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Determination of bariatric surgery outcomes: prospective study

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ABSTRACT

Aims: Obesity and related problems are an important health problem whose prevalence has increased in recent years. Bariatric surgery is one of the accepted clinical treatment methods for obesity. However, the obesity-related problems that bariatric surgery corrects and the problems it causes are not clear. The aim of the study is to determine the recovery status and problems experienced in obesity and related problems in patients who have undergone bariatric surgery.

Methods: 185 individuals who underwent bariatric surgery participated in the study. A 24-question data collection form, prepared by the researchers in line with the literature and including sociodemographic data, pre- and post-operative weight changes, problems experienced due to obesity, problems resolved after surgery, and problems experienced due to surgery, was used.

Results: It was determined that 18.4% (n=34) experienced postoperative complications. most common problems are hair loss (66.4%) and vitamin deficiency (55.1%) after surgery. 74% of individuals reported taking vitamin supplements. After the surgery, it was found that most o related to psychological (60.5%), j f the individuals (41.37%; n=12) had gallbladder surgery. After the surgery, individuals reported improvement in symptoms oint (48.6%), eating and respiratory problems (46.4%; 43.2%). When the type of surgery was compared with revision surgery, presence of complications, postoperative psychological support, and vitamin supplement use, no statistically significant relationship was found (p>0.05).

Conclusion: Our research shows that it is important to monitor the long-term health status of individuals who have undergone bariatric surgery.

Keywords: Bariatric surgery, obesity, complication

INTRODUCTION

Obesity is one of the important health problems whose rate is increasing today.[1] The World Health Organization (WHO) defines obesity as abnormal or excessive fat accumulation that poses a risk to health. According to WHO, individuals with a body mass index over 25 kg/m² are considered overweight, while individuals with a body mass index over 30 kg/m² are called obese.[2] Age, gender, education level, smoking-alcohol use, genetic factors, environmental factors, eating habits and psychological problems are effective in the formation of obesity.[3] Obesity brings with it serious health problems.1 These; insulin resistance, type 2 diabetes, metabolic syndrome, coronary heart disease, hyperlipidemia, gallbladder diseases, stroke, sleep apnea, fatty liver, asthma, musculoskeletal problems, menstrual irregularities, pregnancy complications, and some types of cancer. Obesity is also one of the health problems that increases the risk of complications after surgery.[4] In addition to the physiological effects of obesity, it has been reported that it has psychological effects on individuals such as low self-esteem, depression, anxiety disorders, sexual function and sleep disorders.[5] Recent studies have shown that more than 1,2 million of the deaths in the European region of the World Health Organization are caused by obesity, accounting for 13% of the total causes of death and ranking fourth among the causes of death.[6]

Treatment methods used for obesity are grouped under five groups. These include non-surgical and surgical methods; diet, exercise, behavioral change, pharmacological treatment and surgical treatment.[7] Surgical treatment is applied to those whose body mass index (BMI) is over 40 kg/m² or whose BMI is 35 kg/m² and who has an accompanying disease accompanied by comorbidity. Surgical treatment is a treatment method applied to lose weight and prevent comorbid diseases.[8] The general name given to surgical treatment is bariatric surgery, and there are different types. These are: Gastric bands, Sleeve

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gastrectomy (SG), Biliopancreatic diversion (BPD) Jejunoileal bypass, Combined restrictive and malabsorptive Mini gastric bypass, Roux-Y gastric bypass, BPD with duodenal switch.[8] There are risks of postoperative complications in bariatric surgery, especially those related to obesity. Leak, peritonitis, bleeding, stomal obstruction, internal hernia, marginal ulcer, fistula, gastroesophageal reflux, aletelctasis, pneumonia, long-term vomiting and diarrhea, weight regain, nutritional imbalances, psychosocial problems are among the risks seen after surgery.[9]

It is important to take the necessary precautions against complications that may occur after the surgery, to monitor the patient and to follow up after discharge. In this regard, physicians and nurses play an important role in patient follow-up through multidisciplinary team work. When we look at the literature, there are a limited number of studies revealing the effects of obesity surgery on patients and the care needs of patients. The aim of this study is to determine the recovery levels of obesity-related problems of individuals who have undergone bariatric surgery and the problems they experience after surgery, and to determination of the postoperative care and education needs of patients in this context.

METHODS

Ethics

Before starting the study, ethical approval was obtained from Ankara Yıldırım Beyazıt University Health Sciences Ethics Committee (Date: 16.03.2023, Decision No: 03-95). Additionally, written and verbal consent was obtained from the patients. This study was performed in line with the principles of the Declaration of Helsinki.

Type of Research

It was conducted descriptively in order to determine the recovery levels of obesity-related problems of individuals who underwent bariatric surgery and the problems they experienced after surgery, and to determination of the postoperative care and education needs of the patients in this context.

Population and Sample of the Research

The population of the research online consists of individuals who applied to a physician to receive consultancy services regarding healthy living and weight control between 16.03.2022 and 16.06.2023, and who underwent bariatric surgery. 185 individuals who met the inclusion criteria and volunteered to participate in the study were included in the study without sample selection. It was calculated as 0.99 the power of the study.

Inclusion Criteria

Individuals who agreed to participate in the study, were over 18 years of age, know how to read, write and speak Turkish, had no mental problems, and had at least 3 months and a maximum of one year after surgery were included.

Data Collection Tools

Tha data were collected through a survey containing 24 questions prepared by the researchers in line with the literature, aimed at determining the sociodemographic characteristics of the individuals, the physiological problems they experienced due to obesity and obesity surgery, the problems related to the obesity surgery they had undergone, and the status of receiving psychological support before and after surgery.[2-5]

Collection of Data

To collect data, individuals who received counseling services and underwent bariatric surgery were identified according to the inclusion criteria. The researchers contacted the individuals and explained the purpose of the study. The data collection form prepared for individuals who volunteered to participate in the study was delivered online, and the researchers asked for questions that were not understood.

One's contact information was shared with individuals. Informed consent was obtained from individuals before data collection.

Statistical Analysis

The data were analyzed in computer environment. Percentage distribution, mean, standard deviation, independent groups t test, one-way analysis of variance (ANOVA) test were used to evaluate the data. In all results, $p<0.05$ was considered statistically significant.

RESULTS

42.2% of the individuals participating in the research were in the 26-36 age group, 91.4% were women.

It was determined that 75.1% of them were married and 61.1% had a university education or higher. When the preoperative BMI of the individuals was examined, it was determined that 75.1% were in the group of 40 and more, and when the current BMI was considered, 34.1% were in the group between 25-29.9. 71.4% of the individuals participating in the study had a family history of obesity and 67% It was determined that 6 of them had weight problems in childhood. It was determined that 74.1% of the individuals did regular sports before the surgery, 87% did a regular diet, and 18.9% received psychological support before the surgery (Table 1).

It was determined that 80% of individuals who underwent bariatric surgery had sleeve gastrectomy and 20% had gastric bypass surgery. 3.8% of these individuals underwent revision surgery.

It was determined that 18.4% (n=34) experienced postoperative complications. Individuals; While they reported that the most common problems they experienced after surgery were hair loss (66.4%) and vitamin deficiency (55.1%); 74% of individuals reported taking vitamin supplements. After the surgery, it was found that most of the individuals (41.37%; n=12) had gallbladder surgery.

It was found that 15% of the patients' marital status changed after the surgery and 13.5% received psychological support. When the postoperative nutritional behavior of the individuals was examined, diet compliance behavior was detected in 41.6%, while emotional eating behavior was detected in 30.2% After the surgery, individuals, in order; reported improvement in symptoms related to psychological (60.5%), joint (48.6%), eating and respiratory problems (46.4%; 43.2%) of individuals.

Table 1. Distribution of individuals' descriptive characteristics

	Number	%
Age groups		
25 and less	10	5.4
26-36	78	42.2
37-47	68	36.8
48 and above	29	15.6
The average age	38.47±9.05	
Gender		
Woman	169	91.4
Male	16	8.6
Marital status		
Single	46	24.9
Married	139	75.1
Education status		
Primary education	23	12.4
High school	49	26.5
University and postgraduate	113	61.1
Live		
Marmara	73	39.5
Black Sea	12	6.5
Southeast	10	5.4
East Anatolia	5	2.7
Central Anatolia	44	23.8
Aegean	20	10.8
Mediterrenian	7	3.7
Abroad	14	7.6
Preoperative body mass index		
30 – 34.9 (First degree obese)	9	4.9
35-39.9 (Second degree obese)	37	20.0
40 and more (Third degree obese)	139	75.1
Current body mass index		
18-24.9 (Normal)	25	13.5
25-29.9 (Light fat)	63	34.1
30 – 34.9 (First degree obese)	53	28.6
35 -39.9 (Second degree obese)	30	16.2
40 and more (Third degree obese)	14	7.6
Family history of obesity		
There is	132	71.4
None	53	28.6
History of childhood obesity		
There is	125	67.6
None	60	32.4
Preoperative psychological support status		
Yes	35	18.9
No	150	81.1
Regular exercise before surgery		
Yes	137	74.1
No	48	25.9
Regular diet before surgery		
Yes	161	87.0
No	24	13.0
The impact of psychological factors on the decision to undergo surgery		
Yes	181	97.4
No	5	2.6

It was determined that psychological factors were effective in 97.4% of the patients' decision to undergo surgery (Table 2). When the individuals' age, gender, marital status, family obesity status, weight problem as a child, diet and exercise status, region of residence, pre-operative psychological support, and pre-operative BMI were compared, no statistically significant relationship was found between them (p>0.05).

Table 2. Distribution of individuals' characteristics regarding bariatric surgery and the postoperative period

	Number	%
Surgery type		
Stomach bypass (Roux-en Y gastric bypass, RNY Gastric bypass)	37	20.0
Gastric Sleeve Surgery (Sleeve gastrectomy)	148	80.0
Revision surgery status		
Yes	7	3.8
No	178	96.2
Post-operative re-operation (except revision surgery)		
Cholecystectomy	12	42.9
Skin prolapse	5	17.9
Polyp-cyst	3	10.7
Other*	8	28.5
Postoperative marital status change		
Yes	28	15.1
No	157	84.9
Development of postoperative complication		
Yes	34	18.4
No	151	81.6
Postoperative problems a		
Nausea	37	20.0
Vomiting	48	25.9
Vitamin insufficiency	102	55.1
Dumping syndrome	31	16.7
Hair spill	123	66.4
Constipation	61	32.9
Skin prolapse	64	35.5
Eat less	30	16.2
Other**	95	51.3
Symptom improvement after surgery		
Hypertension	40	21.6

When the type of surgery was compared with revision surgery, presence of complications, postoperative psychological support, and vitamin supplement use, no statistically significant relationship was found (p>0.05).

DISCUSSION

In this study, almost all of the patients reported that psychological reasons were effective in their decision for bariatric surgery. According to individuals' statements, the negative perspective of society seemed to be a big reason for making the decision to have surgery. It has been reported in the literature that the obese adults have 23-36% increased odds of developing depressed mood.[10] Similar to our research result, Callugi and Grave reported in their study that body image and weight concerns of individuals receiving obesity treatment were effective.[11]

Due to postoperative weight loss, an improvement was detected in the most common obesity-related joint, respiratory and eating problems in individuals. Obesity; It

affects osteoarthritis, osteoporosis and systemic inflammatory rheumatic diseases.[12] The fact that patients who lost weight after surgery reported improvement in joint problems may be associated with the positive effects of maintaining the ideal weight on the musculoskeletal system. Obesity also plays a major role in diseases such as obstructive sleep apnea syndrome, obesity hypoventilation syndrome, pulmonary hypertension, pneumonia, asthma is more common in obese individuals, and there is a strong relationship between COPD and obesity.[13] Fat accumulation in the abdominal and thoracic cavities and the mediastinal area causes the diaphragm to remain in an upward position, increasing pleural pressure and decreasing functional residual capacity (FRC). Factors that contribute to reduced lung compliance in obesity include increased thoracic blood volume, mediastinal fat compressing the lung, and closure of dependent airways resulting in atelectasis and increased alveolar surface tension.[14] While Chandrakumar et al.[15] reported an improvement in myocardial infarction,heart failure stroke and cardiovascular problems in individuals who underwent bariatric surgery, Pati et al.[16] reported that about 4-8% of all cancers are attributed to obesity. In our study, individuals; They stated that the problems related to obesity, which improved after surgery, mostly affected their daily life activities. In our research, in addition to the positive changes experienced by individuals after surgery, the problems they experienced were also reported. One of these was that postoperative individuals mostly reported that they had gallbladder surgery. After bariatric surgery, stones develop due to the increase in cholesterol levels in the gallbladder and saturation in bile mucin concentration, and rapid weight loss in a short time, weight loss more than 25% of the preoperative weight, triggers stone formation.[17] It has been reported that gallstones form in 3%-22% of bariatric patients within 12 months after surgery, and in 8%-30% within 24 months after surgery.[18] Approximately 4.7%-12% of obesity patients revealed that they had gallbladder surgery during active weight loss. Studies in the literature were similar to our study.[17-19] In addition, the individuals who participated in our research reported that they mostly experienced hair loss and vitamin deficiency after surgery. Bypassing a part of the gastric mucosa in bariatric surgery may lead to iron and B12 deficiency, and bypassing the duodenum and proximal jejunum may lead to impaired absorption of calcium and vitamin D from the intestines.[20-22] Bariatric surgery has also been reported to lead to decreased absorption of nutrients such as vitamins A, K, iron, selenium, zinc and copper.[23,24] The incidence of vitamin C deficiency in bariatric patients is 10-50%, calcium deficiency occurs in 10-25% at the end of the second year after surgery, 25-48% at the end of the fourth year, and vitamin D deficiency occurs in 17-52% and 50-63% of patients during the same period. deficiency has been reported.[25-28] Nutritional status after bariatric surgery may also affect vitamin deficiency and lead to low protein intake. This situation may cause an increase in hair loss.[20,29] According to the meta-analysis conducted by Zhang et al.[30], the incidence of hair loss in bariatric patients was reported to be 57%. Research results in the literature were similar to our results.

Limitations

This is a study that describes the positive and negative consequences of bariatric surgery. In the research, it would be more useful to check the patients at regular intervals in a clinical environment and support them with measurements of health-related parameters.

CONCLUSION

After bariatric surgery, monitoring the weight loss and improvement in comorbidities in patients is very important for their quality of life. Physiological, psychological and sociological follow-up of the patient in the postoperative period with the understanding of a multidisciplinary team can enable early diagnosis of complications, development of positive eating behavior in patients and increased compliance. Similar to results of this study, it may be recommended to monitor patients' levels such as zinc, biotin, and iron, to take supplements if necessary, and to provide structured training and consultancy services starting in the preoperative period in order to eliminate effects that will negatively affect the body image of patients, such as hair loss. Again, according to the results of our study, it is noteworthy that patients most frequently undergo gallbladder surgery after bariatric surgery. In this context, it is recommended to perform ultrasonography routinely to detect stones and mud before surgery, to follow up patients with pathological findings and provide consultancy services, and to provide patients with a healthy lifestyle regarding proper nutrition and physical activity in the postoperative period.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ankara Yıldırım Beyazıt University Health Sciences Ethics Committee (Date: 16.03.2023, Decision No: 03-95).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Data availability statement

All data generated or analyzed during the present study are included in this published article.

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Laboratory changes and parenchymal changes in computed tomography after COVID-19 pneumonia

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ABSTRACT

Aims: Novel coronavirus-2019 (2019-nCoV) has caused a global pandemic. Fort his reason, our study is to determine the variables of thorax tomography findings and laboratory data after COVID-19 pneumonia in cases with severe COVID-19 pneumonia and to detect the findings of possible interstitial lung diseases.

Methods: In this single-center study, 61 consecutive patients were examined. These patients were admitted to the COVID-19 Pandemic Clinic of Malatya Training and Research Hospital between July 15, 2020 and August 28, 2020 and were hospitalized with a diagnosis of COVID-19 pneumonia. Patients were discharged after the illness, and after 6 months, they applied to the outpatient clinic for follow-up. In this study, we compared the changes in laboratory variables and thorax CT scans at the time of diagnosis and 6 months later. Patients were divided into groups 1 and 2. Group 1: patients who were diagnosed with COVID-19 pneumonia at initial presentation and had thorax CT and laboratory parameters at the time of diagnosis and group 2: patients who presented to the outpatient clinic for 6-month follow-up during the postcovid pneumonia period and had control thorax CT and laboratory parameters.

Results: When the laboratory parameters of group 1 and group 2 patients were statistically compared. In addition to the increase in glucose, creatinine, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, lactate dehydrogenase, aptt, INR, fibrinogen, neutrophil percentage, mean erythrocyte hemoglobin, albumin, the decrease in calcium, sodium, leukocyte, platelet, hemoglobin, lymphocyte count, erythrocyte distribution range variables were found to be statistically significant ($p<0.05$). In our study, ground glass opacity was seen most frequently in Group 1 Thorax CT and was found in 57 patients. In 10 of these 57 patients, ground-glass opacity was positive on Group 1 and Group 2 Thorax CT, while ground-glass opacity was negative on Group 2 Thorax CT in 47 patients. In 50 patients, consolidation was found on Group 1 Thorax CT and consolidation was positive on Group 1 and Group 2 Thorax CT in 5 patients. The changes in fibrosis, parenchymal band, reticular opacity, traction bronchiectasis, irregular interfaces, ground glass opacity, consolidation, and pulmonary nodule variables in Group 2 Thorax CT were statistically significant ($p<0.05$).

Conclusion: Laboratory data is very important in terms of COVID-19 infection diagnosis, prognosis and guiding treatment. It may be due to the fact that patients with residual abnormalities on control thorax CT after COVID-19 pneumonia were older, had more comorbid diseases, and had severe clinical disease at the time of hospitalization.

Keywords: COVID-19 pneumonia, residual abnormalities on thorax CT, laboratory changes

INTRODUCTION

A virus causing unprecedented outbreaks in communities and hospital resources around the world was detected in December 2019.[1] This virus first emerged in the city of Wuhan in the Hubei province of the People's Republic of China. It was identified as a new coronavirus that is of bat origin, infects humans, causes severe respiratory failure, and poses a serious threat to life. In a short time, it crossed the borders of China and spread all over the world, especially to European countries. This virus was named novel coronavirus-2019 (2019-nCoV), then "Serious Acute Respiratory Syndrome-Coronavirus-2 (namely, SARS-CoV-2)" by the World Health Organization (WHO), and the disease it causes was named

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Corona Virus Disease 2019 (COVID-19). On March 11, 2020, WHO reported that this disease caused a global pandemic and turned into a public health problem threatening the whole world.[2] According to WHO data, as of January 10, 2022, an average of 305 million people were infected with this virus and an average of 5.5 million people died due to COVID-19.[3]

Coronaviruses are single-stranded, positive polarized, and enveloped RNA viruses. Coronavirus is a member of the Coronaviridae family that causes mild respiratory disease in humans. Coronaviruses cause the disease in animals and humans by invading the airways.[4] The disease is usually transmitted by airborne droplet transmission of the virus through aerosols. In addition, it was reported in studies that the virus could also be transmitted by a non-infected individual's contact with the infected individual's belongings, clothes, and any place that the infected individual contacted.[5]

According to preliminary data from China, SARS-CoV-2 infection covers a wide spectrum of clinical forms, including asymptomatic infection, mild upper respiratory tract disease in 81% of these patients, or life-threatening severe viral pneumonia such as acute respiratory failure, sepsis, multiple organ failure and death in those with moderate to severe disease.[6] It was reported that 14% of patients with moderate/severe disease progressed to the severe disease stage, 5% progressed to the severe disease stage with life-threatening multiorgan failure, and the mortality rate was reported to be 50% on average in the severe patient group.[7]

COVID-19 is inhaled and the most important site of involvement is the lungs. Therefore, it is very important to demonstrate lung involvement radiologically. Since the diagnosis and treatment of chronic changes and sequelae caused by the virus in the lungs and other organs and laboratory changes will be important parameters in patients with severe disease in the coming months and years, we followed CT and laboratory changes in patients with COVID-19 pneumonia. Although the RT-PCR test is the gold standard for the diagnosis of COVID-19, chest radiography and CT play important roles in the diagnosis, follow-up, and staging of COVID-19 pneumonia.[6-8]

According to the changes in the thorax CT appearance of COVID-19 patients, the disease can be divided into four stages.[8-9]

The early period covers the initial 0-4 days of the disease. Radiologic findings are normal or mild ground-glass opacity (unilateral or bilateral lower lobes, subpleural localization).

The progressive period covers the next 5-8 days. Radiologic findings increase in bilateral, diffuse, multilobar ground-glass opacities with cobblestone appearance and consolidations.

The peak period covers the days 9-13 from the first day. Dense consolidation areas are more prominent. Parenchymal bands may be occasionally seen. Ground-glass and cobblestone appearance may be present.

The regression period covers the 14th day and beyond. In this period, the infection is now under control. Diffuse ground glass opacities may be seen due to regression of consolidation areas. Signs of fibrosis (sequelae fibrotic bands, structural distortion, and traction bronchiectasis) may occur.

This study aimed to evaluate the chronic parenchymal changes and laboratory changes on thoracic CT in patients hospitalized for severe COVID-19 pneumonia infection after 6 months in outpatients who were admitted to the chest diseases outpatient clinic.

METHODS

Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved by the Scientific Ethics Committee of Malatya Training and Research Hospital (Date: 08.07.2020, Decision No: 2020/128). Written informed consent was obtained from all patients that they agreed to participate in the study. The study was supported by İnönü University Scientific Research Projects Coordination (Project No: TSA-2021-2333).

Patients

This study included 61 consecutive patients with severe COVID-19 pneumonia who were hospitalized in the Pandemic Clinic of Malatya Training and Research Hospital between 15.07.2020 and 28.08.2020 and met the inclusion criteria. In this single-center study, between July 15, 2020 and August 28, 2020, patients with a previous diagnosis of COVID-19 infection confirmed by RT-PCR test, whose blood parameters were examined at the time of diagnosis and whose thorax CTs were performed and reported as compatible with COVID-19 pneumonia, and who were clinically and radiologically diagnosed with Covid-19 pneumonia, were selected among the patients who applied to the outpatient clinic in the 6th month of their follow-up. Patients were divided into groups 1 and 2. Group 1; patients who were diagnosed with COVID-19 pneumonia at the first presentation and who had thorax CT and laboratory parameters at the time of diagnosis and group 2: patients who applied to the outpatient clinic for the 6th month control in the postcovid pneumonia period and who had control thorax CT and laboratory parameters.

Clinical/laboratory parameters and demographic data of our patients were recorded. After questioning their backgrounds and physical examinations, thorax CT scans of patients with COVID-19 pneumonia were performed at the time of initial diagnosis. An adult patient with a diagnosis of severe COVID-19 pneumonia was defined as a patient with clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) and severe respiratory distress with any of the following parameters: respiratory rate (RR)>30 breaths/minute and resting oxygen saturation <90%, partial oxygen saturation/fraction of inspired oxygen (PaO_2/FiO_2) ≤300 mm Hg.[10]

After non-contrast CT scanning of Group 2 patients, the comparison and interpretation of the radiologic images of Group 1 and Group 2 patients were evaluated by a radiologist with 9 years of experience who was unaware of the clinical history of the patients. The device was a Philips Medical System MX-128-slice multidetector (Koninklijke Philips N.V., Eindhoven, The Netherlands) with 120 kV, 250 mA and 5 mm slice thickness. During thoracic CT scanning, patients were in the supine position and end-inspiration was performed. Image interpretation Thoracic CT images of the patients at the time of diagnosis and a mean of 6 months later were evaluated at the workstation, and images on PACS were evaluated by the same radiologist using the lung window (width, 1000-1500 HU; level, -300 to -500 HU) and mediastinal window (width, 300-400 HU; level, 30-40 HU).

The main CT findings were described using the international standard nomenclature defined by the Fleischner Society Glossary and the peer-reviewed literature on viral pneumonia, using terms such as ground glass opacity (GGO) and consolidation.[11-13] Other findings most frequently evaluated were fibrosis, parenchymal band, reticular opacity, traction bronchiectasis, irregular interfaces, pulmonary nodule and honeycomb.

The distribution of findings was defined as peripheral (subpleural), central, or diffuse, depending on which third of the lung they were located in, as well as anterior and posterior, depending on which half of the lungs they were located in.

The semi-quantitative CT severity score proposed by Pan et al.[14] was calculated for each of the 5 lobes according to the degree of anatomical involvement as follows: 0, no involvement; 1, <5% involvement; 2, 5-25% involvement; 3, 26-50% involvement; 4, 51-75% involvement; and 5, >75% involvement. The total CT score was the sum of individual lobar scores ranging from 0 (no involvement) to 25 (maximum involvement). Patients were divided into residual and complete resolution groups based on CT scan images and scores at diagnosis and follow-up CT scans.

Thorax CT findings were evaluated according to radiological patterns such as fibrosis, parenchymal band, reticular opacity, traction bronchiectasis, irregular interfaces, ground glass opacity, consolidation, pulmonary nodule, and honeycomb.

Statistical Analysis

The analysis of the data included in the study was carried out with SPSS (Statistical Program in Social Sciences) 27.0 software. The Kolmogorov-Smirnov Test was used to check whether the data fit the normal distribution. The significance level (p) was taken as 0.05 for comparison tests. Since the variables were normally distributed (p>0.05), the analysis was continued with nonparametric test methods. Paired t-test was used to compare continuous dependent data and a marginal homogeneity test was used to analyze categorical dependent data. Number, percentage, mean, and standard deviation values were used as descriptive values.

RESULTS

Main Characteristics of Patients

A total of 61 patients 34 males (55.7%), 27 females (44.3%), ages <40; 2 (3.3%), 40-60;41 (67.2%), >65; 18 (29.5 %) were included in the study. 6 patients (6/55; 9.8%) were active smokers and 55 patients (55/61; 90.2%) had a history of inactive smoking. The patients who participated in the study consumed alcohol (2/59; 3.3%) and 59 patients (59/61; 96.7%) did not consume alcohol. Patients had known comorbid diseases including hypertension (31/30; 50.8%), type 2 diabetes mellitus (23/38; 37.7%), cardiovascular disease (19/42; 31.1%), neurologic disease (2/59; 3.3%) and obstructive pulmonary disease (14/47; 23%)(Table 1).

The study included 8 patients whose general condition deteriorated in the ward and were admitted to intensive care, 30 patients from the ward, and 23 outpatients. The most common clinical findings Group 2 were shortness of breath, fever, chest pain, cough, myalgia, muscle pain, and fatigue.

One of the inpatients with COVID-19 pneumonia was intubated (1/60; 1.6%) and transferred to the intensive care unit. Follow-up was performed in the intensive care unit. 6 of the patients received non-invasive support (6/55; 9.8%). 38 patients (38/23; 62.3%) received oxygen support. Patients with COVID-19 pneumonia received antiviral agents (59/2; 96.7%), antibacterial agents (54/7; 88.5%), glucocorticosteroids (38/23; 62.3%), low molecular weight heparin (47/14; 77%), aspirin (36/25; 59%) as medical treatment (Table 2).

Table 1. Distribution of demographic variables

Variables	Group	Frequency	Percent
Age (years)	<40	2	3.3
	40-60	41	67.2
	>65	18	29.5
Gender (females, males), n(%)	Female	27	44.3
	Male	34	55.7
Smoker, n(%)	Smoker	6	9.8
	Non-smoker	55	90.2
Alcohol consumption, n(%)	Drinking	2	3.3
	Not drinking	59	96.7
Hypertension, n(%)	Present	31	50.8
	Not present	30	49.2
Cardiovascular disease, n(%)	Present	19	31.1
	Not present	42	68.9
Neurological disease, n(%)	Present	2	3.3
	Not present	59	96.7
Obstructive lung disease, n(%)	Present	14	23.0
	Not present	47	77.0
Diabetes mellitus, n(%)	Present	23	37.7
	Not present	38	62.3

Routine blood samples were collected from Group 1 and Group 2 patients. Variables related to COVID-19 pneumonia, acute and 6 months after the acute period were statistically compared. The increase in glucose (mg), creatinine (mg/dL), aspartate aminotransferase (AST) (IU/L), alanine aminotransferase (ALT) (IU/L), gamma glutamyl transferase (GGT) (IU/L), lactate dehydrogenase (LDH) (IU/L), aptt, inr, fibrinogen (mg), neutrophil percentage (%), mean erythrocyte hemoglobin (MCH) (pg) was statistically significant (p<0.05). The decrease in albumin (g/dl), calcium (mg/dl), sodium (Na) (mEq/L), leukocyte, platelet, hemoglobin, lymphocyte count, erythrocyte distribution range variables was statistically significant (p<0.05). However, the increase in urea (mg/dl), creatine kinase (CK) (u/l), ckmb (u/l), protein (g/dl), potassium (k)(mmol), c-reactive protein (CRP)(mg/dl), troponin (ng/ml), platelet distribution range (pdw)(%) was not statistically significant (p>0.05). The decrease in alkaline phosphatase (ALP)(ıu/l), total bilirubin (t.bil)(mg/dl), direct bilirubin (d.bil)(mg/dl), d-dimer (mcg/ml), hematocrit (%), neutrophil count (mcl), mean erythrocyte hemoglobin concentration (MHC)(g/dl), mean erythrocyte volume (MCV)(fl), plateletcrit, mean erythrocyte volume (MCV) was not statistically significant (p>0.05) (Table 3).

When the thorax CT of 61 patients was analyzed, 19 patients (19/61) showed complete resolution of lung findings, while 42 patients (42/61) had residual findings in their lungs. Patients were divided into Group 1 and Group 2. In our study, ground-glass opacity was seen most frequently in Group 1 Thorax CT (Figure 1). In 57 (100%) patients, ground-glass opacity was found and in 4 (100%) patients ground-glass opacity was not observed. Of these 57 patients, 10 (18%) were positive for

Table 2. Distribution of disease-related variables

Variable	Group	Frequency	Percent
Intensive care ward	Intensive care	8	13.1
	Service	30	49.2
	Outpatient	23	37.7
Fire	Present	9	24.6
	Not present	46	75.4
Chest pain	Present	21	34.4
	Not present	40	65.6
Cough	Present	21	34.4
	Not present	40	65.6
Shortness of breath	Present	42	68.9
	Not present	19	31.1
Muscle pain	Present	27	44.3
	Not present	34	55.7
Fatigue	Present	36	59.0
	Not present	25	41.0
Pulmonary function test	Present	48	78.7
	Not present	13	21.3
Invasive	Present	1	1.6
	Not present	60	98.4
Noninvasive	Present	6	9.8
	Not present	55	90.2
Oxygen support	Present	38	62.3
	Not present	23	37.7
Antiviral agent	Present	59	96.7
	Not present	2	3.3
Glucocorticosteroid	Present	38	62.3
	Not present	23	37.7
Antibacterial	Present	54	88.5
	Not present	7	11.5
Low molecular weight heparin	Present	47	77.0
	Not present	14	23.0
Aspirin	Present	36	59.0
	Not present	25	41.0

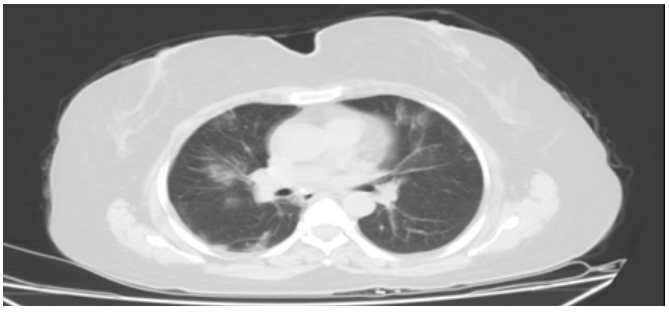

Figure 1. Thoracic computed tomography shows bilaterally located ground-glass opacities

ground-glass opacities in Group 1 and Group 2 Thorax CT, while 47 (82%) were negative for ground-glass opacities in Group 2 Thorax CT. While 4 (100%) of these 4 patients had no ground-glass opacity on Group 1 Thorax CT, 1 (25%) of them had ground-glass opacity on Group 2 Thorax CT, and 3 (75%) had no ground-glass opacity (Table 4). In 50 patients (100%), consolidation was found on Group 1 Thorax CT and no consolidation was observed in 11 patients. Of these, 5 (10%) had positive consolidation on Group 1 and Group 2 Thorax CT, while 45 (90%) had negative consolidation (Figure 2). Consolidation was not seen in Group 1 and Group 2 Thorax CT in these 11 patients (100%) (Table 4).

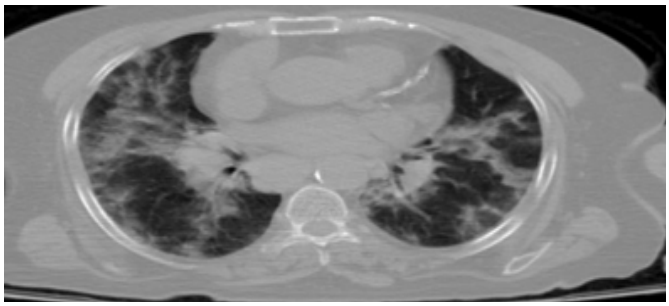

Figure 2. Thoracic computed tomography shows multifocal, segmental, patchy, mostly lower lobe and peripheral localized, irregularly circumscribed consolidations

DISCUSSION

SARS-CoV-2 is a highly contagious and high-mortality viral pneumonia caused by a novel coronavirus of unknown origin. Nearly 4 years after the COVID-19 pandemic, the long-term effects of post-COVID-19 pneumonia on patients have become a popular research topic. As the long-term effects of coronavirus agents that caused the pandemic in previous years have been proven, it has started to be thought that COVID-19 infection may also have the potential to have a permanent effect on patients. So far, there are very few studies in the literature investigating radiologic findings in the lung after COVID-19 pneumonia. In this study, we aimed to evaluate the pulmonary findings of post-COVID-19 pneumonia in the 6th month with CT and to reveal the risk factors that cause these abnormalities, as well as to analyze the variables in laboratory parameters.

In this study, we observed 61 patients diagnosed with COVID-19 pneumonia. In our study, we observed that patients diagnosed with COVID-19 pneumonia were more likely to be male. We also determined that hypertension and diabetes were the most common comorbidities in patients hospitalized with COVID-19 pneumonia. The most common symptoms observed in post-COVID-19 pneumonia patients were chest pain, cough, shortness of breath, myalgia, and fatigue. Fatigue, myalgia, and shortness of breath are frequently reported in other studies.[15-16]

The main routine tests ordered for COVID-19 patients included complete blood count (CBC), tests investigating coagulation and fibrinolysis cascades (PT, aPTT, and D-dimer), and parameters associated with inflammatory biomarkers (ESR, CRP, ferritin and procalcitonin). These blood parameters are used in acute COVID-19 disease and are useful in chronic inflammation.[17] Increased CRP, ferritin, LDH, and fibrinogen levels were also observed in our patients during acute COVID-19 disease. This allowed us to prove that COVID-19 disease is an inflammatory disease by using these markers in our study.

Since the heart, kidneys, and liver, which are our vital organs, are severely affected by the virus and cause deterioration including organ failure, analyzing biochemical parameters is an appropriate way to evaluate the functional activities of these organs.[18] In our study, despite an increase in Glucose, Creatinine, AST, ALT, GGT, LDH, APTT, INR, Fibrinogen, Neutrophil percentage, MCH parameters, a decrease was

Table 3. Comparison of changes in parameters over time

Variables	Group 1	Group 2	p
	Mean±sd	Mean±sd	
Glucose(mg)	160.8±97.52	132.38±59.82	0.029*
Urea(mg/dl)	38.45±21.98	37.51±19.2	0.679
Creatinine(mg/dl)	1.04±1.14	0.98±1.01	0.045*
AST(IU/L)	41.71±40.16	21.43±9.98	<0.001*
ALT(IU/L)	36.2±32.48	26.49±17.02	0.021*
ALP (IU/L),	74.62±22.23	78.67±19.34	0.086
GGT(IU/L)	47.57±31.95	34.58±38.65	0.010*
LDH (U/L)	373.8±251.18	236.9±72.2	<0.001*
CK (U/L),	114.9±77.83	114.67±76.01	0.985
CK-MB (U/L),	23.35±17.7	21.89±37.69	0.786
T.bil(mg/dl)	0.53±0.28	0.55±0.28	0.642
D.bil(mg/dl)	0.22±0.11	0.23±0.1	0.347
Protein(g/dl)	7.21±0.91	7.17±0.88	0.715
Albumin(g/dl),	3.4±0.53	3.92±0.68	<0.001*
Calcium(mg/dl)	8.56±0.67	9.11±0.53	<0.001*
Sodium(mEq/L)	135.7±3.88	138.34±2.83	<0.001*
Potassium(mmol)	4.53±0.57	4.46±0.5	0.336
Crp (mg/dl)	5.51±6.39	0.66±1.16	<0.001*
Troponin(ng/ml)	0.11±0.04	0.11±0.03	0.597
Ferritin (ng/ml)	455.29±573.42	146.02±231.89	<0.001*
NT-proBNP(pg/mL)	401.05±451.53	284.55±935.51	0.36
Procalcitonin(µg/l)	0.15±0.25	0.16±0.22	0.749
Aptt(sec)	25.88±3.79	22.38±3.85	<0.001*
Inr	1.14±0.17	0.8±0.2	<0.001*
Fibrinojen (mg/dl)	429.25±111.65	326.63±105.53	<0.001*
D-dimer (mcg/ml)	0.8±0.9	0.89±1.63	0.663
Leukocyte, $x10^3$/L	7.29±3	8.4±2.52	0.009*
Platelet($x10^3$/L)	249.11±98.63	284.3±82.98	0.011*
Hemoglobin(g/dL)	13.08±1.86	13.43±1.95	0.022*
Hemotokrit(%)	40.26±4.99	40.85±6.39	0.389
Neutrophil count(mcl)	5.09±2.97	5.2±2.44	0.797
Lymphocyte count(mcl)	1.75±1.7	2.49±0.92	0.004*
Neutrophil percentage(%)	68.19±13.98	59.6±11.66	<0.001*
Lymphocyte percentage(%)	23.54±11.91	29.35±10.26	0.001*
Mean erythrocyte hemoglobin (MCH)(pg)	26.82±2.49	27.33±2.53	0.004*
Mean erythrocyte hemoglobin concentration (MCHC)(g/dl)	32.41±1.5	32.55±1.58	0.344
Mean erythrocyte volume (MCV) (fl)	83.03±6.02	83.96±5.36	0.055
Erythrocyte distribution range (RDW) (%)	13.99±1.63	14.42±2.43	0.019*
Plateletcrit	0.26±0.1	0.29±0.08	0.052
Platelet distribution range (PDW) (%)	11.97±1.81	11.74±1.89	0.342
Mean platelet volume(MPV)(fL)	10.3±0.8	10.32±1.03	0.851

sd: standard deviation, p: significance of paired t-test,
The change between measurements was found to be statistically significant at the level of *p<0.05.

Table 4. Comparison of changes in thoracic tomography

Variable	Group	Group 1	Group 2	Total	p
		Present n (%)	Not Present n (%)		
Fibrosis	**Present**	1(100%)	14(23%)	15(25%)	**0.001***
	Not present	0(0%)	46(77%)	46(75%)	
Parenchymal band	**Present**	2(50%)	24(42%)	26(43%)	**0.001***
	Not present	2(50%)	33(58%)	35(57%)	
Reticular opacity	**Present**	0(0%)	11(19%)	11(18%)	**0.013***
	Not present	2(100%)	48(81%)	50(82%)	
Traction bronchiectasis	**Present**	1(50%)	7(12%)	8(13%)	**0.034***
	Not present	1(50%)	52(88%)	53(87%)	
Irregular interfaces	**Present**	0(0%)	11(18%)	11(18%)	**0.001***
	Not present	0(0%)	50(82%)	50(82%)	
Frosted glass opacity	**Present**	10(18%)	1(25%)	11(18%)	**0.001***
	Not present	47(82%)	3(75%)	50(82%)	
Consolidation	**Present**	5(10%)	0(0%)	5(8%)	**0.001***
	Not present	45(90%)	11(100%)	56(92%)	
Pulmonary nodule	**Present**	2(100%)	9(15%)	11(18%)	**0.003***
	Not present	0(0%)	50(85%)	50(82%)	
Honeycomb	**Present**	0(0%)	2(3%)	2(3%)	0.564
	Not present	1(100%)	58(97%)	59(97%)	

n; frequency, %; percent, p; significance of Marginal Homogenity Test, *p<0,05; The change between measurements was found to be statistically significant

observed in Albumin, Calcium, Sodium, Leukocyte, Platelet, Hemoglobin, Lymphocyte count, Erythrocyte distribution range variables at the time of COVID-19 pneumonia diagnosis. These parameters were statistically significant. In a study, white blood cell (WBC), lymphocyte, neutrophil, hemoglobin (HB), and platelet (PLT) values were found to be significantly lower.[19] Clinical laboratory data are indisputably important in the diagnosis of COVID-19 patients and the evaluation of the severity of the disease. In addition to clinical findings, biochemical parameters contribute to the distinction between severe and mild COVID-19 infection and the clinical decision to hospitalize patients. Thus, it is provided in conditions where patients can be differentiated such as hospitalization and/or intensive care unit admission, and more opportunities are provided to patients who need it.

In our study, glucose (mg), creatinine (mg/dL), aspartate aminotransferase (AST) (IU/L), alanine aminotransferase (ALT) (IU/L), gamma glutamyl transferase (GGT) (IU/L) were the control blood values after 6 months, The decrease in lactate dehydrogenase (LDH) (IU/L), APTT, INR, fibrinogen (mg), neutrophil percentage (%), mean erythrocyte hemoglobin (MCH) (pg) was found to be statistically significant ($p<0.05$). The increase in albumin (g/dl), calcium (mg/dl), sodium (Na) (mEq/L), leukocyte, platelet, hemoglobin, lymphocyte count, erythrocyte distribution range variables were found to be statistically significant ($p<0.05$).

Follow-up imaging and pulmonary function tests should be performed in patients with clinically suspected residual disease. We performed thorax CT imaging and pulmonary function tests in our patients.

On control thorax CT scans, 19 patients showed complete resolution of lung findings, while 42 patients had residual findings in the lungs. These residual findings may be due to the severity of the disease clinic at the time of hospitalization (i.e. respiratory rate >30 breaths/min, severe respiratory distress or oxygen saturation <90% in room air, diffuse bilateral ground glass opacities and multifocal segmental, patchy consolidations on thorax CT, i.e. severe respiratory failure and pneumonia).Pneumonia is a common and serious condition in patients with COVID-19 infection and increases the risk of mortality. Although the early clinical manifestations of the disease are well known, it is not clear what kind of sequelae it will leave in the lungs in the long term in patients who have severe pneumonia and survive. Currently, there is no consensus on the frequency and methods of monitoring pulmonary complications that may occur in patients with COVID-19 pneumonia. Radiologic improvement occurs in the early period in most patients. It has been reported that the ideal time for early control is the second week after discharge.[20] In a study investigating the findings 3 months after discharge of 55 patients treated for COVID-19 for long-term follow-up, it was reported that symptoms persisted in 64% of patients and radiological abnormalities in 71%.[21] In our study, lung findings showed complete resolution in 31% of the patients, while 68% had residual findings in the lungs. In our study, ground-glass appearance and consolidations were the most common residual radiological abnormality findings in the lungs at 6 months. When the radiologic course of COVID-19 pneumonia was observed in other studies, the most common tomographic findings at the beginning were bilateral subpleural ground-glass appearance and consolidation in the lower zones.[22-23]

In this study, the presence of middle-aged and elderly patients, radiologically and clinically severe pneumonia in our patients, and underlying diseases such as hypertension, type 2 diabetes mellitus, neurological diseases, and obstructive pulmonary disease were thought to be the reasons for the higher incidence of fibrosis and parenchymal bands. In other studies, the patient's age, severity of the disease, bacterial superinfection, duration of intensive care unit stay, presence of underlying lung disease, and extremely high levels of inflammation markers may be effective

factors in the development of lung fibrosis in patients with COVID-19 pneumonia.[24-25]

In our study, fibrosis (15/46; 25%), parenchymal band (26/35; 43%), reticular opacity (11/50; 18%), traction bronchiectasis (8/53; 13%), pulmonary nodule (11/50; 18%) were observed in Group 2 patients. Subpleural and parenchymal bands are linear striations seen mostly during the healing process. The reticular pattern is a pathological process of the pulmonary interstitium and is characterized by interlobular septal thickening and prominent intralobular striations. They are thought to be mostly sequelae of fibrosis. The presence of traction bronchiectasis is usually thought to be a consequence of fibrosis. However, recent studies have shown that reversible bronchiectasis may occur in cases of severe infection and inflammation and has been named pseudobronchiectasis.[26]

Although pleural pathologies such as pleural effusion and focal pleural thickening have been reported on a case basis, they are rare findings. The presence of pleural fluid is considered a poor prognostic marker.[8] In other studies, airway changes such as endobronchial mucus plug, bronchiectasis, bronchiolectasis, and bronchial wall thickening may also be observed in COVID-19 cases. Opacities of the lung parenchyma with a diameter ≤3 cm are defined as nodules. Nodules are a common finding in viral pneumonia. In studies, it has been reported to be observed in 6-8% of COVID-19 cases.[8]

In Group 2, sequel fibrotic bands, which are one of the signs of fibrosis, and ground-glass opacity, which appears to be the most common (Figure 3 and Figure 4), were examined. There are insufficient studies and evidence on the prevention and treatment of lung fibrosis that may develop after COVID-19 pneumonia.[27-28]

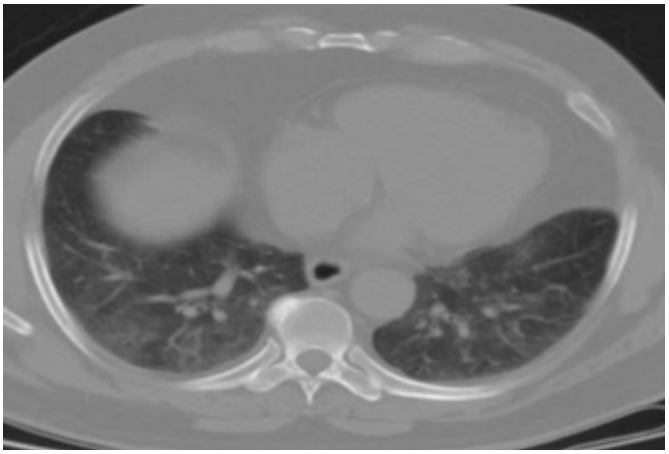

Figure 3. Bilateral irregular limited ground-glass opacities and fibrotic bands located mostly in the lower lobe and periphery on thoracic computed tomography

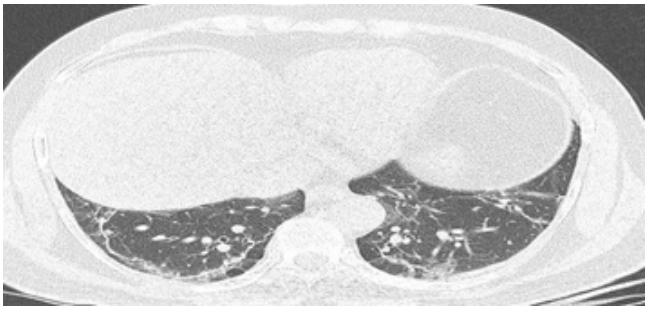

Figure 4. Bilateral fibrotic bands with irregular borders located mostly in the lower lobe and periphery on thoracic computed tomography

The frequency of long-term complications in COVID-19 pneumonia is not yet clear. However, the phylogenetic similarities of SARS-CoV-1 and SARS-CoV-2 viruses and the fact that Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) pneumonia caused by these viruses show very similar clinical, radiologic, and pathologic features with COVID-19 pneumonia suggest that the risk of progression may also be similar.[29]

Although long-term studies on COVID-19 pneumonia are insufficient, permanent damage to the lung parenchyma is expected to be observed in some patients with COVID-19 pneumonia, as seen in SARS and MERS infections. Organized pneumonia, fibrotic bands, reticulation, and honeycomb appearance have been described among CT findings in follow-up.[30]

Limitations

Limitations of our study include that our study was a single-center study. To evaluate the diagnostic power in terms of COVID-19, the initial laboratory values of the patients at the outpatient clinic were taken into account and changes in laboratory parameters during hospitalization were not monitored. Furthermore, laboratory results may have been affected by bacterial co-infections. In addition, the retrospective study design may have led to a high rate of cases with residual abnormalities in the lungs, especially considering that more symptomatic patients presented to the hospital in the post-COVID-19 pneumonia period. Again, due to the retrospective nature of the study, selecting patients with thorax CT at the time of diagnosis and control CT imaging 6 months later led to a decrease in the number of patients. The lack of patients with ARDS/critically severe pneumonia, adequate intensive care, and mechanical ventilation in our study patients provides a limitation to our study. Another limitation was the lack of long-term follow-up of the patients. Long-term follow-up of these patients is needed to understand how much of the findings seen on control CT reflect true fibrosis.

CONCLUSION

In patients who were followed up for 3-6 months after COVID-19 pneumonia, 19 (31%) of 61 patients admitted to the hospital showed complete resolution of pulmonary findings, while 42 (69%) had residual findings in the lungs. Patients with residual abnormalities were older (>40 years of age), had more comorbid diseases (especially HT, DM, CAD, obstructive pulmonary disease), had a severe clinical picture of the disease at the time of hospitalization, i.e. respiratory rate >30 breaths/min, severe respiratory distress or oxygen saturation <90% on room air, severe respiratory failure due to the presence of diffuse bilateral ground-glass opacities and multifocal segmental, patchy consolidations on thorax CT, and severe pneumonia.

Laboratory data is very important in diagnosing COVID-19 infection, prognosis, and guiding treatment. It can be difficult to say that any one blood value may be important in follow-up.

The most common findings in the lungs of patients diagnosed with COVID-19 pneumonia are ground-glass opacity and consolidation. The most common radiologic findings seen on follow-up thorax CT 3-6 months later were ground-glass opacity and consolidation.

There is insufficient evidence on whether fibrosis will develop in the lungs in patients followed up after COVID-19 pneumonia, and if so, whether this fibrosis will affect the patient's quality of life, performance, respiratory functions, whether long-term follow-up should be done, and whether serious clinical consequences such as idiopathic pulmonary fibrosis and findings similar to fibrotic lung disease with severe fibrosis findings on thorax CT will occur.

There is no consensus on how often patients should be followed up after COVID-19 pneumonia. It is also known that radiologic resolution of COVID-19 pneumonia may take a long time.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Scientific Ethics Committee of Malatya Training and Research Hospital (Date: 08.07.2020, Decision No: 2020/128).

Informed Consent

Informed written consent form was obtained from the patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Evaluation of serum natural antioxidant levels in patients with schizophrenia, schizoaffective disorder, and bipolar disorder

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ABSTRACT

Aims: Evidence for the role of oxidative stress in psychiatric disorders is growing. This study aimed to evaluate laboratory parameters related to oxidative stress, such as uric acid, albumin, and total bilirubin, which can be easily measured in serum in patients with schizophrenia, schizoaffective disorder, and bipolar disorder, and to compare them with healthy controls.

Methods: The study included 221 patients diagnosed with schizophrenia, schizoaffective disorder, and bipolar disorder according to DSM-5 criteria and 104 healthy individuals. The patient and control groups were compared in terms of serum uric acid, albumin, and total bilirubin values.

Results: A statistically significant difference was in uric acid levels among the schizophrenia group, schizoaffective disorder, bipolar disorder, and the control group ($p<0.001$ for all). Similarly, significant differences were identified between the patient groups and the control group in terms of albumin levels ($p= 0.002$, $p<0.001$, $p<0.001$, $p<0.001$, respectively). Total bilirubin levels also exhibited significant differences between schizophrenia and schizoaffective disorder, schizoaffective disorder and control group, and bipolar disorder and the control group ($p<0.04$, $p= 0.007$, $p= 0.044$, respectively).

Conclusion: Patients differed from controls in terms of serum natural antioxidants. The findings in our study support a causal relationship between schizophrenia, schizoaffective disorder, and bipolar disorder and uric acid, albumin, and total bilirubin.

Keywords: Psychiatric disorders, oxidative stress, uric acid, albumin, bilirubin

INTRODUCTION

Schizophrenia, schizoaffective disorder, and bipolar disorder are psychiatric illnesses with unclear pathophysiologies and multifactorial etiologies. There is growing evidence of altered immune and oxidative responses in many psychiatric disorders. The number of studies on the role of irregularities in oxidative response in the etiology of these disorders increasing.[1,2]

Oxidative stress is defined as an imbalance between the increased production of reactive oxygen species, or free radicals, part of cellular metabolism, and the body's compromised ability to scavenge these reactive products.[3] It refers to a disruption in the balance between oxidation and the antioxidant defense system, leading to tissue damage, enzyme inactivation, and lipid peroxidation.[4] Antioxidant molecules neutralize the damage, which is caused by oxidant molecules, through both intracellular and extracellular defense. Extracellular defense includes molecules such as uric acid, albumin, bilirubin, transferrin, and ceruloplasmin, whereas intracellular defense involves free radical-scavenging enzymes such as superoxide dismutase, glutathione peroxidase, glutathione reductase, and cytochrome oxidase.[5]

Brain tissue, highly susceptible to free radical damage and oxidative stress due to high oxygen consumption and high lipid content, plays a significant role in the etiology of mental illnesses through these mechanisms. Although there are fewer studies on schizoaffective disorder, research on the etiology of schizophrenia and bipolar disorder focuses on oxidant and antioxidant mechanisms.[6]

There are many parameters to measure oxidative stress, but some of them involve expensive tests. Therefore, there is a need for cheaper and easily available parameters. Uric acid, albumin and bilirubin are simple, relatively inexpensive and easily available laboratory parameters associated with oxidative stress. Therefore, this study aims to evaluate uric acid, albumin, and bilirubin levels as oxidative stress markers in schizophrenia, schizoaffective disorder, and bipolar disorder, where oxidative stress is considered to play a role in etiology and compare them with healthy controls.

METHODS

The study was approved by the Amasya University Non-Invasive Clinical Researches Ethics Committee (Date:16.11.2023, Decision No: 2023/120). All procedures

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were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Antioxidant parameters, particularly uric acid, albumin, and total bilirubin values, for patients and healthy controls were recorded after obtaining them from the hospital record system.

The present study included patients who sought treatment at the Psychiatry outpatient clinic of our hospital between January 1, 2021, and September 1, 2023, and were diagnosed with schizophrenia, schizoaffective disorder, or bipolar disorder by a psychiatric specialist using the DSM-5 criteria. For all patient groups, patients were selected among patients in remission. The control group consisted of age- and gender-matched healthy individuals without any psychiatric disease and psychiatric medication use who applied to our hospital for routine delegation procedures on the same dates.

Individuals with conditions that could potentially influence oxidative stress parameters, such as cardiovascular diseases, inflammatory diseases, liver and kidney diseases, hypertension, and diabetes mellitus, and those using steroids, nonsteroidal anti-inflammatory drugs, antiplatelet agents, anticoagulants, alcohol, or substances, and those with comorbid psychiatric disorders, were excluded from the study.

Statistical Analysis

The study data were tested for normal distribution by using the Kolmogorov-Smirnov test/Shapiro-Wilk (W) test, whereas one-way analysis of variance (ANOVA, Kruskal-Wallis test) was used for the comparison of quantitative data. Correlations between parameters were analyzed using Pearson correlation analysis. The correlation coefficient (r) was interpreted as follows: 0.00-0.24 a weak relationship, 0.25-0.49 a moderate relationship, 0.50-0.74 a strong relationship, and 0.75-1.00 a very strong relationship. Numerical variables were presented as mean±standard deviation, whereas categorical variables were presented as frequency and percentage. The statistical significance level was set at $p<0.05$.

RESULTS

A total of 325 individuals were included in the present study, consisting of 94 individuals diagnosed with schizophrenia, 54 individuals diagnosed with schizoaffective disorder, 73 individuals diagnosed with bipolar disorder, and 104 healthy individuals (controls). The mean age was found to be 38.34±9.12 for the schizophrenia group, 36.69±9.67 for the schizoaffective disorder group, 38.62±9.34 for the bipolar disorder group, and 37.42±9.33 for the control group. The schizophrenia group consisted of 50 (53.2%) males and 44 (46.8%) females; the schizoaffective disorder group consisted of 24 (44.4%) males and 30 (55.6%) females; and the bipolar disorder group consisted of 35 (47.9%) males and 38 (52.1%) females. There were 52 (50.0%) males and 52 (50.0%) females in the control group. There was no significant difference in age or gender between the patient and control groups (all $p>0.05$). The mean duration of illness for schizophrenia patients was 9.81±5.48 years, that of schizoaffective disorder patients was 8.93±4.73 years, and that of bipolar disorder patients was 7.07±4.88 years. The uric acid levels were found to be 5.69±1.06 mg/L in the schizophrenia group, 5.15±1.29 mg/L in the schizoaffective disorder group, 5.13±1.34 mg/L in the bipolar disorder group, and 4.27±0.91 mg/L in the control group. Comparing uric acid levels between groups, there was no statistically significant difference between the schizoaffective and bipolar disorder groups, whereas significant differences were observed between the schizophrenia group and the schizoaffective, bipolar disorder, and control groups ($p=0.029$, $p=0.012$, $p<0.001$, respectively) (Figure 1-A). Significant differences were also found in uric acid levels between the schizoaffective disorder and control groups, as well as between the bipolar disorder and control groups ($p<0.001$, $p<0.001$, respectively). The serum albumin levels were determined to be 43.16±4.44 g/L in the schizophrenia group, 42.75±4.62 g/L in the schizoaffective disorder group, 42.86±4.12 g/L in the bipolar disorder group, and 45.13±2.64 g/L in the control group. Even though there were no significant differences in albumin values between patient groups, there were significant differences between the schizophrenia group, schizoaffective disorder, and bipolar disorder groups and the control group ($p=0.002$, $p<0.001$, $p<0.001$, respectively) (Figure 1-B). The total bilirubin levels were found to be 0.54±0.25 mg/dL in the schizophrenia group, 0.47±0.35 mg/dL in the schizoaffective disorder group, 0.48±0.27 mg/dL in the bipolar disorder group, and 0.55±0.23 mg/dL in the control group. Significant differences were found between the schizophrenia and schizoaffective disorder groups, schizoaffective disorder and control groups, as well as bipolar disorder and control groups ($p<0.04$, $p=0.007$, $p=0.044$, respectively) (Figure 1-C). Descriptive characteristics of the participants and uric acid, albumin, and total bilirubin levels are given in Table 1.

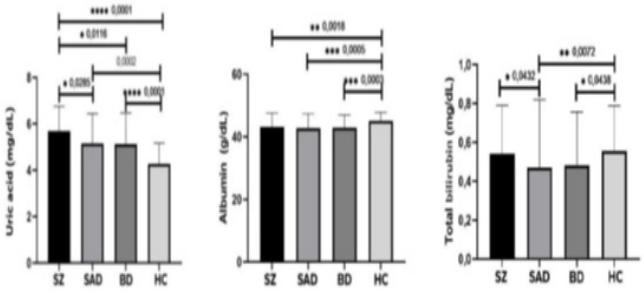

Figure 1. Comparison of uric acid (A), albumin (B) and total bilirubin (C) values in patient and control groups. Lines on the bars indicate statistical significance between groups and show the p-value. Abbreviations; SZ: Schizophrenia, SAD: Schizoaffective disorder, BD: Bipolar disorder; HC: Healthy controls

When examining the correlation between serum albumin, uric acid, total bilirubin levels, and the duration of illness, no significant relationship was observed between the patients' diagnosis duration and the uric acid, albumin, and total bilirubin ($p>0.05$). Correlations between serum parameters and the duration of illness are provided in Table 2.

DISCUSSION

In the present study, simple biochemical parameters associated with oxidative stress were examined by comparing patients with schizophrenia, schizoaffective disorder, and bipolar disorder to healthy controls. Significant differences were found in serum natural antioxidants, specifically uric acid, and albumin, between patient groups and healthy controls. Uric acid levels were significantly higher in schizophrenia, schizoaffective disorder, and bipolar

Table 1. Descriptive characteristics of participants and serum levels of parameters

	Schizophrenia (n=94) n (%) (mean±SD)	Schizoaffective disorder (n=54) n (%) (mean ±SD)	Bipolar disorder (n=73) n (%) (mean ±SD)	Healthy control (n=104) n (%) (mean ±SD)
Variables				
Years (mean ±SD)	38.34±9.12	39.69±9.67	38.62±9.34	37.42±9.33
Gender				
Female/male	44/50 (46.8/53.2%)	30/24 (55.6/44.4%)	38/35 (52.1/47.9%)	52/52 (50.0/50.0%)
Uric acid (mg/L)	5.69±1.06	5.15±1.29	5.13±1.34	4.27±0.91
Albumin (g/L)	43.16±4.44	42.75±4.62	42.86±4.12	45.13±2.64
Total bilirubin (mg/dl)	0.54±0.25	0.47±0.35	0.48±0.27	0.55±0.23
Disease duration (years) (mean±SD)	9.81±5.48	8.93±4.73	7.07±4.88	

SD: standard deviation

Table 2. Relationship between disease duration and other parameters

Variables		Uric acid	Albumin	Total bilirubin
Disease duration	r	0.037	-0.109	-0.109
	p	0.582	0.105	0.106

r: correlation coefficient

disorder when compared to controls, whereas albumin values were significantly lower than healthy controls. However, there was no significant difference in total bilirubin levels between the schizophrenia group and healthy controls, but those in schizoaffective disorder and bipolar disorder groups were found to have significantly lower levels when compared to controls.

Previous studies showed that oxidative stress has harmful effects on human neural tissue and is a significant factor in various neurological and psychiatric disorders.[7] Oxidative stress was investigated in schizophrenia, schizoaffective disorder, and bipolar disorder. In a previous study, higher levels of lipid peroxidation product malondialdehyde (MDA), advanced oxidation protein products (AOPPs), and protein carbonyl (PC) concentrations, along with increased glutathione peroxidase (GSH-Px) activities, were observed in schizophrenia and schizoaffective disorder.[2] Another study reported elevated levels of lipid peroxidation, DNA/RNA damage, and nitric oxide in bipolar disorder compared to healthy controls1. Additionally, serum antioxidants like as uric acid, albumin, and total bilirubin, were investigated in various psychiatric disorders.[8,9]

Serum uric acid is one of the non-enzymatic critical components of the antioxidant defense system of the body. Uric acid, which is an antioxidant naturally occurring in the body, protects cells against the harmful effects of oxidative stress by neutralizing reactive oxygen species.[10] The purinergic system plays a role in cognitive function, mood regulation, motor activity, sleep, and behavior.[11,12] Therefore, it became very popular in studies on psychiatric disorders. Uric acid has been investigated in psychiatric disorders due to its role in the antioxidant defense system. Previous studies examining uric acid levels in schizophrenia reported conflicting results. Even though some studies reported higher uric acid levels in schizophrenia patients when compared to healthy controls, there are also studies reporting lower levels.[13,14] A meta-analysis, however, reported no significant difference in uric acid levels between schizophrenia patients and healthy controls, irrespective of the use of antipsychotic medication.[15] Moreover, Reddy et al.[16] reported that first-episode schizophrenic patients not using medication had lower uric acid levels in comparison to healthy controls. In the present study, significantly higher uric acid levels were determined in schizophrenia patients when compared to controls. This result might be explained by factors such as the changes in the purinergic system in schizophrenia, cellular damage due to oxidative stress, the effects of medications used in schizophrenia treatment, accompanying metabolic disorders, nutritional status, lifestyle factors, smoking, and ethnic background. Some studies even propose that uric acid may not be a causative factor in the onset of schizophrenia but could be influenced by the disorder. It makes uric acid useful in monitoring the course of disease.[17] Elevated uric acid levels during inflammation and oxidative stress can potentially alter the levels of neurotransmitters such as serotonin and dopamine, which are crucial in the pathogenesis of schizophrenia. Furthermore, in the present study, when comparing the uric acid levels among patient groups, schizophrenia patients were found to have significantly higher levels compared to both schizoaffective disorder and bipolar disorder patients. This result might be explained by factors such as medication treatments, lifestyle, and metabolic reasons among patients. In studies evaluating serum uric acid levels in patients diagnosed with bipolar disorder, it was reported that uric acid levels are higher in bipolar disorder patients when compared to healthy controls.[18] The authors associated the increased uric acid levels in bipolar disorder patients with increased purine metabolism and decreased adenosine activity.[18] In the present study, uric acid levels in bipolar patients during the remission period were significantly higher when compared to healthy controls, which is consistent with the literature. Albert et al.[19] similarly reported high uric acid levels in the manic and remission phases of bipolar disorder, whereas Kesebir et al.[20] found significantly higher uric acid levels in remitted bipolar patients in comparison to healthy controls. This finding achieved in this study also indicates the presence of oxidative stress and purinergic dysfunction during the remission period in bipolar disorder.

Moreover, schizoaffective is a condition that exhibits both mood disorder and schizophrenia characteristics. There is limited data on studies evaluating serum uric acid levels in schizoaffective disorder. In one study, serum uric acid levels in schizoaffective disorder patients were found to be higher than in healthy controls.[9] Bülbül et al.[6] reported higher oxidative stress in schizoaffective disorder compared to schizophrenia and bipolar disorder.

Albumin is a significant antioxidant protein with albumin ligand binding and free radical trapping activities. It was reported that

albumin is closely related to oxidative stress and antioxidant capacity.[21] Studies have reported significantly lower levels of albumin in schizophrenia patients in comparison to healthy controls.[8] Another study showed a significant decrease in serum albumin levels after short-term antipsychotic treatment in first-episode untreated schizophrenia patients.[22] In a study examining serum albumin levels in mood disorders, albumin levels were determined to be statistically significantly lower in the control group.[23] In the present study, albumin levels in schizophrenia, schizoaffective disorder, and bipolar disorder patients were significantly lower than in controls. This result supports the hypothesis proposed in previous studies that reduced serum albumin levels might adversely affect the antioxidant defense system, influencing the development of psychiatric disorders.[8]

Bilirubin, the final product of heme metabolism, acts as an endogenous antioxidant with anti-inflammatory properties. It prevents oxidation of low-density lipoprotein and other lipids, eliminating reactive oxygen species through potent antioxidant mechanisms. Studies have demonstrated lower total bilirubin levels in schizophrenia patients compared to healthy controls.[24] On the other hand, Radhakrishnan et al.[25] reported higher total bilirubin levels in schizophrenia patients in comparison to bipolar disorder patients. In the present study, there is no significant difference in total bilirubin levels between schizophrenia patients and healthy controls; however, total bilirubin levels were determined to be significantly lower in schizoaffective and bipolar disorder patients than in healthy controls. These results should be validated in untreated patients, as bilirubin levels might be affected by psychotropic medications.[25]

Examining the correlation between diagnosis duration and serum parameters across all patient groups, no significant relationship was observed between diagnosis duration and any parameter.

Limitations

This study has several limitations. The retrospective design, relatively small sample size, and the lack of consideration for patients' dietary habits, smoking status, and body mass index are among these limitations. Another important limitation of the study is that due to the retrospective nature of the study, tests such as positive and negative symptom rating scales and depression symptom rating scales could not be applied on the patients.

CONCLUSION

The most significant findings in the present study include higher serum uric acid levels and lower albumin levels in schizophrenia, schizoaffective disorder, and bipolar disorder patients when compared to controls. Moreover, total bilirubin levels were statistically significantly lower in schizoaffective and bipolar disorder patients when compared to controls. The results achieved in this study indicate a strong relationship between serum uric acid and albumin levels and schizophrenia, schizoaffective disorder, and bipolar disorder in patients. However, further prospective studies in medication-free patients are necessary to confirm these findings and determine whether these parameters can serve as biomarkers.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was performed in accordance with the Declaration of Helsinki and was approved by the Amasya University Non-invasive Clinical Research Ethics Committee (Date:16.11.2023, Decision No: 2023/120).

Informed Consent

The need for informed consent was waived with the approval of the Amasya University Non-Invasive Clinical Researches Ethics Committee due to the study's retrospective design.

Referee Evaluation Process

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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The relationship between anterior fontanelle and head circumference in term newborns

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ABSTRACT

Aims: At birth, infants have membranous cavities called fontanelles because the angles of the skull bones have not yet formed. Its size is generally accepted as an indicator of cranial development and bone maturation. Head circumference measurement is an important marker for predicting brain development, especially in early childhood.

Methods: Patients followed up in the pediatric outpatient clinic of Kırşehir Training and Research Hospital between January 2020 and January 2024 were retrospectively analyzed. Anterior fontanelle width and head circumference measurements of babies born on the day recorded in the system were recorded.

Results: A total of 340 (M/F:188/152) patients were included in the study. There was a positive correlation between fontanel width and head circumference at birth, at 1 month and at 2 months ($p<0.05$). There was no correlation between fontanel width and head circumference at 3, 4, 6, 9, 12 months ($p>0.05$).

Conclusion: A significant relationship was found between anterior fontanelle width and head circumference in the first months of life. It is considered to be taken into consideration in the follow-up of healthy children. However, further studies are needed in this context and our study will contribute to future studies.

Keywords: Child, anterior fontanel, head circumference

INTRODUCTION

At birth, infants have membranous cavities called fontanelles because the angles of the skull bones have not yet formed. The largest and systematically palpated anterior fontanelle (ACF) is diamond-shaped.[1] Its dimensions and closure are evaluated by physical examination.[2] The mean anteroposterior diameter is 1.5-2.5 cm closure, which begins around the 3rd month after birth, is commonly regarded as a marker of cranial growth and ossification.[1-3] An increase in anterior fontanelle size may reflect increased intracranial pressure, osteogenesis imperfecta, achondroplasia, hypothyroidism or other skeletal system anomalies, whereas a decrease may reflect craniosynosis, hyperthyroidism and microcephaly.[3-4] Its width is evaluated by palpation under the scalp in the form of a rhombus on physical examination. Head circumference measurement is an important marker in predicting brain development especially in early childhood.[10-11] Abnormal values in head circumference (microcephaly, macrocephaly) may be an early harbinger of many diseases including developmental retardation and may also be familial. Heritability estimates for head circumference variation show that approximately half of normal head circumference variations are familial and are most likely genetically determined.[12]

In this study, our primary objective was to investigate the potential correlation between fontanelle size and head circumference in healthy infants.

METHODS

Our study was conducted by retrospectively examining the follow-ups of healthy infants admitted to the Pediatric Outpatient Clinic of Kırşehir Training and Research Hospital between January 2020 and January 2024 and recording anterior fontanelle and head circumference data. In your outpatient clinic, newborn babies are typically examined at birth and during the first week, followed by monthly check-ups for the first 6 months, then every 3 months until 18 months, and finally every 6 months until they reach 5 years of age. Infants who attended regular child health follow-up were included in the study. The study included infants with a gestational age between 36 and 40 weeks, normal birth weight for gestational age (AGA), and no prenatal, natal, or postnatal medical issues. Infants outside this gestational age range, with small (SGA) or large (LGA) birth weight for gestational age, or with chronic diseases or congenital anomalies, were excluded from the study. The study gathered and documented data from 340 robust, full-term

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newborns who satisfied the inclusion criteria for subsequent analysis. Head circumference data were used, which included longitudinal and transverse measurements of the anterior fontanelle and measured using a narrow, non-stretchable tape passing over the supraorbital processes on the child's forehead and the occiput posteriorly. Anterior fontanelle patency was evaluated by physical examination and fontanelle dimensions were calculated by dividing the sum of anteroposterior and transverse dimensions by 2 using the method described by Popich and Smith.[5]

The study received ethical clearance from the Ahi Evran University Faculty of Medicine Ethics Committee (Date: 20.02.2024, Decision No: 2024-05/33). The research adhered to the ethical guidelines outlined in the Declaration of Helsinki.

Statistical Analysis

The statistical analyses for the study were carried out utilizing the Statistical Package for Social Sciences version 25.0 software for Windows (IBM SPSS Statistics for Windows, Version 25.0, IBM Corp., Armonk, NY, USA). The normality assumption was assessed using both the Kolmogorov-Smirnov and Shapiro-Wilk tests. The descriptive statistics of the variables were presented as mean±standard deviation and median (min-max). Group comparisons were assessed using the Kruskal-Wallis test. For post hoc comparisons of groups with significant differences, the Mann-Whitney U test, which is the post hoc test for the Kruskal-Wallis test, was employed. The relationships between variables were examined using Spearman correlation analysis and ANOVA. A significance level of $p<0.05$ was considered statistically significant for all analyses.

RESULTS

In the study, a total of 340 patients were enrolled, with 55.3% (n=188) being boys and 44.7% (n=152) girls.

The fontanelle width was larger in boys than in girls, but there was no difference between the sexes in head circumference (Table 1). In the study conducted by the user, a positive correlation was observed

Table 1. Distribution of cases according to fontanel and head circumference width

	Average	Standard deviation	p
Fontanel width (cm)	155.9043 (Male)	22.14395	>0.05
	148.5526 (Female)	24.76801	
Head circumference	313.8989 (Male)	8.86593	
	312.0066 (Female)	7.92556	

between fontanelle width and head circumference at birth, at 1 month, and at 2 months ($p<0.02$, $p<0.15$, $p<0.36$) (Table 2). In the study, there was no correlation found between fontanelle width and head circumference at 3, 4, 6, 9, and 12 months. ($p>0.96$, $p>0.141$, $p>0.141$, $p>146$, $p>0.439$, $p>0.88$) (Table 2). Additionally, in the user's study, there was no correlation observed between fontanelle width and head circumference when all the evaluated months were combined and analyzed together. ($p>0.85$) (Table 2).

DISCUSSION

Since an abnormal fontanelle in infants may indicate serious problems, evaluation of the fontanelle is part of the routine physical examination.

Table 2. Relationship between fontanel and head circumference of the cases according to months

	Fontanel/head circumference ratio by months	p
FC0/BC0	181.469 a	.002
FC1/BC1	173.508 a	.015
FC2/BC2	181.743 a	.036
FC3/BC3	49.147 a	.969
FC4/BC4	359.113 a	.141
FC6/BC6	159.823 a	.146
FC9/BC9	102.826 a	.439
FC12/BC12	222.561 a	.088
FC Total/BC total	17924.154 a	.854

a: R Squared=.049 (Adjusted R Squared=.037), FP: Fontanel diameter, WC: Head circumference

There are various studies showing the anterior fontanel (ACF) dimensions in infants. Boran P. et al.[11] used the Popich method to determine the size of the ACF in 321 healthy term infants from birth to 24 months and created percentage charts. In this study, they reported the mean fontanel closure time as 9.7±5.0 months.

In a study conducted by Neyzi et al.[12] in our country, the difference between the head circumferences of boys and girls was 0.4 cm at birth and 1.3 cm at 12 months and 24 months . In our study, although head circumference was larger in boys than in girls, no significant difference was found (Table 1).

It has been observed that there is a difference between anterior fontanel dimensions and races.[13]

When the time of fontanel closure was examined in studies, it was found that fontanelles were still open at the age of 2 years.[14-15] The common result of these studies was that fontanel dimensions increased between 0-2 months and reached the highest value in the 2nd month and then gradually decreased.[18-19] In our research, fontanel dimensions were found to be larger in the first two months compared to the other months. In one study, the anterior fontanel width was found to be significantly larger in male newborns than in female newborns.[24] In addition, fontanel width was found to be larger in boys than in girls. No other study has been found to investigate whether there is a relationship between head circumference and fontanel width. In our study, a significant relationship was identified between fontanelle width and head circumference during the first two months of life. However, no correlation was found in the other months of follow-up. When we analyzed whether there was a relationship between head circumference and fontanel width in all the months followed up, no significant result was found. In a recent study, birth weight and head circumference were found to be risk factors for anterior fontanelle width.[25]

Duc and Largo[4] also found that the percentage of closed fontanelles was higher in boys than in girls, although not statistically significant. Similar findings regarding the higher percentage of closed fontanelles in boys compared to girls, without statistical significance, have been documented in other studies as well.[1-4,10,13,22]

About half of the normal variation in head size may have a familial component. Weaver and Christian did not find a significant maternal effect on the child's head size. However, they observed that mothers of children diagnosed with microcephaly also had microcephaly, while fathers of children with macrocephaly also had macrocephaly.[20]

Maternal nutrition has been found to have an effect on head circumference.[23]

In patients with an abnormal fontanelle, ultrasonography (US), CT and magnetic resonance imaging (MR) can be used to evaluate ventricular dimensions and subarachnoid distance widths, and to exclude space-occupying lesions and many other pathologies. However, US is preferred in patients with an open fontanelle because of the disadvantages of CT including radiation exposure and MR including cost and sedation.[3-6,16,17,21] Fontanelle abnormalities constitute a significant portion of patients referred to radiology for transfontanel US. It is important to know the normal distribution in order to detect abnormal fontanelle and to refer the patient for imaging to exclude pathologies that may cause this abnormality. In addition, head circumference follow-up is extremely important for the early diagnosis of future pathologies.

CONCLUSION

Regular follow-up of fontanelle opening and head circumference is extremely important in the follow-up of healthy children. There is no previous study investigating the relationship between fontanel width and head circumference. Our study is the first in this sense. In our research, a significant relationship was identified between fontanelle width and head circumference during the first two months of life. However, further studies are needed to reinforce this finding.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ahi Evran University Faculty of Medicine Ethics Committee (Date: 20.02.2024, Decision No: 2024-05/33).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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The impact of surgical resection on prognosis in gastric neuroendocrine tumors

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ABSTRACT

Aims: This study aimed to investigate the pathological factors influencing prognosis in patients undergoing surgical resection for GNETs, in the context of the World Health Organization 2010 staging system.

Methods: This retrospective study included 27 patients who underwent surgical resection for GNETs diagnosis between 2001 and 2015. Patients were clinically categorized into four types based on GNET characteristics: type 1 tumors, which are typified by hypergastrinemia and develop on a background of atrophic gastritis; type 2 tumors, which are related with gastrinomas; type 3 tumors, which have low serum gastrin levels and no underlying mucosal pathology, and type 4, which are characterized by neuroendocrine carcinoma. Additionally, all patients were classified according to the TNM staging system.

Results: The median age of the patients was 56 years (range: 33-81), and most patients were identified as type I (55.6%), with subsequent groups being type IV (25.9%) and type III (18.5%). The majority of type I patients were classified as stage I, while the majority of type III patients were in stage IIA, and most type IV patients were in stage IIIB. Type III and type IV groups exhibited a higher rate of lymph node metastasis compared to type I group (Type I: 13.3% vs. Type II: 80.0% vs. Type IV: 57.1%, $p < 0.001$). The mortality rate was higher in the Type IV group compared to other groups (Type I: 0% vs. Type II: 20% vs. Type IV: 57.1%, $p<0.001$). The Ki-67 levels were higher in patients with lymph node metastasis than in those without.

Conclusion: Type III and IV GNETs are at a higher risk of lymph node metastasis and mortality. The Ki-67 value assessed through preoperative endoscopic biopsy may serve as a guide for deciding on the necessity of lymph node dissection.

Keywords: Classification, Ki-67, neuroendocrine tumor, stomach, prognosis

INTRODUCTION

Gastric neuroendocrine tumors (GNETs) originate from the excessive multiplication of enterochromaffin-like (ECL) cells, mainly situated in the fundus of the stomach. This proliferation is associated with an increase in plasma gastrin levels, resulting in various neoplastic transformations.[1] A study utilizing the Surveillance, Epidemiology, and End Results (SEER) database demonstrated that the age-adjusted annual incidences of GNETs were 0.30.[2] Results from the SEER database show that at the time of diagnosis, localized disease is identified in 53% of NET patients, while locoregional and distant metastatic diseases are found in 20% and 27% of patients, respectively.[3] The management and treatment of GNETs are of prognostic significance.

GNETs are associated with pronounced lymph node and liver metastases, and exhibits a high level of malignancy. However, the classification, pathology, and treatment strategies for GNETs are still largely unclear.[4] The low occurrence of GNETs continues to fuel debates regarding the appropriate treatment methods and the identification of the most effective treatment.[5] The World Health Organization (WHO) revised its classification scheme in 2010, segmenting it into three separate groups: type 1 tumors, which are typified by hypergastrinemia and develop on a background of atrophic gastritis; type 2 tumors, which are related with gastrinomas; type 3 tumors, which have low serum gastrin levels and no underlying mucosal pathology, and type 4, which are characterized by neuroendocrine carcinoma.[6] However, studies evaluating GNETs using this classification and comparing surgical outcomes are limited.

This study aimed to investigate the pathological factors influencing prognosis in patients undergoing surgical resection for GNETs, in the context of the WHO 2010 staging system.

METHODS

This retrospective study was conducted on patients diagnosed with GNETs at the Ege University Faculty of Medicine, Department of General Surgery, between January 2001 and December 2005. This study received approval from the Ege University Faculty of Medicine Ethics Committee and was

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performed in accordance with relevant ethical guidelines, including the Declaration of Helsinki (2013 Brazil revision). Informed consent requirements were waived by the Ethics Committee due to the study's retrospective nature. This research is derived from the thesis titled 'Effect of surgical resection on prognosis in gastric neuroendocrine tumors".

The study retrospectively assessed 27 patients (≥18 years old) who were diagnosed with GNETs and underwent surgical resection. Patients under 18 years of age, those with a previous history of malignancy, and those with incomplete data were excluded from the study. The patients' demographic, clinical, and survival data were sourced from the hospital database, as well as pathology and radiology archives. Tumor size, lymph node status, lymphovascular invasion, and Ki-67 percentage were evaluated based on pathology findings. According to the WHO 2010 guidelines, GNETs were classified into four categories based on clinicopathological features: type I, type II, type III, and poorly differentiated neuroendocrine carcinomas (NECs, type IV).[6] In the pathology findings, the positivity of chromogranin, synaptophysin, and neuron-specific enolase were used as confirmatory evidence in the classification of GNETs. The overall survival time of the patients was monitored through the Death Notification System (https://obs.saglik.gov.tr). The death dates of deceased patients were recorded. The overall survival time for each patient was calculated in terms of months.

Statistical Analysis

The normality of numerical data was evaluated with the Kolmogorov-Smirnov test. Data were presented as mean±standard deviation or median (min-max) according to normal distribution. Depending on the normality of distribution for numerical variables, the Student's t-test and Mann-Whitney U test were used for comparisons between two groups, while the ANOVA and Kruskal-Wallis tests were employed for comparisons among more than two groups. Categorical variables are presented as numbers and percentages, and inter-group comparisons were conducted using Chi-square and Fisher's exact tests. Overall survival plots were created using Kaplan-Meier analysis. Values of $p<0.05$ were considered statistically significant. All data were analyzed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA).

RESULTS

The median age of the patients was 56 years (range: 33-81), and 51.9% were male (n=14). Among the patients, 44% (n=12) had abdominal pain, 22.2% (n=6) experienced nonspecific symptoms, 18.5% (n=5) had dysphagia, and 14.8% (n=4) were afflicted with fatigue. The majority of the patients had tumors located in the corpus (37%), followed by the fundus (29.6%), antrum (18.5%), and cardia (14.8%). Based on GNETs classifications, most patients were identified as type I (55.6%), with subsequent groups being type IV (25.9%) and type III (18.5%). There were no cases identified as type II associated with Zollinger-Ellison syndrome (ZES) and multiple endocrine neoplasia 1 (MEN-1). It was found that total gastrectomy was performed on 11 patients (40.7%), subtotal gastrectomy on 9 patients (33.3%), and wedge resection on 7 patients. The median duration of hospitalization was 18.5 days (range: 6-35 days). The median follow-up period for the patients was 42 months (range: 1-171 months), and the mortality rate was 18.5% (n=5). No recurrence was observed in the remaining 22 patients throughout their follow-up period. The demographic and clinical characteristics of the patients were detailed in Table 1.

Table 1. The demographic and clinical characteristics of the patients with gastric neuroendocrine tumors

Variables	All population n=27
Age, years	56 (33-81)
Gender, n (%)	
Male	14 (51.9)
Female	13 (48.1)
Clinical symptoms, n (%)	
Abdominal pain	12 (44.0)
Dysphagia	5 (18.5)
Fatigue	4 (14.8)
Nonspecific symptoms	6 (22.2)
Tumor location, n (%)	
Corpus	10 (37.0)
Fundus	8 (29.6)
Antrum	5 (18.5)
Cardia	4 (14.8)
Tumor diameter, cm	2 (0.2-22)
TNM stage, n (%)	
I	10 (37.0)
IIA	7 (25.9)
IIB	2 (7.4)
IIIA	-
IIIB	7 (25.9)
IV	1 (3.8)
Type of GNETs, n (%)	
Type I	15 (55.6)
Type II	-
Type III	5 (18.5)
Type IV	7 (25.9)
Surgical procedures, n (%)	
Total gastrectomy	11 (40.7)
Subtotal gastrectomy	9 (33.3)
Wedge resection	7 (25.9)
Vascular invasion, n (%)	13 (48.1)
Lymph node metastasis, n (%)	10 (37.0)
Duration of hospitalization, days	19 (6-35)
Follow-up time, months	42 (1-171)
Mortality, n (%)	5 (18.5)

Categorical variables were shown as number percentages. Numerical variables are mean ± SD or median (min-max). TNM, tumor, node, and metastasis; GNETs, gastric neuroendocrine tumors

The distribution of age and gender was similar across GNET types. The majority of type I patients were classified as stage I, while the majority of type III patients were in stage IIA, and most type IV patients were in stage IIIB. The rates of vascular invasion were similar between type III and type IV groups. However, these groups exhibited a higher rate of vascular invasion compared to type I group (Type I: 20% vs. Type II: 80% vs. Type IV: 85.7%, $p < 0.001$). Type III and type IV groups exhibited a higher rate of lymph node metastasis

compared to type I group (Type I: 13.3% vs. Type II: 80.0% vs. Type IV: 57.1%, p < 0.001). The mortality rate was higher in the Type IV group compared to other groups (Type I: 0% vs. Type II: 20% vs. Type IV: 57.1%, p < 0.001) (Table 2) (Figure 1A). According to TNM stages, the mortality risk in patients with Stage III-IV was higher compared to other stages (Figure 1B). The deceased patients had a median tumor diameter of 5 cm, all exhibited vascular invasion, and the lymph node metastasis rate was at 80%.

Table 2. The distribution of TNM staging and prognostic findings according to GNET types

Variables	Type I n=15	Type III n=5	Type IV n=7	p
Age, years	53 (33-75)	56 (35-72)	58 (35-81)	0.845
Gender, n (%)				
Male	8 (53.3)	3 (60.0)	3 (42.9)	0.369
Female	7 (46.7)	2 (40.0)	4 (57.1)	
TNM stage, n (%)				
I	10 (66.7)	-	-	<0.001*
IIA	2 (13.3)	3 (60.0)	2 (28.6)	
IIB	-	2 (40.0)	-	
IIIB	3 (20.0)	-	4 (57.1)	
IV	-	-	1 (14.3)	
Surgical procedures, n (%)				
Total gastrectomy	5 (33.3)	2 (40.0)	4 (57.1)	<0.001*
Subtotal gastrectomy	3 (20.0)	3 (60.0)	3 (42.9)	
Wedge resection	7 (46.7)	-	-	
Vascular invasion, n (%)	3 (20.0)	4 (80.0)	6 (85.7)	<0.001*
Lymph node metastasis, n (%)	2 (13.3)	4 (80.0)	4 (57.1)	<0.001*
Duration of hospitalization days	16 (6-30)	19 (6-32)	20 (8-35)	0.126
Follow-up time, months	46 (24-171)	40 (8-164)	28 (1-118)	0.035*
Mortality, n (%)	-	1 (20.0)	4 (57.1)	<0.001*

Categorical variables were shown as number percentages. Numerical variables are mean ± SD or median (min-max). * p <0.05 shows statistical significance. TNM, tumor, node, and metastasis; LNM, gastric neuroendocrine tumors

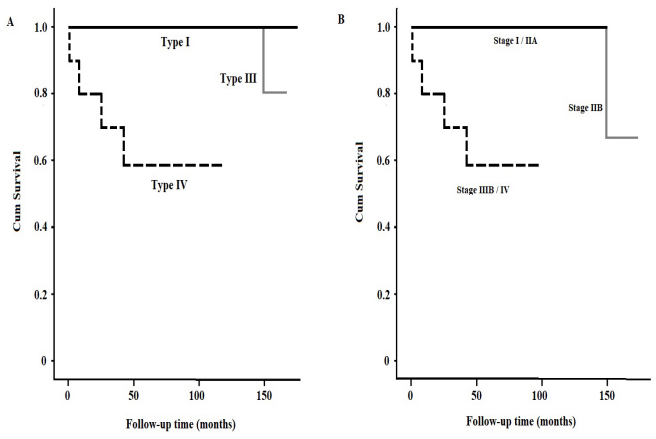

Figure 1. Survival findings of patients according to GNETs types (A) and TNM stages (B)

No significant relationship was found between Ki-67 and tumor diameter or vascular invasion (p>0.05). However, the Ki-67 levels were higher in patients with lymph node metastasis than in those without (Figure 2).

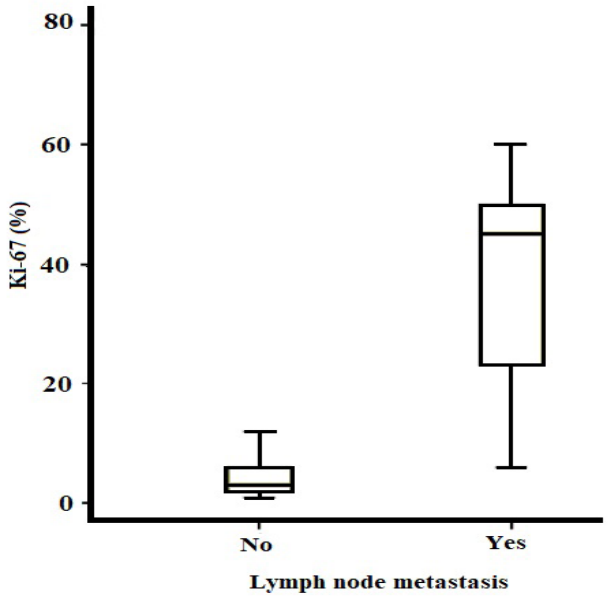

Figure 2. The distribution of Ki-67 levels according to the presence of lymph node metastasis

DISCUSSION

Globally, the TNM staging system is not widely accepted as the standard for neuroendocrine tumors. The classification embraced by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) corresponds to the classification related to carcinoids, which are designated as well-differentiated benign lesions by the WHO. In the classification accepted by the European Neuroendocrine Tumor Society (ENETS), carcinoids are defined as high-grade lesions.[7-10] However, either classification can be employed for gastric cancer cases. Type 1 and Type 2 GNETs often present as stage I or stage IIa, while Type III GNETs and NECs frequently appear as stage 2a, 2b, and stage 3b, and rarely as stage 4.[10] Similar to the literature, we found that the majority of type 1 patients were in stages I and IIA, while type 3 and NECs were in stages IIB, IIIB, and IV.

Although total gastrectomy is recommended for GNETs patients with tumor diameters below 2 cm, endoscopic excision has been shown to be safely applicable in Type 1 and 2 GNETs with lesions smaller than 1 cm.[11-13] In lesions with a tumor diameter greater than 1 cm, antrectomy can be performed along with the excision of accessible lesions.[14,15] Consistent with existing literature, these patients have undergone total gastrectomy, subtotal gastrectomy, and local excision procedures in our clinic. For patients who had deceased, the size of the tumor was above 3 cm. Moreover, during the median monitoring period of 42 months, there was no observed recurrence among the patients who survived.

Good prognostic factors for GNETs are their restriction to the mucosa and submucosa, the lack of vascular invasion, tumor diameters less than 1 cm, the absence of endocrine syndrome, and relationships with chronic atrophic gastritis (CAG) or MEN1-ZES.[16,17] The majority of type 1-CAG related GNETs are known to have a favorable prognosis.[11] NETs with aggressive characteristics demonstrate a poor prognosis due to their invasion past the muscularis propria, tumor diameters under 1 cm, vascular invasion, initial presentation with endocrine syndrome, elevated mitotic activity, and sporadic

occurrence.[14,18,19] NECs are frequently associated with a poor prognosis.[20] Also, it has been demonstrated that having a tumor diameter over 2 cm markedly increases the risk of metastasis in gastric NECs.[21] Previous studies have demonstrated that the rates of lymph node metastasis for GNETs type were 3-20% for type I, 12-30% for type II, 59-71% for type III, and 58-72% for NECs.[22-27] The present study found that the rates of lymph node metastasis were 13% for Type 1, 75% for Type 3, and 57% for NECs. It has been shown that primary tumor resection contributes to a better prognosis compared to non-surgical treatment in patients with Stage IV gastric NECs.[28] However, the mortality rate was higher in patients with NECs. This is consistent with patients with NECs having a worse prognosis.[20] Hence, patients with Type 3 and NECs should be closely monitored for 5 years compared to those with Type 1, due to the higher risk of a worse prognosis.[29,30] It has been proposed in various studies that employing endoscopic approaches like polypectomy, endoscopic mucosal resection, and endoscopic submucosal dissection (ESD) could be advantageous for excising small GNETs.[25,31,32] Additionally, it has been reported that in patients with submucosal gastric tumors who underwent wedge resection, no recurrence or metastasis was observed during a follow-up period of 61 months.[33] In this study, wedge resection was performed on about half of the patients with Type 1 GNETs, and there was no observation of recurrence or mortality throughout the follow-up.

Previous studies have demonstrated that the Ki-67 is an important tumor marker in predicting prognosis.[34,35] On the other hand, it has been shown that Ki-67 is significantly associated with a poor prognosis in early-stage gastric cancer but does not serve as a marker for poor prognosis in late-stage gastric cancer.[36] The differences between studies may be attributed to the clinical-demographic characteristics of the patients, such as age, stage, and tumor location, as well as the sample sizes of the studies. In this study, the lack of a significant relationship between Ki-67 levels and tumor diameter or vascular invasion suggests that while Ki-67 may serve as an indicator of proliferation, it does not directly correlate with these specific pathological features in GNETs. However, the higher Ki-67 levels in patients with lymph node metastasis indicate its potential utility as a prognostic marker for more aggressive disease courses. In the cases of GNETs, which are subject to discussions about lymph node dissection, evaluating the Ki-67 index via preoperative endoscopic biopsy could provide guidance on the necessity of performing lymph node dissection.

Limitations

This study has several limitations. The main limitation of the study was its single-center and retrospective design. Additionally, the small number of patients, the lack of standardization in the parameters evaluated by pathology varying over the years, and the uneven distribution of patients according to stages and GNETs types were other significant limitations. Lastly, the absence of GNETs associated with MEN1 and ZES precluded evaluations related to endocrine syndrome.

CONCLUSION

This study underscores the significant impact of surgical resection on the prognosis of patients with GNETs, utilizing the WHO 2010 staging system for classification. Our findings highlight the variability in outcomes based on tumor type, with type I GNETs showing a markedly better prognosis compared to the more aggressive type III and type IV tumors. The observed differences in mortality rates among GNET types, especially the significantly higher rate in type IV patients, point to the necessity of a tailored approach in the management of GNETs. The Ki-67 value assessed through preoperative endoscopic biopsy may serve as a guide for deciding on the necessity of lymph node dissection. Future studies with larger sample sizes and a multi-center approach are needed to validate these findings and further explore the role of Ki-67 and other markers in the prognostication and management of GNETs.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethical Committe of Ege University (Date: 24.12.2014, Decision No: 14.12-1T/58).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Availability of Data and Material

The data that support the findings of this study are available on request from the corresponding author.

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Ankyra Medical Journal
LETTER TO EDITOR DOI: 10.51271/ANKMJ-0011

Comparison of novel oxidative stress and systemic inflammation marker levels in patients with bipolar disorder and schizophrenia

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Dear Editor,

Bipolar disorder (BD) and schizophrenia (SCZ) are chronic mental disorders with mood and psychotic episodes, respectively, which significantly affect functioning and quality of life. The pathophysiology of both BD and SCZ is still poorly understood; however, accumulating evidence indicates the role of aberrant immune-inflammatory processes.[1] The pathophysiological mechanisms of SCZ and BD require further investigation. It is vital to develop a validated methodology that searches for cheap and easily accessible biomarkers and results in an accurate diagnosis.[2] A better understanding of the pathophysiology of these chronic mental illnesses is crucial for the discovery of new targets that may lead to better outcomes in their treatment.[3]

Studies on inflammation in BD and SCZ have generally been performed using cytokines, chemokines or other oxidative stress markers. However, many inflammation-related biomarkers are expensive and have limited use in clinical practice. Therefore, combined biomarkers based on routine peripheral blood cell tests, including neutrophil/high-density lipoprotein (HDL) ratio (NHR), lymphocyte/HDL ratio (LHR), monocyte/HDL (MHR) ratio, platelet/HDL ratio (PHR), atherogenic index of plasma (AIP; logarithmically transformed ratio of triglyceride to HDL molar concentrations), and atherogenic coefficient (AC; non-HDL/HDL), have received increasing attention for identifying simple, inexpensive, and routinely obtained biomarkers of systemic inflammation and oxidative stress.[4] A few recent studies have evaluated MHR, NHR, LHR, PHR, AIP, and AC levels in patients with BD and SCZ.[2,4-6] This study aimed to examine whether the levels of these markers differed in patients with acute mood (BD) or psychotic episodes (SCZ), after adjusting for confounding factors.

The first blood tests of patients with BD-mania (BD-M, n=52), BD-depression (BD-D, n=51), and SCZ (n=61) hospitalized in the psychiatry department of Çanakkale Onsekiz Mart University Hospital were analyzed retrospectively. The sociodemographic and clinical characteristics of the patients are shown in Table 1. Sociodemographic and clinical characteristics did not differ between the groups (p<0.05), except for sex (p=0.03) and number of hospitalizations (p=0.044).

Table 1. Sociodemographic and clinical characteristics of the patients

Characteristics	BD-M (n=52)	BD-D (n=51)	SCZ (n=61)	p-value
Age (years)	40.9±13.1	44.9±11	42.4±13.2	.282
Gender (female)	36 (69.2%)	34 (66.7%)	25 (41%)	.003*
Age at disorder onset (years)	30.4±14	31.3±11.9	31.7±13	.505
Marital status (married)	26 (50%)	29 (56.9%)	21 (34.4%)	.083
Occupation (employed)	18 (34.6%)	22 (43.1%)	19 (31.1%)	.408
Duration of disorder (years)	9.7±9.1	12.9±9.5	9.4±10.8	.139
Number of hospitalisation	2.54±1.9	3±2	2.1±1.8	.044*
Having comorbidity	24 (46.2%)	27 (52.9%)	21 (34.4%)	.156
Active smoking	25 (48.1%)	24 (47.1%)	38 (62.3%)	.205

Note: Plus-minus values are given as mean±standard deviation. * significant p-value. BD-M: Bipolar disorder, mania; BD-D: Bipolar disorder, depression; SCZ: schizophrenia.

Analyses of covariance (ANCOVA) were performed by controlling for age, sex, presence of medical disease, and active smoking to examine whether there was a difference in inflammatory ratios between the groups. Table 2 presents the results. When controlling for confounding factors, there was no difference in any inflammatory ratio among the three groups (all p<0.05).

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Table 2. ANCOVA results of inflammatory ratios among groups

	BD-M (n=52)	BD-D (n=51)	SCZ (n=61)		
Inflammatory ratios	Estimated marginal means±standard error			F	p
MHR	0.12±0.001	0.12±0.001	0.12±0.001	.192	.825
LHR	0.056±0.004	0.055±0.004	0.051±0.004	.42	.658
NHR	9.385±0.498	9.335±0.504	9.417±0.482	.007	.993
PHR	6.074±0.37	5.646±4.895	5.665±0.344	.43	.651
AIP	0.439±0.042	0.486±0.042	0.396±0.039	1.156	.318
AC	2.993±0.195	3.334±0.205	2.774±0.175	2.083	.129

Note: ANCOVA: analyses of covariance; MHR: monocyte/HDL ratio; LHR: lymphocyte/HDL ratio; NHR: neutrophil/HDL ratio; PHR: platelet/HDL ratio; AIP: atherogenic index of plasma; AC: atherogenic coefficient.

In this study, new inflammatory ratios such as MHR, LHR, NHR, PHR, AIP, and AC did not differ between acute mood episodes in patients with BD and acute psychotic episodes in SCZ. In previous studies in patients with BD or SCZ, these inflammatory ratios were compared with those in healthy controls, and significant differences were usually found.[2,4,5] This suggests that these inflammatory ratios were not predictors for differentiating SCZ patients from BD in acute episodes. These biomarkers may be peripheral trait biomarkers that reflect the enhanced inflammatory signaling in SCZ, BD-M, and BD-D. Longitudinal studies with a larger sample size comparing BD and SCZ patients with healthy controls will increase our knowledge of this subject.

ETHICAL DECLARATIONS

Reviewer Evaluation Process

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Ankyra Medical Journal

LETTER TO EDITOR DOI: 10.51271/ANKMJ-0012

Is there a relationship between chronic low back pain and spinal sagittal balance? A prospective controlled study

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Dear Editor,

With great interest, I read the article titled "Is there a relationship between chronic low back pain and spinal sagittal balance? A prospective controlled study." by Korkmaz et al.[1] The authors evaluated the relationship between chronic low back pain and spinal sagittal alignment. They showed that deviations from normal sagittal verticalaxis (SVA) are a significant contributor to low back pain. I congratulate the authors for their contribution to this topic. However, I have some comments regarding this study.

The authors measured SVA, thoracic kyphosis (TK), and lumbar lordosis (LL) values on the lateral whole-spine radiograph, but they did not include the other spinopelvic parameters such as, sacral slope, pelvic tilt and spinosacral angle. In the literature, association between these sagittal parameters and spinal sagittal balance function has been reported in patients with low back pain.[2,3] Spinopelvic parameters and balance function are associated with a greater risk of low back pain. Therefore, the role of sacral slope, pelvic incidence, spinosacral angle and pelvic tilt could not be neglected. It may be beter to combine the information from both SVA, TK, LL and these spinopelvic parameters to assess the spinal sagittal balance function and postural instability.

Additionaly, Niu et al.[2] also measured T1 pelvic angle, T1 spino-pelvic inclination and T9 spino-pelvic inclination to assess the sagittally imbalanced spine, which may affect the posture and low back pain. I would prefer to see the effects of these parameters and their relationship between chronic low back pain and posture, which could improve the understanding of spinal misalignment.

Moreover, spinopelvic parameters were measured using lateral whole-spine radiograph. However, 3D analysis of the spine surface for posture assessment provides more precise results. With 4D technology, which pioneered functional clinical measurement technology, measurement accuracy is increased, and postural variants can be avoided. While such technologies allow for more diagnostic imaging of the spinal misalignment, X-rays are more readily available and less expensive. Although whole-spine radiograph is easily accessible, It would be beter if the authors could use the more sensitive and radiation-free measuremen tsystems, such as three-dimensional motion analysis of the spine and pelvis, which could affect their results. In this regard, rasterstereographic analysis of the spine and pelvis has been reported to be a valuable tool in patients with lowback pain and spinopelvic disorders.[4,5]

Finally, how did the authors calculate the sample size in this study? Although the authors stated that the small number of subjects was a limitation for the study, they did not explained the determination of the sample size of the study.

ETHICAL DECLARATIONS

Referee Evaluation Process

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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