METHODS:

Treatment and to examine the relation between antipsychotic polypharmacy and MetS. Further, we aimed to compare the practices of polypharmacy and monotherapy in terms of the rationale and compatibility of the prevalence of metabolic syndrome and related factors in outpatients with SMI who were in antipsychotic monotherapy or polypharmacy. Although there are many studies on the treatment of patients with schizophrenia and other SMI, studies about prevalence and characteristics of antipsychotic polypharmacy and its metabolic outcomes are limited in Turkey. The aim of this study was to examine the prevalence of metabolic syndrome and related factors in outpatients with SMI who were in antipsychotic monotherapy or polypharmacy. Further, we aimed to compare the practices of polypharmacy and monotherapy in terms of the rationale and compatibility of the treatment and to examine the relation between antipsychotic polypharmacy and MetS.

METHOIDS:

This study included 290 patients with SMI between 18 and 65 years of age who were followed at KTU Psychiatry Department Schizophrenia-Bipolar Disorder outpatient clinic. Data of patients who were diagnosed with schizophrenia, schizoaffective disorder or bipolar disorder according to DSM-IV-TR between January 2007 and December 2014 were screened. Data were obtained from clinical records in the charts and electronic medical records. The data for patients who were on antipsychotic monotherapy or polypharmacy with effective doses of antipsychotic drugs for at least 8 weeks and whose complete metabolic data was fully recorded for the same time period were taken into the study. MetS was diagnosed according to NCEP ATP III (National Cholesterol Education Program Adult Treatment Panel) definition.

RESULTS:

The mean age of the 290 patients included in this study was 39.8±11.2 years, 57.6% were male and 42.4% were female. 183 patients (63.1%) were diagnosed with schizophrenia, 85 patients (29.3%) were diagnosed with bipolar disorder and 22 patients (7.6%) were diagnosed with schizoaffective disorder. 93 patients (32.1%) were receiving antipsychotic polypharmacy. Combinations of two second-generation antipsychotics were most common (n=73, 78.5%), followed by combinations of a first- with a second-generation antipsychotic (n=19, 20.4%). There was no significant difference between monotherapy and polypharmacy groups in terms of MetS prevalence (n=62, 31.5%, n=31, 33.3%, p=0.751 respectively). Patients with a diagnosis of schizoaffective disorder were receiving the highest number of psychotropic drugs (3.13±1.16). Schizoaffective disorder patients were followed by bipolar disorder patients (2.84±1.09) and schizophrenia (2.30±1.07) in terms of co-prescribed psychotropic drugs. In this regard, patients with schizoaffective disorder differ significantly from those with bipolar disorder and schizophrenia (p=0.000). However, the number of total psychotropic drugs did not indicate a significant difference between patients with or without MetS (2.53±1.20 vs. 2.51±1.09, p=0.932).

Overall MetS prevalence was 32.1% (n=93) according to ATP-III. The prevalence of MetS was higher among women, but this difference was not significant statistically (n=123, 35% vs. n=167 29.9%, p=0.365). High triglyceride level, increased waist circumference, and low HDL were frequent among the patients (54.8%, 58.3% and 46.9%, respectively). The high frequency of positive triglyceride criteria in males (60.5% vs. 47.2%, p=0.024) and waist circumference criteria in females (75.6% vs. 45.5%, p=0.000) were remarkable.

The prevalence of MetS increased significantly with age (p=0.002). Also we found that mean age is significantly different between patients with or without MetS (2.53±1.20 vs. 2.51±1.09, p=0.932).

Frequency of smokers was higher in patients with MetS but the difference was not significant statistically (50.5% vs. 48.2%, p=0.713). The prevalence of MetS was 30.6% in schizophrenia patients, 36.4% in schizoaffective disorder patients, and 34.1% in bipolar disorder patients according to ATP III. The differences in MetS prevalence between diagnostic categories were not significant (p=0.767). When schizophrenia and schizoaffective disorder were combined into a category termed “schizophrenia spectrum disorders”, the prevalence of MetS in this combined group was 31.2% (n=64). However, the difference in MetS prevalence between this combined group and bipolar disorder still was not significant (p=0.63).

We conducted logistic regression analysis to examine the relevance of variables for the presence of MetS. For the multivariate analyses, we entered into the model all variables that possibly determinant for metabolic syndrome. However, in logistic regression analysis, MetS was significantly associated with higher BMI (r2: 0.121, p<0.01).

CONCLUSION:

Depending on MetS criteria used, gender, ethnicity, country, age groups, and antipsychotic treatment, percentages vary considerably. In this cross-sectional retrospective study of outpatients with SMI who were on antipsychotic monotherapy or polypharmacy, the prevalence of MetS was 32.1% according to ATP III. This was similar to the previous studies from Turkey and other
countries. Women were more likely to be diagnosed with MetS, which is consistent with recent studies.

In a large adult population sample representing all geographical regions of Turkey, Sanisoglu and associates reported MetS prevalence across the country as 17.9% and specifically in the Black Sea region as 14.2% according to IDF (International Diabetes Federation)1. Yazıcı et al. have reported the prevalence of MetS as 34.2% in a Turkish cohort. In another study from Turkey, it was found that MetS prevalence according to IDF criteria was 32% among chronic inpatients hospitalized in the regional mental health hospital2.

While several studies found MetS to be more common in older patients, fewer studies reported no age differences2,3,4. In the present study, the prevalence of MetS increased with age significantly. Similarly, in a study conducted in our country (METSAR), it was reported that MetS incidence increased with age in the adult population (20 years and over).

The mean BMI was significantly higher in patients with MetS. Kato et al. (2004) posited that the relationship between MetS and central obesity was stronger than the relationship between MetS and obesity (as determined by BMI)5. In the present study, increased waist circumference was the most common MetS criterion, and females were significantly more likely to meet this criterion. This finding was consistent with the recent literature about MetS. This suggest that waist circumference is an important criterion for monitoring patients. We did not find any difference in terms of duration of illness or number of exacerbations and hospitalizations between patients with and without MetS. Smoking was not different between SMI patients with or without MetS in the recent studies. This was consistent with our results.

In our study, there was no significant difference between monotherapy and polypharmacy groups in terms of MetS prevalence. Correl and associates found MetS prevalence 34.4% in a monotherapy group and 50% in a polypharmacy group in patients with schizophrenia. In our study, consistent with prior studies (Cerit et al. 2008, Gulec, Oyekcin 2009, Songur et al. 2012), there was no significant difference between monotherapy and polypharmacy groups in terms of MetS prevalence.

It is known that atypical antipsychotics can trigger weight gain and related metabolic changes; however, in the present study there was no relationship between the type of drugs used and MetS diagnoses, which is similar to what was reported by Kato et al. (2004), Heiskanen et al. (2003), Sarisoy et al. (2013) and Cerit et al. (2008). It has been repeatedly found in recent studies that people with SMI exhibit a higher MetS prevalence than their peers in the general population across the world1,4,5. Our finding supports that information. It is found that higher BMI is a powerful predictor of MetS and the prevalence of MetS increased with age significantly. Moreover, in logistic regression analyses, metabolic syndrome was significantly associated with higher BMI.

We could not compare antipsychotic subgroups in terms of MetS prevalence due to the sample heterogeneity and small number of cases. Further research is needed to determine the metabolic effects of specific antipsychotic combinations, duration of treatment and individual dosage used in polypharmacy.

In conclusion, our results confirm previous reports that patients with SMI are most likely to receive antipsychotic polypharmacy and MetS is highly prevalent among patients treated with SMI. We are not able to generalize our findings to the general population. But it is important that our findings have shown similar findings to those of recent studies conducted in the Black Sea region which have shown that MetS prevalence is higher in SMI patients compared to the general population (Sanisoglu et al. 2006, Boke et al. 200, Sarisoy et al. 2013). This might be caused by certain characteristics shared by the specific population in the Black Sea region such as genetic features, dietary habits or other variables that are related with MetS in this particular region of Turkey.

Finally, we have not found any significant effects of antipsychotic medication (such as monotherapy, polypharmacy, same-class/multiclass polypharmacy, typical/atypical, high-risk medication like clozapine, olanzapine and others) on metabolic syndrome. In order to determine the complex effects of not only antipsychotic but also other psychotropic drugs on metabolic syndrome, further studies with control groups and medicine sub-groups being distributed homogeneously are needed. However, in the light of our results, we believe we can hypothesize that in the patients with SMI, there are many more factors that determine the risk of metabolic syndrome besides antipsychotic medication, and most of those have not been elucidated yet.

**Keywords**: antipsychotic monotherapy, antipsychotic polypharmacy, metabolic syndrome, severe mental illness

**References:**


