# METABOLIC SYNDROME IN PATIENTS WITH SCHIZOAFFECTIVE DISORDER AND RELATIONSHIP WITH THE ANTIPSYCHOTICS

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***ABSTRACT***

***Introduction****: Metabolic syndrome is highly prevalent in patients with schizophrenia. The use of atypical antipsychotics also increases the risk of metabolic syndrome. This study aimed to evaluate the association between schizoaffective disorder and risk of incident metabolic syndrome and the relationship with the drugs used.*

***Materials and methods****: This cross-sectional study included patients diagnosed with schizoaffective disorder. The study group consisted of 77 outpatients aged 18 to 65 years, prescribed any antipsychotic medication between September 2013 and August 2014. Metabolic syndrome was defined using the criteria of the National Cholesterol Education Program - Adult Treatment Protocol and the National Cholesterol Education Program - Adapted Adult Treatment Protocol.*

***Results****: Metabolic syndrome was found in 33.8% according to National Cholesterol Education Program - Adult Treatment Protocol diagnostic criteria, 36.4% according to National Cholesterol Education Program - Adapted Adult Treatment Protocol diagnostic criteria of the patients. When we grouped patients treated with typical antipsychotic, atypical antipsychotics and typical & atypical antipsychotics in combination, there was no significant difference for prevalence of metabolic syndrome among any groups. Metabolic syndrome prevalence was significantly higher in study subjects using antidepressants in combination with antipsychotics.*

***Conclusions****: The results suggest that metabolic syndrome risk is common among patients with schizoaffective disorder. Our data shows that systemic inflammation plays a key role in both schizoaffective disorder and metabolic syndrome so chronic comorbid disorders should be treated concurrently and all risk factors like that weight loss, regular physical activity, smoking cessation should be eliminated by modifying life style.*

***Keywords****: Schizoaffective disorder, metabolic syndrome, antipsychotic, systemic inflammation, dyslipidemia.*

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## Introduction

Schizoaffective disorder, a chronic mental illness with the characteristics of both schizophrenia and mood disorders and its lifetime prevalance is about 0.2-0.3 percent[1,2]. In general, the prognosis of schizoaffective disorder lies between schizophrenia and mood disorders[3].

Patients with concurrent schizophrenic and mood symptoms are often treated with complex pharmacologic regimens of antipsychotics, antidepressants, and mood stabilizers[4].

The metabolic syndrome (MetS) consists of a cluster of metabolic disorders, which increase the risk of cardiovascular disease events. MetS comprises a spectrum of metabolic disorders including

glucose intolerance (type 2 diabetes, impaired glucose tolerance or impaired fasting glucose) obesity, dyslipidemia and hypertension[5]. MetS has been associated with an 2-fold increased risk of developing cardiovascular outcomes and 1.5-fold increase in mortality due to all causes[6].

MetS is a determinant of systemic inflammation in generally and systemic inflammation has been well documented in schizoaffective disorder[7]. Systemic inflammation may play a determinant role in the relationship between MetS and schizoaffective disorder.

The prevalence of MetS has been reported to be 22% in the United States, according to the NHANES III (National Health and Nutrition Examination Survey)[8]. In the Southeastern Anatolia Region where our study group is located, the prevalence of MetS is 29.7% in the general population (Gaziantep %29) (9).

Prevalence of MetS in schizophrenic patients is 2-4 times higher than in general population[10]. Schizoaffective disorder was mostly investigated in small groups with other psychotic disorders and similar results were obtained[11]. The prevalence of MetS is very high in a study entirely in patients with schizophrenia or schizoaffective disorder[12]. The use of antipsychotics increases the risk of metabolic syndrome[13].

The first objective of this study was to establish the prevalence of metabolic syndrome in schizoaffective disorder. In this cross sectional study, we also aimed to evaluate the association between schizoaffective disorder and risk of incident MetS and the relationship with the drugs used.

## Materials and methods

The study population included all patients with schizoaffective disorder who were referred to Gaziantep University Medical Faculty, Turkey., between September 2013 and August 2014. This study was approved by the ethics committee of the Gaziantep University of Medical Faculty before the collection of data.

The total sample consisted of 77 schizoaffective patients. Schizoaffective disorder was diagnosed by psychiatrists according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders IV.

The patient exclusion criteria were as follows: aged under 18 years old or above 65 years old, substance abuse or dependence, the presence of non mental chronic medical illness, pregnancy, dementia, moderate or severe mental retardation.

Anthropometric parameters including weight, height, body mass index (BMI), blood presure were assessed. Venous blood sample taken from the antecubital vein. Metabolic parameters including fasting glucose (mg/dL), serum triglycerides, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol (mg/dL) were assessed. MetS was defined using the NCEP-ATP III (National Cholesterol Education Program -Adult Treatment Protocol), NCEP-ATP IIIA (National Cholesterol Education Program-Adapted Adult Treatment Protocol)[14] (Table I).

| Risk Factor | Definition |
|---|---|
| Abdominal obesity | Male > 102 cm |
| (Waist circumference) | Female > 88 cm |
| Triglyceride | ≥ 150 mg/dl |
| HDL | Male < 40 mg/dl |
| | Female < 50 mg/dl |
| Blood pressure | ≥ 130/85 mmHg |
| Fasting blood glucose | ≥110 (according to ATP III) |
| | ≥100 (according to ATP III A) |

**Table I**: ATP III ve ATP III A Metabolic Syndrome Diagnostic Criteria.

Statistical analyses were performed using the SPSS 21.0 software package and the significance level used was $p<0.05$. Relationships between discontinuous variables were tested by chi-square analysis. The compliance of the data with a normal distribution is analyzed via the Shapiro-Wilk test. In comparison of two independent groups, the Student's t-test was used to compare means between continuous variables, Mann Whitney U Test was used for variables that don't have normal distribution.

## Results

This study was conducted in a psychiatric outpatient clinic of Gaziantep University of Medical Faculty. In total, we enrolled 77 schizoaffective disorder patients (61% male). The average age of these patients was 36.47.23 ± 11.25 years, desease onset age was 23,81 ± 8,6. Sociodemographic and clinical features of patients are shown in Table II.

| | | |
|---|---|---|
| Age | 36,47±11,251 | |
| Disease onset age | 23,81±8,607 | |
| Sex | Male | 47 (%61) |
| | Female | 30 (%39) |
| Disease duration | 12,6±9,0 | |
| Body mass index | 29,12±5,0 | |
| Smoking | Yes | 38 (%49,4) |
| | No | 39 ( %50,6) |
| Suicide attempt story | Yes | 29 (%37,7) |
| | No | 48 (%62,3) |

**Table II**: Sociodemographic and Clinical Characteristics of Patients.

All study subjects were on antipsychotic medication at least for three months. The most commonly prescribed antipsychotics have been risperidone and quetiapine. The patients treated with combined therapy (more than one antipsychotic) were 64.9%, monotherapy (only one antipsychotic) 35.1% and long acting injectable antipsychotics 40.3%. When we grouped patients treated with typical antipsychotic, atypical antipsychotics and typical & atypical antipsychotics in combination, we observed that 85.7% of patients treated atypical antipsychotic alone. The most commonly prescribed mood stabilizer was valproic acid (37.7%). 31.2% of patients were also taking an antidepressant and the most commonly prescribed antidepressants were citolopram (7.8%) and escitolopram (7.8%).

The prevalence of metabolic syndrome was 33.8% according to ATP III; 36,4% according to ATP III A (Table III). There was a significant correlation between the frequency of MetS and patient ages in our patients (p = 0.012).

| | ATP III | ATP III A | IDF |
|---|---|---|---|
| One diagnosed with metabolic syndrome (n) | 26 | 28 | 34 |
| One not diagnosed with metabolic syndrome (n) | 51 | 49 | 43 |
| Frequency of metabolic syndrome (%) | 33,8 | 36,4 | 44,2 |

**Table III**: Frequency of metabolic syndrome according to ATP III, ATP III A and IDF definitions.

Among atypical antipsychotics, clozapine is mostly associated with higher prevalence of metabolic syndrome, followed by quetiapine = risperidone, depot form, olanzapine, aripiprazole, amisulpride = paliperidone, sulpiride, haloperidol = chlorpromazine = trifluperazine (according to ATP III and IIIA diagnostic criteria). There was no significant for MetS frequency among any drug groups.

MetS was not detected in patients using flupentixol and ziprasidone according to all three diagnostic criteria. MetS prevalence was significantly higher in study subjects using antidepressants in combination with antipsychotics (p=0.043). When we grouped patients treated with typical antipsychotic, atypical antipsychotics and typical & atypical antipsychotics in combination, there was no significant difference for MetS among any groups, according to ATP III (p>0,05).

## Discussion

The prevalence of metabolic syndrome was found 33.8% according to ATP III; 36,4% according to ATP III A. Significant risk factors for MetS in the study group included age, using antidepressants in combination with antipsychotics. No significant relationships were identified between MetS and any other demographic/clinical characteristic or antipsychotic treatment groups.

Studies have indicated a higher prevalence of metabolic syndrome in people with psychiatric diseases[10,15]. In the CATIE trial; according to the definition of national cholesterol education and treatment panel (NCEP), about one-third of patients diagnosed with schizophrenia have MetS (36% in males and 51.6% in females)[16]. In a multicenter study, it was found that the frequency of MetS was 26.5% in 268 schizoaffective patients and that MetS was associated with age and severity of disease[17]. In also our study it was observed that the frequency of MetS increased with the age in the schizoaffective population by supporting previous studies (p<0,05).

In this study the association between different antipsychotic medication used in the treatment of schizoaffective disorder and metabolic syndrome has been explored. Atypical antipsychotics are associated with severe side effects like weight gain and disruption of glucose metabolism, MetS and the related disorders[18]. It is reported that the metabolic changes such as weight gain, lipid and glucose metabolism disorders began to be seen more prevalent with the widespread use of atypical antipsychotic drugs than typical antipsychotic drug use[19].

In some studies found that there was no significant difference between typical and atypical antipsychotic drug use in terms of the frequency of MetS[20]. In our study, we grouped patients treated with typical antipsychotics, atypical antipsychotics and typical & atypical antipsychotics in combination, no significant difference was detected in terms of the frequency of MetS between the groups according to ATP III.

Some antidepressants unfavourably influence the lipid milieu; increase weight gain and lead to dyslipidemia in some patients[21]. A large-scale study showed that the patients using tricyclic antidepressants had a higher MetS risk than the patients not using any antidepressant[22]. In our study it was observed that MetS prevalence was significantly higher in study subjects using antidepressants in combination with antipsychotics.

Despite the use of valproic acid and lithium are known to be closely associated with metabolic changes[23], no significant difference was found between the frequency of MetS with the use of the mood stabilizers in our study .

It was found that maximum increase in hyperlipidemia and MetS occured in clozapine and olanzapine; less with the use of quetiapine and risperidone; minimal with the use of ziprasidone and aripiprazole[24]. In our study, clozapine is mostly associated with higher prevalence of metabolic syndrome, followed by quetiapine = risperidone, depot form, olanzapine, aripiprazole, amisulpride = paliperidone, sulpiride, haloperidol = chlorpromazine = trifluperazine according to ATP III. There was no significant for MetS among any drug groups.

An elevated rates of metabolic syndrome was found in polytherapy, compared with antipsychotic monotherapy (50.0% vs. 34.3%)[25]. In our study, there was no statistically significant relationship between MetS frequency with the use of antipsychotic polytherapy.

It was showed that long disease duration and old age is an important risk factor in the emergence of the MetS[26, 27]. There was a significant correlation between the frequency of MetS and patient ages in our subjects ($p = 0.012$), but no significant difference was found with the disease duration ($p = 0.073$).

Our study has some limitations mainly because of its cross-sectional design, does not show similarity for the number of patient of different drug groups and has no control group. The fact that the distribution of patients is different according to gender makes comparison difficult, however the increased risk in schizoaffective disorder patients is noteworthy when considering large-scale MetS studies conducted with healthy population in our city and country. Further systematic investigations based on long term observation have to be performed in order to confirm the prevelance of MetS in schizoaffective disorder.

In conclusion, our data shows that there are also a high MetS risk in schizoaffective disorder like schizophrenia. Systemic inflammation plays a key role in both schizoaffective disorder and MetS so chronic comorbid disorders should be treated concurrently and all risk factors should be eliminated by modifying life style (e.g. weight loss, regular physical activity, smoking cessation).

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