



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.



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)
Clinical Nutrition Open Science
journal homepage:
www.clinicalnutritionopenscience.com



Original Article

Assessment of anorexia and weight loss during the infection and recovery period of patients with coronavirus disease 2019 (COVID-19)

Masoumeh Khalighi Sikaroudi ^a, Sanaz Rezaei Zonooz ^b, Zohreh Ebrahimi ^b,
Hanieh Jebraili ^a, Farnaz Farsi ^c, Atefeh Talebi ^c, Mohsen Masoodi ^{c,*}

^a Department of Health Sciences and Nutrition, Tehran University of Medical Sciences, Tehran, Iran

^b Department of Nutrition, School of Public Health, Iran University of Medical Sciences, Tehran, Iran

^c Colorectal Research Center, Iran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article history:

Received 4 July 2021

Accepted 6 November 2021

Available online 13 November 2021

Key words:

SARS-CoV-2

COVID-19

Anorexia

Weight loss

SUMMARY

Objectives: Patients with coronavirus disease 2019 (COVID-19) can present anorexia and weight loss due to their symptoms and eating disorder which can lead to immune system weakness and increase the duration of recovery time. We aim to assess the severity and duration of anorexia and weight loss within the infection and recovery period in these patients.

Method: We retrospectively identified 233 COVID-19 patients (older than 18 years) were admitted to the Rasoul-e Akram Hospital, from August to December 2020. Their medical records were reviewed by researchers. Then, patients who had inclusion criteria were asked about duration and severity of anorexia, and also weight alternation during the infection and after the recovery period.

Result: Analyzed data were collected from 233 COVID-19 patients showed the mean duration of anorexia was 7.08 ± 10.41 days with a significant loss of appetite (-75.55 ± 88.09 , P -value < 0.001) at the period of anorexia compare to appetite improvement. Also,

Abbreviations: ARDS, acute respiratory distress syndrome; BMI, Body mass index; COVID-19, Coronavirus disease 2019; COPD, chronic obstructive pulmonary disease; GI, Gastrointestinal; HADs, Hospital Anxiety and Depression Scales; ICU, intensive care unit; IgM, Immunoglobulin M; IgG, Immunoglobulin G; MERS-CoV, Middle East respiratory syndrome coronavirus; PCR, Polymerase chain reaction; PHEIC, public health emergency of international concern; RNA, Ribonucleic acid; SD, standard deviation; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VASs, visual analog scales; WHO, World Health Organization.

* Corresponding author. Colorectal Research Center, Iran University of Medical Sciences, Tehran, 1445613131, Iran.

E-mail address: masoodi47@yahoo.com (M. Masoodi).

<https://doi.org/10.1016/j.nutos.2021.11.001>

2667-2685/© 2021 Published by Elsevier Ltd on behalf of European Society for Clinical Nutrition and Metabolism. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

results demonstrated patients, especially males and severe illness subjects, significantly lost weight (P-value <0.001).

Conclusion: anorexia and weight loss occur in people infected with the coronavirus and may affect the recovery process of these patients by reducing their food intake. The underlying mechanisms of SARS-CoV-2 related to interaction to the gastrointestinal tract and development of anorexia in these patients need to clarify in future studies.

© 2021 Published by Elsevier Ltd on behalf of European Society for Clinical Nutrition and Metabolism. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

A novel coronavirus, named as SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) has infected people worldwide since January 7, 2020. Thus, the World Health Organization declared this novel spread as public health emergency of international concern (PHEIC) [1,2]. Three types of coronaviruses as the largest positive stranded RNA viruses with a nucleocapsid, SARS-CoV, MERS-CoV, and SARS-CoV-2 can lead to lower respiratory tract infections, ARDS, or even death [1,3]. According to recent studies, most patients are middle-aged men (40–60 years old) with underlying diseases such as hypertension, diabetes, COPD, cardiovascular disease and malignancy [4,5]. Clinical manifestations of SARS-CoV-2 are classified as mild symptoms to severe pneumonia with organ function damage. The most common symptoms are fever, cough, fatigue, shortness of breath, myalgia, sputum production and headache. Symptoms that are less common include sore throat, rhinorrhea, chest pain, hemoptysis, conjunctivitis redness, diarrhea, nausea, and vomiting [5,6]. Loss of appetite and reduced nutrient intake are parts of the symptoms present in infected patients with fever, headache, myalgia, and malaise [7]. Also, studies have shown that the prevalence of gastrointestinal (GI) symptoms among patients infected by COVID-19 is about 18% [8], accompanied by other symptoms, and can be associated with anorexia and food intolerance in these patients [9]. A meta-analysis of 25,252 cohorts among the first and second waves by Elshazli *et al.* [10] showed that 20.3% of patients presented GI manifestations, 19.9% of whom had anorexia. A study in China on seven COVID-19 patients showed that the participants had symptoms of anorexia for 7–22 days [9]. A recent 2020 study of the early COVID-19 effects on 1,000 individuals with eating disorders from the US and The Netherlands showed a total of 62% participants was increasing anxiety and alarming eating behaviors during the pandemic and respective 69% of the individuals had anorexia nervosa [11]. Parts of evidence have shown that COVID-19 can cause GI hypomotility on the nervous system and this may exacerbate anorexia in patients [12]. Moreover, the impact of COVID-19 on central nervous system, and also anxiety, quarantine, and hospitalization period can lead a person to eating disorder and negatively affect appetite [13]. Due to anorexia, insufficient food intake, and weight loss, macro and micronutrient deficiency (malnutrition) and immune system weakness can occur [14,15] (Fig. 1).

To the best of our knowledge, no prior studies have been performed to evaluate the anorexia status and weight loss in COVID-19 patients. Therefore, present study set for evaluate the severity and duration of anorexia and weight loss within the infection and recovery period in COVID-19 patients.

2. Method

2.1. Study design and patients

A retrospective cohort study was conducted on SARS-COV-2 patients in January 2021 at the Rasoul-Akram Hospital, Tehran, Iran. We examined patients who were hospitalized or referred to Infectious Diseases Clinic from August to December, 2020 (in second wave), and had one of the diagnostic criteria

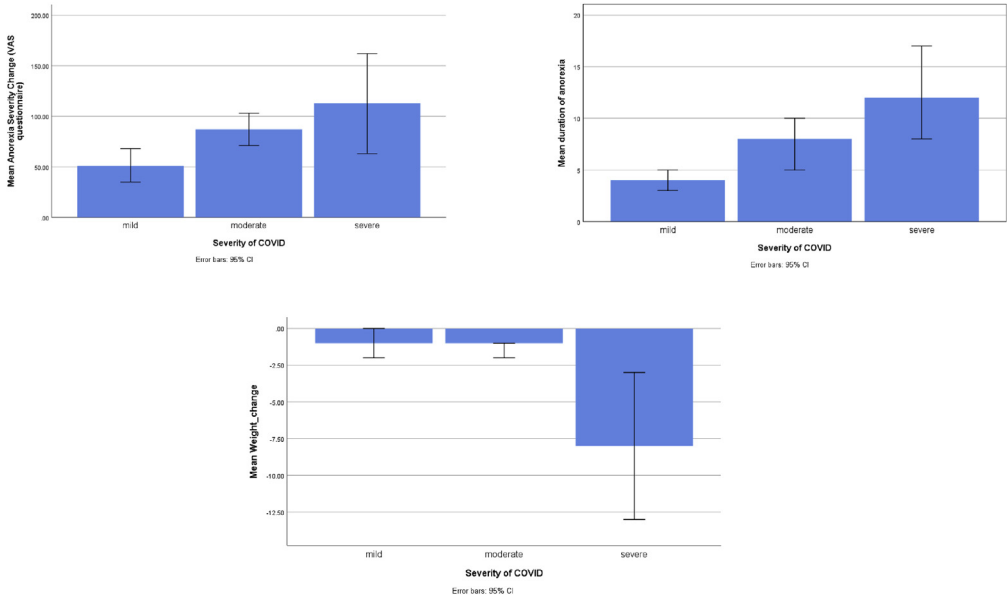


Fig. 1. Descriptive of duration and severity of anorexia and weight loss in different illness severity.

(nasopharyngeal positive polymerase chain reaction (PCR) or chest scan). We included patients who were i) adult (18 years and older), ii) suffered mild, moderate, or severe symptoms of COVID-19, iii) had no critical symptoms and history of ICU admission and connection to the ventilator, iv) without any malignant disease which can affect appetite such as cancer, renal or liver or heart failure, neurological diseases, etc., v) not being pregnant or lactating women. Also, we excluded patients reluctant to continue cooperation with the researchers or patients who died after discharge from the hospital.

This study was reviewed and approved by the ethic committee of Iran University of Medical Sciences (IR.IUMS.REC.1399.1114). The objective of the study was explicitly stated to the participants.

2.2. Data collection

Demographic data, past medical history, smoking, lab tests (PCR, IgG, and IgM), severity of illness based on physician diagnosis and symptoms (mild, moderate, and severe), and clinical symptoms (fever, cough, shortness of breath, chest pain, redness of the conjunctiva of the eye, sore throat, loss of sense of smell or taste, shivering, pain, feeling exhausted, nausea and vomiting, and diarrhea) were collected retrospectively from patient electronic records. Severity of COVID described as: 1. Asymptomatic or presymptomatic infection: Individuals who test positive for severe SARS-CoV-2 but have no symptoms, 2. Mild illness: Individuals with any of various signs and symptoms (eg, fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnea, or abnormal imaging, 3. Moderate illness: Individuals with evidence of lower respiratory disease by clinical assessment or imaging and an oxygen saturation (SaO2) over 93% on room air at sea level, 4. Severe illness: Individuals with a respiratory frequency of over 30 breaths per minute, SaO2 up to 93% on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) below 300, or more than 50% lung infiltrates, 5. Critical illness: Individuals with respiratory failure, septic shock, and/or multiple organ dysfunction [16,17]. We had telephone calls with patients who hospitalized in the 3 month ago (in the peak of infection), to gather anthropometric indices (height, wight, and body mass index) and their alterations after relief symptoms and anorexia. Also, appetite assessment questionnaire with visual analog scales (VASs) method which included three sets of identical questions (hungry, desire to eat, and fullness), was administered in the same order on a 100-mm line for patients

and recorded during the anorexia (during the hospitalization) and after relief symptoms (may be during the hospitalization or after discharge). The VASs were designed to reflect retrospective ratings of motivation to eat rather than the state at the time and according to studies, the average VAS score above 50 was considered suitable for the patient, and the score below 50 was assumed poor [18].

We used Hospital Anxiety and Depression Scales (HADs) [19] questionnaire, which is a 14-item self-rating scale, assessing anxiety and depression symptoms in different diseases associated with psychological disorders. The questionnaire consisted of seven questions related to anxiety, and seven questions to depression. Each item has a rating of 0–3; the higher rates indicate greater anxiety or depression symptoms. The total score ranged in each part from 0 to 21. Scores from 0 to 7 indicated a normal scale, 8 to 10 borderline, and scores 11 to 21 illustrated clinical problems. This questionnaire was asked telephonically after the discharge of patients.

2.3. Statistical analysis

Data was analysed by SPSS 25 for Windows. Descriptive statistics were reported for qualitative variables using frequencies with number and percentages, and for quantitative variables using mean and standard deviation (SD). Chi-square or Fisher exact test were also be used to examine the relationship between the two qualitative variables. Graphical methods assessed the normality distribution of data; the degree of skewness and normality tests were determined by Kolmogorov–Smirnov and Shapiro-Wilk tests. The paired sample T-test was used to compare mean in two dependent groups. Moreover, the analysis of variance was performed to compare mean in more than two independent groups. The correlation between the quantitative normal variables was investigated using Pearson correlation coefficient test. Statistical significance was considered at P-values <0.05.

3. Results

3.1. Study population and baseline demographics

Among 565 patients hospitalized or referred to the clinic with confirmed COVID-19, 233 patients (136 females, 97 males; mean age 38.41 ± 11.52 years) were included in the study after excluding patients who had critical severity of illness, malignant disease, or died after discharge from hospital. About 161 (69.1%) COVID-19 patients had not any past medical history. Of these, 91 (39.1%), 124 (53.2%), and 18 (7.7%) had mild, moderate, and severe illness severity, respectively. Also, the mean duration of illness was 17.08 ± 11.18 days. Patient characteristics are shown in [Table 1](#).

3.2. Anorexia duration

The mean duration of anorexia during infection and recovery was 7.08 ± 10.41 days. There was no significant difference in the duration of anorexia between female and male patients. The longest duration of anorexia was seen in patients with severe disease. Also, patients who had past history of GI problem with nausea and vomiting as COVID-19 symptoms, had experienced a longer period of anorexia. Full data are shown in [Table 2](#).

3.3. Anorexia severity

Totally anorexia was observed significantly (-75.55 ± 88.09 , P-value < 0.001) in patients during the illness and recovery as compared to appetite improvement. Also, each item for appetite assessment including hungry, desire to eat, and fullness, it decreased significantly (-27.17 ± 35.53 , -30.43 ± 36.00 , and -17.96 ± 40.89 , respectively; all P-value <0.001). Males and patients with severe illness and diarrhea as COVID-19 symptoms showed more severe anorexia. In addition, there was no significant correlation between the severity of anorexia and total score of stress and depression. Data are reported in [Table 2](#).

Table 1
Characteristic of study participants

Characteristics	COVID-19 patients (n=233)
Age (years) ^b	38.41 (11.52)
Sex ^a	
Male	97 (41.60%)
Female	136 (58.40%)
Height (Cm) ^b	169 (10)
Weight (Kg) ^b	75.60 (18.28)
BMI (Kg/m ²) ^b	26.29 (4.98)
Smoking ^a	
Nonsmoker	224 (96.1%)
Smoker	9 (3.9%)
Duration of illness ^b	17.08 (11.18)
Duration of anorexia ^b	7.08 (10.41)
Severity of COVID ^a	
mild	91 (39.1%)
moderate	124 (53.2%)
severe	18 (7.7%)
COVID symptoms ^a	
Fever	134 (57.5%)
Cough	125 (53.6%)
Shortness of breath	88 (37.8%)
Chest pain	82 (35.2%)
Pink eye (conjunctivitis)	37 (15.9%)
Sore throat	76 (32.6%)
Loss of sense of smell or taste	125 (53.6%)
Shivering	119 (51.1%)
Pain	185 (79.4%)
Feeling exhausted	184 (79%)
Nausea and vomiting	67 (28.8%)
Diarrhea	79 (33.9%)
Hospital Anxiety and Depression Scale ^b	
Stress (total score)	6.69 (4.95)
Depression (total score)	5.33 (4.44)
Past medical history ^a	
Healthy	161 (69.1%)
Renal disorders	10 (4.3%)
Cardiovascular diseases	23 (9.9%)
Diabetes	17 (7.3%)
Gastrointestinal disorders	28 (12%)
Hypothyroidism	22 (9.4%)
Diagnostic test ^a	
PCR	136 (58.4%)
IgG	42 (18%)
IgM	38 (16.3%)
Chest image	96 (41.2%)
Appetite indexes ^b	
Hungry	40.94 (32.34)
Desire to eat	44.76 (33.70)
Fullness	43.51 (31.98)
Total	129.29 (77.15)

^a Data are shown numbers (%).
^b Data are shown as mean ± SD.

3.4. Weight and BMI alternation

The mean body weight and BMI of patients before infection were 75.62 ± 18.28 and 26.29 ± 4.98, respectively. There was no significant difference between the bodyweight of subjects with mild (74.48 kg ± 19.05), moderate (76.66 kg ± 17.93), and severe (74.17 kg ± 17.20) severity illness at the beginning of the study. The analysis showed that the patients significantly lost weight (-2.34 kg ± 4.90) and BMI

Table 2
Descriptive of duration and severity of anorexia and weight loss in different sex, illness severity, PMH, and COVID-19 symptoms

	Anorexia duration	Anorexia severity (change)	Weight (change)	BMI (change)
Sex				
Female	7.57 ± 12.64	-60 ± 80.12	-1.43 ± 3.46	-0.55 ± 1.27
Male	6.39 ± 6.05	-97.37 ± 94.34	-3.61 ± 6.21	-1.15 ± 1.94
P-value	0.394	0.001	0.001	0.005
Illness severity				
Mild	4.65 ± 5.53	-51.70 ± 79.00	-1.61 ± 3.84	-0.54 ± 1.22
Moderate	8.03 ± 12.65	-87.58 ± 89.00	-2.00 ± 3.97	-0.70 ± 1.35
Severe	12.83 ± 9.28	-113.33 ± 99.65	-8.39 ± 9.72	-2.81 ± 3.08
P-value	0.003	0.002	<0.001	<0.001
PMH				
Healthy	7.15 ± 11.41	-74.07 ± 81.50	-2.04 ± 4.42	-0.70 ± 1.43
Diabetes	5.88 ± 4.90	-104.71 ± 92.60	-4.88 ± 5.95	-1.60 ± 1.85
CVD	7.17 ± 7.64	-62.61 ± 122.37	-2.74 ± 6.95	-0.93 ± 2.36
Hypothyroidism	6.36 ± 5.83	-75.45 ± 75.83	-1.95 ± 6.88	-0.72 ± 2.31
Renal disorder	8.30 ± 9.38	-108 ± 80.66	-2.45 ± 4.60	-0.94 ± 1.80
GI problem	9.07 ± 9.05	-96.79 ± 88.65	-3.50 ± 4.93	-1.73 ± 1.50
COVID-19 symptoms				
Fever	8.61 ± 12.71	-85.22 ± 85.04	-2.8 ± 5.86	-0.94 ± 1.91
Loss of smell or taste	8.06 ± 12.52	-74.16 ± 81.34	-2.23 ± 4.18	-0.77 ± 1.40
Pain	7.72 ± 11.25	-79.70 ± 91.41	-2.39 ± 5.29	-0.81 ± 1.73
Feeling exhausted	7.80 ± 11.24	-77.83 ± 91.15	-2.58 ± 5.16	-0.87 ± 1.69
Nausea and vomiting	10.61 ± 16.16	-80.15 ± 92.91	-3.29 ± 5.43	-1.12 ± 1.81
Diarrhea	8.25 ± 7.67	-97.97 ± 87.70	-2.22 ± 4.00	-0.78 ± 1.33

COVID-19: Coronavirus Disease 2019; PMH: Past medical history; CVD: Cardiovascular disease; GI: gastrointestinal.

Data are shown as mean ± SD.

P-value ≤ 0.05 was considered significant.

(-0.80 ± 1.61) during anorexia (P-value <0.001). This rate of weight loss was significantly correlated with decreased appetite in these patients (P-value= 0.001). Also, the most weight loss was seen in males and severe COVID-19 patients. Data are provided in [Table 2](#).

4. Discussion

In this study, the results of analysis on 233 adult COVID-19 patients with different amounts of the illness severity demonstrated that the average duration of anorexia was 7 days. During illness and recovery time, the patients significantly lost their weight. Also, the most loss of appetite and weight loss followed anorexia were seen in the males and severe illness patients.

One of the important complications of infection by SARS-COV-2 is anorexia [9,13]. The loss of appetite and reduced nutrient intake are parts of the symptoms presented in infected patients with fever, headache, myalgia and malaise [7]. Also, some symptoms including GI symptoms can highly reduce appetite. The main receptor for mediating SARS-CoV entry into host cells is angiotensin-converting enzyme 2 (ACE-2) [20]. Recent studies have shown that the ACE receptor is present in most parts of the GI tract, hence, some complications were reported in the digestive system by many patients with COVID-19 [21,22]. According to the results, most patients had moderate illness severity with a short duration and mild anorexia accompanied by nausea-vomiting (28.8%) and diarrhea (33.9%) as a GI symptom. The study was carried out by Ai *et al.* [9] on the clinical characteristics of seven COVID-19 patients with GI symptoms; they observed that each person had anorexia in the range of 7–22 days along with other symptoms including diarrhea, upper abdominal discomfort, nausea, and vomiting. Similarly, the current study showed seven days loss of appetite as an average period of anorexia. However, the advantage of present study over the previous study was the evaluation of anorexia with a larger sample size and also the use of the VASs questionnaire for the assessment of anorexia severity.

In addition, studies have been shown that the serum level of Leptin (hormone of satiety) in COVID-19 patients were significantly higher compared to the control group with a similar BMI, which can be one of the reasons why more severe symptoms are seen in people with more fat mass [23]. In a normal

range, leptin has a critical regulator of immunity and functions as a pro-inflammatory cytokine (not in obese or starved patients) [24]. The ACE2 utilization by the virus might be enhanced by an increase in leptin production induced by SARS-CoV-2 infection of visceral fat [23]. It can be a reason for anorexia in COVID-19 patients as other infectious diseases with increased inflammation and serum level of leptin. The average of BMI in our patients revealed their range of overweight. Further, studies in this area are needed to be conducted on these patients with different BMI.

Another causes of anorexia in these patients can be stress and fear of disease [13]. The stress of COVID-19 and the quarantine increased depression, anxiety and other mental health issues [25,26]. Stress can cause changing in appetite, energy, desires, and interests [27]. Studies reported an increased restriction in COVID-19 patients with anorexia nervosa [28,29]. Although anorexia can weaken the immune system by reducing the intake of micro and macro-nutrients, studies have shown that the levels of various pro-inflammatory cytokines and tumor necrosis factor increase in anorexia nervosa [30].

As expected and observed in our study, weight loss and decreased BMI following anorexia occurred during the disease. Inadequate nutrition is further worsen by diarrhea, malabsorption, loss of appetite, diversion of nutrients for the immune response, and urinary nitrogen loss, all of which lead to nutrient losses and damage to defense mechanisms. In addition, fever increases both energy and micronutrient requirements [31]. Also, systematic inflammation is directly related to the reduction of muscle mass. In this regard, Filippo *et al.* [32] indicated that patients with high C-reactive protein had lost >5% of initial body weight. As compared to prior to the infection, patients in our study had 3% reduction in weight.

This is the first study to evaluate the duration and severity of anorexia and weight loss during this period in COVID-19 patients. Also, we evaluated the duration and severity of anorexia and weight loss in various genders and illness severity with different COVID-19 symptoms. However, the study has some limitations. Considering the retrospective nature of the study, weight and appetite changes were based on the patients' self-reports and there was a possibility of error. The study also suffered from relatively small sample size, single-center hospital-based study, and lack of validated symptom instruments.

This study demonstrated that anorexia and weight loss occur among COVID-19 patients in the infection and recovery period and may affect the recovery process of these patients by reducing their food intake. The underlying mechanisms of SARS-CoV-2 related to the interaction with the gastrointestinal tract and development of anorexia and also the effect on hormone of satiety and hunger in these patients need to be clarified in future studies.

Author contributions

MKS and MM designed the study and reviewed the manuscript. MKS, SRZ, ZE, FF, and HJ collected data. MKS and AT performed the statistic analysis. MKS, MM, and HJ summarized the data and drafted the manuscript. All authors were responsible for the final approval of the version to be published.

Funding

This work was supported by the Colorectal Research Center (99-2-49-19132).

Declaration of competing interest

The authors declare that there were no conflicts of interest.

Acknowledgements

The authors would like to acknowledge the ongoing support of the Rasoul-e-Akram Hospital staffs and honorable participants who patiently helped us to advance this project.

References

- [1] Ge H, Wang X, Yuan X, Xiao G, Wang C, Deng T, et al. The epidemiology and clinical information about COVID-19. *Eur J Clin Microbiol Infect Dis* 2020;1–9. <https://doi.org/10.1007/s10096-020-03874-z>.
- [2] Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. *JAMA* 2020;324:782–93. <https://doi.org/10.1001/jama.2020.12839>.
- [3] Amawi H, Abu Deiab GI, Aljabali AA, Dua K, Tambuwala MM. COVID-19 pandemic: an overview of epidemiology, pathogenesis, diagnostics and potential vaccines and therapeutics. *Ther Deliv* 2020;11:245–68. <https://doi.org/10.4155/tde-2020-0035>.
- [4] Zhang J, Dong X, Cao Y, Yuan Y, Yang Y, Yan Y, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy* 2020;75:1730–41. <https://doi.org/10.1111/all.14238>.
- [5] Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020;382:1708–20. <https://doi.org/10.1056/NEJMoa2002032>.
- [6] Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020;8:475–81. [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5).
- [7] Eccles R. Understanding the symptoms of the common cold and influenza. *Lancet Infect Dis* 2005;5:718–25. [https://doi.org/10.1016/S1473-3099\(05\)70270-X](https://doi.org/10.1016/S1473-3099(05)70270-X).
- [8] Cheung KS, Hung IFN, Chan PPY, Lung KC, Tso E, Liu R, et al. Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples From a Hong Kong Cohort: Systematic Review and Meta-analysis. *Gastroenterology* 2020;159:81–95. <https://doi.org/10.1053/j.gastro.2020.03.065>.
- [9] Ai J-W, Zi H, Wang Y, Huang Q, Wang N, Li L-Y, et al. Clinical Characteristics of COVID-19 Patients With Gastrointestinal Symptoms: An Analysis of Seven Patients in China. *Front Med* 2020;7:308. <https://doi.org/10.3389/fmed.2020.00308>.
- [10] Elshazli RM, Kline A, Elgaml A, Aboutaleb MH, Salim MM, Omar M, et al. Gastroenterology manifestations and COVID-19 outcomes: A meta-analysis of 25,252 cohorts among the first and second waves. *J Med Virol* n.d.;n/a. <https://doi.org/10.1002/jmv.26836>.
- [11] Dumitraşcu MC, Şandru F, Carsote M, Petca RC, Gheorghisan-galateanu AA, Petca A, et al. Anorexia nervosa: COVID-19 pandemic period (Review). *Exp Ther Med* 2021;22:1–5. <https://doi.org/10.3892/etm.2021.10236>.
- [12] Kaafarani HMA, El Moheb M, Mwabejire JO, Naar L, Christensen MA, Breen K, et al. Gastrointestinal Complications in Critically Ill Patients With COVID-19. *Ann Surg* 2020;272:e61–2. <https://doi.org/10.1097/SLA.0000000000004004>.
- [13] Touyz S, Lacey H, Hay P. Eating disorders in the time of COVID-19. *J Eat Disord* 2020;8:19. <https://doi.org/10.1186/s40337-020-00295-3>.
- [14] Taylor AK, Cao W, Vora KP, De La Cruz J, Shieh W-J, Zaki SR, et al. Protein energy malnutrition decreases immunity and increases susceptibility to influenza infection in mice. *J Infect Dis* 2013;207:501–10. <https://doi.org/10.1093/infdis/jis527>.
- [15] Batool R, Butt MS, Sultan MT, Saeed F, Naz R. Protein-energy malnutrition: a risk factor for various ailments. *Crit Rev Food Sci Nutr* 2015;55:242–53. <https://doi.org/10.1080/10408398.2011.651543>.
- [16] **Diagnosics for Coronavirus Disease 2019 (COVID-19) Patients: What is the incubation period for coronavirus disease 2019 (COVID-19)?, What is the range of illness severity of patients with coronavirus disease 2019 (COVID-19)?, What are the signs and symptoms of patients with coronavirus disease 2019 (COVID-19)?, 2020.**
- [17] Maier HE, Kuan G, Saborio S, Bustos Carrillo FA, Plazaola M, Barilla C, et al. Clinical spectrum of SARS-CoV-2 infection and protection from symptomatic re-infection. *Clin Infect Dis Off Publ Infect Dis Soc Am* 2021. <https://doi.org/10.1093/cid/ciab717>.
- [18] Molfino A, Kaysen GA, Chertow GM, Doyle J, Delgado C, Dwyer T, et al. Validating Appetite Assessment Tools Among Patients Receiving Hemodialysis. *J Ren Nutr Off J Counc Ren Nutr Natl Kidney Found* 2016;26:103–10. <https://doi.org/10.1053/j.jrn.2015.09.002>.
- [19] Zigmund AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–70.
- [20] Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. *J Virol* 2020;94. <https://doi.org/10.1128/JVI.00127-20>.
- [21] Zhang H, Kang Z, Gong H, Xu D, Wang J, Li Z, et al. The digestive system is a potential route of 2019-nCoV infection: a bioinformatics analysis based on single-cell transcriptomes. *BioRxiv* 2020. <https://doi.org/10.1101/2020.01.30.927806>.
- [22] Chen H, Xuan B, Yan Y, Zhu X, Shen C, Zhao G, et al. Profiling ACE2 expression in colon tissue of healthy adults and colorectal cancer patients by single-cell transcriptome analysis. *MedRxiv* 2020. <https://doi.org/10.1101/2020.02.15.20023457>.
- [23] van der Voort PHJ, Moser J, Zandstra DF, Muller Kobold AC, Knoester M, Calkhoven CF, et al. Leptin levels in SARS-CoV-2 infection related respiratory failure: A cross-sectional study and a pathophysiological framework on the role of fat tissue. *Heliyon* 2020;6:e04696. <https://doi.org/10.1016/j.heliyon.2020.e04696>.
- [24] Maurya R, Bhattacharya P, Dey R, Nakhasi HL. Leptin Functions in Infectious Diseases. *Front Immunol* 2018;9. <https://doi.org/10.3389/fimmu.2018.02741>.
- [25] Fernández-Aranda F, Casas M, Claes L, Bryan DC, Favaro A, Granero R, et al. COVID-19 and implications for eating disorders. *Eur Eat Disord Rev* 2020;28:239–45. <https://doi.org/10.1002/erv.2738>.
- [26] Panchal N, Kamal R. The implications of COVID-19 for mental health and substance use. KFF; 2021. 2021. <https://www.kff.org/coronavirus-covid-19/issue-brief/the-implications-of-covid-19-for-mental-health-and-substance-use/>. [Accessed 21 March 2021].
- [27] Swaffield JB, Guo Q. Environmental stress effects on appetite: Changing desire for high- and low-energy foods depends on the nature of the perceived threat. *Evol Mind Behav* 2020;18:1–13. <https://doi.org/10.1556/2050.2018.00008>.
- [28] Ünver H, Rodopman Arman A, Erdöğdu AB, İlbasım Ç. COVID-19 pandemic-onset anorexia nervosa: Three adolescent cases. *Psychiatry Clin Neurosci* 2020;74:663–4. <https://doi.org/10.1111/pcn.13160>.
- [29] Frayn M, Fojtu C, Juarascio A. COVID-19 and binge eating: Patient perceptions of eating disorder symptoms, tele-therapy, and treatment implications. *Curr Psychol* 2021. <https://doi.org/10.1007/s12144-021-01494-0>.

- [30] Gibson D, Mehler PS. Anorexia Nervosa and the Immune System—A Narrative Review. *J Clin Med* 2019;8. <https://doi.org/10.3390/jcm8111915>.
- [31] Farhadi S, Ovchinnikov RS. The relationship between nutrition and infectious diseases: A review. *Biomed Biotechnol Res J BBRJ* 2018;2:168. https://doi.org/10.4103/bbrj.bbrj_69_18.
- [32] Di Filippo L, De Lorenzo R, D'Amico M, Sofia V, Roveri L, Mele R, et al. COVID-19 is associated with clinically significant weight loss and risk of malnutrition, independent of hospitalisation: A post-hoc analysis of a prospective cohort study. *Clin Nutr Edinb Scotl* 2020. <https://doi.org/10.1016/j.clnu.2020.10.043>.