to note that most obese patients suffer from a variety of metabolic disorders such as diabetes (Huang et al., 2020a; Sattar et al., 2020), which has been proposed as an independent risk factor of the severe form of COVID-19 (Palaiodimos et al., 2020).

A meta-analysis of 27,007 people with COVID-19 showed that obesity and overweight (BMI > 25) were associated with a 268% increased risk of death (Hussain et al., 2020). However, in a study, although high body mass index (BMI) in people over 60 years of age did not increase the risk of COVID-19 disease severity, in patients under 60 years of age, BMI above 30 kg/m2 increased it by 100% (Lighter et al., 2020).

It is also important to understand the impact of obesity on the outcome of COVID-19 disease in those patients who require hospitalization in the intensive care unit (ICU). Clinically, the timing of the outcome is also very important. This means that it takes a few days from the time of admission to the ICU to the time of the event (discharge or death).

The aim of this study was to analyze the survival of patients with COVID-19 admitted to the ICU wards of Amir-Al-Momenin Hospital in Arak, considering BMI as an independent variable with the control of known confounding factors such as age, underlying disease status, prescribed drugs and nutritional supplements, and some other clinical and biochemical parameters at the time of admission to ICU.

2. Methods & Materials

This study was reviewed by the ethics committee of Arak University of Medical Sciences and approved with the ethics code IR. ARAKMU.REC.1400.080. At the beginning of hospitalization, informed written consent was obtained from all patients for confidential use of their medical records.

In a study by Jennifer Lighter et al. (2020), the risk of developing severe Covid disease in patients with a body mass index above 35 was associated with an 80% increase (1.8; 95% CI, 1.2–2.7; P = 0.006). Accordingly, in this study, HR (Hazard Ratio) = 1.8 with a standard deviation of 0.38 [(2.7-1.2)/3.92] was predicted.

Taking into account the first type error of 0.05 and statistical power of 0.85, the sample size of 180 people was estimated. The sample size was calculated based on the analytical approach of the COX regression model and using STATA v.12 software [Syntax: power cox, hratio (1.8) sd (0.38) effect (hratio) power (0.85)].

Patients with COVID-19 admitted to the intensive care units of Amir Al-Momenin Hospital in Arak city in Iran were included in the study from the mid-April 2021. Inclusion criteria included COVID-19 infection according to the diagnosis recorded in the medical record, admission to the intensive care unit, age over 18 years, and informed consent to enter the study.

COVID-19 infection had been confirmed by polymerase chain reaction (PCR) from nasal and throat swabs, as well as clinical signs examines by expert physicians. At this stage, by reviewing the patients’ medical records, variables of sex, height, weight, body mass index, age, underlying disease status, prescribed drugs, and nutritional supplements, and clinical and laboratory parameters at the beginning of admission including oxygen saturation, systolic and diastolic blood pressure, serum glutamate-pyruvate transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), fasting blood sugar (FBS), blood urea nitrogen (BUN), and serum creatinine (Cr) were extracted.

Then, the final event of each patient (death), and the days elapsed from the admission to the ICU until the event (time-to-event) were also reviewed and recorded.

Finally, data analysis was performed using the Cox regression model, and its backward conditional selection model. In this model, death was considered as main outcome variable and BMI was considered as an independent variable. The effects of other variables were also controlled in the model. Kaplan-Meier estimate was also used to compare the survival rate in three categories of BMI (less than 25 kg/m2, 25–30 kg/m2 as overweight, higher than 30 kg/m2 as obesity).

STATA statistical software (version 12; STATA Corporation, College Station, TX, USA) was used to analyze the data.

2.1. Theory

BMI seems to be a factor determining the survival in COVID-19 patients admitted to the ICU.

3. Results

In this study, 193 patients with COVID-19 admitted to the ICU were studied. Ninety-five patients were female, and the rest were male. During the follow-up period, 59 people were discharged from the ICU ward and 134 people (59 women and 75 men) died. The mortality rate was significantly higher in men than women (p = 0.03). Furthermore, there was no significant difference in mortality between obese patients (22 out of 33), overweight (54 out of 83), and normal patients (58 out of 77) (p = 0.35). In addition, the mortality rate was not different in patients with hypertension, diabetes mellitus or cardiovascular diseases compared to those without these diseases (Table 1).
Mean and standard deviation (SD) of weight, height, BMI, systolic and diastolic blood pressure (SBP), FBS, and creatinine at the time of admission in the expired and discharged patients were not statistically significant, but the difference between age, BUN, and arterial blood oxygen saturation at the beginning of admission in both groups were statistically significant (Table 2).

Comparison of patients’ survival based on different levels of BMI (less than 25, 25 to 30, more than 30) showed that the survival rate in these three levels of BMI was not statistically significant (Fig. 1).

In the Cox regression model, while inserting sex, age, BMI, spo2, diabetes mellitus, remdesivir, meropenem, vitamin C, vitamin B12, vitamin B-complex, vitamin D3, multivitamin, pantoprazole, famotidine, dexamethasone, vancomycin, and zinc sulfate in the model, only oxygen saturation percentage and taking famotidine had a significant effect on the survival rate at any given day from the admission date to the ICU (Table 3). Using the Cox regression Backward Conditional selection and setting the elimination cutoff at 0.2, sex, spo2, remdesivir, MULTIVIT, famotidine, dexamethasone, pantoprazole remained in the model, in which only spo2 (p < 0.001) and taking famotidine (p = 0.014) had a significant effect. (Table 4). In addition, when BMI was also used as a categorical variable (less than 25 as indicator, 25–30, higher than 30 kg/m²) in the Cox regression model (backward conditional selection), it was removed in the first step, i.e., it’s HRs at the last two levels compared to the first level were not statistically significant.

4. Discussion

The main purpose of this study was to investigate the effect of BMI on the survival rate of COVID-19 patients admitted to the ICU. In this study, we tried to control as many variables as possible that could distort the relationship. The results of this study showed that BMI was not related to the survival rate in COVID-19 patients admitted to the ICU.

It was shown that percentage of arterial blood oxygen saturation, as well as taking Famotidine were the significant determinant of mortality, but not the other variables.

The effect of obesity on the event of COVID-19 disease has been questioned in various studies (Yates et al., 2020; Rychter et al., 2020). Although in some studies the effect of BMI has been studied (Pranata et al., 2021; de Siqueira et al., 2020; Huang et al., 2020b), but rarely confounding variables have been controlled. Except for a few cases (Giacomelli et al., 2020), the time to the event has not been assessed.

In a study by Giacomelli et al. (2020), monitoring of 233 patients showed that obesity was independently associated with an increase in the hazard-to-death ratio in COVID-19 patients.

A study of 200 patients (Palaiodimos et al., 2020), showed that a BMI above 35 had a significant relationship with the mortality rate of COVID-19 patients (OR: 3.78; 95% CI: 1.45–9.83; p = 0.006). They also showed that male gender and older age increased the risk of death, with the latter two factors being consistent with the results of our study. We believe that in the regression analysis in our study, more confounding factors were controlled, and also the BMI variable was continuously entered in the model, which makes the relationship between this variable and the event more reliable. Furthermore, in our study, chi-square test showed that the ratio of normal, overweight, and obese people in the two groups of expired and discharged patients was not statistically significant.

In a study with a sample size of 43,995 COVID-19 patients aged 25–79 years in Spain (Fresán et al., 2021), the relative risk of age-adjusted mortality showed that severe obesity was an important risk factor for hospitalization and the severity of COVID-19. Another study in Wuhan, China, surveyed 95 COVID-19 patients and found that obese patients had more underlying disease and higher mortality rates than non-obese patients. In addition, obese patients also showed a more severe pathological changes in lung, as well as higher blood lymphocytes, IL-6, CRP, alanine aminotransferase (ALT), and ESR.

Recent systematic review and meta-analysis studies (de Siqueira et al., 2020; Huang et al., 2020b) concluded that obesity increases the need for hospitalization, the need for ICU admission, the need for mechanical ventilation, and the risk of death in COVID-19 patients, and increased abdominal fat with more severe consequences are associated. The difference in the results of our study with the results of the mentioned studies can be due to several reasons: 1- Difference in controlled confounder variables, 2- Small sample size in our study, 3- High mortality in our study (probably due to high hospitalization loading which was in the fourth domestic

### Table 1
Comparison of gender, HTN (hypertension), DM, CVD (cardiovascular diseases), and BMI levels between expired and discharged patients admitted to ICU.

| Gender | Expired | Discharged | p   |
|--------|---------|------------|-----|
| f      | 36      | 59         | 0.03|
| m      | 23      | 75         |     |
| HTN    |         |            |     |
| 0      | 31      | 69         | 0.89|
| 1      | 28      | 65         |     |
| DM     |         |            |     |
| 0      | 31      | 90         | 0.053|
| 1      | 28      | 44         |     |
| CVD    |         |            |     |
| 0      | 46      | 110        | 0.5 |
| 1      | 13      | 24         |     |
| BMI    |         |            |     |
| <25    | 19      | 58         | 0.35|
| 25–30  | 29      | 54         |     |
| >30    | 11      | 22         |     |
### Table 2
Comparison of continuous variables between expired & discharged patients regarding gender.

|                | Expired (134) |                | Discharged (59) |                | p   |
|----------------|---------------|----------------|-----------------|----------------|-----|
|                | Mean          | SD             | Mean            | SD             |     |
| **Age**        |               |                |                 |                |     |
| Men (98)       | 69.43         | 13.53          | 58.35           | 14.49          | 0.001 |
| Women (95)     | 64.61         | 15.65          | 63.28           | 17.23          | 0.699 |
| Total          | 67.31         | 14.64          | 61.36           | 16.27          | 0.013 |
| **Weight**     |               |                |                 |                |     |
| Men (98)       | 74.53         | 12.09          | 79.13           | 14.01          | 0.128 |
| Women (95)     | 73.64         | 12.27          | 72.53           | 13.16          | 0.677 |
| Total          | 74.14         | 12.14          | 75.10           | 13.77          | 0.628 |
| **Height**     |               |                |                 |                |     |
| Men (98)       | 172.41        | 6.04           | 172.00          | 6.99           | 0.783 |
| Women (95)     | 164.22        | 6.21           | 163.06          | 6.87           | 0.396 |
| Total          | 168.81        | 7.33           | 166.54          | 8.15           | 0.058 |
| **BMI**        |               |                |                 |                |     |
| Men (98)       | 25.05         | 3.76           | 26.73           | 4.42           | 0.076 |
| Women (95)     | 27.27         | 4.08           | 27.29           | 4.99           | 0.988 |
| Total          | 26.03         | 4.04           | 27.07           | 4.74           | 0.12 |
| **SBP**        |               |                |                 |                |     |
| Men (98)       | 126.75        | 18.89          | 130.30          | 16.22          | 0.42 |
| Women (95)     | 128.03        | 18.88          | 126.72          | 18.21          | 0.74 |
| Total          | 127.31        | 18.82          | 128.12          | 17.41          | 0.78 |
| **DBP**        |               |                |                 |                |     |
| Men (98)       | 76.96         | 11.30          | 76.96           | 9.74           | 0.999 |
| Women (95)     | 77.73         | 12.24          | 78.97           | 9.33           | 0.602 |
| Total          | 77.30         | 11.69          | 78.19           | 9.46           | 0.608 |
| **BUN**        |               |                |                 |                |     |
| Men (98)       | 151.63        | 88.23          | 148.09          | 52.57          | 0.856 |
| Women (95)     | 159.27        | 102.83         | 158.94          | 85.61          | 0.987 |
| Total          | 154.99        | 94.64          | 154.71          | 74.16          | 0.984 |
| **Cr**         |               |                |                 |                |     |
| Men (98)       | 1.92          | 2.11           | 1.24            | 1.24           | 0.138 |
| Women (95)     | 1.55          | 1.30           | 2.15            | 2.50           | 0.128 |
| Total          | 1.76          | 1.80           | 1.80            | 2.08           | 0.895 |
| **P<sub>O2</sub>** |               |                |                 |                |     |
| Men (98)       | 85.00         | 12.00          | 85.00           | 13.00          | 0.116 |
| Women (95)     | 80.00         | 20.00          | 92.00           | 9.00           | 0.0001 |
| Total          | 84.00         | 15.00          | 90.00           | 11.00          | <0.0001 |

**Fig. 1.** Comparison of patients’ survival based on different levels of BMI (less than 25, 25 to 30, more than 30) showed that the survival rate in these three levels of body mass index was not statistically significant. (p = 0.71).
pandemic peak time in Iran) which can increase or decrease the actual effect of variables. Some variables in the cox model included nutritional supplements prescribed by physicians or nutritionists. From the beginning of the COVID-19 pandemic, various questions arose about the effectiveness of dietary supplements, and many physicians began prescribing these supplements. Among micronutrients, vitamin D (Abbas et al., 2020; Rojas-Osornio et al., 2019), zinc (Skalny et al., 2020; de Almeida Brasil, 2020) and vitamin C (Feyaerts and Luyten, 2020; Cheng, 2020) received the most attention from researchers and physicians. The results of this study showed that after adjusting for other variables, administration of any of these nutrients had no statistically significant effect on patient survival. However, in this study, laboratory evaluation of these nutrients was not performed (due to non-prescription by physicians) and the dose of supplements and their frequency of use were not recorded. In addition, multivitamin, B-complex, and vitamin B12 supplements had no effect on survival rate.

In this study, the effect of prescribed drugs included remdesivir, meropenem, famotidine, dexamethasone, vancomycin, and pantoprazole on survival was also investigated, in which only famotidine had a statistically significant effect on the reduction mortality at any given day following admission to ICU. However, in a meta-analysis of observational study famotidine has been shown to not be associated with a reduced risk of mortality, intubation, and/or ICU admission in COVID-19 patients, but the heterogeneity of studies was high, and due to lack of power a possible protective effect has been proposed (Chiu et al., 2021). On the other hand, in a randomized, double-blind, clinical trial famotidine has been shown that lead to earlier resolution of COVID-19 symptoms and inflammation (Brennan et al., 2022). An in-vitro study proposed that famotidine acts as a direct inhibitor of SARS-CoV-2 replication (Loffredo et al., 2021).

Overall, only arterial oxygen pressure at the beginning of admission, and famotidine had a statistically significant effect on patient survival. It should be considered that this was an observational study and the selection of the patient to receive a drug or supplement was based on physician judgment, therefore those receiving any given drug or dietary supplement may have a better or worse clinical situation than others. This affects the results of observational studies, and the result should be interpreted in this regard. That’s why well-conducted randomized controlled trials should be also reviewed for each of the mentioned drugs and supplements.

5. Conclusions

In this study BMI was not related to the survival rate in COVID-19 patients admitted to the ICU. On the other hand, that percentage of arterial blood oxygen saturation, and taking Famotidine were the significant determinant of survival rate in these patients.

Table 3
Cox regression model. While adjusting for potential confounding variables, BMI has no significant effect on the risk of mortality of the COVID-19 patients admitted to the ICU.

| HR     | 95% CI      | p   |
|--------|-------------|-----|
| Sex (m)| 1.25        | 0.84| 1.88 | 0.27 |
| Age    | 1.01        | 0.99| 1.02 | 0.32 |
| BMI    | 0.99        | 0.94| 1.04 | 0.69 |
| SpO2   | 0.97        | 0.96| 0.99 | <0.001 |
| DM     | 1.16        | 0.77| 1.76 | 0.48 |
| Remdesivir | 0.69    | 0.46| 1.06 | 0.09 |
| Meropenem | 0.97   | 0.65| 1.47 | 0.90 |
| Vitamin C | 0.96  | 0.64| 1.45 | 0.86 |
| Vitamin B12 | 0.78  | 0.48| 1.27 | 0.31 |
| B-complex | 0.97  | 0.64| 1.48 | 0.90 |
| Vitamin D3 | 1.26  | 0.73| 2.16 | 0.40 |
| Multivitamin | 0.57 | 0.27| 1.21 | 0.14 |
| Famotidine | 0.63 | 0.42| 0.96 | 0.03 |
| Dexamethasone | 0.65 | 0.41| 1.04 | 0.07 |
| Vancomycin | 0.95 | 0.63| 1.44 | 0.82 |
| Pantoprazole | 0.74 | 0.47| 1.15 | 0.17 |
| Zinc   | 1.21        | 0.51| 2.90 | 0.66 |

Table 4
Cox regression model, the last step of backward conditional selection. Only SpO2, and taking famotidine, had a significant effect on the survival rate of COVID-19 patients admitted to the ICU. BMI did not remain in the model.

| HR     | 95% CI      | p   |
|--------|-------------|-----|
| SEX (M)| 1.28        | 0.89| 1.84 | 0.19 |
| SPO2   | 0.97        | 0.96| 0.99 | <0.001 |
| REMDESIVIR | 0.68  | 0.45| 1.01 | 0.057 |
| MULTIVITAMIN | 0.60 | 0.30| 1.22 | 0.16 |
| FAMOTIDINE | 0.61 | 0.42| 0.90 | 0.014 |
| DEXAMETHASONE | 0.66 | 0.42| 1.03 | 0.066 |
| PANTOPRAZOLE | 0.69 | 0.46| 1.06 | 0.088 |
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CRediT authorship contribution statement

Morteza Zangeneh: Data acquisition, Investigation, Resources, Validation, Visualization, Writing – review & editing. Touraj Valeh: Data curation, Funding acquisition, Resources, Writing – review & editing. Amrollah Sharifi: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

None.

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References

Abbas, A.M., Fathy, S.K., Fawzy, A.T., Salem, A.S., Shawky, M.S., 2020. The mutual effects of COVID-19 and obesity. Obes. Med. 19, 100250.

Almond, M.H., Edwards, M.R., Barclay, W.S., Johnston, S.L., 2013. Obesity and susceptibility to severe outcomes following respiratory viral infection. Thorax 68 (7), 684-686.

Andersen, C.J., Murphy, K.E., Fernandez, M.L., 2016. Impact of obesity and metabolic syndrome on immunity. Adv. Nutr. 7 (1), 66–75.

Brennan, C.M., Nadella, S., Zhao, X., Dima, R.J., Jordan-Martin, N., Demestichas, B.R., et al., 2022. Oral famotidine versus placebo in non-hospitalised patients with COVID-19: a randomised, double-blind, data-intense, phase 2 clinical trial. Gut 71 (5), 879–888.

JMDD Cheng, R.Z., 2020. Can early and high intravenous dose of vitamin C prevent and treat coronavirus disease 2019 (COVID-19)?. Med. Drug Discov. 5, 100028.

Chiu, L., Shen, M., Lo, C.H., Chiu, N., Chen, A., Shin, H.J., et al., 2021. Effect of famotidine on hospitalized patients with COVID-19: a systematic review and meta-analysis. PLoS One 16 (11), e0259514.

Chowdhury, A.U., Alam, M.R., Rabbi, M.F., Rahman, T., Reza, S., 2021. Does higher body mass index increase COVID-19 severity? A systematic review and meta-analysis. Obes. Med. 23, 100340.

de Almeida Brasil, P.G., 2020. The key role of zinc in elderly immunity: a possible approach in the COVID-19 crisis. Clin. Nutr. ESPEN 38, 65–66.

de Siqueira, J.V.V., Almeida, L.G., Zica, B.O., Brum, J.B., Barcelo, A., de Siqueira Galil, A.G., 2020. Impact of obesity on hospitalizations and mortality, due to COVID-19: a systematic review. Obes. Med. 25, 100352.

Feyaerts, A.F., Layten, W., 2020. Vitamin C as prophylaxis and adjunctive medical treatment for COVID-19? Nutrition 79, 110948.

Frezian, U., Guevara, M., Elis, R., Alhenia, E., Burgui, C., Castilla, J., 2021. Independent role of severe obesity as a risk factor for COVID-19 hospitalization: a Spanish population-based cohort study. Obesity 29 (1), 29–37.

Giacomelli, A., Ridolfo, A.L., Milazzo, L., Oreni, L., Bernachia, D., Siano, M., et al., 2020. 30-day mortality in patients hospitalized with COVID-19 during the first wave of the Italian epidemic: a prospective cohort study. Pharmacol. Res. 158, 104931.

Grasselli, G., Zangrillo, A., Zanella, A., Antonelli, M., Calvi, L., Castelli, A., et al., 2020. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. JAMA 323 (16), 1574–1581.

Houdek, M.T., Griffin, A.M., Ferguson, P.C., Wunder, J.S., 2019. 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). 14 (1), 114–120.

Huang, J.F., Wang, X.B., Zheng, K.I., Liu, W.Y., Chen, J.J., George, J., et al., 2020a. Letter to the Editor: obesity hypovitaminosis syndrome and severe COVID-19. Metabolism 108, 154249.

Huang, Y., Lu, Y., Huang, Y.M., Wang, M., Ling, W., Sui, Y., et al., 2020b. Obesity in patients with COVID-19: a systematic review and meta-analysis. Metabolism 113, 154378.

Hussain, A., Mahawar, K., Xia, Z., Yang, W., El-Hasani, S., 2020. Obesity and mortality of COVID-19. Meta-analysis. Obes. Res. Clin. Pract. 14 (4), 295–300.

Kang, Y.J., 2020. Mortality rate of infection with COVID-19 in Korea from the perspective of underlying disease. Disaster Med. Public Health Prep. 14 (3), 384–386.

Li, M.Y., Li, L., Zhang, Y., Wang, X.S., 2020. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infect. Dis. Poverty 9 (1), 45.

Lighter, J., Phillips, M., Hochman, S., Sterling, S., Johnson, D., Francois, F., et al., 2020. Obesity in patients younger than 60 Years is a risk factor for COVID-19 hospital admission. Clin. Infect. Dis. 71 (15), 896–897.

Loffredo, M., Lucero, H., Chen, D.Y., O’Connell, A., Bergqvist, S., Munawar, A., et al., 2021. The in-vitro effect of famotidine on sars-cov-2 proteases and virus replication. Sci. Rep. 11 (1), 5433.

Louie, J.K., Acosta, M., Samuel, M.C., Schechter, R., Vugia, D.J., Harriman, K., et al., 2011. A novel risk factor for a novel virus: obesity and 2009 pandemic influenza A (H1N1). Clin. Infect. Dis. 52 (3), 301–312.

Mizumoto, K., Kagaya, K., Zarebski, A., Chowell, G., 2020. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill. 25 (10), 2000180.

Mucoguiri, G., Pugliese, G., Barrea, L., Savastano, S., Colao, A., 2020. Experimental: Commentary: obesity: the “Achilles heel” for COVID-19? Metabol. Clin. 108, 108609.

O’Shea, D., Corrigan, M., Dunne, M.R., Jackson, R., Woods, C., Gaoatswe, G., et al., 2013. Changes in human dendritic cell number and function in severe obesity may contribute to increased susceptibility to viral infection. Int. J. Obes. 37 (11), 1510–1515, 2005.

Paladiminos, L., Kokkinidis, D.G., Li, W., Karamanis, D., Ogbinene, J., Arora, S., et al., 2020. Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality, in a cohort of patients with COVID-19 in the Bronx, New York. Metabolism 108, 154262.

Pranata, R., Linn, M.A., Yonas, E., Vania, R., Lukito, A.A., Siwabanto, E.B., et al., 2021. Body mass index and outcome in patients with COVID-19: a dose-response meta-analysis. Diabetes Metab. 47 (2), 101178.

Rojas-Osorio, S.A., Cruz-Hernandez, T.R., Drago-Serrano, M.E., Campos-Rodriguez, R., 2019. Immunity to influenza: impact of obesity. Obes. Res. Clin. Pract. 13 (5), 419–429.

Ruan, Q., Yang, K., Wang, W., Jiang, L., Song, J., 2020. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 46 (5), 846–848.

Rychter, A.M., Zawada, A., Ratajczak, A.E., Dobrowolska, A., Krela-Kazmierczak, I., 2020. Should patients with obesity be more afraid of COVID-19? Obes. Rev. 21 (9), e13083.

Sartaj Sohrab, S., I. Atkinson, R., M Alawi, M., I Azhar, E., 2017. Viral infection and obesity: current status and future prospective. Curr. Drug Metabol. 18 (9), 798–807.
Sattar, N., McInnes, I.B., McMurray, J.J.V., 2020. Obesity is a risk factor for severe COVID-19 infection: multiple potential mechanisms. Circulation 142 (1), 4–6.

Shrestha, E., Charkviani, M., Musurakis, C., Kansakar, A.R., Devkota, A., Banjade, R., et al., 2021. Type 2 diabetes is associated with increased risk of critical respiratory illness in patients COVID-19 in a community hospital. Obes. Med. 22, 100316.

Skalny, A.V., Rink, L., Ajsuvakova, O.P., Aschner, M., Gritsenko, V.A., Alekseenko, S.I., et al., 2020. Zinc and respiratory tract infections: perspectives for COVID-19. Int. J. Mol. Med. 46 (1), 17–26.

Sureshchandra, S., Marshall, N.E., Messaoudi, I., 2019. Impact of pregravid obesity on maternal and fetal immunity: fertile grounds for reprogramming. J. Leukoc. Biol. 106 (5), 1035–1050.

Wu, Z., McGoogan, J.M.J.J., 2020. 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 323 (13), 1239–1242.

Yates, T., Razieh, C., Zaccardi, F., Davies, M.J., Khunti, K., 2020. Obesity and risk of COVID-19: analysis of UK biobank. Prim. Care Diabetes 14 (5), 566–567.