ENDOCRINOLOGY RESEARCH AND PRACTICE

SOCIETY OF ENDOCRINOLOGY AND METABOLISM OF TÜRKİYE

Evaluation of Coronavirus Disease 2019-Related Morbidity and Mortality in Lipodystrophy Patients During the Pandemic Period

ORIGINAL ARTICLE
Endocrinol Res Pract. 2024;28(3):151-155

ABSTRACT

Objective: Coronavirus Disease 2019's (COVID-19) impact on rare disease populations such as lipodystrophy syndromes is unknown. We assessed COVID-19 infection outcomes in lipodystrophy syndromes and aimed to investigate the effect of restricted access to the hospital during the pandemic on metabolic parameters.

Methods: A survey form consisting of descriptive questions about the situation of the patients during the COVID-19 pandemic was created. The survey was performed by phone in February and March 2021; all patients gave verbal consent. Patients diagnosed with lipodystrophy syndromes participated in our study. Demographic parameters were recorded. They were asked if they were diagnosed with COVID-19; if so, the hospitalization, intensive care unit need, oxygen requirement, and COVID-19 treatment were questioned. Laboratory data were recorded from the hospital records.

Results: Seventy-one patients were investigated. Lipodystrophy patients in our study had at least 1 comorbid disease. Diabetes mellitus was the most common (87.1%). Six patients stated they had a COVID-19 infection (6/71, 8.5%). Three cases (50.0%) were hospitalized, and 1 (16.6%) patient was followed up in the intensive care unit. There were no deaths in our cohort. When the laboratory parameters of the entire group were evaluated, spot urine microalbumin increased significantly compared to the prepandemic period ($P = .013$).

Conclusion: Lipodystrophy patients may experience COVID-19 more severely due to their numerous comorbidities. Further research should be conducted with larger patient cohorts to investigate this relationship.

Keywords: COVID-19, lipodystrophy, mortality

Gökçen Güngör Semiz[1]

Tevfik Demir[2]

Ilgın Yıldırım Şimşir[3]

İsmail Selimoğlu[4]

Müge Yılmaz[5]

Hülya Ellidokuz[6]

Hüseyin Onay[7]

Ramazan Gen[8]

Bahri Evren[9]

[1]*Division of Endocrinology and Metabolism, Buca Seyfi Demirsoy Training and Research Hospital, İzmir, Türkiye*
[2]*Division of Endocrinology and Metabolism, Department of Internal Medicine, Dokuz Eylul University Faculty of Medicine, İzmir, Türkiye*
[3]*Division of Endocrinology and Metabolism, Department of Internal Medicine, Ege University Faculty of Medicine, İzmir, Türkiye*
[4]*Department of Internal Medicine, Dokuz Eylul University Faculty of Medicine, İzmir, Türkiye*
[5]*Department of Internal Medicine, Ege University Faculty of Medicine, İzmir, Türkiye*
[6]*Department of Preventive Oncology, Institute of Oncology, Dokuz Eylül University, İzmir, Türkiye*
[7]*Department of Medical Genetics, Ege University Faculty of Medicine, İzmir, Türkiye*
[8]*Division of Endocrinology and Metabolism, Department of Internal Medicine, Mersin University Faculty of Medicine, Mersin, Türkiye*
[9]*Division of Endocrinology and Metabolism, Department of Internal Medicine, İnönü University Faculty of Medicine, Malatya, Türkiye*

Corresponding author:
Gökçen Güngör Semiz
✉ ggungor28@hotmail.com

Received: September 17, 2023
Revision Requested: September 29, 2023
Last Revision Received: December 24, 2023
Accepted: January 16, 2024
Publication Date: March 4, 2024

Cite this article as: Güngör Semiz G, Demir T, Yıldırım Şimşir I, et al. Evaluation of coronavirus disease 2019-related morbidity and mortality in lipodystrophy patients during the pandemic period. *Endocrinol Res Pract.* 2024;28(3):151-155.

DOI: 10.5152/erp.2024.23352

Introduction

Lipodystrophic syndromes are a rare group of diseases characterized by the complete or partial absence of subcutaneous adipose tissue with hereditary or acquired defects.[1] There are 4 defined forms of lipodystrophic syndromes: congenital generalized lipodystrophy (CGL), familial partial lipodystrophy (FPLD), acquired partial lipodystrophy (APL), and acquired generalized lipodystrophy (AGL).

In some lipodystrophic syndromes, pathological fat accumulation occurs in other body parts, including the liver. Fatty liver increases hepatic and extrahepatic morbidity in patients with lipodystrophy. The degree of fat loss correlates with the severity of metabolic abnormalities. Insulin resistance and related comorbidities occur in patients with severe lipodystrophy.[2]

Congenital generalized lipodystrophy and FPLD are the 2 most common genetic lipodystrophies. Individuals with CGL experience complete or near-complete depletion of body fat, resulting in the abnormal accumulation of ectopic fat in organs like the liver and muscles. Familial partial lipodystrophy is a rare genetic disorder that leads to the partial loss of fat, predominantly affecting the limbs, trunk, and gluteal areas. The FPLD is linked to insulin-resistant diabetes, hypertriglyceridemia, low HDL cholesterol, hepatosteatosis, and an elevated risk of cardiovascular disorders.[3,4] Acquired generalized and partial lipodystrophies are mainly autoimmune and show complement abnormalities.[1]

In late winter 2019, the appearance of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) led to the coronavirus disease 2019 (COVID-19) pandemic, which first occurred in the spring of 2020. More than 150 million cases of COVID-19 have been declared.[5]

Coronavirus disease 2019 is a viral disease mainly affecting the pulmonary system, such as interstitial pneumonia and acute respiratory distress syndrome (ARDS).[6] During this outbreak, patients with chronic diseases are at higher risk for the life-threatening effects of COVID-19.[7] These conditions are ischemic cerebrovascular disease, chronic renal failure, chronic obstructive pulmonary disease, diabetes mellitus, cancer, obesity, and pregnancy. These comorbidities have been associated with severe COVID-19.[8,9] According to data from the Chinese Center for Disease Control and Prevention, mild disease is 81%, severe disease (e.g., shortness of breath, hypoxia, or >50% lung involvement) is 14%, and critical illness (e.g., respiratory failure, multi-organ dysfunction, or shock) is 5% reported. The overall case mortality rate was 2.3%.[10] As of the date of that report (November 26, 2021), a total of 8 700 641 cases have been diagnosed in Türkiye, according to the Turkish Ministry of Health data, and the case fatality rate was 0.8 %.[11]

During the COVID-19 pandemic, standard control applications in health institutions have decreased in our country within the scope of isolation measures, as in the rest of the world. In this process, the follow-up of diabetes, cardiovascular diseases, neurological disorders, and similar chronic diseases has also become difficult, and their course has deteriorated. The impact of the COVID-19 pandemic on rare diseases, such as patients with lipodystrophy, is unknown.

This study aimed to examine COVID-19 morbidity, mortality, and illness progression in patients with lipodystrophy syndromes. Additionally, we sought to investigate the impact of restricted hospital access during the pandemic on metabolic parameters within this patient population.

Materials and Methods

The Ethics Commiitee of Dokuz Eylül University Faculty of Medicine approved the protocol for this study (approval number: 2021/10-03, date March 29, 2021). Seventy-one patients diagnosed with lipodystrophy were included in the study. These patients were under follow-up at the hospitals of 4 universities: Dokuz Eylül University Faculty of Medicine, Ege University Faculty of Medicine, Mersin University Faculty of Medicine, and Malatya İnönü University Faculty of Medicine. Lipodystrophy patients were divided into 4 groups according to their clinical characteristics. The clinical diagnosis of CGL was made with the complete or near-complete loss of body fat tissue present since birth. The clinical diagnosis of FPLD was made with varying degrees of subcutaneous fat tissue loss in the extremities and trunk, starting during childhood and puberty. The clinical diagnosis of AGL was made in patients who started in adulthood and observed a gradual loss of subcutaneous fat throughout the body. The diagnosis of APL was made in patients with gradual loss of fat, especially from the upper part of the body (head, neck, upper extremities).[1] A survey form consisting of descriptive and straightforward questions was created. The survey was conducted by phone in February and March 2021; all patients gave verbal consent. Age, gender, weight, height, comorbid diseases, and patients' treatments were recorded. They were asked if they had COVID-19 so far; if so, the hospitalization and oxygen requirement, COVID-19 treatment, and ongoing findings after COVID-19 infection were questioned. COVID-19 positivity in the patients was confirmed by real-time polymerase chain reaction (RT-qPCR) (sampled with a nasopharyngeal swab). In patients whose nasopharyngeal swab sample tested negative for RT-qPCR, the diagnosis was made based on lung tomography findings and laboratory findings. Laboratory data (HbA1c, spot urine microalbumin, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) were recorded from the hospital records retrospectively, and the results after the COVID-19 period, if any, were obtained from the patients.

Statistical Analysis

As this was a retrospective study, the entire population was included in the study. Descriptive statistics, frequencies, percentages, means, and SDs of the patients were calculated to evaluate the data. Chi-square and Fisher's exact tests were used to analyze the variables indicated by count. The Mann–Whitney *U*-test was used for the independent group comparison to analyze the variable denoted by the measurement, and the Wilcoxon test was used for the dependent group analysis. Statistical Package for the Social Sciences (version 24.0, IBM Corp., Armonk, NY, USA) was used in data analyses. The statistical significance level was accepted as $P < .05$.

Results

Patient Characteristics

Of the 71 patients in our study, 57 (80.3%) were female, and 14 (19.7%) were male. The median age of the surveyed cases was 39.5 ±14.3 years (range: 17-73). If we look at the age distribution, there were 32 patients (45.1%) between the ages of 17 and 35 years, 34 patients (47.9%) between the ages of 36 and 64 years, and 5 cases (7.0%) were over 65. When the body mass index (BMI) was examined, there were 8 cases with <18.5 kg/m^2, 38 patients in the range of 18.5-24.9 kg/m^2, and 25 patients with >25 kg/m^2.

According to the subtypes of lipodystrophy, there were 20 (28.1%) patients in the CGL group, 1 (1.4%) in the AGL group, 44 (61.9%) in the FPLD group, and 6 (8.4%) in the APL group. Demographic analysis of all patients and analysis according to subgroups is given in Table 1.

Comorbidities and Therapies

Lipodystrophy patients in our study had at least one comorbid disease. Diabetes mellitus was the most common (87.1%), and hyperlipidemia was the second (48.6%). Most of the patients were taking more than one drug. In particular, 21.5% of those with diabetes followed up with diet and lifestyle changes, while 47.7% of them were receiving insulin therapy (basal or intensive insulin), and 30.8% of them were taking OADs. While the number of patients who received leptin treatment was 11 (15.5%), the treatment was discontinued in 2 cases. All patients receiving leptin were CGL patients.

The Course of Coronavirus Disease 2019 in Lipodystrophic Patients and the Impact of the Pandemic

Six patients stated that they had a COVID-19 infection (8.5%). Five of these patients had real-time polymerase chain reaction (RT-qPCR)

MAIN POINTS

- Lipodystrophic syndromes are a rare group of diseases. Coronavirus disease 2019's (COVID-19) impact on rare disease populations like lipodystrophy syndromes is unknown.
- Lipodystrophies, along with multiple comorbidities, may make the COVID-19 infection more severe. Further research should be conducted with larger patient cohorts to investigate this relationship.
- The pandemic may lead to deterioration in some metabolic parameters in patients with rare diseases.

Table 1. Demographic Analysis and Comorbid Conditions of the Patients

	All patients (n = 71)	CGL (n = 20)	AGL (n = 1)	FPLD (n = 44)	APL (n = 6)
Age (years ± SD)	39.49 ± 14.29	28.75 ± 8.36	20.00	44.09 ± 14.09	44.83 ± 11.42
Females	57 (80.3)	14 (70)	1 (100)	36 (81.8)	6 (100)
BMI (kg/m^2) mean ± SD	24.19 ± 5.05	22.14 ± 3.92	14.45	25.13 ± 4.79	25.81 ± 7.38
DM	61 (87.1)	20 (100)	1 (100)	35 (81.4)	5 (83.3)
HT	30 (42.9)	7 (35)	0 (0)	20 (46.5)	3 (50)
HL	34 (48.6)	10 (50)	0 (0)	21 (48.8)	3 (50)
CAD	10 (14.3)	0 (0)	0 (0)	10 (23.3)	0 (0)
HF	3 (4.3)	0 (0)	0 (0)	3 (7)	0 (0)
CKD	5 (7.1)	3 (15)	0 (0)	2 (4.7)	0 (0)
CVD	1 (1.4)	0 (0)	0 (0)	1 (2.2)	0 (0)
Hypothyroidism	11 (15.7)	2 (10)	0 (0)	8 (18.6)	1 (16.7)
Leptin treatment (yes)	11 (15.49)	11 (55)	0	0	0

Data are shown as n (%) and given as mean ± SD.
AGL, acquired generalized lipodystrophy; APL, acquired partial lipodystrophy; BMI, body mass index; CAD, coronary artery disease; CGL, congenital generalized lipodystrophy; CKD, chronic kidney disease; CVD, cerebrovascular disease; DM, diabetes mellitus; FPLD, familial partial lipodystrophy; HF, heart failure; HL, hyperlipidemia; HT, hypertension; OAD, oral antidiabetics.

positivity (samples were taken with a nasopharyngeal swab); 1 (16.6%) of them had RT-qPCR negativity (the diagnosis was determined through clinical findings, laboratory examinations, and imaging results). Of the 6 cases (8.5%) with COVID-19, 4 were female and 2 were male; all had diabetes. Three were in the CGL group, and 3 were in the FPLD group. Three out of 6 patients were admitted to the hospital, and 1 was later transferred to the intensive care unit. Two of these 6 patients required oxygen. There were no deaths from COVID-19 in our cohort. Table 2 compares the demographic characteristics of patients with and without COVID-19. The risk of contracting COVID-19 was assessed based on age, gender, BMI, lipodystrophy subtype, and comorbid conditions. There was no significant correlation between the age of patients and the acquisition of COVID-19 ($P = .60$). Also, there was no significant statistical difference in the risk of contracting COVID-19 based on gender ($P = .38$). Since other parameters aside from age and gender do not conform to the normal distribution, "*P* values" are not provided.

All patients stated that they received favipiravir treatment. Two patients had received corticosteroid therapy due to lung involvement and hypoxia. Immune plasma was not given to any of the patients. The most common findings that continued after COVID-19 were weakness and shortness of breath. It was ongoing in 2 cases (33.3%) (post-COVID seventh month).

Patients stated they were infected in August, September, November, December 2020, and January 2021. Only 1 patient was transmitted from their family, while the others had no contact with anyone with COVID-19.

Table 2. Comparison of Patients With and Without Coronavirus Disease 2019 in Terms of Demographic Characteristics and Comorbidities

	COVID-19 Positive (n = 6)	COVID-19 Negative (n = 65)
Gender n (%)		$P = .381$*
Female	4 (66.6)	53 (81.5)
Male	2 (33.3)	12 (18.5)
Age groups n (%)		$P = .605$**
17-35	3 (50.0)	29 (44.6)
36-64	3 (50.0)	31 (47.6)
65+	0 (0)	5 (7.8)
LPD type n (%)		
CGL	3 (50.0)	17 (26.1)
AGL	0 (0)	1 (1.7)
FPLD	3 (50.0)	41 (63.0)
APL	0 (0)	6 (9.2)
BMI groups n (%)		
<18.5	1 (16.6)	7 (10.7)
18.5-24.99	2 (33.4)	36 (55.4)
>25	3 (50.0)	22 (33.9)
DM n (%)	6 (100)	55 (84.6)
HT n (%)	3 (50)	27 (41.5)
HL n (%)	2 (33.3)	32 (49.2)
Leptin treatment n (%)	3 (50)	8 (12.3)

Data are shown as n (%).
AGL, acquired generalized lipodystrophy; APL, acquired partial lipodystrophy; BMI, body mass index; CGL, congenital generalized lipodystrophy; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; FPLD, familial partial lipodystrophy; HL, hyperlipidemia; HT, hypertension; LPD, lipodystrophy.
*Pearson chi-square.
**Mann–Whitney *U*-test.

The changes in the laboratory parameters of the whole group before and after the pandemic were examined. Only spot urine microalbumin increased significantly compared to the period before COVID-19 ($P = .013$) (Table 3). There was no substantial alteration observed in the other laboratory parameters of patients when compared to the prepandemic period ($P > .05$)

Table 3. Comparison of Metabolic Parameters During the Pandemic Period with the Prepandemic Period in all Patients

	Prepandemic Period	Pandemic Period	*P*
HbA1c (%)	7.08±1.69	7.29 ± 1.82	.741
Spot urine microalbumin (mg/dL)	311.61 ± 1050.32	371.52 ± 749.84	**.013***
TC (mg/dL)	186.09 ± 72.68	178.91 ± 84.35	.545
LDL cholesterol (mg/dL)	98.36 ± 71.50	92.00 ± 52.67	.451
HDL cholesterol (mg/dL)	40.05 ± 23.04	36.53 ± 15.48	.593
TG (mg/dL)	340.81 ± 392.77	379.83 ± 687.51	.379

Data are given as mean ± SD. The value in bold indicates statistical significance.
HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglycerides.
*Wilcoxon signed-rank test.

Discussion

Lipodystrophy syndromes are rare syndromes characterized by multiple comorbidities. In this retrospective evaluation of patients diagnosed with lipodystrophy, 8.5% were found to have contracted COVID-19, with half of those patients requiring hospitalization (3/6), and 1 patient was monitored in the intensive care unit. All of the COVID-19 cases in the study had diabetes, recognizing that these patients often have multiple comorbidities besides diabetes. Although 14.3% of men and 7% of women had the infection, no significant relationship was found between gender and the development of COVID-19, and there was no significant correlation between the age of patients and the acquisition of COVID-19.

To our knowledge, another study has been conducted in Brazil examining the progression of COVID-19 in patients with lipodystrophy. That study assessed 22 patients diagnosed with congenital generalized lipodystrophy.[12] In our study, we examined the data of 71 patients, including all lipodystrophy subgroups. The risk of contracting COVID-19 within subgroups could not be assessed due to noncompliance with a normal distribution in the group's numbers.

In meta-analyses and observational studies to date, male gender, advanced age, and various comorbid conditions have been associated with COVID-19 infection severity and mortality. These comorbid conditions are cardiovascular disease, diabetes mellitus, chronic obstructive pulmonary disease, and other lung diseases; cancer (in particular hematologic malignancies, lung cancer, and metastatic disease); pregnancy; cerebrovascular disease; chronic kidney disease; solid organ or hematopoietic stem cell transplantation; smoking; and obesity.[8,9] Our study found no relationship between the risk of disease and older age and gender ($P > .05$).

In a recently published article from our country, the rate of severe pneumonia at COVID-19 in hospitalized patients is 14.1%.[13] Although the number of patients in our cohort was small, half of those (3/6) who had COVID-19 were hospitalized; 2 of these 6 patients required oxygen, and 1 patient was monitored in the intensive care service. The fact that these rates are relatively high compared to Turkish data can be attributed to the multiple comorbidities of the patients. In addition, in a recent study with a large number of patients from Türkiye, the course of the disease in patients hospitalized due to COVID-19 was compared between patients with and without diabetes. T2DM patients hospitalized for COVID-19 have higher mortality rates (13.6% vs 8.7%), longer hospitalizations, and higher intensive care unit admissions (22.5% vs 16.1%).[14]

In the study conducted in Brazil, 22 CGL patients were evaluated. All recovered mildly from COVID-19. There were no hospitalizations or deaths. They attributed the patients' mild COVID-19 infection to their young age (median age 13.5 years).[12]

When considering the entire study group, there is a statistical increase in the spot urine microalbumin levels of the patients compared to the pre-pandemic period. The rise of microalbumin levels may be because patients spend more time at home, stay sedentary, disrupt their dietary habits, and are inconsistent with their treatment. Furthermore, patients may have taken additional vitamins or supplements to enhance their immune system. This may have also impacted microalbuminuria. Restriction and isolation measures taken during the pandemic, people's reluctance to enter the hospital environment, and disruptions to their normal check-ups can also cause this situation.

Limitations of our study include a restricted sample size and incomplete access to laboratory results from all patients. Due to the pandemic, regular patient check-ups were disrupted. It should be noted that some individuals may have contracted COVID-19 without exhibiting any noticeable symptoms. Only patients with laboratory or imaging-confirmed COVID-19 were considered positive cases. That is why there may be patients whose COVID-19 infection has not been detected. During the pandemic, patients may have taken supplements and vitamins or consumed food, which could have affected their metabolic parameters positively or negatively.

In our study exploring the morbidity and mortality of COVID-19 in patients with lipodystrophy, no deaths were recorded. Half of the patients with COVID-19 were admitted to the hospital, and 1 patient was monitored in the intensive care unit. All of the COVID-19 cases in this study had diabetes, recognizing that these patients often have multiple comorbidities besides diabetes. Additionally, the pandemic period may lead to deterioration in some of the metabolic parameters of rare disease patients. Thus, larger patient cohorts are necessary for a comprehensive study.

Data availability statement: The datasets used and/or analyzed in this study are available upon reasonable request from the corresponding author.

Ethics Committee Approval: Ethical approval of the study was obtained from the Ethics Committee of Dokuz Eylül University Faculty of Medicine (approval number: 2021/10-03, date March 29, 2021).

Informed Consent: Verbal informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – T.D., I.Y.Ş.; Design – T.D., I.Y.Ş., R.G., B.E.; Supervision – T.D., I.Y.Ş., H.E.; Resource – T.D., I.Y.Ş., R.G., B.E., H.O.; Materials – T.D., I.Y.Ş., R.G., B.E., H.O.; Data Collection and/or Processing – G.G.S., İ.S., M.Y.; Analysis and/or Interpretation – H.E.; Literature Search – G.G.S., İ.S., M.Y.; Writing – G.G.S.; Critical Review – T.D., I.Y.Ş., H.E.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: Preparation for publication of this article is supported by the Society of Endocrinology and Metabolism of Türkiye.

References

1. Garg A. Clinical review#: Lipodystrophies: Genetic and acquired body fat disorders. *J Clin Endocrinol Metab*. 2011;96(11):3313-3325. [CrossRef]
2. Polyzos SA, Perakakis N, Mantzoros CS. Fatty liver in lipodystrophy: a review focusing on therapeutic perspectives of adiponectin and leptin replacement. *Metabolism*. 2019;96:66-82. [CrossRef]
3. Chan D, McIntyre AD, Hegele RA, Don-Wauchope AC. Familial partial lipodystrophy presenting as metabolic syndrome. *J Clin Lipidol*. 2016;10(6):1488-1491. [CrossRef]
4. Hegele RA. Insulin resistance in human partial lipodystrophy. *Curr Atheroscler Rep*. 2000;2(5):397-404. [CrossRef]
5. CDC COVID-19 Response Team. Severe outcomes among patients with coronavirus disease 2019 (COVID-19) - United States, February 12-March 16, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(12):343-346. [CrossRef]
6. Landi F, Barillaro C, Bellieni A, et al. The new challenge of geriatrics: saving frail older people from the SARS-COV-2 pandemic infection. *J Nutr Health Aging*. 2020;24(5):466-470. [CrossRef]
7. McMichael TM, Currie DW, Clark S, et al. Epidemiology of COVID-19 in a long-term care facility in King County, Washington. *N Engl J Med*. 2020;382(21):2005-2011. [CrossRef]

8. Centers for Disease Control and Prevention. [updated Oct 14, 2021; cited 2021 December]. Available at: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/underlying-evidence-table.html
9. Centers for Disease Control and Prevention. [updated Oct 14, 2021; Cited 2021 Dec 11]. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html
10. 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):1239-1242. [CrossRef]
11. Ministry of Health, the Republic of Turkey. *COVID-19 Information Platform* Accessed 2021 Dec 11. Available at: https://covid19.saglik.gov.tr/
12. Madeira MP, Freire EBL, Fernandes VO, et al. SARS-COV-2 infection outcomes in patients with congenital generalized lipodystrophy. *Diabetol Metab Syndr*. 2021;13(1):65. [CrossRef]
13. Kokturk N, Babayigit C, Kul S, et al. The predictors of COVID-19 mortality in a nationwide cohort of Turkish patients. *Respir Med*. 2021;183:106433. [CrossRef]
14. Sonmez A, Demirci I, Haymana C, et al. Clinical characteristics and outcomes of COVID-19 in patients with type 2 diabetes in Turkey: A nationwide study (TurCoviDia). *J Diabetes*. 2021;13(7):585-595. [CrossRef]