e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(12); 173-178

Risk Factors for Clinically Significant Weight Gain in Psychiatric Patients on Treatment: A Case Control Study

Jumi Jacob[1], Rakhesh LR[2], Sanitha Kuriachan[3], Mahesh Kumar D[4]

[1]MBBS, MD, Assistant Professor, Department of Pharmacology, Jubilee Mission Medical College and Research Institute, Thrissur, Kerala, India.

[2]MBBS, MD, Assistant Professor, Department of Pharmacology, Dr. Moopen's Medical College, Wayanad, Kerala, India.

[3] MBBS, MD, Associate Professor, Department of Pharmacology, Amrita school of Medicine, Amrita Institute of Medical sciences, Amrita Vishwa Vidyapeetham, Ernakulam, Kerala, India.

[4]MBBS, MD, Associate Professor, Department of Pharmacology, Amrita school of Medicine, Amrita Institute of Medical sciences, Amrita Vishwa Vidyapeetham, Ernakulam, Kerala, India.

Received: 25-09-2023 / Revised: 23-10-2023 / Accepted: 18-11-2023

Corresponding Author: Mahesh Kumar D

Conflict of interest: Nil

Abstract:

Background: This study focuses on the various risk factors for weight gain in psychiatric patients receiving treatment. It helps the clinician to treat accordingly to prevent comorbidities associated with weight gain in psychiatric patients. This in turn can prolong the lifespan of these patients and can also improve their quality of life.

Aims and Objectives: To evaluate the risk factors of clinically significant weight gain, defined as more than 7% of initial weight over 3 months in psychiatric patients of age group between 18 to 45 years receiving treatment in a tertiary care setting.

Materials and Methods: 145 psychiatric patients who gained weight more than 7% during treatment were selected as cases and 145 psychiatric patients without weight gain were selected as controls. Data collected from patients by direct interviews were recorded in a proforma and the various risk factors studied were socio-demographic factors, family history of overweight, psychiatric diagnosis and psychotropic medications. Data was analyzed by SSPS 17 statistical software. Chi Square Test was used for comparison of proportions. Odds ratios and their confidence intervals were calculated to determine the strength of association. Binary logistic regression was then used to find the adjusted odds ratios and their confidence intervals and thereby its statistical significance.

Results: Psychiatric patients treated with Clozapine and Olanzapine were associated with clinically significant weight gain on univariate analysis. Multivariate analysis showed that patient's age (adjusted odds ratio i.e. AOR=0.964, 95% confidence interval(CI): 0.937-0.992), and the use of atypical anti-psychotic agents like Clozapine (AOR=2.290, 95% CI:1.422-5.996), Olanzapine (AOR=3.474, 95% CI:1.805-6.685), Quetiapine (AOR=4.060, 95% CI:1.193-13.821), and Risperidone (AOR=2.224, 95% CI:1.189-4.233) were associated with clinically significant weight gain.

Conclusion: Patient's age and the use of psychotropic drugs like Clozapine, Olanzapine, Risperidone and Quetiapine were associated with clinically significant weight gain in psychiatric patients.

Keywords: Psychotropic drugs, atypical antipsychotics, weight gain, Clozapine, Olanzapine, Risperidone, Quetiapine.

Introduction

The connection between obesity and psychiatric disorders is an important public health issue. Mentally ill patients have an increased risk of weight gain and obesity than the general population. [1,2] Both these conditions have major implications for health care systems and account for a proportion of the global burden of disease. Both conditions have been shown to influence each other, leading to a complex interplay that contributes to a range of health challenges. Individuals with obesity may be at a higher risk of developing these mental health conditions, and conversely, those with depression [3,4] or anxiety [5] may be more susceptible to weight gain. This highlights the interconnectedness of mental and physical well-being.

The reason for weight gain and obesity, as well as its associated medical complications, in severe mentally ill patients is multi-factorial. It includes lifestyle factors, genetic factors plus drug related

factors. Many psychotropic medications used in mental disorders predisposes to weight gain. [1,6,7] In addition, mentally ill patients may have limited access to health care for the prevention and treatment of the above medical conditions.[8,9]

Psychotropic drug related weight gain can affect the compliance to pharmacotherapy as it can cause stigmatization and is indirectly responsible for psychosis relapses. Moreover, it increases the risk for metabolic syndrome with associated cardiovascular complications. With this background, this study was intended to evaluate the risk factors of clinically significant weight gain in psychiatric patients in a tertiary care center.

Methodology

This case control study was conducted at the Department of Psychiatry, Government Medical College, Thiruvananthapuram from May 2015 to April 2016 for a period of 1 year after obtaining ethical clearance from The Human Ethics Committee Medical College, Thiruvananthapuram. (IEC No. 01/29/2015/MCT dated 09/01/2015). Patients attending tertiary care setting for the treatment of psychiatric disorders were screened for inclusion and exclusion criteria; and were enrolled after obtaining written informed consent in their regional language (or attendants, when the patients were not competent to give consent). Patients, of the age group of 18 to 45 years, who were free of psychotropic drugs for at least six months prior to the initiation of treatment and those who had a record of weight at the onset of treatment were included in the study. Exclusion criteria were patients with endocrine disorders such as abnormal function of thyroid or pituitary glands, patients who were on steroids for other medical illness and, pregnant or lactating women. Confidentiality and anonymity of the patient's information was maintained during and after the study.

290 patients satisfying inclusion criteria were selected for the study and psychiatric diagnosis as per DSM IV TR by a qualified psychiatrist was recorded. Cases were defined as subjects in the age group 18-45 years seeking treatment for psychiatric illness with clinically significant weight gain over a period of 3 months of treatment. Controls were defined as subjects seeking psychiatric treatment without clinically significant weight gain over 3 months of treatment. Clinically significant weight gain was defined as more than 7% of initial body weight over a period of 3 months. 145 cases and 145 controls were enrolled into the study. Socio-demographic profile and clinical data were collected from the patients and/or attendants and the variables considered relevant for the study were age, sex, socio-economic status, primary psychiatric diagnosis, history of substance abuse and details of psychotropic medications consumed by the patient. Family history of obesity and dietary habits were also noted. Baseline weight was pre-recorded at the onset of treatment in psychiatric outpatient department. Same weighing machine was used throughout the study. The scale precision was calculated as+/- 0.1kg.

Statistical Methods

The sample size for this study was determined using the formula: $N = [Z_\alpha + e^{(\varphi 2/4)} Z_\beta]^2 (1+2p\delta)/ p\varphi^2$ where δ is calculated as: $\delta = [1+(1+\varphi^2)\ e^{(5\varphi 2/4)}]\ [1+e^{(\varphi 2/4)}]^{-1}$. For 1:1 ratio of cases to controls, given a significance level (α) of 5%, power ($1-\beta$) of 80%, an expected odds ratio (ϕ) of 2.5, and a with 10 % prevalence of weight gain in control population (p), the calculated sample size for each arm was 145.

The data collected was analyzed using SPSS version 17 and the results were interpreted accordingly. Chi Square Test was used for comparison of proportions. Independent T test and Mann- Whitney U tests were used for the comparison of continuous variables. Binary logistic regression was then used to find the adjusted odds ratios and their confidence intervals and its statistical significance.

Results

The mean age of the patients was 28.5±8.6 among cases and 33.6±7.1 among controls. As per the data shown in TABLE 1, Majority (128 patients) were in the age group below 30, of which 73 were cases and 55 were controls. Males and females were relatively equally distributed in both groups. The substance abuse observed in these patients was tobacco smoking which was not statistically significant between groups.

Table 1: Sociodemographic details of patients

Variable %(n)		Controls (n=145)	Cases (n=145)	Total (N=290)	P value
Age Group	<30	37.9(55)	50.3(73)	44.1(128)	0.083
	30 – 40	23.4(34)	21.4(31)	22.4(65)	
	>40	38.6(56)	28.3(41)	33.4(97)	
Gender	Male	53.1(77)	46.9(68)	50(145)	0.291
	Female	46.9(68)	53.1(77)	50(145)	
socio-economic status	Upper	7.6(11)	6.9(10)	7.2(21)	0.642
	Middle	44.8(65)	50.3(73)	47.6(138)	
	Lower	47.6(69)	42.8(62)	45.2(131)	

Family history of obesity	Yes	19.3(28)	15.9(23)	17.6(51)	0.441
	No	80.7(117)	84.1(122)	82.4(239)	
Dietary habit	Non vegetarian	93.8(136)	93.1(135)	93.4(271)	0.812
	Vegetarian	6.2(9)	6.9(10)	6.6(19)	
Substance abuse	Yes	8.3(12)	9.7(14)	9(26)	0.681
	No	91.7(133)	90.3(131)	91(264)	

290 psychiatric patients included in the study had different diagnosis like Psychosis, Depression, bipolar disorder, panic disorder, generalized anxiety disorder**,** organic mood disorder, schizophrenia, alcohol use disorder, obsessive compulsive disorder and conversion disorder. (TABLE 2) The maximum number of patients had bipolar disorder followed by depression.

Table 2: Clinical profile of patients

Diagnosis %(n)	Control (n=145)	Cases (n=145)	Total (n=290)	P value
Psychosis	6.9(10)	7.6(11)	7.2(21)	0.681
Depression	22.1(32)	26.9(39)	24.5(71)	
Bipolar disorder	39.3(57)	28.3(41)	33.8(98)	
Panic disorder	1.4(2)	0	0.7(2)	
Generalized anxiety disorder	4.1(6)	4.1(6)	4.1(12)	
Organic mood disorder	0	3.4(5)	1.7(5)	
Schizophrenia	14.5(21)	17.2(25)	15.9(46)	
Alcohol disorder	2.1(3)	6.2(9)	4.1(12)	
Obsessive compulsive disorder	6.9(10)	4.1(6)	5.5(16)	
Conversion disorder	2.8(4)	2.1(3)	2.4(7)	

Prescribed drugs included antipsychotics, anti-depressants, benzodiazepines, and mood stabilizers. (Table 3) Prescribed drugs were typical antipsychotic namely Haloperidol; Atypical antipsychotics: Clozapine, Olanzapine, Risperidone, Quetiapine and Aripiprazole; Antidepressants: Clomipramine, Sertraline, Fluvoxamine, Escitalopram, Duloxetine, Fluoxetine, Venlafaxine, Mirtazapine; Benzodiazepines: Etizolam, Lorazepam, Clonazepam and Mood stabilizers like Lithium, Valproate and Oxcarbazepine. The maximum number of patients were treated with Valproate followed by Escitalopram. Prescription rates of Clozapine and Olanzapine among cases were significantly high when compared to the control group. Mean weight gain for cases was 6.9±2.8 kg and for the controls it was 0.6±0.8 kg (p value<0.001).

Table 3: Drug prescription pattern of the Cases and controls

Drugs	Control (n=145)	Cases (n=145)	Total (n=290)	P value
Haloperidol	2.8(4)	2.8(4)	2.8(8)	1.000
Clozapine	9.7(14)	18.6(27)	14.1(41)	0.028*
Olanzapine	12.4(18)	24.8(36)	18.6(54)	0.007*
Risperidone	14.5(21)	22.8(33)	18.6(54)	0.070
Quetiapine	2.8(4)	6.2(9)	4.5(13)	0.156
Aripiprazole	4.1(6)	2.8(4)	3.4(10)	0.520
Clomipramine	1.4(2)	0	0.7(2)	0.498
Sertraline	2.8(4)	1.4(2)	2.1(6)	0.409
Fluvoxamine	3.4(5)	1.4(2)	2.4(7)	0.251
Escitalopram	22.1(32)	27.6(40)	24.8(72)	0.277
Duloxetine	2.1(3)	0.7(1)	1.4(4)	0.314
Fluoxetine	1.4(2)	1.4(2)	1.4(4)	1.000
Venlafaxine	1.4(2)	1.4(2)	1.4(4)	1.000
Mirtazapine	2.8(4)	3.4(5)	3.1(9)	0.735
Etizolam	0	0.7(1)	0.3(7)	1.000
Lorazepam	1.30(15)	6.9(10)	8.6(25)	0.296
Clonazepam	20.7(30)	17.9(26)	19.3(56)	0.552
Lithium	11(16)	14.5(21)	12.8(37)	0.379
Valproate	24.8(36)	29(42)	26.9(78)	0.427
Oxcarbazepine	6.9(10)	4.8(7)	5.9(17)	0.453

Univariate analysis shows that the patients treated with Clozapine and Olanzapine are associated with clinically significant weight gain. The results revealed a statistically significant association for both Clozapine ($\chi2 = 4.801$, df = 1, p = 0.028) and Olanzapine ($\chi2 = 7.373$, df = 1, p = 0.007). Adjusted Odds Ratios (AOR) and their corresponding 95% confidence intervals (CI) indicated that individuals taking Clozapine were [2.141 (95% CI: 1.072–4.276)] times more likely to experience weight gain compared to those not taking Clozapine. Similarly, for Olanzapine, AOR was [2.330 (95% CI: 1.252–4.336)], suggesting an increased likelihood of weight gain in individuals on Olanzapine. Five variables which are significantly associated with weight gain ($p<0.2$) have been subjected to multivariate analysis of binary logistic regression. (TABLE 4) A logistic regression model reveals that patient's age, use of Clozapine, Risperidone, Olanzapine and Quetiapine are significantly associated with weight gain with adjusted odds ratio of 0.964, 2.920, 2.244, 3.474 and 4.060 respectively.

Table: 4 Binary logistic regression model

	B	S.E.	Wald	Df	p	OR	95% C.I. for OR	
							Lower	Upper
Age	-0.037	0.015	6.452	1	0.011	0.964	0.937	0.992
Clozapine	1.072	0.367	8.519	1	0.004	2.920	1.422	5.996
Risperidone	.808	0.324	6.223	1	0.013	2.244	1.189	4.233
Olanzapine	1.245	0.334	13.901	1	0.008	3.474	1.805	6.685
Quetiapine	1.401	0.625	5.026	1	0.025	4.060	1.193	13.821
Constant	-.590	0.172	11.808	1	0.001	0.554		

Discussion

The present study analyzed the risk factors for clinically significant weight gain in psychiatric patients on treatment, to identify strategies for the prevention and control of this health issue. Multivariate analysis showed that the patient's age is a risk factor for clinically significant weight gain for psychiatric patients on treatment for 3 months. For each one-unit increase in age, the odds of weight gain decrease by approximately 3.6%. This finding is contradictory to a study by Kivimäki M et al. [10] where the risk of obesity increased with increasing age in the presence of mental disorders (p = 0.004). This difference could be due to the selection of younger population (18-45 years) in our study as compared to the age group between 35-74 years in the other. [10] It is believed that healthy elderly persons, in contrast to younger subjects, are more conscious of their external physical appearance and are also more positive in their self-evaluations of body competence. [11]

Both univariate and multivariate analysis suggest that gender is not a risk factor for clinically significant weight gain for psychiatric patients on treatment for a period of 3 months (p = 0.291). This is similar to the findings in the study by Kivimaki M et al. The risk of weight gain did not vary by gender in that study (p = 0.92). Similarly, socio-economic status is not a risk factor for clinically significant weight gain for psychiatric patients on treatment for 3 months (p= 0.812). These findings go hand in hand with the study by Ross MJ et al[11], where it is seen that the risk of weight gain did not vary by socioeconomic status (p = 0.82).

Dietary habit is not a risk factor for clinically significant weight gain in psychiatric patients on treatment for 3 months (p = 0.812). Family history of obesity is also not associated with weight gain in psychiatric patients (p = 0.441). It is observed that psychiatric disorders are not a risk factor for clinically significant weight gain for psychiatric patients on treatment for 3 months (p =0.681). In the present study, there is no significant weight gain in patients with anxiety disorders. This is in accordance to the findings in cross-sectional population-based studies by Bruffaerts *et al. [12],* McLaren *et al*. [13], Simon *et al*. [14]. In these studies, there was no association between anxiety disorders and obesity. [15]

Patients with short duration of exposure to Clozapine and Olanzapine had a weight gain when compared to control group on univariate analysis. On multivariate analysis, patients treated with Quetiapine and Risperidone also had clinically significant weight gain. These findings are consistent with findings in Cross sectional study by Tarricone et al. [16] These medications are known to affect various neurotransmitter systems, including histamine, serotonin and dopamine, which can influence appetite, metabolism, and energy balance thereby induce weight gain.

Based on the knowledge from available literature that assesses risk factors, the current study aims to highlight the importance of a possible association between factors like age, gender, socio-economic status, dietary habits, psychiatric disorders, substance abuse, psychotropic drugs versus weight gain. Among psychotropic drugs, use of Clozapine, Olanzapine, Quetiapine and Risperidone are associated with clinically significant weight gain.

Age is also an important factor for clinically significant weight gain in psychiatric patients. This is an important finding that can be put into use in clinical practice, and it highlights the importance of screening and the need for early interventions to prevent weight gain and associated co-morbidities in future.

Limitations of the Study

The study's three-month duration may limit the ability to capture long-term effects on weight gain. A more extended observation period could provide a comprehensive understanding of the dynamics over time. The study's focus on patients aged 18-45 years may limit the generalizability of findings to older age groups. Additionally, characteristics such as ethnicity and comorbid medical conditions were not addressed, potentially influencing results. Variables like dietary habits and substance abuse rely on self-reported data, introducing the possibility of recall bias and social desirability bias. The study did not consider variations in medication dosages or patient compliance, which could influence the magnitude of weight gain associated with psychotropic drug use.

Conclusion

The present study has provided valuable insights into the risk factors associated with clinically significant weight gain in psychiatric patients undergoing treatment for three months. Gender, socioeconomic status, dietary habits, family history of obesity, and psychiatric disorders were not identified as significant risk factors for clinically significant weight gain in this study. These findings align with existing research, supporting the notion that weight gain in psychiatric patients may be more strongly influenced by factors such as age and specific psychotropic drug use. The implications of these findings for clinical practice are substantial. Identifying age and specific psychotropic drug use as significant factors allows for targeted screening and early interventions to prevent weight gain and mitigate associated health risks in psychiatric patients. It underscores the importance of a personalized approach to medication management, taking into consideration the potential impact on body weight.

Acknowledgments:

We are extremely grateful to Dr. Asha. S, Professor and Head, Department of Pharmacology, Govt. Medical College, Manjeri; Dr. Vidhukumar, Additional Professor, Department of Psychiatry, Govt. Medical College, Thiruvananthapuram; Dr. Ramani. P.T, Professor and Head, Department of Pharmacology, Government Medical College Thiruvananthapuram for the encouragement and valuable suggestions provided at various stages of the study and for all the efforts in facilitating the smooth conduct of the study.

References

1. Torrent C, Amann B, Sánchez-Moreno J, Colom F, Reinares M, Comes M, et al. Weight gain in bipolar disorder: pharmacological treatment as a contributing factor. Acta Psychiatr Scand. 2008 Jul;118(1):4–18.
2. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, Obesity NAA for the S of. Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. Diabetes Care [Internet]. 2004 Feb 1;27(2):596–601.
3. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BWJH, et al. Overweight, Obesity, and Depression: A Systematic Review and Meta-analysis of Longitudinal Studies. Arch Gen Psychiatry [Internet]. 2010 Mar 1;67(3):220–9.
4. Atlantis E, Baker M. Obesity effects on depression: systematic review of epidemiological studies. Int J Obes (Lond). 2008 Jun;32(6):881–91.
5. Lykouras L, Michopoulos J. Anxiety disorders and obesity. Psychiatrike. 2011;22(4):307–13.
6. Nihalani N, Schwartz TL, Siddiqui UA, Megna JL. Weight gain, obesity, and psychotropic prescribing. J Obes. 2011;2011:893629.
7. McCloughen A, Foster K. Weight gain associated with taking psychotropic medica tion: an integrative review. Int J Ment Health Nurs. 2011 Jun;20(3):202–22.
8. Stahl SM, Mignon L, Meyer JM. Which comes first: atypical antipsychotic treatment or cardiometabolic risk? Acta Psychiatr Scand [Internet]. 2009 Mar 1;119(3):171–9.
9. De Hert M, Dekker JM, Wood D, Kahl KG, Holt RIG, Möller H-J. Cardiovascular disease and diabetes in people with severe mental illness position statement from the European Psychiatric Association (EPA), supported by the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ES. Eur Psychiatry. 2009 Sep; 24(6):412–24.
10. Kivimäki M, Batty GD, Singh-Manoux A, Nabi H, Sabia S, Tabak AG, et al. Association between common mental disorder and obesity over the adult life course. Br J Psychiatry. 2009 Aug;195(2):149–55.
11. Ross MJ, Tait RC, Grossberg GT, Handal PJ, Brandeberry L, Nakra R. Age differences in body consciousness. J Gerontol. 1989 Jan;44 (1):P23-4.
12. Bruffaerts R, Demyttenaere K, Vilagut G, Martinez M, Bonnewyn A, De Graaf R, et al. The relation between body mass index, mental

health, and functional disability: a European population perspective. Can J Psychiatry. 2008 Oct;53(10):679–88.
13. McLaren L, Beck CA, Patten SB, Fick GH, Adair CE. The relationship between body mass index and mental health. A population-based study of the effects of the definition of mental health. Soc Psychiatry Psychiatr Epidemiol. 2008 Jan;43(1):63–71.
14. Simon GE, Von Korff M, Saunders K, Miglioretti DL, Crane PK, van Belle G, et al. Association Between Obesity and Psychiatric Disorders in the US Adult Population. Arch Gen Psychiatry [Internet]. 2006 Jul 1;63(7): 824–30.
15. Gutiérrez-Bedmar M, Villalobos Martínez E, García-Rodríguez A, Muñoz-Bravo C, Mariscal A. Psychiatric Status across Body Mass Index in a Mediterranean Spanish Population. PLoS One. 2015;10(12):e0145414.
16. Tarricone I, Casoria M, Gozzi BF, Grieco D, Menchetti M, Serretti A, et al. Metabolic risk factor profile associated with use of second generation antipsychotics: a cross sectional study in a community mental health centre. BMC Psychiatry [Internet]. 2006;6(1):11.