Metabolic derangements with olanzapine and risperidone in schizophrenia spectrum and other psychotic disorders: A 24-week prospective study

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ABSTRACT

Background and Aims: Schizophrenia spectrum and other psychotic disorders are common disorders often requiring long-term treatment with atypical antipsychotics, which might cause metabolic dysfunctions. We aimed to study the metabolic dysfunctions with olanzapine and risperidone in patients with schizophrenia spectrum and other psychotic disorders. We also explored the incidence of new-onset metabolic syndrome and its predictors. Methods: This was a 24-week prospective observational study conducted at a teaching hospital in North India. The patients were prescribed olanzapine or risperidone. Anthropometric measurements (waist circumference, weight, body mass index, blood pressure) and biochemical investigations (triglycerides, high-density lipoproteins, fasting plasma glucose) were recorded at baseline and after 24 weeks. Metabolic syndrome was defined using the International Diabetes Federation definition. Statistical tests used were Fisher’s exact test, paired t-test, unpaired t-test, and logistic regression. Results: A total of 45 patients, 30 on olanzapine and 15 on risperidone completed the study. Statistically significant changes occurred in all variables with olanzapine while with risperidone statistically significant changes occurred in all variables except waist circumference and fasting plasma glucose. Statistically greater changes in mean values between the two were noted only for high-density lipoprotein with olanzapine. 20% of patients developed metabolic syndrome with non-significant between drug differences. Baseline triglyceride predicted the development of the metabolic syndrome. Conclusions: Olanzapine and risperidone cause metabolic derangements and statistically significant differences may not exist between them. Baseline triglyceride levels might predict subsequent metabolic syndrome.

Keywords: Metabolic dysfunction, metabolic syndrome, olanzapine, risperidone, schizophrenia spectrum and other psychotic disorders, triglycerides

Introduction

The schizophrenia spectrum and other psychotic disorders are common mental disorders. The prevalence of schizophrenia globally is 0.45% in adults (World Health Organisation) and in India is 0.3%.⁶,⁷

Metabolic syndrome is characterized by central obesity, high blood pressure, high triglycerides, low high-density lipoprotein cholesterol, and insulin resistance. It is a predictor of type 2 diabetes mellitus, cardiovascular events, and stroke.⁹

The schizophrenia spectrum disorders are primarily treated with antipsychotic medications, especially atypical antipsychotics, which might cause a range of metabolic derangements.⁴,⁵ Often these patients require long-term treatment which compounds these metabolic derangements. Different antipsychotics have a varying propensity for
metabolic derangements with significant interindividual variations.\[5\]

Considering the ever-increasing prevalence of metabolic syndrome and mental disorders, primary care physicians are very likely to encounter patients on atypical antipsychotics who may develop metabolic derangements with treatment.

Hence, we studied the metabolic dysfunction with olanzapine and risperidone, the two most commonly used atypical antipsychotics for the treatment of schizophrenia spectrum and other psychotic disorders. We also compared the risk of development of metabolic derangements and metabolic syndrome between these two drugs and establish predictors if any, for the development of the metabolic syndrome.

**Material and Methods**

The study was approved by the Institutional Ethics Committee and written informed consent was taken.

This study was a prospective 24-week observational study with purposive sampling. All patients attending the psychiatry department of a teaching hospital in north India for one-year were assessed using a pre-structured proforma. A detailed history, general physical examination, and mental status examination were completed, and the diagnosis was made using DSM-5 criteria for schizophrenia spectrum and other psychotic disorders. The inclusion criteria were being diagnosed with schizophrenia spectrum and other psychotic disorders. We compared the mean values of variables at baseline and week 24 using paired t-test. A statistically significant increase in WC was due to the treatment. Data were verified, tabulated, and entered into Google sheets and analyzed. Fisher’s exact test, paired and unpaired t-tests, and multiple logistic regression were applied.

**Results**

A total of 65 patients were included in the study, of which 41 were prescribed olanzapine (group 1) and 24 risperidone (group 2).

At the end of the study, 45 patients; 30 from the olanzapine group and 15 from the risperidone group were available for analysis. Rest 20 were either lost to follow-up or were dropped from the study.

Mean maintenance doses of olanzapine and risperidone were 11.85 ± 2.35 mg/day, respectively.

The majority of patients were aged 20–30 years (46.67%) with a mean of 28.16 ± 1.61 years. The majority were married (57.78%), urban dwellers (53.33%), and from nuclear families (57.78%). Participants were less educated (only 15.56% had intermediate or higher education) and largely skilled or unskilled workers (48.89%). In terms of socioeconomic status, 95.55% belonged to the lower middle class or below [Table 1].

There were no significant differences in socio-demographic, biochemical, or anthropometric parameters between subjects prescribed olanzapine and risperidone and between those who were dropped/lost to follow-up and those who completed the study.

All the parameters under study showed an increase except HDL which decreased in both the olanzapine group and risperidone group. In the olanzapine group at baseline, the mean values of WC, TGs, HDL, FPG, SBP, DBP, weight, and body mass index (BMI) were 76.48 ± 9.03 cm, 117.03 ± 47.36 mg/dl, 47.80 ± 6.74 mg/dl, 88.35 ± 15.88 mg/dl, 111.93 ± 10.74 mm Hg, 73.00 ± 8.93 mm Hg, 60.18 ± 9.02 kg, 22.53 ± 2.35 kg/m², respectively. At 24 weeks, the corresponding values were 80.17 ± 8.40 cm, 151.94 ± 72.46 mg/dl, 37.85 ± 6.37 mg/dl, 101.79 ± 14.99 mg/dl, 115.93 ± 7.91 mm Hg, 75.33 ± 6.05 mm Hg, 64.63 ± 8.84 kg, 23.79 ± 2.52 kg/m², respectively. In the risperidone group at baseline, the mean values of WC, TGs, HDL, FPG, SBP, DBP, weight, and BMI were 77.97 ± 5.18 cm, 110.55 ± 39.37 mg/dl, 45.51 ± 8.44 mg/dl, 91.42 ± 19.64 mg/dl, 117.33 ± 10.80 mm Hg, 75.20 ± 9.26 mm Hg, 63.17 ± 8.66 kg, 23.20 ± 2.40 kg/m², respectively. At 24 weeks, the corresponding values were 80.20 ± 4.84 cm, 122.68 ± 43.61 mg/dl, 40.83 ± 6.53 mg/dl, 97.80 ± 12.25 mg/dl, 120.67 ± 10.60 mm Hg, 78.40 ± 7.31 mm Hg, 63.17 ± 8.66 kg, 23.88 ± 2.46 kg/m², respectively [Table 2].

We compared the mean values of variables at baseline and week 24 using paired t-test. A statistically significant increase in WC was...
noted for the olanzapine group (P < 0.01) but not the risperidone group. The increase in TGs was found to be statistically significant with both olanzapine (P < 0.01) and risperidone (P < 0.05). The decrease in HDL was statistically significant for both drugs (P < 0.001 for both). FPG significantly increased in the olanzapine group (P < 0.001) only. Statistically significant increases occurred for both SBP (P < 0.01 for both olanzapine and risperidone) and DBP (P < 0.05 for both olanzapine and risperidone) in patients treated with either of the two drugs. The increment in weight and BMI were again statistically significant with both drugs (P < 0.001 for both weight and BMI) [Table 2].

Females had a statistically significant greater risk of weight gain and raised WC compared to males. Unskilled workers showed a significantly greater rise in TGs compared to other occupations. Living in an urban area and joint family was associated with a greater risk of weight gain. No significant relationship between other variables and sociodemographic factors existed.

The changes in means of different parameters over 24 weeks between the two groups were calculated and compared using the unpaired t-test. The WC increased by 3.69 ± 6.03 cm in the olanzapine group vs 2.23 ± 4.35 cm in the risperidone group. Serum TGs increased by 34.91 ± 57.16 mg/dl in the olanzapine group vs 12.13 ± 21.84 mg/dl in the risperidone group. Subjects on olanzapine had a decrease of 9.95 ± 7.75 mg/dl in HDL levels compared to a decrease of 4.68 ± 4.02 mg/dl in subjects on risperidone. In the olanzapine group, FPG increased by 13.44 ± 12.83 mg/dl while in the risperidone group FPG increased by 6.38 ± 25.08 mg/dl. In the olanzapine group, SBP increased by 4 ± 6.83 mm Hg and DBP by 2.33 ± 5.31 mm Hg while in the risperidone group SBP increased by 3.34 ± 3.68 mm Hg and DBP by 3.2 ± 5.0 mm Hg. Patients on olanzapine experienced a weight gain of 3.95 ± 2.99 kg while patients on risperidone experienced a weight gain of 2.26 ± 1.79 kg. The increment in BMI was 1.26 ± 1.41 kg/m² in the olanzapine group and 0.85 ± 0.73 kg/m² in the risperidone group.

| Table 1: Sociodemographic characteristics of the study population |
|---------------------------------------------------------------|
| **Group 1 (Olanzapine) n=30** | **Group 2 (Risperidone) n=15** | **Total (Group 1 + Group 2) n=45** |
| Age (mean±s.d.) in years | 27.10±10.75 | 30.27±10.24 | 28.6±1.61 |
| Age Groups | 12 (40%) | 9 (60%) | 21 (46.67%) |
| 18-20 | 3 (10%) | 3 (20%) | 6 (13.33%) |
| 20-30 | 4 (13.34%) | 1 (6.67%) | 5 (11.11%) |
| 30-40 | 2 (6.67%) | 1 (6.67%) | 3 (6.67%) |
| Sex | 15 (50%) | 11 (26.67%) | 26 (57.78%) |
| Male | 15 (50%) | 4 (73.33%) | 19 (42.22%) |
| Female | 1 (6.67%) | 9 (60%) | 13 (28.89%) |
| Religion | 25 (83.33%) | 13 (86.67%) | 38 (84.44%) |
| Hindu | 5 (16.67%) | 2 (13.33%) | 7 (15.56%) |
| Muslim | 1 (6.67%) | 9 (60%) | 10 (22.22%) |
| Marital status | 15 (50%) | 11 (26.67%) | 26 (57.78%) |
| Married | 15 (50%) | 4 (73.33%) | 19 (42.22%) |
| Unmarried | 10 (22.22%) | 7 (46.67%) | 17 (37.78%) |
| Locality | 13 (43.33%) | 8 (53.33%) | 21 (46.67%) |
| Rural | 17 (56.67%) | 7 (46.67%) | 24 (53.33%) |
| Urban | 5 (16.67%) | 2 (13.33%) | 7 (15.56%) |
| Occupation Skilled/Professional | 3 (10%) | 2 (13.33%) | 5 (11.11%) |
| Unskilled | 9 (30%) | 8 (53.33%) | 17 (37.78%) |
| Housewife | 7 (23.33%) | 2 (13.33%) | 9 (20%) |
| Student | 8 (26.67%) | 0 (0%) | 8 (17.78%) |
| None | 3 (10%) | 3 (20%) | 6 (13.33%) |
| Education | 2 (6.67%) | 2 (13.33%) | 4 (8.89%) |
| Graduate or higher | 7 (23.33%) | 1 (6.67%) | 8 (17.78%) |
| Intermediate | 8 (26.67%) | 6 (40%) | 14 (31.11%) |
| Secondary | 10 (33.33%) | 6 (40%) | 16 (35.56%) |
| Primary | 0 (0%) | 0 (0%) | 0 (0%) |
| Illiterate | 1 (3.33%) | 1 (6.67%) | 2 (4.44%) |
| Socioeconomic status | 9 (30%) | 1 (6.67%) | 10 (22.22%) |
| Upper | 11 (36.67%) | 3 (20%) | 14 (31.11%) |
| Upper middle | 9 (30%) | 10 (66.67%) | 19 (42.22%) |
| Lower middle | 1 (6.67%) | 1 (6.67%) | 2 (4.44%) |
| Lower | 0 (0%) | 0 (0%) | 0 (0%) |
| Family type | 17 (56.67%) | 9 (60%) | 26 (57.78%) |
| Nuclear | 13 (43.33%) | 6 (40%) | 19 (42.22%) |
A statistically significant difference between the two groups was noted only for HDL levels with olanzapine causing greater changes ($P < 0.05$) [Table 3].

At baseline, two patients in the olanzapine group and none in the risperidone group had raised WC. At end of the study, this increased to 9 in the olanzapine group and 2 in the risperidone group. 6 and 1 patients had raised TG levels in the olanzapine and risperidone group at baseline compared to 10 and 3 patients at study completion. Four patients on olanzapine and five patients on risperidone had raised blood pressure at baseline while at end of the study 2 subjects on olanzapine group and 6 on risperidone had raised blood pressure. The subjects with raised FPG increased from 3 to 8 in the olanzapine group and from 2 to 4 in the risperidone group from baseline to the end of the study. A total of 9 (20%) patients had newly diagnosed metabolic syndrome at end of the study, of whom 7 (23.33%) were from the olanzapine group and 2 (13.33%) were from the risperidone group [Table 4]. No significant difference was noticed between olanzapine and risperidone for the number of individuals meeting any of the individual or the complete criteria of metabolic syndrome.

Using logistic regression, we inferred that among different individual parameters of metabolic syndrome, baseline TG levels significantly predicted the appearance of metabolic syndrome at end of the study after adjusting for age and sex [Table 5]. With every patient having 1-unit higher TG levels as compared to the other at the baseline, the odds of having metabolic syndrome increased by 4.3%. No significant relationship was found between sociodemographic factors, weight, BMI, and the appearance of metabolic syndrome.

### Discussion

Out of 65 patients enrolled, only 45 completed the study. 20 (30.77%) were either lost to follow-up or dropped from the study. Perez-Iglesias et al.[7] and Saddichha et al.[8] have reported a dropout of 12% and 10%, respectively. Relatively higher dropouts in our study were due to loss to follow-up and exclusion due to changes in treatment.

Greater representation of the younger age reflects the usual age of onset of schizophrenia spectrum and other psychotic disorders.

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### Table 2: Metabolic parameters and anthropometric measures at baseline and 24 weeks

| Variables (mean±s.d.) | Group 1 (Olanzapine) | Group 2 (Risperidone) | $P$ |
|-----------------------|----------------------|-----------------------|-----|
| WC (cm)               | 76.48±9.03           | 80.17±8.40            | <0.01 |
| TG (mg/dl)            | 117.03±47.36         | 151.94±72.46          | <0.01 |
| HDL (mg/dl)           | 47.80±6.74           | 37.85±6.37            | <0.001 |
| Systolic BP (mm Hg)   | 111.93±10.74         | 115.93±7.91           | <0.01 |
| Diastolic BP (mm Hg)  | 73.00±8.93           | 75.33±6.05            | <0.05 |
| FPG (mg/dl)           | 88.35±15.88          | 101.79±14.99          | <0.001 |
| Weight (kg)           | 60.18±9.02           | 64.13±8.84            | <0.001 |
| BMI (kg/m²)           | 22.53±2.35           | 23.79±2.52            | <0.001 |

### Table 3: Comparison of mean changes in metabolic parameters and anthropometric measures with olanzapine and risperidone

| Variables (mean±s.d.) | Group 1 (olanzapine) | Group 2 (risperidone) | $P$ |
|-----------------------|----------------------|-----------------------|-----|
| WC (cm)               | 3.69±6.03 (5.27%)    | 2.23±4.35 (3.08%)     | 0.398 |
| TG (mg/dl)            | 34.91±57.16 (35.53%) | 12.13±21.84 (12.63%)  | 0.058 |
| HDL (mg/dl)           | -9.95±7.75 (19.88%)  | -4.68±4.02 (9.59%)    | <0.05 |
| Systolic BP (mm Hg)   | 13.44±12.83 (16.78%) | 6.38±25.08 (10.88%)   | 0.334 |
| Diastolic BP (mm Hg)  | 42.6±13.83 (3.9%)    | 3.34±3.68 (2.92%)     | 0.541 |
| FPG (mg/dl)           | 2.33±3.51 (3.84%)    | 3.2±5.0 (4.84%)       | 0.654 |
| Weight (kg)           | 3.95±2.99 (6.87%)    | 2.26±1.79 (3.75%)     | 0.527 |
| BMI (kg/m²)           | 1.26±1.41 (5.79%)    | 0.85±0.73 (3.75%)     | 0.264 |

### Table 4: Number of patients meeting the individual metabolic syndrome criterion and the complete criterion at end of the study period between the two groups

| Groups       | Group 1 (olanzapine) | Group 2 (risperidone) | $P$ |
|--------------|----------------------|-----------------------|-----|
| WC           | 2 9                  | 0 2                   | 1   |
| TG           | 6 10                 | 1 3                   | 1   |
| BP           | 4 2                  | 5 6                   | 0.61 |
| HDL          | 10 15                | 5 6                   | 1   |
| FPG          | 3 8                  | 2 4                   | 1   |
| MetS         | 0 7                  | 0 2                   | 1   |
The study group had a male predominance as males have an earlier onset of illness and are more likely to use substances like cannabis which is associated with schizophrenia spectrum disorders.

The higher representation of lower socioeconomic and underprivileged strata is due to the study being conducted in a state-run institution providing treatment at minimal costs. The sociodemographic characteristics are similar to what has been reported by Rathor et al[9] from a state-run mental health institute that caters to a similar population and geographical area as ours except that most of their study patients were from a rural background.

The mean maintenance dose of both medications was in the usual range and similar to other studies, although olanzapine was used at comparatively lower doses.

A statistically significant increase in WC was noted for the olanzapine group (P < 0.01) only. A plausible explanation is that change in WC reflected a return to health state before illness with no further increase in the risperidone group, while in the olanzapine group, WC showed increment over and above the state before the illness. The baseline WC may have been affected by the loss of appetite, withdrawn behavior, or excessive psychomotor activity in individual cases. Similarly, Gupta et al[14] also found that in long term only olanzapine and not risperidone is associated with a significant increase in WC while Saddichha et al[10] Medved et al[11] Gautam et al[12] Oriot et al[13] reported significant increases in WC with antipsychotic treatment including both olanzapine and risperidone.

The increase in TGs was found to be statistically significant for both (P < 0.01 for the olanzapine group, P < 0.05 for the risperidone group). Saddichha et al[8] Gautam et al[12] Asaad et al[14] Zahan et al[13] Kaushal et al[14] have also reported that significant changes occur in TG levels with atypical antipsychotics including risperidone and olanzapine whereas Misiak et al[17] Garyfallos et al[18] Wu et al[19] Perez-Iglesias et al[20] and Nanotkar et al[21] reported a significant increase in TG with olanzapine only. Pillinger and colleagues[5] in their meta-analysis found that olanzapine and not risperidone causes significant changes in TG levels. In contrast, Medved et al[11] Krakowski et al[22] Sengupta et al[25] did not find a significant change in TG levels even with olanzapine.

The decrease in HDL was statistically significant for both treatment groups (P < 0.001 for both). Gautam et al[12] Asaad et al[14] Kaushal et al[14] Goswami et al[24] have also made similar observations. Meanwhile, Oriot et al[13] Misiak et al[17] Sengupta et al[25] reported no significant change in serum HDL after treatment with atypical antipsychotics including olanzapine and risperidone. Interestingly, Saddichha et al[8] Zahan et al[13] and Mubarak et al[25] reported increased HDL with risperidone. Metanalysis by Pillinger et al[5] also failed to show any strong evidence of change in HDL levels with either olanzapine or risperidone.

In our study, the increase in FPG was statistically significant only for the olanzapine group. This is in agreement with studies by Nanotkar et al[21] Ingole et al[28] and Lindenmayer et al[27] that found only olanzapine to be associated with adverse glycemic outcomes. This is further substantiated by a recent meta-analysis by Pillinger et al[5] who reaffirmed changes in glucose concentration with olanzapine but not risperidone. Saddichha et al[8] Gupta et al[14] Gautam et al[12] Oriot et al[13] Asaad et al[14] Kaushal et al[14] Goswami et al[24] found both olanzapine and risperidone to result in raised blood sugar levels while Misiak et al[17] Wu et al[19] Sengupta et al[25] Perez-Iglesias et al[25] found no statistically significant changes in blood sugar levels with antipsychotic treatment.

A statistically significant increase was found for both SBP (P < 0.01 for both olanzapine and risperidone group) and DBP (P < 0.05 for both olanzapine and risperidone group) with either drug. Similar results have been obtained by Saddichha et al[8] and Gautam et al[12] while Nanotkar et al[21] found significant increases only with olanzapine. Gupta et al[8] found a significant increase only in DBP and not SBP with these agents.

The increase in weight and BMI was statistically significant with both drugs (P < 0.001 for all for both weight and BMI) similar to observations by Saddichha et al[8] Gautam et al[12] Asaad et al[14] Zahan et al[13] Garyfallos et al[18] Nanotkar et al[21] Krakowski et al[25] Ingole et al[28] while Wu et al[19] Comley et al[28] found a significantly elevated mean BMI with olanzapine and not risperidone. Conversely, Guha and colleagues[25] found no significant change in body weight or BMI with olanzapine.

Mean change in all individual parameters was higher in the olanzapine group compared to the risperidone group except in DBP where risperidone was associated with greater numerical change. Interestingly, a significant difference in change in means between the olanzapine and risperidone group was noted only for serum HDL (P < 0.05) with olanzapine causing a greater decrease. Our findings are in line with Meyer et al[20] who also found no significant differences between mean changes in WC,

### Table 5: Logistic regression for baseline values of individual parameters in the definition of metabolic syndrome and the risk of development of the metabolic syndrome

| Variables      | β   | P   |
|---------------|-----|-----|
| Sex           | -1.097 | 0.591 |
| Age           | -0.037 | 0.611 |
| WC Baseline   | -0.056 | 0.612 |
| TG Baseline   | -0.043 | 0.008 |
| HDL Baseline  | -0.207 | 0.060 |
| DBP Baseline  | -0.019 | 0.868 |
| SBP Baseline  | 0.007  | 0.945  |
| FBS Baseline  | -0.019 | 0.611  |

The increase in WC was found to be statistically significant for both (P < 0.01 for the olanzapine group, P < 0.05 for the risperidone group). Saddichha et al[8] Gautam et al[12] Asaad et al[14] Zahan et al[13] Kaushal et al[14] have also reported that significant changes occur in TG levels with atypical antipsychotics including risperidone and olanzapine whereas Misiak et al[17] Garyfallos et al[18] Wu et al[19] Perez-Iglesias et al[20] and Nanotkar et al[21] reported a significant increase in TG with olanzapine only. Pillinger and colleagues[5] in their meta-analysis found that olanzapine and not risperidone causes significant changes in TG levels. In contrast, Medved et al[11] Krakowski et al[22] Sengupta et al[25] did not find a significant change in TG levels even with olanzapine.

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Mean change in all individual parameters was higher in the olanzapine group compared to the risperidone group except in DBP where risperidone was associated with greater numerical change. Interestingly, a significant difference in change in means between the olanzapine and risperidone group was noted only for serum HDL (P < 0.05) with olanzapine causing a greater decrease. Our findings are in line with Meyer et al[20] who also found no significant differences between mean changes in WC,
SBP, DBP, HDL, fasting glucose, and TGs between olanzapine and risperidone. Medved et al. found that olanzapine resulted in a greater increase in WC and risperidone in TGs levels but changes in other parameters were not different. Mubarak et al. found significant differences between olanzapine and risperidone for changes in WC, weight, TGs, and HDL but not for blood sugar, albeit risperidone leads to a rise in HDL and greater increase in TGs. On the other hand, Nanotkar et al. reported significantly greater changes in mean weight, BMI, TGs, HDL, fasting sugars, SBP, and DBP with olanzapine compared to risperidone. As is evident, like us many have reported greater numerical changes with olanzapine compared to risperidone but intergroup differences have often failed to reach statistically significant levels.

In our study, a total of 9 (20%) patients developed metabolic syndrome after 24 weeks of treatment. Independently, 7 (23.33%) were from the olanzapine group and 2 (13.33%) were from the risperidone group had new-onset metabolic syndrome with antipsychotic medication. Similar rates have been reported by Saddichha et al. (total 18.2%, olanzapine group 25.7% and risperidone group 24.2%) and Gautam et al. (total 11.66%, olanzapine group 23.3%, and risperidone group 10%) in India. Although 10–70% of the patients may develop metabolic syndrome with antipsychotic treatment, most have reported rates between 20 and 50%.[11] This wide variation is accounted for by different methodologies, differing definitions of metabolic syndrome, and varying characteristics of study populations including ethnic, racial, and genetic disparities.

No significant difference was present between olanzapine or risperidone for the number of patients developing metabolic syndrome or meeting its different individual criteria at end of the study. Again, for the number of individuals developing metabolic syndrome with olanzapine and risperidone no significant difference was noted by Meyer et al., Grover et al., Lee et al., Nanotkar et al., Straker et al., and for its components no difference was noted by Kaushal et al., Lindenmayer et al. and Nanotkar et al.[21] Hence, both olanzapine and risperidone lead to increased risks of metabolic derangements with no apparent difference.

Weight gain was higher in females, urban dwellers, and those from joint families while increased BMI was likely in those from joint families. Females also experience a greater increase in WC. Unskilled workers showed a greater rise in TGs. In our study, baseline TG levels significantly predicted the development of metabolic syndrome after adjusting for age and sex and so may help identify those at greater risk. No association was found for other parameters and metabolic syndrome.

Hence, both these drugs are associated with metabolic abnormalities and the above-stated variables might help identify those at risk of metabolic derangements leading to the institution of appropriate preventive remedial measures.

The limitations of this study are a lack of randomization, unequal number of patients receiving olanzapine and risperidone, flexible dosing schedule, no control group, small sample size, and high dropout rates. Further, duration of illness, diagnosis, type of presentation, history of prior treatment, nutritional status, physical activity, occupational status, dietary patterns, and smoking habits were also not considered. No method or rating scale to monitor illness and treatment response was used.

Future studies should be planned to address these lacunae.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

References
1. Schizophrenia. WHO.int. 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/schizophrenia. [Last accessed on 2022 Feb 02].
2. Sagar R, Dandona R, Gururaj G, Dhaliwal R, Singh A, Ferrari A, et al. The burden of mental disorders across the states of India: The Global Burden of Disease Study 1990–2017. Lancet Psychiatry 2020;7:148–61.
3. Eckel R, Grundy S, Zimmet P. The metabolic syndrome. Lancet 2005;365:1415–28.
4. Huhn M, Nikolakopoulou A, Schneider-Thoma J, Krause M, Samara M, Peter N, et al. Comparative efficacy and tolerability of 32 oral antipsychotics for the acute treatment of adults with multi-episode schizophrenia: A systematic review and network meta-analysis. Lancet 2019;394:393–51. 5. Pillinger T, McCutcheon R, Vano L, Mizuno Y, Arumuham A, Hindley G, et al. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: A systematic review and network meta-analysis. Lancet Psychiatry 2020;7:64–77.
6. Alberti K, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabet Med 2006;23:469–80.
7. Perez-Iglesias R, Mata I, Pelayo-Teran J, Amado J, Garcia-Unzueta M, Berja A, et al. Glucose and lipid disturbances after 1 year of antipsychotic treatment in a
drug-naive population. Schizophr Res 2009;107:115-21.
8. Saddichha S, Manjunatha N, Ameen S, Akhtar S. Metabolic syndrome in first episode schizophrenia — A randomized double-blind controlled, short-term prospective study. Schizophr Res 2008;101:266-72.
9. Rathor D, Kumar S, Tiwari D, Jain R, Sisodia A. Prevalence of metabolic syndrome in drug-naive patients with schizophrenia. Int J Med Sci Public Health 2016;5:2574.
10. Gupta A, Dadheech G, Yadav D, Sharma P, Gautam S. Metabolic issues in schizophrenic patients receiving antipsychotic treatment. Indian J Clin Biochem 2014;29:196-201.
11. Medved V, Kuzman M, Jovanovic N, Grubisin J, Kuzman T. Metabolic syndrome in female patients with schizophrenia treated with second generation antipsychotics: A 3-month follow-up. J Psychopharmacol 2008;23:915-22.
12. Gautam S, Meena P. Drug-emergent metabolic syndrome in patients with schizophrenia receiving atypical (second-generation) antipsychotics. Indian J Psychiatry 2011;53:128-33.
13. Oriot P, Feys J, Mertens de Wilmars S, Misson A, Ayache L, Fagnart O, et al. Insulin sensitivity, adjusted β-cell function and adiponectinaemia among lean drug-naive schizophrenic patients treated with atypical antipsychotic drugs: A nine-month prospective study. Diabetes Metab 2008;34:490-6.
14. Asaad T, Meguid M, El Missiry M, Ali R, Bassim R, Taha S. Metabolic dysfunction related to typical and atypical antipsychotics in drug-naive patients with nonaffective psychosis. Middle East Curr Psychiatry 2017;24:93-101.
15. Zahan T, Akther N, Mullick M, Dewan Z. Metabolic risk factor-profile in patients on treatment with second generation antipsychotics. Bangladesh Med Res Counc Bull 2015;41:144-50.
16. Kaushal J, Bhutani G, Gupta R. Comparison of fasting blood sugar and serum lipid profile changes after treatment with atypical antipsychotics olanzapine and risperidone. Singapore Med J 2012;53:488-92.
17. Misiak B, Frydecka D, Laczmański Ł, Słężak R, Kiejna A. Effects of second-generation antipsychotics on selected markers of one-carbon metabolism and metabolic syndrome components in first-episode schizophrenia patients. Eur J Clin Pharmacol 2014;70:1433-41.
18. Garyfallos G, Dimelis D, Kouniakis P, Sidiropoulos N, Karastergiou A, Lavrentiadis G, et al. Olanzapine versus risperidone: Weight gain and elevation of serum triglyceride levels. Eur Psychiatry 2003;18:320-1.
19. Wu R, Zhao J, Liu Z, Zhai J, Guo X, Guo W, et al. Effects of typical and atypical antipsychotics on glucose-insulin homeostasis and lipid metabolism in first-episode schizophrenia. Psychopharmacology 2006;186:572-8.
20. Perez-Iglesias R, Crespo-Facorro B. A 12-week randomized clinical trial to evaluate metabolic changes in drug-naive, first-episode psychosis patients treated with haloperidol, olanzapine, or risperidone. J Clin Psychiatry 2007;68:1733-40.
21. Nanotkar S, Choure B, Gosavi D. A comparative study of the effects of risperidone and olanzapine on metabolic parameters of schizophrenic patients. Int J Basic Clin Pharmacol 2016;5:814-9.
22. Krakowski M, Czobor P, Citrome L. Weight gain, metabolic parameters, and the impact of race in aggressive inpatients randomized to double-blind clozapine, olanzapine or haloperidol. Schizophr Res 2009;110:95-102.
23. Sengupta S, Klink R, Stip E, Baptista T, Malla A, Joobr R. Weight gain and lipid metabolic abnormalities induced by olanzapine in first-episode, drug-naive patients with psychotic disorders. Schizophr Res 2005;80:131-3.
24. Goswami N, Gandhi A, Patel P, Dikshit R. An evaluation of the metabolic effects of antipsychotic medications in patients suffering from psychiatric illness. J App Pharm Sci 2014;4:14-9.
25. Mubarak A, El sawy H, Morad H, Abu-Hammar S. Study of biological parameters of schizophrenics during 6 months of different anti psychotics treatment. J Schizophr Res 2018;5:1035.
26. Ingole S, Belorkar N, Waradkar P, Shrivastava M. Comparison of effects of olanzapine and risperidone on body mass index and blood sugar level in schizophrenic patients. Indian J Physiol Pharmacol 2009;53:47-54.
27. Lindenmayer J, Czobor P, Volakova J, Citrome L, Shetman B, McEvoy J, et al. Changes in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics. Am J Psychiatry 2003;160:290-6.
28. Conley R, Mahmoud R. A randomized double-blind study of risperidone and olanzapine in the treatment of schizophrenia or schizoaffective disorder. Am J Psychiatry 2001;158:765-74.
29. Guha P, Roy K, Sanyal D, Dasgupta T, Bhattacharya K. Olanzapine-induced obesity and diabetes in Indian patients: A prospective trial comparing olanzapine with typical antipsychotics. J Indian Med Assoc 2005;103:660-4.
30. Meyer J, Davis V, Goff D, McEvoy J, Nasrallah H, Davis S, et al. Change in metabolic syndrome parameters with antipsychotic treatment in the CATIE schizophrenia trial: Prospective data from phase 1. Schizophr Res 2008;101:273-86.
31. Malhotra N, Grover S, Chakrabarti S, Kulhara P. Metabolic syndrome in schizophrenia. Indian J Psychol Med 2013;35:227-40.
32. Grover S, Aggarwal M, Dutt A, Chakrabarti S, Avasthi A, Kulhara P, et al. Prevalence of metabolic syndrome in patients with schizophrenia in India. Psychiatry Res 2012;200:1035-7.
33. Lee N, Kim S, Jung D, Kim E, Yu H, Sung K, et al. The prevalence of metabolic syndrome in Korean patients with schizophrenia receiving a monotherapy with aripiprazole, olanzapine or risperidone. Prog Neuropsychopharmacol Biol Psychiatry 2011;35:1273-8.
34. Straker D, Correll C, Kramer-Ginsberg E, Abdulhamid N, Koshi F, Rubens E, et al. Cost-effective screening for the metabolic syndrome in patients treated with second-generation antipsychotic medications. Am J Psychiatry 2005;162:1217-21.