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DERLEME / REVIEW

Bipolar Mood Disorder in Older Age Individuals

İleri Yaş Bireylerde Bipolar Duygudurum Bozukluğu

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Abstract

Since geriatric individuals are a rapidly growing segment of the population, the number of patients with bipolar mood disorder is increasing gradually. Treatment options become more difficult as a result of increasing organic diseases and comorbid psychiatric disorders with increasing age, and the treatment of geriatric bipolar mood disorder patients can be more complex than that of younger patients, considering the sensitivity to side effects due to pharmacological treatments. The aim of this study is to present the prevalence of bipolar mood disorder in the older age group, the symptoms affecting them, and the current status of comorbid disorders by collecting information from the studies in the related literature. It is of critical importance examining the neurodegeneration of bipolar mood disorder in more detail in future studies. With more interventional studies, it will be possible to support organic diseases and psychiatric comorbidities that occur with advancing age. Local studies on the treatment protocols will help to reduce the burden created on patients.

Keywords: Bipolar mood disorder, older age, treatment, mania, depression.

Öz

Geriatrik bireylerin nüfusun hızla büyüyen bir kesimi olmasından dolayı ileri yaşta bipolar duygudurum bozukluğu hasta sayısı da giderek artmaktadır. Yaşın ilerlemesi ile beraber artan organik hastalıklar ve komorbid olarak görülen psikiyatrik bozukluklar sonucunda tedavi seçenekleri zorlaşmakta, farmakolojik tedavilere bağlı yan etkilere duyarlılık dikkate alındığında da geriatrik bipolar duygudurum bozukluğu hastalarının tedavisi genç yaştaki hastalara göre daha karmaşık olabilmektedir. Bu çalışmanın amacı, ileri yaş grubunda bipolar duygudurum bozukluğunun yaygınlığını, bunları etkileyen semptomları, komorbid olarak gelişen rahatsızlıkların güncel durumunu ilgili literatürde yapılan araştırmalardan bilgi toplayarak özet bir çalışma olarak sunmaktır. Daha fazla girişimsel çalışmalar yardımıyla ilerleyen yaşla birlikte ortaya çıkan organik hastalıkların ve psikiyatrik ek tanıların desteklenmesi mümkün olabilecektir. Tedavi protokollerine ilişkin yapılacak olan çalışmalar hastaların üzerinde oluşan yükün azaltılmasına yardımcı olacaktır.

Anahtar Kelimeler: Bipolar duygudurum bozukluğu, ileri yaş, tedavi, mani, depresyon.

1. Introduction

Aging begins with birth, continues through childhood and adulthood, and as time progresses, the individual's mental and physical independence decreases. It refers to all the changes that cause a decline in motor and cognitive performance in the musculoskeletal system (1). According to the new data from the WHO, old age is considered to be over 65 years of age based on calendar age (2). Nowadays, the world's elderly population tends to increase rapidly due to the improvement of living conditions and the development of medical care services (3). Bipolar mood disorder (BMD) is a serious psychiatric disorder that is characterized by mania, hypomania, depression, and mixed attacks, in which normal mood can be seen between attacks, genetic predisposition is dominant, and it causes deterioration in quality of life. The estimated incidence of BMD in adults is reported as 2.8-6.5%, and in the patient group over 65 years of age, between 1-0.5%, and it is supported by studies in which geriatric individuals constitute 25% of the patient group with BMD (4 -6).

1.1. Epidemiology of Bipolar Disorder in Old Age Patients

Due to the decrease in birth rates worldwide and the improvement of living conditions, the human lifespan is increasing, and older individuals represent a rapidly growing group of the population. According to the Turkish Statistical Institute's internet site data accessed on November 10, 2023; the population aged 65 and over, which is considered the elderly population, was 6 million 895 thousand 385 people in 2017, increasing by 22.6% in the last five years and reaching 8 million 451 thousand 669 people in 2022. According to population projections, the elderly population rate is predicted to increase by 12.9% in 2030, 16.3% in 2040, 22.6% in 2060, and 25.6% in 2080 (Chart 1) (7).

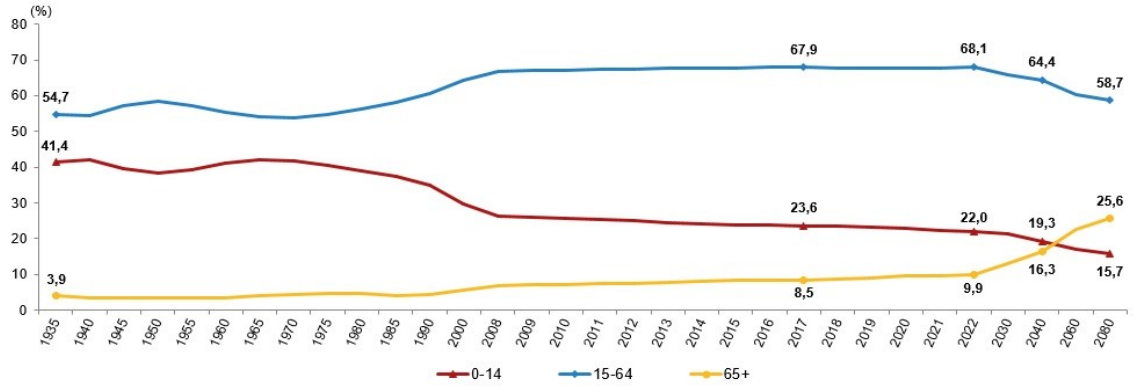

Chart 1. Population Rate by Age Group, 1935-2080

Although mood disorders are common, the lifetime prevalence of BMD is accepted as 1-5% (8). The average age of onset of bipolar disorder is between 15 and 25 years of age, and it occurs in less than 10% of cases after the age of 50 (9,10). The fact that there is an increasing proportion of the elderly population around the world and that studies focusing on elderly BMD patients as a result of the serious clinical data obtained from the research results have also managed to draw attention to patients with geriatric BMD. According to the results of the research, it was concluded that BMD represents approximately 20% of mood disorders in older individuals and accounts for approximately 8-10% of psychiatric admissions (11,12). In epidemiological studies, the prevalence of BMD I and II in the older age group is 0.5-1%, indicating that the rate of BMD in older individuals is lower compared to the younger patient group (13,14). It has been found that the rate of BMD in older individuals living in nursing homes is 3-10%, and the prevalence of manic attacks in older individuals receiving inpatient psychiatric treatment is 6%, and 44% of them have late-onset mania (12,15,16).

1.2. Aetiology of Bipolar Mood Disorder in Old Age Patients

Advanced-age BMD disease appears as a heterogeneous group, including early and late-onset BMD patients. For this reason, individuals with different pathogenesis, clinical course, and treatment options can be seen in the older patient group. In addition to genetic and biochemical factors, advanced declines in cognitive processes, neurological diseases, somatic factors such as head trauma and tumors, and complications arising from multiple drug use appear to be effective in the etiology of advanced-age BMD (Figure 1).

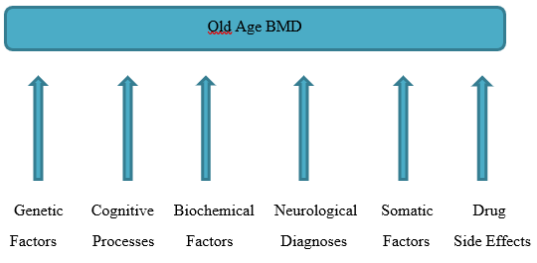

Figure 1. Old Age BMB Etiological Factors

Although it is not clear today exactly how BMD occurs, it is documented as a result of research that genetic, neurobiological, biochemical, and environmental factors play an important role in the etiology of BMD (17). Studies on families and twins demonstrate the importance of genetic factors affecting susceptibility to bipolar disorder and suggest that there is significant genetic and phenotypic complexity (18). While genetic factors are more dominant in early-onset BMD patients, the conclusion that neurological diagnoses, cognitive decline, or somatic factors are more effective in late-onset BMD patients is supported by study findings (19-22). In most patients who have their first manic episode at an advanced age, vascular changes or other brain pathologies are held responsible for this condition (23). In late-onset BMD, manic attacks may occur due to disorders such as somatic disorders, inflammatory diseases, head trauma, and stroke, rather than having an organic origin and as a side effect of the drugs used for their treatment (24,25). This concept, which is defined as secondary mania, is accepted as an episode that occurs as a result of a pharmacological, metabolic, or somatic condition (25).

1.3. Differences Between Early-Onset and Late-Onset Bipolar Mood Disorder

In BMD, where genetic predisposition is dominant, familial predisposition predominates in early-onset patients and manifests itself as a secondary disorder mostly caused by organic diseases, pharmacological treatments, and neurological diseases in the elderly patient group. According to the results of a study conducted with 57 individuals over the age of 60, mood swings are significantly associated with organic diseases, cognitive disorders, and disability. It was concluded that 60% of the patients had endocrine diseases, musculoskeletal system disorders, vascular disorders, and breast system disorders, and more severe depressive episodes were significantly associated with organic comorbidities and cognitive disorders (26). As a result of magnetic resonance imaging (MRI) studies in BMD patients, it was determined that there were some structural changes compared to healthy individuals. Gray matter reductions in cortical and subcortical brain structures that are responsible for emotion regulation in young BMD patients, together with a decrease in structural integrity in white matter that connects these brain structures, are associated with BMD symptoms, and it has been concluded that structural brain differences are also seen in elderly BMD patients (27). Although white matter hyperintensity has been frequently reported in BMD patients, it supports the opinion that cardiovascular and metabolic comorbidities may contribute to higher rates of white matter hyperintensity in patients with advanced age and late-onset BMD (28). Studies show that older individuals are more likely to have their first manic episode during antidepressant treatment than younger adults, which is in line with the fact that tricyclic antidepressants have long been considered a risk factor for secondary mania (29). According to retrospective research findings, the time from the onset of BMD to rapid cycling and the duration of episodes were shorter in the early-

onset patient group than in the late-onset patient group, and lithium carbonate used in the manic attack periods and antidepressant treatment used in the depressive phase were more effective in treating the attacks of the late-onset group than in the early-onset patient group. It has been found that rapid cycling caused by antidepressants manifests itself more clearly in patients with late-onset BMD (30). It is observed that late-onset BMD patients have longer hospital stays and more applications for outpatient treatment compared to the early-onset BMD patient group, as a result of the increased burden of comorbid medical diseases, more side effects of the drugs used, and less favorable treatment (31-33).

1.4. Cognitive Processes in Old Age Bipolar Mood Disorder

BMD is known to be chronic and cause disability. The cause of the sequelae seen in elderly BMD patients may be largely due to the accumulation of cognitive impairments seen before advancing age (34). Dysfunction in cognitive functions mostly occurs in verbal memory, executive function, and processing speed in relation to the severity of the disease, and it is supported by studies including first-degree relatives of patients (35). Although the etiology of the deterioration in cognitive functions is not fully clarified, the dysfunction in dopamine and glutamate release is due to a neurodevelopmental and/or neurodegenerative process such as oxidative stress (34,36). As a result of a prospective study, it was concluded that older BMD patients had more cognitive dysfunction than the healthy control group matched for age and education level, and cognitive decline increased more rapidly as a result of further follow-up (37). Another prospective study supported these findings through cognitive evaluation tests and MRI scans which showed that, as compared to the healthy control group, there were more decreases in hippocampal volume and temporal lobe gray matter in BMD patients at the beginning and at the end of the 4-year follow-up period. The study also found that these observed decreases were closely related to the decline in cognitive function and the number of mood attacks in the follow-up period (38). According to the results of many studies, having a diagnosis of BMD is an important predictor of cognitive dysfunction and cognitive decline over time, and it is emphasized that cognitive dysfunction seen in elderly patients with BMD is an important comorbidity associated with mood disorder (37). It is among the remarkable findings that cognitive dysregulation is seen not only in the attack periods but also in the euthymic periods in BMD patients. A 6-year prospective study found that adult BMD patients in the euthymic period experienced a serious regression in executive memory, processing speed, and verbal memory compared to the healthy control group (39). A meta-analysis study conducted with elderly BMD patients also showed that there are cognitive impairments in the euthymic period, which supports the data in the literature (40).

1.5. Dementia Comorbidity in Old Age Bipolar Mood Disorder

Whether the deterioration in cognition is progressive or not and its relationship with the increased risk of dementia in BMD patients are among the issues that need to be investigated in detail. The results of a study conducted using a nationwide database showed that the risk of dementia increases in patients after the diagnosis of bipolar disorder (41). Dementia is a neurological disease that poses a significant burden on patients and caregivers, and the number of dementia cases is expected to reach 81 million in 2040 (42). There are studies in the literature showing that the diagnosis of BMD increases the risk of dementia. As a result of a meta-analysis study with a sample size of 3.026, it was concluded that the diagnosis of BMD greatly increased the incidence of dementia and that there was a significant correlation between advanced age BMD and the risk of dementia (43). Neurobiological factors in patients are dysregulated as a result of manic and/or hypomanic episodes, which are characteristic symptoms of BMD. BMD may cause medical comorbidities such as diabetes, obesity, and sleep apnea, as well as behaviors that may endanger health, such as smoking, risky sexual acts, and diet programs. In addition, many studies in the literature revealed that BMD causes morphological damage in certain parts of the brain and increases the risk of dementia in clinical dimensions (44-46).

1.6. Death in Elderly/Geriatric Patients with BMD

The high mortality level seen in BMD patients is closely associated with a large number of comorbid medical diseases and suicidal behaviours that are commonly observed (47). Studies found that individuals who attempt suicide have a higher risk of cognitive dysfunction, and as a result, they are diagnosed with dementia at higher rates (48,49). It was found that geriatric patients newly diagnosed with dementia attempted suicide at a higher rate than the control group matched in terms of age and education level, and the suicide rate increased by 54% within 1 year after the diagnosis of dementia (50). It has been reported that suicide risk poses a greater risk for individuals aged 74 years and younger (51). Inadequate cognitive control, dysregulation in executive functions, and problem-solving skills reduce the ability to cope with life problems in a healthy way, and in this case, the risk of suicide increases (52). According to the results of a study conducted to determine the determinants of suicidal ideation in geriatric BMD patients as well as in young adults, depressive symptoms, cognitive deficits, alcohol abuse, and life dissatisfaction cause an increase in suicidal ideation, and sleep disturbance has an indirect effect on suicide (53). According to the results of another study conducted with 37,768 male patients diagnosed with BMD; an increased mortality level is associated with the presence of BMD and that suicide is one of the highest causes of death in this patient group (54).

1.7. Sleep in Old Age Bipolar Mood Disorder

Difficulties in the process of transitioning to sleep, maintaining it, and arranging the appropriate time are common complaints among patients with significant psychiatric diagnoses and are significantly associated with disability, cognitive impairment, anxiety, and decreased quality of life (55-57). In a study investigating the relationship between sleep disorder and increased suicide risk in BMD patients, it was concluded that sleep dysregulation triggers suicidal behaviour and that interrupted sleep and sleeping late are the most effective sleep disorder parameters for suicide (58). With advancing age, qualitative and quantitative changes occur in sleep at a level that can be taken seriously (59). According to the studies, there is an increase in the mortality rate with advancing age, and individuals with cognitive impairment have a high share of this rate (60,61). It is supported by research findings in the literature that there is a significant relationship between cognitive dysregulation

and sleep disorders, which are especially common in geriatric individuals (59). Sleep disturbances are seen among the primary symptoms of BMD because decreased need for sleep is a prominent symptom of the manic period and insomnia is a problem associated with depressive episodes (62,63). The most prominent sleep features seen in manic periods are the delay in the REM period, in which rapid eye movements occur; on the other hand, total sleep time decreases in the depressive period (64).

1.8. Treatment for Bipolar Mood Disorder in Old Age

The diagnosis and treatment process of psychiatric disorders seen in older individuals may be more challenging than in adult patients. The main reasons for this are organic diseases that occur as a result of advancing age, comorbid disorders, and secondary factors that develop due to them. There are also complications caused by multiple drug use, and the perception of mental health problems that occur in the clinical symptoms of neurological disorders such as dementia and Alzheimer's as the natural process of old age. The diagnostic tools are used to diagnose mental diseases. The tools and scale items have been developed for children and adults, and there is a lack of a reliable scale to measure mental diseases in elderly patients. For the treatment of geriatric BMD, there is a need for treatment options that are planned according to the specific factors and needs caused by the somatic and cognitive changes seen with aging (65). The lack of adequate studies on treatment protocols applied to advanced-age BMD patients is due to the fact that they carry a higher risk of medical complications and therefore are not included in phase 3 studies (65,66). As a result of a meta-analysis study, it is suggested that the basic principles applied to treat geriatric BMD patients, somatic comorbid diseases, and the risk of interaction with the drugs used for their treatment should be much more careful, and therapeutic lithium serum levels are also lower as a result of the tests performed (67).

Lithium is seen as the golden standard protocol for the treatment of BMD. As a result of epidemiological and neuroimaging studies, it has been reported that cortical grey matter volume is better preserved and the risk of dementia and possible cancer is reduced in adult BMD patients treated with lithium (68-70). Although pharmacological treatments used in psychiatric diseases are very effective, they are also methods that have side effects. It is detected that lithium in geriatric BMD patients increases the risk of Parkinson's disease, hypercalcemia, chronic kidney failure, and triggered hypothyroidism (71-74).

Valproic acid is one of the drugs frequently used alone or in combination with other antipsychotics in the treatment of mania in geriatric BMD patients because it is well tolerated (66,75). Although it is an effective drug, valproic acid has serious side effects, and approximately 11% of valproate use during pregnancy causes anomalies such as neurolethal tube defects and a cleft palate. It has been reported to cause a three-fold increase in difficulty speaking, delay in walking, memory problems, low-level intellectual abilities, and pervasive developmental disorders such as autism (76-79). Among the side effects seen in adults aretremors, fatigue complaints, gait disturbances, gastrointestinal complaints, a decrease in thrombocyte level, rarely liver damage, and encephalopathy (66,75). In the treatment of mania in adult BMD patients, serum levels above 90 ug/ml should be aimed at; however, for the treatment of geriatric BMD patients, there are no studies in the literature containing adequate valproic acid pharmacology (80).

Carbamazepine, which belongs to the dibenzoazepine family, is an antiepileptic drug that acts as a sodium channel and is thought to block calcium channels (81,82). Blurring of vision, involuntary rapid movement of the eye in certain directions, indications such as pathological blurring, agitation, and changes in blood count such as aplastic anemia, allergic reactions, and irregularities in the level of salt in the blood resulting from the use of the drug in high doses are more common than other mood stabilizers, and especially in geriatric BMD patients, blood dyscrasias with carbamazepine may occur at higher levels. Although it is not prescribed in many countries due to its indications, it is preferred as a secondary treatment option in elderly BMD patients, and its neurochemical action mechanisms support that it is an effective mood stabilizer in preventing recurrence (83-86).

Lamotrigine is an antiepileptic drug that is in the phenyl triazine family, is used in the treatment of BMD and epilepsy, and is licensed by the US Food and Drug Administration to prevent relapses (87). Available evidence from a population-based cohort study found lamotrigine to be equivalent to lithium in the prevention of (hypo) manic or depressive episodes (88). Oral clearance of lamotrigine appears to be reduced by 20-35% in the elderly, and dose adaptation may be required (89).

Antipsychotics are preferred in the first-line treatment of acute mania; their combination with benzodiazepines is a common protocol, but there are not enough studies on their efficacy on acute mania and prevention of attacks in geriatric BMD patients (39). It has been reported that the risk of parkinsonism increases as a result of long-term use of antipsychotics, especially in geriatric BMD patients (90).

It has recently become an accepted fact that pharmacotherapy alone is insufficient to prevent BMD attacks, cannot alleviate the symptoms that occur after the episodes, and cannot rationalize functional impairment. Research shows that, as a result of the combined use of pharmacotherapies and psychotherapies, the disease remission period is prolonged, the relapse period is delayed, and BMD plays an active role in permanent and life-long factors in the development of neurobiological mechanisms, vocational skills, and psychosocial skills (91). Individual and group psychoeducation programs, individual and group cognitive behavioral therapy (CBT), family-focused therapy, interpersonal social rhythm therapy, and electroconvulsive therapy (ECT) are frequently used psychotherapy methods in the treatment of BMD.

Psychoeducation consists of structured sessions that focus on providing information to help individuals diagnosed with BMD become aware of episode symptoms and create a conscious response plan (92). Studies show that, compared to pharmacotherapy applied alone, psychoeducation is associated with a decrease in the number of relapses of patients' first manic attacks, improvement in social and occupational functionality, a significant decrease in relapse and hospitalization rates, a prolongation of the remission period, and increased medication compliance (92,93).

Cognitive behavioral therapy applied in BMD is based on the belief that emotions, thoughts, and behaviors are interrelated and that changes in psychological and cognitive processes during emotional periods play an active role in behaviors, and all of these can lead to a vicious

circle that has negative effects on the disease (94). In CBT, the clinician helps people understand the connection between their mood, emotions, thoughts, and behaviors, become aware of symptoms, develop externally observable strategies for symptoms, learn basic CBT techniques, and improve their impaired functionality (95).

Family-focused therapy is structured skill training carried out together with a patient and family members with the aim of providing information about disease symptoms and the clinical course of the disease on the basis of maintaining strong communication (96).

Interpersonal social rhythm therapy is a therapy method aimed at establishing the order of daily routines, regulating circadian rhythms that affect the sleep-wake cycle, identifying interpersonal problems caused by emotional dysregulation, and providing solutions (96).

ECT has been proven effective in treating acute attacks of both mania and depression in BMD patients with psychotic features or a high risk of self-harm and who are resistant to pharmacological treatment (97). Studies show that ECT applied to older BMD patients can treat depression and manic attacks that develop after discontinuation of pharmacological treatment and prevent repeated hospitalizations (98,99).

2. Conclusion and Recommendations

The presence of BMD among geriatric individuals escapes attention. Although the disease includes symptoms seen in other age groups, it also includes some distinctive features in geriatric patients. The prevailing opinion is that BMD in older individuals is mostly a cause of secondary factors, and existing research findings that were conducted with individuals diagnosed with BMD over the age of 60 reveal that organic disorders and advanced cognitive losses are closely related to the disease (26). Cognitive dysregulation, which is seen at increasing rates in older BMD patients, also constitutes the basis for many neurological diseases and causes an increase in suicidal behaviors. In a study investigating the predictors of suicidal behavior in older BMD patients, it was found that cognitive dysregulation predisposes to suicide both directly and indirectly (53). Sleep disturbance, which is one of the general symptoms of BMD, causes cognitive and physiological damage in geriatric individuals, which results in a worse clinical course of the disease. A study examining sleep and the clinical course of BMD disease concluded that insufficient and irregular sleep causes relapses, reduces quality of life, causes impairments in cognitive functions, increases risk-taking behavior and impulsivity, and triggers mania and hypomania attacks (62). Comorbid medical diseases and mental health problems are more common in elderly BMD patients than in other age groups. As a result of organic diseases and comorbid psychiatric disorders that increase with age, treatment options become more difficult, and the risk of interaction of the drugs used with each other is striking. Studies in the literature show that lithium, which is used for the treatment of manic attacks in BMD, poses a risk for Parkinson's disease, hypercalcemia, chronic renal failure, and hypothyroidism in older individuals diagnosed with BMD (71-74). In cases where there is no adequate response to pharmacotherapy or complications arise from multiple drug use, which are common in older individuals, ECT or psychotherapy methods should be used alone or in combination with drug therapy in CBT treatment. Acting in cooperation with BMD patients, their families, or caregivers increases patients' treatment compliance, and the information provided by clinicians about the causes of the disease, its clinical course, and coping strategies through psychoeducation provides the ability to cope with the disease symptoms, a decrease in hospitalization rates, and a decrease in functionality. As a result of all these, the burden on the patient and caregiver will decrease, which is a possible outcome. A study that compared the effectiveness of pharmacotherapy and CBT in the treatment of BMD concluded that CBT reduced the relapse rate, increased medication compliance, and reduced hospitalization rates compared to drug treatment (94). In future studies, it is critical to investigate the neurodegeneration of BMD disease in more detail, to support comorbid organic diseases and psychiatric comorbidities with advancing age with more interventional studies, and to alleviate the burden they create on patients.

3. Contribution to the Field

Elderly individuals represent a rapidly increasing segment of the population. In addition to the somatic diseases seen in geriatric individuals, the presence of psychiatric diseases is a neglected issue that is usually confronted.

Since studies on bipolar mood disorder seen in older individuals are insufficient, there is a need to conduct large-scale and longitudinal evaluation studies on pharmacological and psychotherapy treatment needs applied to individuals diagnosed with BMD. Side effects seen in elderly patients, comorbidities with organic diseases, and their sensitivity to possible risks due to the disease should also be taken into account. It is thought that this study will shed light on future research.

Conflict of Interest

This article did not receive any financial fund. There is no conflict of interest regarding any person and/or institution.

Authorship Contribution

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