

## PAPER DETAILS

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# Metabolic Monitoring of the Patients with Serious Mental Illness (SMI) in a Community Mental Health Center (CMHC) During the COVID-19 Pandemic

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## ABSTRACT

**Purpose:** Metabolic monitoring of patients with serious mental illness (SMI) has been interrupted during the COVID-19 pandemic. Our aim in this study is to compare the metabolic parameters of patients at baseline (before pandemic) and 12 months after the COVID-19 pandemic in a community mental health center (CMHC).

**Methods:** In this retrospective cohort study, we compared the metabolic parameters such as body mass index (BMI), waist circumference (WC), high-density lipoprotein (HDL), atherogenic index of plasma (AIP) at baseline (before pandemic) and 12 months after pandemic.

**Results:** BMI ( $p<0.001$ ), WC ( $p<0.001$ ), and HDL levels ( $p<0.001$ ) were significantly higher at month 12 when compared with baseline for both schizophrenia ( $n=17$ ) and bipolar disorder ( $n=17$ ) groups. The prevalence of obesity was significantly higher at month 12 when compared with baseline.

**Conclusion:** Social restrictions and physical inactivity during COVID-19 pandemic cause deteriorating effect on metabolic parameters. BMI, AIP, WC, and fasting glucose can be used for metabolic monitoring. Common vaccination programs and releasing of social restrictions provided opportunities to assess and intervene metabolic health of patients with SMI. Taken into consideration that obesity cause an increased risk of hospitalization, severe disease, and death due to COVID-19 infection, metabolic monitoring of patients with SMI should be done rigorously.

**Keywords:** COVID-19, Serious Mental Illness, Community Mental Health Center, Metabolic Monitoring, Physical activity

## Bir Toplum Ruh Sağlığı Merkezinde (TRSM) İzlenen Ciddi Ruhsal Hastalığı (CRH) Olan Hastaların COVID-19 Pandemisi Döneminde Metabolik Takibi

### ÖZET

**Amaç:** Ciddi Ruhsal Hastalığı (CRH) olan hastaların metabolik izlemi, COVID-19 pandemisi döneminde ciddi düzeyde aksamış. Bu çalışmadaki amacımız, bir Toplum Ruh Sağlığı Merkezindeki (TRSM) hastaların başlangıçtaki (pandemi öncesi) ve COVID-19 pandemisinden 12 ay sonraki metabolik parametrelerini karşılaştırmaktır.

**Yöntemler:** Bu retrospektif kohort çalışmada, vücut kitle indeksi (VKİ), bel çevresi (BÇ), yüksek yoğunluklu lipoprotein (HDL), aterojenik plazma indeksi (API) gibi metabolik parametrelerin başlangıç (pandemi öncesi) ve pandemiden 12 ay sonraki değerlerini karşılaştırdık.

**Bulgular:** VKİ ( $p<0.001$ ), BÇ ( $p<0.001$ ) ve HDL düzeyleri ( $p<0.001$ ) 12. ayda hem şizofreni ( $n=17$ ) hem de bipolar bozukluk ( $n=17$ ) grupları için başlangıça göre anlamlı olarak daha yüksekti. Obezite prevalansı, 12. ayda başlangıça kıyasla önemli ölçüde daha yüksekti.

**Sonuç:** COVID-19 pandemisi sırasındaki sosyal kısıtlamalar ve fiziksel hareketsizlik metabolik parametreler üzerinde kötüleştirici etkiye neden olmaktadır. Metabolik izlem için VKİ, API, BÇ ve açlık glukozu kullanılabilir. Yaygın aşılama programları ve sosyal kısıtlamaların azaltılması, CRH tanılı hastaların metabolik sağlığını değerlendirmek ve müdahale etmek için fırsatlar sağladı. Obezitenin COVID-19 enfeksiyonuna bağlı hastaneye yatış, ağır hastalık ve ölüm riskinde artışa neden olduğu göz önüne alındığında, CRH tanılı hastaların metabolik izlemi dikkatle yapılmalıdır.

**Anahtar Kelimeler:** COVID-19, Ciddi Ruhsal Hastalık, Toplum Ruh Sağlığı Merkezi, Metabolik İzlem, Fiziksel Aktivite

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**S**chizophrenia, bipolar disorder, and other psychotic disorders are chronic and severe mental disorders. Worldwide, they are associated with considerable disability and may affect educational and occupational performance. The life expectancy of severe mental illness (SMI) patients is 8 to 32 years shorter than the general population. This is often due to higher rates of smoking, unhealthy diets, antipsychotic drugs that increase the risk for metabolic syndrome, and preventable physical diseases such as cardiovascular disease and infections (1, 2). Hence, metabolic monitoring of SMI patients in a multidisciplinary approach is critical within psychiatric care. There is clear evidence that old-style mental health hospitals are not effective in the management of metabolic and psychological health of SMI patients. Therefore, a community-based mental health model is being adopted all over the world (3).

After the second half of the twentieth century, psychiatric services in Western Europe underwent serious conceptual and structural transformations. Community-based psychiatric services played a key role as a milestone for modern psychiatric treatments. Institutions such as community mental health centers (CMHCs) have been established to provide services to SMI patients. CMHCs implement the holistic approach, which incorporates both mental health and metabolic monitoring, and collaborate with dietitians, family physicians, cardiologists, and endocrinologists in case of a metabolic problem. Social skills training in CMHCs significantly improves psychopathology, functionality, depression level, insight, and drug compliance of SMI patients (3, 4).

The coronavirus disease 2019 (COVID-19) pandemic, which has been going on for more than a year, has also shaken the metabolic balance of the world with the curfew restrictions it has imposed, along with many other challenges (5). The closure of many workplaces, flexible and home office working resulted in decreased organized physical activity, increase in sedentary lifestyle and screen time with the possibility of stress-induced indulgence in high calorie-dense and sugary foods, resulting in higher susceptibility to weight gain (6). In this study, it was stated that the COVID-19 pandemic caused weight gain in one-half of the respondents in their systematic scoping review, in which they examined 19 out of 396 articles conducted using online self-report surveys. In this review, significant weight gain was reported, associated with a 36.3% to 59.6% increase in total food consumption and a 61.4% to 67.4% decrease in physical activities (6).

SMI patients are at higher risk for metabolic syndrome than the general population (7). COVID-19 is known to exhibit a more severe clinical picture in individuals with metabolic syndrome. Increased metabolic risk due to the physical restrictions of the COVID-19 leads to a vicious circle, and the situation becomes more tragic. SMI patients have more diminished and restricted social networks than the general population (8). Social restrictions during the COVID-19 pandemic have diminished the social network of SMI patients through interrupted general health and CMHC services and curfews. COVID-19 pandemic may decline the size of the social network of SMI patients. Researchers have already sounded the alarm on how the COVID-19 pandemic may affect the mental health of the general population, and more specifically, SMI patients (9). Studies on this group of patients who already experience social, psychological, and physical negative outcomes due to the COVID-19 pandemic are not at the desired level yet. Although it is known that metabolic parameters are regularly recorded in many CMHCs, there is no study comparing the metabolic and functional parameters of SMI patients before and after COVID-19. In this study, we aimed to assess changes in metabolic profiles and functionality of patients with SMI who regularly attend the CMHC, which is interrupted by the COVID-19 pandemic. We hypothesized that during the pandemic, there would be substantial changes in lipid profile, weight, waist circumference, and social functioning in patients with SMI.

## MATERIAL AND METHODS

### *Study Design*

This retrospective cohort study was conducted in CMHC of Elazığ Mental Health and Diseases Hospital. Patients diagnosed with schizophrenia and bipolar disorder, according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), were included (10).

### *Inclusion and Exclusion Criteria*

537 SMI patients were recruited from the CMHC of Elazığ Mental Health and Diseases Hospital. We included patients who were > 18 years old, had regular medication, had past (before COVID-19 pandemic) and recent (at the end of the first year of COVID-19 pandemic) blood test results, anthropometric parameters, and psychometric measurements. The patients whose medication schedule and doses are stable at least for the last two years were assessed retrospectively from CMHC records between January 2020 and March 2021. The patients with missing data were excluded from the study. The patients with a known history of diabetes and hypertension before the

COVID-19 pandemic, the patients who were hospitalized at the psychiatry clinic in the last year, were excluded from the study. The patients who had a history of alcohol and drug dependence and who had a history of COVID-19 infection were excluded. The flowchart is shown in Figure 1.

#### *Anthropometric, Metabolic, and Psychometric Measurements*

Functionality was assessed by the Global Assessment Scale (GAS) and the Personal and Social Performance Scale (PSP). Changes in psychiatric symptoms were assessed by the Brief Psychiatric Rating Scale (BPRS) (11-14). Variables such as body mass index (BMI), waist circumference, fasting glucose, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), and total cholesterol (TC) were evaluated. BMI ( $\text{kg}/\text{m}^2$ ) was calculated from weight (measured in light clothing without shoes) and height (measured without shoes). BMI groups defined as underweight ( $\text{BMI} < 18.5 \text{ kg}/\text{m}^2$ ), normal weight ( $\text{BMI} 18.5\text{-}24.9 \text{ kg}/\text{m}^2$ ), class I obesity - overweight ( $\text{BMI} 25.0\text{-}29.9 \text{ kg}/\text{m}^2$ ), class II obesity - obesity ( $\text{BMI} 30.0\text{-}39.9 \text{ kg}/\text{m}^2$ ), class III obesity - extreme obesity ( $\text{BMI} > 40 \text{ kg}/\text{m}^2$ ) (15). Waist circumference (cm) was measured from the midpoint between the lowest rib and iliac crest by using a Gulick II tape measuring tape (16). A total of 5-10 ml of venous blood sample was collected every 6 months for routine metabolic monitoring in CMHC. Peripheral venous blood samples were taken one hour after awakening (8.00 am) and when patients are fasting for 12 hours. Blood samples are analyzed without waiting. Assay parameters were evaluated by medical biochemistry specialist. Atherogenic index of plasma (AIP), which is calculated as the logarithm of plasma triglyceride to HDL ratio, has shown an independent association with cardiovascular risk (17).

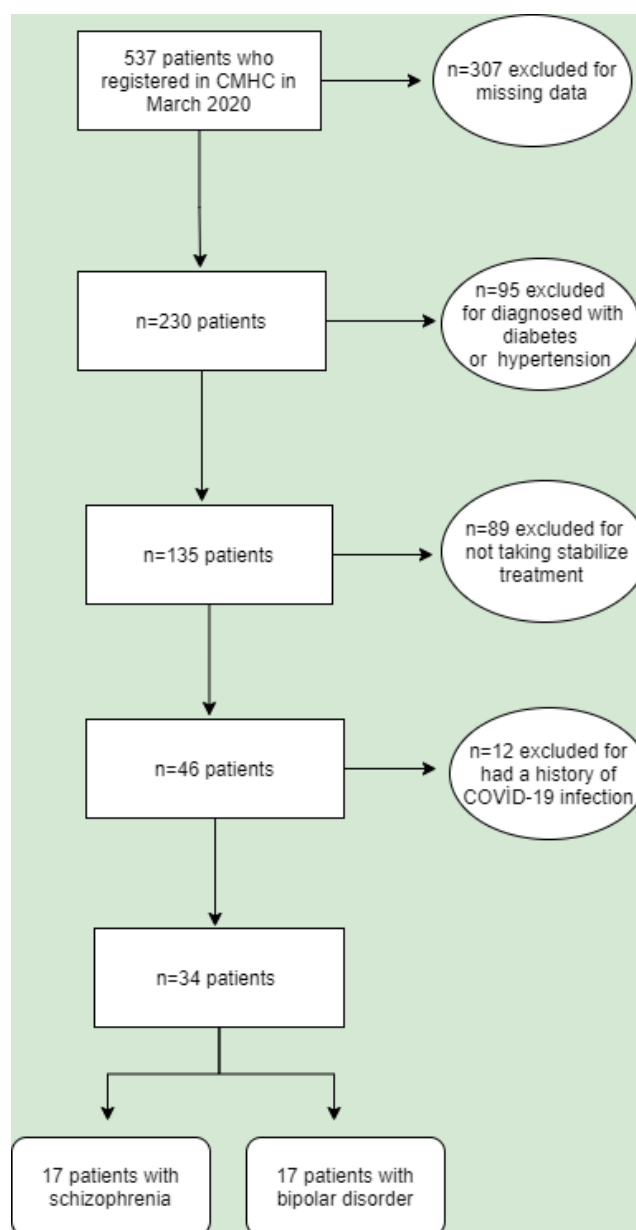
#### *Biochemical Analyses*

Venous blood samples were obtained from the antecubital vein of patients between 8 and 9 a.m. after at least 12 hours of starvation. The samples were centrifuged within 30 minutes and on the same day (4000 rpm for 10 minutes), centrifugation was followed in the Beckman Coulter AU480 Biochemical Auto-Analyser (Beckman Coulter, Inc.; CA, USA) device at our hospital biochemistry laboratory.

#### *Statistical Analyses*

Statistical analysis was performed using Windows SPSS 22.0 (Statistical Package for the Social Sciences Inc.). Descriptive statistics and continuous variables were given as mean  $\pm$  standard deviation, and categorical variables were given as frequency and percentage. The Chi-square

test was used to analyze the categorical data. Normal distribution suitability was assessed using the Kolmogorov-Smirnov test. Paired Sample T-test was used to compare the measurements at two time points (baseline and month 12) for metabolic and functioning parameters. The Marginal Homogeneity test was used to compare the change in BMI groups between baseline and month 12. A value of less than 0.05 (p-value) was considered statistically significant.



**Figure 1.** The Flowchart: Selection of Participants

## RESULTS

The mean age of participants (n=34) was  $42.41 \pm 8.25$  years (min: 24, max: 58); mean duration of education was  $10.32 \pm 4.35$  years; mean duration of illness was  $19.94 \pm 7.55$  years; mean age at first diagnosis was  $22.47 \pm 5.36$  years; the mean number of hospitalization was  $8.91 \pm 8.36$ ; the mean number of suicide attempts was  $0.41 \pm 0.89$ .

Table 1 shows the comparison of clinical parameters of patients at baseline and month 12. BMI groups of the patients (n=34) at baseline and month 12 are shown in Table 2. Owing to BMI change during one year, six of the patients transited to the higher BMI group (2 patients: normal weight to overweight and 4 patients: overweight to obese). The prevalence of obesity was significantly higher at month 12 when compared with baseline. HDL levels were significantly higher at month 12 when compared with baseline for both smokers and non-smokers.

Parameters	Baseline (n=34) (Mean $\pm$ SD)	Month 12 (n=34) (Mean $\pm$ SD)	p value
BMI (kg/m <sup>2</sup> )	27.55 $\pm$ 4.89	29.21 $\pm$ 5.51	<0.001**
Waist Circumference	95.44 $\pm$ 12.57	101.52 $\pm$ 13.87	<0.001**
Fasting Glucose (mg/dl)	97.9 $\pm$ 15.6	96.1 $\pm$ 23.5	0.636
HDL (mg/dl)	44.64 $\pm$ 13.03	51.08 $\pm$ 11.33	<0.001**
LDL (mg/dl)	107.50 $\pm$ 29.90	104.82 $\pm$ 28.90	0.433
Triglycerides (mg/dl)	164.52 $\pm$ 74.21	184.55 $\pm$ 103.06	0.185
Total cholesterol (mg/dl)	185.82 $\pm$ 39.62	198.32 $\pm$ 50.57	0.050
AIP	0.53 $\pm$ 0.29	0.51 $\pm$ 0.28	0.509
BPRS	14.05 $\pm$ 6.46	20.17 $\pm$ 9.69	<0.001**
GAS	63.58 $\pm$ 12.24	57.97 $\pm$ 13.83	<0.001**
PSP	66.55 $\pm$ 14.99	58.50 $\pm$ 15.29	<0.001**

\*p<0.05; \*\*p<0.001; In statistical analysis, Paired Sample T-Test was used; Abbreviations: SD: Standard Deviation; BMI: Body Mass Index; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein; AIP: Atherogenic Index of Plasma; BPRS: Brief Psychiatric Rating Scale; GAS: Global Assessment Scale; PSP: Personal and Social Performance Scale

Clinical parameters of patients with schizophrenia (n=17) were compared between baseline and month 12. BMI (p=0.006), waist circumference (p=0.006), and HDL levels (p=0.006) were significantly higher at month 12 when compared with baseline. Clinical parameters of patients with bipolar disorder (n=17) were compared between baseline and month 12. BMI (p<0.001), waist circumference (p=0.001), and HDL levels (p=0.005) were significantly higher in month 12 compared with baseline.

Table 2. BMI Groups of Patients at Baseline and Month 12

BMI Groups	Baseline (n=34) n (%)	Month 12 (n=34) n (%)	p value
Underweight	1 (%2.9)	1 (%2.9)	0.014*
Normal Weight	10 (%29.41)	8 (%23.52)	
Overweight	13 (%38.23)	11 (%32.35)	
Obese	9 (%26.56)	13 (%38.31)	
Severe Obese	1 (%2.9)	1 (%2.9)	

\*p<0.05; In statistical analysis, Marginal Homogeneity test was used; Abbreviations: BMI: Body Mass Index

Patients were divided into two groups as schizophrenia and bipolar disorder as shown in Table 3. The use of a mood stabilizer was significantly higher in bipolar disorder (p<0.001).

The change rates ([Month 12 Value - Baseline Value] / Baseline Value) in clinical and metabolic parameters within one year after the COVID-19 pandemic was compared between schizophrenia and bipolar groups. There was no significant difference between two groups in change rates of BPRS (p=0.709), GAS (p=0.550), PSP (p=0.114) scores, BMI (p=0.224), AIP (p=0.122), LDL (p=0.955), HDL (p=0.426), waist circumference (p=0.375), TC (p=0.206), and TG (p=0.335). The change rates of the clinical and metabolic parameters between baseline and month 12 were compared between employed (n=11) and unemployed (n=23) patients; between married (n=11) and single (n=19); between those who used one or more drugs such as olanzapine, clozapine, quetiapine, and risperidone (n=20) and those who did not use any of these drugs (n=14); between smoking (n=21) and non-smoking (n=13) patients, and no significant difference was found (p>0.05).

## DISCUSSION

We found that BMI, waist circumference, and HDL levels significantly increased at the end of the first year of the COVID-19 pandemic when compared with baseline. Our findings showed that at the end of the first year of the COVID-19 pandemic, psychiatric symptoms and functioning deteriorated when compared with baseline. When the schizophrenia and bipolar disorder groups were evaluated separately; BMI, waist circumference, and HDL levels increased in both groups. Change rates of clinical and metabolic parameters in one year after the COVID-19 pandemic were similar between schizophrenia and bipolar disorder groups. We found that employment, marital status, and smoking status did not affect change rates of metabolic and clinical parameters.

Table 3. Comparison of Sociodemographic and Clinical Parameters of Patients with Schizophrenia and Bipolar Disorder

Parameter		Schizophrenia	Bipolar Disorder	p value
Gender	Female	3 (42.9%)	4 (57.1%)	0.671
	Male	14 (51.9%)	13 (48.1%)	
Marital Status	Single	12 (63.2%)	7 (36.8%)	0.209
	Married	4 (36.4%)	7 (63.6%)	
	Widowed	1 (25.0%)	3 (75.0%)	
Living Area	Parent	13 (59.1%)	9 (40.9%)	0.504
	Partner/Child	2 (28.6%)	5 (71.4%)	
	Brother/Sister	1 (50.0%)	1 (50.0%)	
	Alone	1 (33.3%)	2 (66.7%)	
Working Status	Yes	5 (45.5%)	6 (54.5%)	0.714
	No	12 (52.2%)	11 (47.8%)	
Socioeconomic Status	Lower	8 (61.5%)	5 (38.5%)	0.558
	Middle	8 (42.1%)	11 (57.9%)	
	Upper	1 (50.0%)	1 (50.0%)	
Smoking Status	Yes	10 (47.6%)	11 (52.4%)	0.724
	No	7 (53.8%)	6 (46.2%)	
Depot AP Use	Yes	8 (44.4%)	10 (55.6%)	0.492
	No	9 (56.3%)	7 (43.8%)	
Mood Stabilizer Use	Yes	6 (27.3%)	16 (72.7%)	<0.001**
	No	11 (91.7%)	1 (8.3%)	
Oral AP Use	Yes	15 (53.6%)	13 (46.4%)	0.368
	No	2 (33.3%)	4 (66.7%)	
AD Use	Yes	14 (46.7%)	16 (53.3%)	0.287
	No	3 (75.0%)	1 (25.0%)	

\*\*p<0.001; In statistical analysis, Chi-Square Test was used; Abbreviations: AP: Antipsychotic; AD: Antidepressant

The COVID-19 pandemic has caused a more common sedentary lifestyle due to strict rules set by governments. A study showed that 41.8-42.2% of the participants, who exercised regularly before the COVID-19 pandemic, reported a decrease in walking, jogging, and sports during the COVID-19 pandemic (18). According to this study, most of the participants reported an "increase" in watching TV (72.3%), using electronics (82.7%), and logging into social media (81.9%). In another study, which has participants aged 18-35, there was a significant decrease in the physical activities of individuals during the COVID-19 pandemic when compared with before the COVID-19 pandemic, and individuals spent more time on sleep and sedentary activities (19). Besides physical inactivity, unhealthy dietary habits also become more common during the COVID-19 pandemic. A study evaluated the effect of the quarantine during the COVID-19 pandemic on the dietary habits and found that almost half of the respondents (49.4%) ate more than usual, 45.1% increased snacking, and 62.1% cooked at home more often (20). Physical activity and dietary habits have sharply changed in the whole population during the COVID-19 pandemic. SMI patients, who have a greater risk for metabolic problems than the general

population, should be rigorously monitored for metabolic parameters during the COVID-19 pandemic. In our study, we showed that weight gain and abdominal obesity risk of SMI patients increased at the end of the first year of the COVID-19 pandemic. Possible reasons for this increase are thought to be physical inactivity, increasing sedentary lifestyle, and changing dietary habits. Weight gain and abdominal obesity during the COVID-19 pandemic in SMI patients, who have already more metabolic risk than the normal population, may be overlooked due to interruption in the healthcare system. Several studies have shown that obesity is a very important risk factor for hospitalization, severe disease, and death due to COVID-19 infection (21, 22). When taking into consideration the COVID-19 pandemic still goes on, the metabolic health of patients would affect mortality rates due to the COVID-19 infection. COVID-19 vaccination programs provided by health institutions gradually come back to normal. Patients who could not reach to hospital and CMHC during the pandemic may refer after releasing of restrictions. Clinicians should be alert about the deteriorating effects of the COVID-19 pandemic on the weight gain of these patients.



We found a marked deterioration in the general and social functioning levels of SMI patients at the first year of the pandemic when compared with baseline. We found also psychiatric symptoms increased during the first year of the pandemic. These results may be related to social distancing, physical inactivity, difficulty reach to CMHC and hospital during the first year of the pandemic. A study showed that a longer period of social distancing and self-reported history of previous psychiatric disorders were strongly associated with higher severity of psychiatric symptoms (23). Sepúlveda-Loyola et al.'s narrative review including 20.069 individuals from ten descriptive cross-sectional papers demonstrated that the main outcomes of the COVID-19 pandemic were anxiety, depression, and poor sleep quality during the isolation period (24). This situation may lead to the emergence of anxiety and depression problems in addition to their current main psychiatric diagnoses and to worsening of their already poor social functioning. Community-based psychiatric entities such as CMHC help to reduce the social and psychological problems experienced by this patient group (4). Interruption of CMHC services during the pandemic may be related to the decreased social and general functioning of patients.

The most interesting finding in this study is the increased HDL levels detected in patients at the end of the first year of the COVID-19 pandemic when compared with pre-pandemic levels. HDL is synthesized in the liver and intestines and mainly facilitates reverse cholesterol transport, which is a mechanism for removing excess cholesterol from peripheral tissue and delivering them to the liver (25). The long-standing notion that lower HDL levels are directly related to cardiovascular disease has shaken with recent studies. HDL-functionality may have a more important role in atheroprotection than circulating HDL levels (26). In recent studies, there is no clear evidence on the relation of the exercise-HDL level. A study showed that only one meta-analysis showed good quality among 23 meta-analyses on the relation of exercise-HDL levels, the rest had a high risk of bias (27). Research has recently focused on HDL functionality. A study suggested regular and prolonged exercise improves some measures of HDL function (28). Larger studies are needed to determine what dose of exercise needs to provide improvements in HDL levels and function. Taken decreased importance on evaluating the cardiovascular risk of HDL levels when compared with HDL functions, we propose AIP levels instead of HDL levels to assess cardiovascular risk in SMI patients.

AIP is a novel index composed of HDL and triglycerides. AIP, as a biomarker, is an independent risk factor

for coronary artery disease (29). There was no change in AIP levels, which means no increase in cardiovascular risk ratio at the end of the first year of the pandemic. It has been used as an optimal indicator of dyslipidemia and cardiovascular diseases (30). Also, AIP levels use as a predictor of mortality in patients with COVID-19 (31). AIP should be considered when estimating current and future cardiovascular disease risk, along with other traditional risk factors (32). AIP as a predictor for both prognosis of COVID-19 and cardiovascular disease risk may have an important role during the COVID-19 pandemic. As a result, metabolic parameters such as BMI, waist circumference, AIP, fasting glucose should take into consideration for optimal metabolic monitoring of SMI patients.

SMI patients are more vulnerable to infectious diseases due to predisposing metabolic risk factors. Management of abiding by the rules during the pandemic and complying with COVID-19 treatment during infection can be challenging for SMI patients due to lack of insight, insufficient social support. Common vaccination program provides partial renormalization of mental health services. The vaccination status of patients admitted to CMHCs should be followed and hesitation over the vaccination should be dealt with by giving information and correcting the myths about COVID-19 vaccines.

## CONCLUSION

Reactivation of mental health services in CMHCs with common vaccination and social distance rules provides an opportunity to detect, assess and intervene with psychosocial and metabolic impacts of the COVID-19 pandemic. Psychiatrists and nurses who work in CMHCs should be alert to the deteriorating effects of the COVID-19 pandemic on metabolic health and keep on metabolic monitoring, which is interrupted during the pandemic. It should be followed whether the COVID-19 vaccine, which is the most effective way to protect against COVID-19 disease, is administered and the hesitation or lack of knowledge of SMI patients in CMHCs about vaccines should be intervened.

The retrospective nature of this study is a significant limitation. There was no objective information about the diet and physical activity habits of the patients during the COVID-19 pandemic. The possible effect of these habits on the results should be investigated in future studies. Although patients using a stable treatment regimen for at least two years were included, the effect of psychotropic drugs on metabolic parameters could not be excluded.

Larger and longitudinal studies are required to assess the effects of the COVID-19 pandemic on metabolic parameters and functioning of CMHCs patients with SMI.

## DECLARATIONS

### Funding

The present study was not funded by any corporation

### Conflicts of Interest

The author declares no conflict of interest.

### Ethics Approval

All protocols for this study were approved by the Firat University Ethics Committee (Decision No: 2021-07-07).

### Authors Contributions

Establishing the main idea and hypothesis of the study: A.B.T. and H.K.; Developing the hypothesis and designing the materials and methods section: A.B.T. and H.K.; Evaluation of data: A.B.T., H.K. and M.H.O.; Writing the introductory part of the article: A.B.T., H.K. and M.H.O.; Writing the conclusion and discussion sections of the article: A.B.T., H.K. and M.H.O.; Writing the draft of the article: A.B.T., H.K. and M.H.O.; Assessing the final version of the article and making necessary corrections: A.B.T., H.K. and M.H.O.

### Availability of Data

Available upon request.

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