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Assessment of vitamin D levels and adipokines mediated obesity among psychiatric patients on treatment and treatment naïve: A comparative cross-sectional study

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Abstract

Background and aims: Antipsychotic treatment may contribute to low vitamin D levels and have impact on direct anti-inflammatory activity such as adiponectin activity and indirect proinflammatory activity such as leptin and resistin activity. However, vitamin D levels and adipokines mediated effect on weight gain and increased adiposity are not well evaluated. This study, therefore, assessed vitamin D and adipokines-mediated obesity among Ghanaian psychiatric patients.

Methods: This comparative cross-sectional study was conducted at psychiatric unit of Komfo Anokye Teaching Hospital, Kumasi, Ghana. Anthropometric measurements, sociodemographic and previous medical history were taken from 300 antipsychotics treatment naïve and active patients. Obesity was classified using World Health Organization (WHO) body mass index (BMI)-specific cut-offs. Blood samples were collected for serum vitamin D and adipokines (adiponectin, leptin, and resistin) analysis using enzyme-linked immunosorbent assay. Statistical analyses were done using SPSS version 26.0 and GraphPad Prism version 8.0.

Results: We observed higher prevalence of obesity among treatment active psychiatric patients (40.7%) compared to treatment naïve group (16.8%). Vitamin D insufficiency and deficiency prevalence were significantly higher among the treatment active group (25.3%; 39.5%; $p < 0.001$) and associated with increased odds of obesity (91.8%; cOR = 91.84, 95% confidence interval [CI]: 24.94–338.13). Moreover, adiponectin (84.2%: cOR = 14.15, 95% CI: 5.52–36.27), leptin (55.6% cOR = 2.20, 95% CI: 1.04–4.67), and resistin (79.4%: cOR = −8.34, 95% CI: 3.39–20.55) were significantly associated with increased odds of obesity among treatment active psychiatric. Furthermore, treatment active psychiatric patients exhibited inverse correlation for adiponectin and leptin with BMI ($r = -0.62$; −0.24), and WHtR ($r = -0.53$; −0.24); however, a moderate positive correlation for resistin with BMI ($r = 0.80$), HC ($r = 0.67$), and WHtR ($r = 0.65$).

Conclusion: Obesity is more prevalent in psychiatric patients on antipsychotics such as Olanzapine and Clozapine. Obesity among treatment active psychiatric patients is associated with vitamin D insufficiency and deficiency, low adiponectin and leptin levels but higher resistin level.

KEYWORDS
adipokines, antipsychotic treatment, leptin, obesity, resistin, vitamin D

1 | INTRODUCTION

Psychiatric disorders (PD) are uncontrolled emotional or cognitive impaired behaviors associated with medically relevant distress. PD has been linked with malfunction in social, occupational, and neurodevelopmental dysfunctions.[1] Globally, psychiatric disorder affecting adults is a highly predominant health threat.[2] The World Health Organization (WHO) estimated that more than 450 million people globally are suffering from mental and neurological disorders. Moreover, WHO estimated 3% of Ghana's population suffer from a severe mental disorder, whilst another 10% suffer from a moderate to mild mental disease, with a handful of them being antipsychotic treatment active.[3]

In Ghana, people with psychiatric disorder are commonly treated with antipsychotics such as clozapine (12.5–50 mg), olanzapine (5–10 mg), and risperidone (2 mg).[4] However, studies show that people with PD on antipsychotic treatment are almost certain to become overweight/obese, with increasing cardiovascular disease risk factors such as dyslipidemia, diabetes, and hypertension.[5] These comorbidities consequently link with PD and predispose to a patient to cardiovascular diseases.[6,7] Moreover, people with psychiatric disorder are known to have 2–3 times tendency to die earlier than the general population with clearly diminished life expectancy.[8,9] PD, notably anxiety and depression, are estimated to be the fourth most common cause of morbidity and early mortality worldwide.[10]

Likewise, antipsychotic pharmacotherapy has also been associated with obesity in psychiatric patients via metabolic and inflammatory dysregulations, however, levels of vitamin D and adipokines such as adiponectin, leptin, and resistin in psychotics on pharmacotherapy have not been well evaluated in Ghana. An earlier study in Greece found higher levels of adiponectin, leptin, and resistin in drug-naïve, first-episode patients with normal body mass index (BMI), however, they reported that increasing weeks of antipsychotic treatment leads to reduced levels of leptin with no change in adiponectin and resistin levels. Other studies have also reported increased leptin levels among psychiatric patients under long-term antipsychotic treatment due to antipsychotic medication.[11,12] In addition, decreased adiponectin levels have been reported in antipsychotic medication and have been associated with metabolic syndrome.[13,14]

Antipsychotic has been suggested to induced diabetes mellitus through weight gain, decreased insulin secretion from pancreatic β-cells, and impaired leptin action.[15] Again, the effect of vitamin D on atypical antipsychotic-induced metabolic disorders is unknown. Whilst studies that evaluated the efficacy of vitamin D against antipsychotic-induced metabolic side effects were hampered by statistically insufficient sample sizes.[16,17] Others found that antipsychotic-induced hyperglycemia could be caused by vitamin D deficiency,[18] however, this study based its conclusions from animal models with clozapine treatment induced weight gain, which may contradict clinical results. Understanding the role of vitamin D and adipokines in obesity among psychiatric patients on treatment is warranted to aid in the psychological and therapeutic management of psychiatric patients. This study, therefore, assessed the role of vitamin D and adipokines in obesity among psychiatric patients.

2 | MATERIALS AND METHODS

2.1 | Study design and site

This comparative cross-sectional study was conducted among newly diagnosed Ghanaian psychiatric patients aged 18 and 60 years, and those on antipsychotic treatment at the Psychiatric Unit of the Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana. The Psychiatric Unit of the Komfo Anokye Teaching Hospital is well-known for providing excellent mental health treatment to patients across Ghana. It provides specialist psychiatric care such as psychotherapy and counseling, psychometric testing and assessments, research, advocacy, and media outreach programs to clients of all ages with mental health challenges. The unit also renders specialist out-patient clinics, and a 24-h, 11-bed capacity ward for patients who require hospitalization on weekdays.[19]

2.2 | Study participants

This study recruited 150 newly diagnosed adult psychiatric patients and 150 psychiatric patients who have been on antipsychotic treatment for over 3 months at the Psychiatric Unit of the KATH, Kumasi, Ghana. A simple selective sampling technique was used in the recruitment of participants. The diagnosis of Psychiatric disorder was carried out by a qualified specialist in Psychiatry using the guidelines in reporting psychiatric disorder in Ghana adapted from the World Health Organization Assessment Instrument for Mental

Health Systems (WHO-AIMS).[20] Psychiatric patients who did not and/or were not able to give consent, pregnant women, and children below 18 years with PD were excluded from the study. Additionally, study participants with previous hypertension, diabetes mellitus, and cardiovascular disease (CVD), who were on any pharmacotherapy treatments (such as drugs for diabetes management, drugs for weight and lipid management, and antihypertensives) before their recruitment were excluded from the study.

2.3 | Sample size calculation

The lowest number of patients to be recruited from each study group was estimated by the formula proposed by Fleiss et al.[21] Approximately 26 samples in each study group were required for the study. To increase statistical power, 150 participants in each group being the antipsychotic naïve group and the antipsychotic treatment group were considered for this study.

2.4 | Ethical considerations

Ethical approval was obtained from the Committee on Human Research, Publications and Ethics, of the Kwame Nkrumah University of Science and Technology, School of Medical Sciences, and the Research and Development Committee of the KATH, Kumasi (CHRPE/AP/364/15). Written informed consent was also obtained from all study participants after a thorough explanation of the study protocol and assurance of anonymity was made to the participants.

2.5 | Questionnaire administration

A well-structured questionnaire was designed in the English language and administered to study participants. Translations of every question on the questionnaire into the local language and explanation for clarity in the local dialect to study participants who had difficulties in reading and comprehending in the English Language was carried out by a certified language translator. Sociodemographic data such as age, gender, occupation, religion, level of education, religious affiliation of participants, past medical history, and the type and duration of antipsychotic treatment participants were managed with, was obtained using the questionnaire.

2.6 | Anthropometric measurements

Using a wall-mounted ruler and standard bathroom scale (Zhongshan Camry Electronic Co. Ltd.), without footwear and light clothing, height and weight were measured and approximated to the nearest centimeter and 0.1 kg, respectively. BMI was estimated by dividing the weight (kg) by the height (m^2). Obesity was classified using the WHO BMI-specific cut-off. Thus, BMI of over 25 is considered overweight, and over 30 is obese.[22] Again, using Gulick II spring-loaded measuring tape, waist circumference, located between the inferior angle of the ribs and the suprailiac crest was obtained. The widest circumference over the buttocks region in meters was quantified as the waist circumference (cm) and waist to hip ratio was estimated by dividing the waist circumference (cm) by the hip circumference (m). Additional anthropometric parameters measured and calculated includes; blood pressure, waist to hip ratio (WHR), waist to height ratio (WtHR), and the classical anthropometric parameters namely conicity index (CI), abdominal volume index (AVI), and body adiposity index (BAI).

Additional anthropometric formulae used includes[23–25]:

$$\text{Waist to height ratio (WtHR): } \frac{\text{Waist circumference (cm)}}{\text{Height (cm)}},$$

$$\text{Conicity index (CI)} = \frac{\text{Waist circumference (m)}}{0.109\sqrt{\frac{\text{Weight (kg)}}{\text{Height (m)}}}},$$

$$\text{Abdominal volume index (AVI)} = \frac{2\ \text{cm (waist)}^2 + 0.70\ \text{cm}}{1000} \times (\text{waist circumference} - \text{hip circumference})^2,$$

$$\text{Body adiposity index (BAI)} = \frac{\text{Hip (cm)}}{\text{Height (m)} \times \sqrt{\text{Height (m)}}} - 18.$$

2.7 | Blood sample collection and biochemical assay

A total volume of 5 ml of venous blood specimen was taken from the antecubital vein of the study participants after an overnight fast (12–16 h). Four milliliters of blood were transferred into Gel Activator Tubes. It was centrifuged at 2000 rpm for 10 min and serum obtained was transferred into storage tubes until assay period. Vitamin D and adipokines (adiponectin, leptin, and resistin) were assayed using Enzyme Immunosorbent Assay (ELISA). Vitamin D insufficiency and deficiency was defined as serum 25(OH)D of 21–29 ng/ml and 25(OH)D of <20 ng/ml, respectively.[26]

2.8 | Statistical analysis and evaluation

Statistical analyses were performed using SPSS version 26.0 and GraphPad Prism version 8.0. Differences in general characteristics of participants with antipsychotic naive and those on antipsychotic treatment were compared using a chi-squared test or Student's *t*-test, where appropriate. Skewed variables were presented using median and interquartile ranges (IQR) and compared between the two groups using Wisconsin rank test. Prevalence of obesity, vitamin D insufficiency, and deficiency was presented using bar chart. An estimate of the association between vitamin D status, adipokines levels, and antipsychotic treatment were estimated using age and

sex-adjusted logistic regression models. Correlation tests were done to determine the influence of adipokines on obesity indices. All analysis was conducted separately for the treatment and nontreatment group, whilst adjusting for the effect of gender and age. A two-sided *p*-value of 0.05% and 95% confidence interval was considered statistically significant.

3 | RESULTS

3.1 | Baseline characteristics of the study groups

Table 1 shows the baseline characteristics of study groups. Gender was disproportionately distributed between the antipsychotic naïve vs active patients ($p = 0.024$). However, age ($p = 0.136$) and religion ($p = 0.310$) were comparable between antipsychotic naïve and antipsychotic active groups.

Moreover, blood pressure and biochemical indices in the treatment active group and treatment naïve group. All obesity-related indices (BMI, WC, WHtR, AVI, BAI, and CI) other than WHR ($p = 0.994$), were significantly higher among treatment active patients compared with the treatment naïve group ($p < 0.05$). Also, mean arterial pressure ($p < 0.001$) and systolic BP ($p < 0.001$) were significantly elevated among the treatment active group compared to the treatment naïve group. In terms of biochemical parameters, statistically, significant differences were observed in all parameters ($p < 0.001$).

3.2 | Prevalence of obesity, vitamin D deficiency, and insufficiency among the study groups

Figure 1 shows prevalence of obesity, vitamin D insufficiency, and deficiency among treatment naive and treatment active group. Class I and Class II obesity were more prevalent among the treatment active group (26% and 14.7%) compared to the treatment naïve group (16% and 0.7%).

Moreover, the prevalence of vitamin D insufficiency and vitamin D deficiency was significantly higher among treatment active group (25.3% vs. 39.5%) compared to treatment naïve group (12.7%; $p = 0.003$; 11.2%; $p < 0.001$).

3.3 | The interrelationship between antipsychotic treatment type and vitamin D insufficiency and deficiency

Table 2 shows the age and gender-adjusted association between type of antipsychotic agent and vitamin D status. Patients receiving treatment with Olanzapine were significantly associated with increased odds of vitamin D insufficiency (aOR = 4.35, 95% CI: 1.56–12.13) and vitamin D deficiency (aOR = 7.05, 95% CI: 2.95–16.85). Also, patients receiving treatment with Clozapine were associated with high risk of both vitamin D insufficiency (OR = 21.66, 95% CI: 6.45–72.71) and deficiency (aOR = 33.17, 95% CI: 11.09–99.19).

TABLE 1 Baseline characteristics of the study participants

Variables	Treatment naïve (*n*= 50)	Treatment active (*n* = 150)	*p*-Value
Mean age (years)*	35.73 ± 13.61	35.87 ± 12.76	0.927
Age group (years)			0.136
<30	60 (40.0)	52 (34.7)	
30–39	48 (32.0)	40 (26.7)	
40–49	17 (11.3)	34 (22.7)	
50–59	17 (11.3)	16 (10.7)	
≥60	8 (5.3)	8 (5.3)	
Gender			
Male	66 (44.0)	47 (31.3)	
Female	84 (56.0)	103 (68.7)	**0.024**
Religion			
Christian	144 (96.0)	147 (98.0)	
Muslim	6 (4.0)	3 (2.0)	0.310
Anthropometric indices			
BMI* (Kg/m^2)	26.12 ± 3.82	29.75 ± 4.99	**<0.001**
WC (cm)*	89.54 ± 8.42	95.07 ± 11.03	**<0.001**
HC (cm)*	99.75 ± 10.38	105.49 ± 10.88	**<0.001**
WHR*	0.90 ± 0.08	0.90 ± 0.06	0.994
WHtR*	0.54 ± 0.07	0.60 ± 0.07	**<0.001**
AVI*	16.29 ± 3.14	18.42 ± 4.20	**<0.001**
BAI*	29.39 ± 6.86	35.44 ± 5.86	**<0.001**
CI*	0.19 ± 0.02	1.28 ± 0.09	**<0.001**
Adiponectin (pg/ml)*	150.93 ± 23.05	131.95 ± 27.05	**<0.001**
Leptin (μg/L)#	5.21 (4.97–7.59)	8.12 (5.67–10.73)	**<0.001**
Resistin (μg/L)#	0.85 (0.74–1.89)	1.88 (1.49–1.94)	**<0.001**
Vitamin D (pg/ml)#	35.66 (17.51–45.58)	12.45 (11.45–23.62)	**<0.001**

Note: Independent sample *t*-test was used to obtained *p*-values for normally distributed variables whilst Mann–Whistney U-test was used to obtained *p*-values for nonparametric variables. $p < 0.05$ and in bold value indicates a statistically significant difference.

Abbreviations: AVI, abdominal volume index; BAI, body adiposity index; BMI, body mass index; CI, conicity index; WC, waist circumference; WHR, waist-to-hip ratio; WtHR, waist-to-height ratio.

*Normally distributed variables are presented as mean and standard deviations (π ± SD), whilst #nonparametric variables are presented as median (IQR).

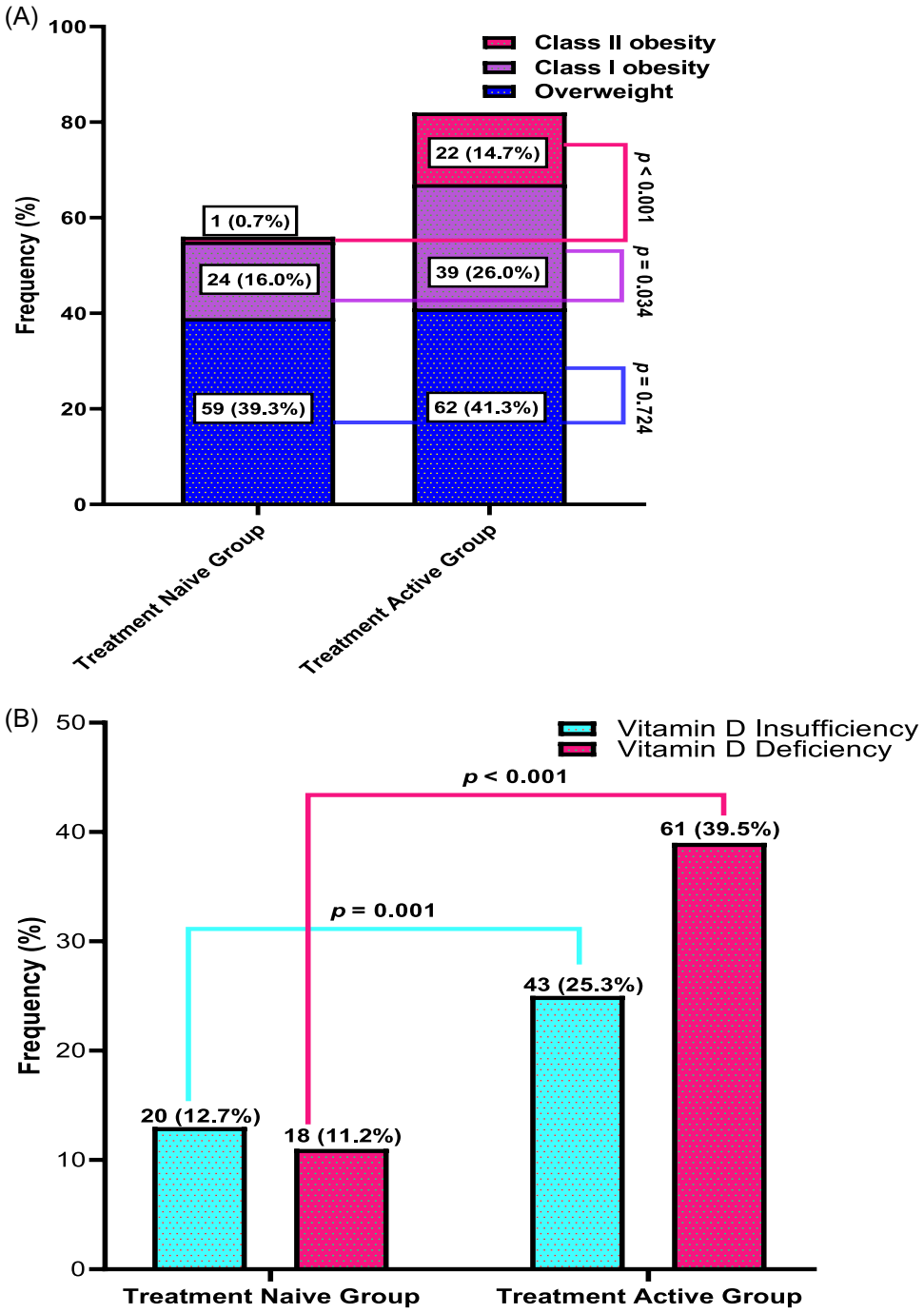

FIGURE 1 Prevalence of obesity (A), vitamin D insufficiency, and deficiency (B) among psychiatric patients on antipsychotic treatment and treatment naïve group

3.4 | Association between vitamin D insufficiency and deficiency with obesity prevalence

Table 3 depicts the association between vitamin D Insufficiency and Deficiency and obesity among psychiatric patients. In the treatment naive and treatment active groups, vitamin D deficiency was significantly associated with increased odds of obesity (52.0%; cOR = 21.67, 95% CI: 6.57–71.41) and (91.8%; cOR = 91. 84, 95% CI: 24.94–338.13), respectively.

3.5 | Association between the adipokines (adiponectin, leptin and resistin) and prevalence of obesity among study groups

Table 4 depicts association between adipokines and the prevalence of obesity among psychiatric patients. In both treatment naïve and treatment active groups, adiponectin was significantly associated with increased odds of obesity (51.4%: cOR = 17.43, 95% CI: 6.31–48.13) and (84.2%: cOR = 14.15, 95% CI: 5.52–36.27)

respectively. Likewise, in both treatment naïve and treatment active groups, Leptin associated with increased odds of obesity prevalence (51.4%: cOR = 17.43, 95% CI: 6.31–48.13) and (55.6% cOR = 2.20 95% CI: 1.04–4.67), respectively. Again, resistin was associated with increased odds of obesity prevalence in both treatment naïve and treatment active groups (43.3%: cOR = 6.70, 95% CI: 2.67–16.81) and (79.4%: cOR = 8.34, 95% CI: 3.39–20.55), respectively.

3.6 | Correlation between adipokines, vitamin D and obesity indices among study groups

Table 5 depicts correlation between adipokines, vitamin D and Obesity indices among study groups. Compared to the treatment naïve group, there were moderate negative correlation for adiponectin with BMI (r = −0.62 vs. −0.60), abdominal volume index (r = −0.51 vs. −0.44), waist circumference (r = −0.50 vs. −0.42), and waist to height ratio (r = −0.53 vs. −0.47). Moreover, compared to the treatment naïve group, psychiatric patients on treatment had resistin correlation with BMI (r = 0.80 vs. 0.67), hip circumference (r = 0.67 vs. 0.08), waist to height ratio (r = 0.65 vs. 0.05), abdominal volume index (r = 0.65 vs. 0.55), (r = 0.64 vs. 0.57), waist circumference (r = 0.64 vs. 0.53). Again, compared to treatment naïve group, psychiatric patients on antipsychotics had negative Leptin correlation with BMI (r = −0.24 vs. 0.03), BAI (r = −0.16 vs. 0.15), CI (r = −0.10 vs. 0.02), HC (r = −0.16 vs. 0.08) and WHtR (r = −0.24 vs. 0.05)

TABLE 2 Association between type of treatments and vitamin D status

Insufficiency	Proportion	Odds ratio	95% confidence interval
Olanzapine	14/35	4.05	1.50–11.13
Clozapine	23/32	21.66	6.25–72.01
Risperidone	6/22	3.09	0.83–10.44
OCF	0/10	N/c	N/c
Overall		6.96	3.11–15.55
Deficiency			
Olanzapine	21/42	7.05	2.85–16.85
Clozapine	27/36	33.17	11.09–99.01
Risperidone	3/19	1.23	0.29–5.12
OCF	10/10	N/c	N/c
Overall		9.67	4.80–19.47

Note: Association adjusted for age, gender, and anthropometrics; N/c, not computed because of zero cells.

4 | DISCUSSION

Obesity has been associated with metabolic and inflammatory dysregulations in people with PD treated with antipsychotics. Antipsychotic therapy may cause low vitamin D levels and may affect both direct anti-inflammatory activity like adiponectin and indirect proinflammatory activity like leptin and resistin activity. This study evaluated the prevalence of obesity with vitamin D deficiency and insufficiency as well as adipokine levels in psychiatric patients on treatment compared to those newly diagnosed psychiatric patients. We observed that Class I and Class II obesity were more prevalent among treatment active group (26%; 14.7%) compared to the treatment naïve group (16%; 0.7%). The prevalence of vitamin D insufficiency and deficiency were significantly higher among treatment active group (25.3%; 39.5%) compared to treatment naïve group (12.7%; 11.2%; $p < 0.001$) and were also significantly associated with increased chances of obesity among psychiatric patients on Olanzapine and Clozapine. Moreover, adiponectin, leptin, and resistin levels were significantly associated with increased chances of obesity among the treatment active psychiatric patients. Furthermore, it was observed that, treatment active psychiatric patients exhibited inverse correlation among adiponectin and Leptin with BMI (r = −0.62; −0.24), and waist to height ratio (r = −0.53; −0.47; −0.24); however, higher moderate positive correlation among resistin with BMI (r = 0.80), hip circumference (r = 0.67), and waist to height ratio (r = 0.65).

The finding of higher prevalence of obesity among psychiatric patients on treatment such as Olanzapine and Clozapine compared to treatment naïve participants is consistent with studies of Dayabandara et al.,[27] and Annamalai et al.,[28] who observed that treatment with Olanzapine, and Clozapine atypical antipsychotics elevated the risk of obesity in psychiatric disorder and the degree of weight gain varied with the antipsychotic type.[27,28] Atypical

TABLE 3 Association between vitamin D status and obesity prevalence among psychiatric patients

Variables	Treatment naïve (n = 150)		Treatment active (n = 150)	
	Odds ratio (95% confidence interval)	p-Value		p-Value
Obesity				
Normal vitamin D level	1.00	-	1.00	-
Vitamin D insufficiency	9.01 (0.095–12.05)	0.059	32.03 (2.08–50.078)	**<0.0001**
Vitamin D deficiency	21.67 (6.57–71.41)	**<0.0001**	91.84 (24.94–338.13)	**<0.0001**

Note: Association adjusted for age, gender, and anthropometrics, values in bold indicate a statistically significant association.

TABLE 4 Association between adipokines and prevalence of obesity among psychiatric patients

Variable	Treatment naïve Adipokines Adiponectin level	cOR (95% confidence interval [CI])	Treatment active Adipokines Adiponectin level	cOR (95% CI)
Obesity				
Q1	51.4	**17.43 (6.31–48.13)**	84.2	**14.15 (5.52–36.27)**
Q2	0	N/c	65.8	3.96 (1.84–8.54)
Q3	4.9	0.23 (0.06–0.91)	0	N/c
Q4	11.8	0.66 (0.22–1.96)	11.4	**0.15 (0.05–0.42)**
	Leptin level		**Leptin level**	
Obesity				
Q1	5	0.24 (0.06–0.94)	10	0.11 (0.04–0.33)
Q2	11.1	0.60 (0.20–1.79)	0	N/c
Q3	0	0	55.6	**2.20 (1.04–4.67)**
Q4	51.4	**17.43 (6.31–48.13)**	100	N/c
	Resistin level		**Resistin level**	
Obesity				
Q1	4.9	0.23 (0.06–0.91)	10.3	0.11 (0.04–0.32)
Q2	11.4	0.63 (0.21–1.87)	20.5	0.27 (0.12–0.64)
Q3	13.6	0.76 (0.29–1.99)	64.7	**3.35 (1.52–7.40)**
Q4	43.3	**6.70 (2.67–16.81)**	79.4	**8.34 (3.39–20.55)**

Note: Q1 to Q4 indicates Quartile 1 to Quartile 4, values in bold indicate a statistically significant association, N/c, not computed due to zero cells.

antipsychotics like olanzapine, and clozapine have lower incidence of side effects compared to typical antipsychotics but high metabolic side effects.[29] The high metabolic effects could explain the reason that atypical antipsychotics have additional compatibility for various neurotransmitter receptor subtypes, which include serotonin receptors (5HT1A, 5HT2C, 5HT6, and 5HT7) and dopamine receptors (D1, D3, and D4), as well as the histamine receptor H1, muscarinic receptors (M1, M2, M3, M4, and M5) and adrenergic receptors (α1 and α2).[30] This may account for the weight gain among treatment active psychiatric patients on these atypical antipsychotics.

Moreover, we observed higher significant prevalence of vitamin D insufficiency and deficiency among psychiatric patients on treatment. This finding is in concordance with the studies of Melanie et al.,[31] and Cuomo et al.,[32] who also observed vitamin D insufficiency and deficiency were prevalence among more than two-thirds of psychiatric inpatients. Similar to this finding, Petter et al.,[33] also found that, the use of some antipsychotics such as clozapine, olanzapine, or depot injectable antipsychotics nominally decrease vitamin D levels causing vitamin D insufficiency and deficiency.[32,34,35] Concurrently, our study observed that vitamin D insufficiency and deficiency among psychiatric patients on treatment significantly increased the chances of obesity; which confirms the fact that obesity and vitamin D deficiency is more prevalent in treatment active psychiatric patients. These outcomes could be explained by the active form of vitamin D, 1.25(OH)D, impeding adipogenesis via vitamin D receptor modulated actions.[36,37] This becomes impossible if vitamin D concentrations are highly deficient, thereby promoting adipogenesis. This could also be attributed to elevated parathyroid hormone concentrations due to vitamin D deficiency, aggravating lipogenesis by increased calcium influx in adipose tissue. The decreased vitamin D among psychiatric patients may be due to dietary deficiencies, little or no exposure to sunlight, antipsychotic pharmacotherapy side effects, decreased vitamin D synthesis in the skin and general physical inactivity.[32] The importance of sunlight in the synthesis of vitamin D cannot be over emphasized, therefore it is imperative that psychiatric patients are encouraged to spend more time outdoors to gain adequate exposure to sunlight as low physical activity correlates with less exposure to sunlight resulting in low level of vitamin D among the psychiatric patients. This also puts psychiatric patients on treatment at risk for CVD occurrence. Additionally, the decreased activity of hormones such as serotonin and dopamine- which play a major role in the control of mood and happiness; by the action antipsychotics may decrease willingness for physical activities in the psychiatric patients.

In this study, we found that adiponectin, leptin, and resistin levels were significantly associated with increased chances of obesity among treatment active psychiatric patients and correlated with obesity indices such as BMI, hip circumference, and waist to height

TABLE 5 Correlation between adipokines, vitamin D, and obesity indices within the study groups

Variables	BMI	AVI	BAI	CI	WC	HC	WHR	WHtR
Treatment naïve								
Adiponectin (pg/ml)	−0.60	−0.44	−0.56	0.25	−0.42	−0.54	0.22	−0.47
Resistin (μg/l)	0.67	0.55	0.57	−0.28	0.53	0.62	−0.19	0.52
Leptin (μg/l)	**0.03**	−0.01	**0.15**	**0.02**	−0.03	**0.08**	−0.14	**0.05**
Leptin/Resistin	0.03	0.08	0.25	0.17	0.08	0.14	−0.08	0.18
Adiponectin/Resistin	−0.62	−0.48	−0.59	0.25	−0.47	−0.59	0.23	−0.50
Adiponectin/leptin	−0.43	−0.38	−0.55	0.07	−0.36	−0.5	0.23	−0.43
Vitamin D (ng/ml)	−0.31	−0.39	−0.57	−0.08	−0.37	−0.48	0.21	−0.46
Treatment active								
Adiponectin (pg/ml)	**−0.62**	**−0.51**	−0.51	−0.11	**−0.50**	−0.50	−0.07	**−0.53**
Resistin (μg/l)	**0.80**	**0.65**	**0.64**	0.11	**0.64**	**0.67**	0.06	**0.65**
Leptin (μg/l)	−0.24	−0.22	−0.16	−0.10	−0.24	−0.16	−0.21	−0.24
Leptin/Resistin	−0.33	−0.14	0.11	0.25	−0.14	−0.04	−0.21	−0.04
Adiponectin/Resistin	−0.66	−0.57	−0.61	−0.14	−0.56	−0.60	0.00	−0.59
Adiponectin/leptin	−0.46	−0.44	−0.59	−0.23	−0.44	−0.51	0.09	−0.51
Vitamin D (ng/ml)	−0.43	−0.47	−0.58	−0.27	−0.47	−0.56	0.12	−0.50

Note: R = 0.00–0.3 = weak correlation. R = 0.3–0.7 = moderate correlation. R = 0.8–0.9 = strong correlation. Bold data shows significant correlation.
Abbreviations: AVI, abdominal volume index; BAI, body adiposity index; BMI, body mass index; CI, conicity index; WC, waist circumference; WHR, waist-to-hip ratio; WtHR, waist-to-height ratio.

ratio. This is in agreement with previous studies by Mondelli et al., Lu et al., and Aprahamian et al., who reported that antipsychotic drugs may have different impacts on the immune system, having both a direct anti-inflammatory activity such as adiponectin and an indirect proinflammatory activity such as those of Leptin and Resistin, mediated by their weight gain and elevated obesity impact.[38–40] These observations prove that atypical antipsychotics lead to irregularities of anti-inflammatory and proinflammatory adipokine levels in psychiatric patients which put them at risk of developing obese states.

Obesity, insulin resistance, and type II diabetes have been well proven to be strongly linked with chronic inflammation, presented by inflammatory signaling pathway triggering and by untypical production of cytokines. Lu et al.[38] suggested that alterations in leptin and adiponectin concentrations is largely by direct antipsychotic pharmacotherapy effect rather than secondary to weight gain.[38] In agreement with our study finding, Lu et al.[38] also found that psychiatric patients on a long period of clozapine treatment have lower serum levels of adiponectin as compared to healthy subjects.[38] Again, as observed in our study, it has been suggested that there are low levels of adiponectin with low BMI, body fat mass, and visceral adipose tissue; as larger adipocytes have the ability to lower adiponectin levels.[39,41] Similarly, Kardas et al.[42] reported an inverse relationship between adiponectin and obesity indices.[42] This could be further explained by the effect of Leptin on appetite, energy expenditure, adipose synthesis, and insulin activity with its main impact on the amount of adipose tissue control and weight of the body. Similarly, it could also be due to failure of leptin to cross the blood-brain barrier contributing to decreased receptor activation in key brain regions implicated in energy homeostasis; this was proposed as a likely mechanism of leptin resistance.

Resistin, an adipocyte-specific protein contributes to adiposity associated with metabolic and cardiovascular disease.[43] Previous studies, found elevated resistin in obesity.[44,45] In the study of Makni et al.[43] it was demonstrated that resistin has higher correlations with obesity which agrees with our current study.[43] Sequel to the well-known association between adipokines and metabolic alteration in obese states and metabolic syndrome, metabolic changes linked with psychiatric disorder can also be potentially mediated by adipokines, among other factors including antipsychotic administration, sedentary lifestyle, obesity, psychological stress, and genetic predisposition.[46]

Our current findings have established that antipsychotic treatment affect anti- and proinflammatory adipokine levels which results in obese states and low vitamin D levels; as a later consequence, increased cardiovascular risk. It is imperative that psychiatric patients on treatment regimen, though mentally unstable, should be exposed to more physically activity instead of a sedentary lifestyle. Moreover, antipsychotic treatment regimen should be given for shorter periods of time where possible. Treatment active psychiatric patients in the current study were on antipsychotic treatment for about 3 years.

This study was limited by the inability to assess the levels of calcium and parathyroid hormone (PTH). There is a need to include

the measurement of calcium and parathyroid hormone in psychiatric patients to distinguish between other possible biological effects on total vitamin D serum concentrations. Moreover, information on dietary and physical activity could not be obtained and evaluated in this present study. Poor dietary and sedentary habits could influence excessive weight gain in psychiatric patients.

5 | CONCLUSION

Obesity is more prevalence in psychiatric patients on antipsychotics such as Olanzapine and Clozapine. Obesity among treatment active psychiatric patients is influenced by vitamin D insufficiency and deficiency, low adiponectin and Leptin levels but high resistin. This calls for the effective monitoring of psychiatric patients on treatment to enhance early management of any likely adverse effects.

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AUTHOR CONTRIBUTIONS

Linda A. Fondjo: Conceptualization; data curation; investigation; methodology; project administration; resources; supervision; validation; visualization; writing – original draft; writing – review and editing. **Olivia Osei**: Conceptualization; data curation; investigation; methodology; resources; validation; writing – original draft; writing – review and editing. **William K. B. A. Owiredu**: Conceptualization; investigation; methodology; project administration; resources; supervision; validation; writing – original draft; writing – review and editing. **Christian Obirikorang**: Methodology; resources; supervision; validation; writing – original draft; writing – review and editing. **Ebenezer Senu**: Data curation; formal analysis; investigation; methodology; software; validation; writing – original draft; writing – review and editing. **Ruth Owusu-Antwi**: Methodology; resources; validation; writing – original draft; writing – review and editing. **Eugene F. J. Brefo**: Data curation; investigation; methodology; writing – original draft; writing – review and editing.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article can be requested from the corresponding author.

TRANSPARENCY STATEMENT

The lead author Linda Ahenkorah Fondjo affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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