



<Research Article>

Mineral nutrition remains adequate in hospitalized patients with mental illness despite visceral fat obesity

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Summary Many studies have been conducted worldwide to identify micronutrient deficiency (a lack of vitamins and/or minerals) associated with obesity. As obesity is commonly observed in individuals with mental illness, this study was designed to examine whether mineral deficiencies are present in Japanese patients with mental illness and obesity. We analyzed the serum mineral levels and visceral fat areas (VFA) in 77 hospitalized patients with mental illness, and visceral fat obesity ($100 \text{ cm}^2 \leq \text{VFA} \leq 251 \text{ cm}^2$) was observed in 57.1% of the patients. The prevalence of mineral deficiency (i.e., serum concentrations < cutoff levels) in patients with obesity ($100 \text{ cm}^2 \leq \text{VFA} \leq 251 \text{ cm}^2$) was not different from that in patients without obesity ($\text{VFA} < 100 \text{ cm}^2$) for serum levels of iron, zinc, magnesium, sodium, potassium, calcium, and phosphorus, which was < 10% for all the minerals, except zinc. Half of both obese and non-obese patients had a marginal zinc deficiency. Serum levels of phosphorus were negatively associated with VFA. No significant or negative associations were observed for the other minerals. Our results indicate that only slight mineral deficiency is expected to develop in patients with mental illness, despite the presence of visceral fat obesity due to the consumption of diets that followed the recommended dietary allowances (RDAs) for Japanese individuals. The high prevalence of marginal zinc deficiency was unrelated to obesity.

Key words: Micronutrient deficiency, Visceral fat area, Schizophrenia, Phosphorous, Zinc

1. Introduction

Obesity is defined as the accumulation of visceral and subcutaneous fat in the body, and it is fundamentally caused by overeating high-calorie foods and/or lowered energy expenditure¹. Visceral fat accumulation is more strongly linked to metabolic disease and insulin resistance than subcutaneous fat accumulation. Moreover, obesity can arise from

secondary causes, including endocrine disorders, genetic syndromes, central nervous system disorders, mental factors (binge eating disorders and bulimia nervosa), and weight-gain-promoting medicines (immune-suppressive agents, steroid hormone drugs, and psychotropic drugs)². Recently, overweight and obese individuals have been reported to have lower levels of serum concentrations of micronutrients (minerals [iron, selenium, zinc, sodium, potassium, calcium, phosphorus, and magnesium] and vitamins

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[β -carotene as the precursor of vitamin A, folate, vitamin B12, and 25-hydroxyvitamin D)]³⁻⁸. Moreover, serum concentrations of potassium, magnesium, 25-hydroxyvitamin D, and folate were reported to be significantly and negatively correlated with body mass index (BMI) in obese Australian individuals with a BMI between 25 and 50 kg/m², whereas no negative correlation was observed for the serum concentrations of iron, zinc, sodium, calcium, vitamin C, vitamin B12, vitamin A, and vitamin E⁷. Obesity-related micronutrient deficiencies can be explained mainly by the overconsumption of foods that are high in calories but low in vitamins and/or minerals⁹, and the increased demand for micronutrients corresponds to increased body size¹⁰.

On the other hand, a higher prevalence of overweight and obesity has been observed worldwide in patients with mental illnesses, including schizophrenia, mental retardation, and manic-depressive illness (60.1%), than that in the general population¹¹. In Japanese patients with schizophrenia, the prevalence of obesity was 48.9% and 23.1% among outpatients and inpatients, respectively¹². Obesity in mentally ill patients may result from overeating, reduced physical activity, and the use of psychotropic medications that induce obesity. However, to the best of our knowledge, the prevalence of mineral deficiency in hospitalized patients with mental illness and obesity has not been consistently reported in Japan. Given this background, we questioned whether a mineral deficiency was observed in patients with obesity with mental illness. In this preliminary study, we investigated the presence of mineral deficiencies in 77 hospitalized patients with mental illness.

2. Patients and Methods

Participants

We included 13 patients in addition to the 64 patients with schizophrenia who participated in a previous study¹³; these 77 hospitalized patients with mental illness (aged 23–72 years; 50 men and 27 women), comprising 65 patients with schizophrenia (84%); 8, with mental retardation; 4, with manic-depressive illness (Table 1). Age was confirmed to

be matched between patients with and without visceral fat obesity. However, the number of female patients was half that of the male patients; thus, the iron levels of men and women were separately examined.

The average duration of illness in all patients was 29.4±11.3 years (median 30 years, range 1–57 years). Patients had multiple illnesses other than mental illness, including hypertension (n= 30), dyslipidemia (n= 32), diabetes mellitus including suspected diabetes (n= 14), hyperuricemia (n= 9), decreased renal function (n= 8), hypothyroidism (n= 3), liver diseases (n= 4), gastrointestinal diseases (n= 4), arrhythmia (n= 4), sequelae of cerebral infarction (n= 2), and anemia (n= 2). Patients were medicated with antipsychotic agents (i.e., quetiapine, risperidone, perospirone, haloperidol, lithium carbonate, timiperone, nemonapride, carbamazepine, zotepine, and mianserin). These medications are associated with weight gain and the development of obesity, but although the degree of these effects can depend on among individuals¹⁴⁻¹⁹. Although serum zinc concentrations have been reported to decrease with lithium carbonate and carbamazepine medications²⁰, we found no significant difference in serum zinc concentrations between patients on these two medications (77.8±9.3 µg/dL, n= 20) and those on other psychotropic medications (82.2±12.4 µg/dL, n= 50, *p* > 0.05), in our cohort. Antihypertensive, hypolipidemic, and hypoglycemic agents were prescribed to patients with hypertension, dyslipidemia, and hyperglycemia, respectively. Many antihypertensive drugs have been reported to reduce serum zinc concentrations²¹, but we found no statistically significant difference between antihypertensive drug users (82.0±11.3 µg/dL, n= 30) and non-users (79.7±12.3 µg/dL, n= 47, *p* > 0.05) in our cohort. The relationship between lipid-lowering drugs and serum zinc concentrations remains uncertain in our experience.

All patients were classified by the presence of visceral fat obesity (defined as VFA ≥ 100 cm²) and by BMI (kg/m²) (underweight, BMI < 18.5; normal range, 18.5 ≤ BMI < 25.0; pre-obese, 25.0 ≤ BMI < 30.0; obesity class I, 30.0 ≤ BMI < 35.0) based the

Table 1 Characteristics of patients with or without visceral fat obesity.

	Patients with mental illness		Significance ^a
	< 100	≥ 100	
VFA (cm ²)			
range	21.0 – 98.8	100.7 – 251.4	
	61.5 ± 23.8	152.1 ± 36.4	p < 0.01
No. of patients	33 (42.9%)	44 (57.1%)	
Men / Women	20 / 13	30 / 14	ns
Age (years)	54.1 ± 10.6	56.7 ± 7.6	ns
Illness duration (years)	32.6 ± 12.6	27.3 ± 10.0	p < 0.05
BMI (kg/m ²)	22.7 ± 3.3	26.8 ± 2.6	p < 0.01
SBP (mmHg)	120.2 ± 13.8	125.6 ± 15.3	ns
DBP (mmHg)	74.0 ± 10.4	78.1 ± 8.5	p < 0.05
No. of patients with UW/NR/PO/OCI	2 / 23 / 8 / 0	0 / 8 / 31 / 5	
No. of patients with SCZ/MR/MDI	28 / 3 / 2	37 / 5 / 2	

Values are mean±SD. ^a Significance between participants with VFA < 100 cm² and VFA ≥ 100 cm². ns: not significant (p > 0.05).

VFA, visceral fat area; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; UW, underweight (BMI < 18.5); NR, normal range (18.5 ≤ BMI < 25.0); PO, pre-obese (25.0 ≤ BMI < 30.0); OCI, obese class I (30.0 ≤ BMI < 35.0); SCZ, schizophrenia; MR, mental retardation; MDI, manic-depressive illness.

guideline established by Japan Society for the Study of Obesity²². Guidelines recommend the use of VFA to assess the accumulation of visceral fat.

Hospitalized patients were provided meals containing calories, nutrients, and dietary fiber that fulfilled the recommended dietary allowances (RDAs) for the Japanese population²³. Those aged < 60 years were given 2127 kcal/day, 71.2 g/day of protein, 45.8 g/day of lipids, 348 g/day of carbohydrates, and 19 g/day of dietary fiber, and those aged ≥ 60 years were given 1635 kcal/day, 68.0 g/day of protein, 47.9 g/day of lipids, 230 g/day of carbohydrates, and 19 g/day dietary fiber—both along with RDA-based amounts of minerals and vitamins.

The patients finished all hospital meals provided. In addition to hospital-provided meals, some patients often ate snacks brought by themselves and drank high-calorie beverages. The patients did not take any additional dietary supplements.

Ethics

In compliance with the Helsinki Declaration,

written informed consent was obtained from all patients; for patients under Hospitalization for Medical Care and Protection, informed consent was additionally obtained from family members. This study was compliant with the guidelines established by the Protection of Human Subjects Committee of Aizunishi Hospital (Ethics Committee approval number 1101).

Assays

After somatometry (height and body weight) and visceral fat area (VFA) measurement by CT (Hitachi Radix Turbo CT scanner, Ibaraki, Japan) combined with image analysis software Fat Scan version 3.0 (N2 system Co., Osaka, Japan), venous blood samples were collected from the patients before breakfast and submitted for the following analyses in addition to the regular medical examinations. VFA is a better indicator of obesity in the Japanese population, considering that the most common type of obesity among the Japanese is abdominal visceral fat obesity²⁴. Constituents in

blood related to obesity (fasting plasma glucose [FPG], hemoglobin A1c [HbA1c], immunoreactive insulin [IRI], triglyceride [TG], total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C]) and minerals (iron, zinc, magnesium, sodium, potassium, calcium, and phosphorous) were measured at a commercial laboratory (SRL, Inc., Tokyo, Japan). Blood plasma and whole blood were used as specimens for FPG and HbA1c measurements, respectively. Low-density lipoprotein cholesterol (LDL-C) levels were calculated using the Friedewald equation.

Cutoff levels for diagnosing hyperglycemia (≥ 110 mg/dL), high HbA1c level ($\geq 6.5\%$), hypertriglyceridemia (≥ 150 mg/dL), hyper-LDL cholesterolemia (≥ 140 mg/dL), and hypo-HDL cholesterolemia (< 40 mg/dL) were defined according to guidelines established by the Japan Diabetes Society²⁵, Japan Society for the Study of Obesity²², and Japan Atherosclerosis Society²⁶. We evaluated mineral deficiencies using the universally accepted cutoff levels²⁷ for iron (65 μ g/dL for men, 50 μ g/dL for women), magnesium (1.6 mg/dL), sodium (136 mmol/L), potassium (3.5 mmol/L), calcium (albumin-adjusted calcium, 8.6 mg/dL), and phosphorus (2.4 mg/dL). For zinc (80 μ g/dL, marginal deficiency), cutoff level established by the Japanese Society of Clinical Nutrition²⁰ was used. Serum mineral levels are not superior indicators of body storage, but measuring body stores is difficult. Therefore, following previous studies⁴⁻¹⁰, we estimated the presence of mineral deficiency based on the presence of serum concentrations below the cutoff levels.

Statistics

Values are expressed as mean \pm SD, if not indicated otherwise. The Mann-Whitney U test was used to compare the differences in patients' age, BMI, blood pressure, duration of illness, and serum (or blood) levels of constituents related to obesity and micronutrients between the groups of patients with VFA ≥ 100 cm² and VFA < 100 cm². The prevalence of patients with levels exceeding the cutoff levels for serum (or blood) constituents related to obesity, along with mineral deficiency, was analyzed using

the z-test. To measure the strength and direction of association between two variables, Spearman's Rank correlation coefficient (ρ) was calculated. Statistical significance was defined as $p < 0.05$.

3. Results

Baseline characteristics of patients

VFA levels in the overall patient population ranged from 21.0 to 251.4 cm² and 57.1% of the patients had visceral fat obesity (VFA ≥ 100 cm²) (Table 1). Although the BMI levels in patients having visceral fat obesity were significantly higher than those in those without visceral fat obesity, eight patients were classified as "normal range" by BMI regardless of having visceral fat obesity, while another eight were classified by BMI as "overweight" without having visceral fat obesity. BMI therefore misdiagnosed the presence or absence of visceral fat accumulation in some cases.

Serum or blood levels of constituents related to obesity and minerals in patients with or without visceral fat obesity

Serum or blood levels of constituents related to obesity and minerals in patients with mental illness are shown in Table 2. Serum or blood levels of constituents related to obesity were significantly higher in patients having visceral fat obesity (VFA ≥ 100 cm²) than those in patients without it (VFA < 100 cm²) for FPG, HbA1c, IRI, TG, TC, and LDL-C levels. Serum HDL-C levels were significantly lower in patients with VFA ≥ 100 cm² than those in patients with VFA < 100 cm².

Regarding minerals, serum levels of iron, zinc, magnesium, sodium, potassium, calcium, and phosphorous did not differ significantly between our patients with mental illness who had VFA of ≥ 100 cm² vs those with VFA of < 100 cm². However, serum levels of iron (only in the men) and phosphorous tended to be lower in patients with VFA of ≥ 100 cm² vs those with VFA of < 100 cm².

The numbers and frequencies (%) of patients with serum or blood levels of constituents related to obesity and mineral levels outside the cutoff levels

Table 2 Serum or blood levels of constituents related to obesity and minerals in patients with or without visceral fat obesity.

	Cutoff levels	Patients with mental illness		Significance ^a
		VFA < 100 cm ²	VFA ≥ 100 cm ²	
		20 men and 13 women	30 men and 14 women	
Constituents related to obesity				
FPG (mg/dL)	≧ 110	94.1 ± 12.3 (2: 6.1)	103.8 ± 20.6 (10: 22.7) ^b	p < 0.01
HbA1c (%)	≧ 6.5	5.23 ± 0.34 (0: 0.0)	5.66 ± 0.69 (5: 11.4)	p < 0.01
IRI (μU/mL)	–	8.27 ± 8.95	11.04 ± 8.65	p < 0.05
TG (mg/dL)	≧ 150	104.1 ± 42.9 (4: 12.1)	158.3 ± 82.0 (19: 43.2) ^b	p < 0.01
TC (mg/dL)	–	181.6 ± 26.8	208.5 ± 38.5	p < 0.01
LDL-C (mg/dL)	≧ 140	108.0 ± 20.4 (2: 6.1)	131.6 ± 33.6 (14: 31.8) ^b	p < 0.01
HDL-C (mg/dL)	< 40	53.4 ± 8.7 (2: 6.1)	45.3 ± 7.9 (10: 22.7) ^b	p < 0.01
Minerals				
Iron (Men: μg/dL)	< 65	119.2 ± 25.5 (0: 0.0)	113.9 ± 37.9 (3: 6.8)	ns
Iron (Women: μg/dL)	< 50	82.7 ± 39.1 (3: 9.1)	88.1 ± 24.8 (1: 2.3)	ns
Zinc (μg/dL)	< 80	79.1 ± 11.5 (21: 63.6)	81.6 ± 12.4 (23: 52.3)	ns
Magnesium (mg/dL)	< 1.6	2.31 ± 0.22 (0: 0.0)	2.32 ± 0.17 (0: 0.0)	ns
Sodium (mmol/L)	< 136	141.7 ± 3.0 (1: 3.0)	141.9 ± 4.2 (2: 4.5)	ns
Potassium (mmol/L)	< 3.5	4.12 ± 0.28 (0: 0.0)	4.20 ± 0.34 (0: 0.0)	ns
Calcium (mg/dL)	< 8.6	9.37 ± 0.55 (2: 6.1)	9.59 ± 0.65 (1: 2.3)	ns
Phosphorus (mg/dL)	< 2.4	3.59 ± 0.56 (1: 3.0)	3.45 ± 0.50 (0: 0.0)	ns

Values are mean ± SD (prevalence: %). ^a Significance of serum or blood concentrations between participants with VFA < 100 cm² and VFA ≥ 100 cm². ^b Significant prevalence (p < 0.05) between participants with VFA < 100 cm² and VFA ≥ 100 cm². ns: not significant (p > 0.05).

FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; IRI, immunoreactive insulin; TG, triglyceride; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

are shown in Table 2. Compared with patients without obesity, patients with obesity had a significantly higher prevalence of hyperglycemia (22.7%), hypertriglyceridemia (43.2%), hyper-LDL cholesterolemia (31.7%), and hypo-HDL cholesterolemia (22.7%). The prevalence of mineral deficiencies appears to be quite high (> 50%) in terms of serum zinc levels regardless of the presence of visceral fat obesity. No patients had serum levels of magnesium and potassium lower than the cutoff levels. The prevalence of deficiencies of other minerals was lower (< 10%) as compared to that of zinc in patients with and without visceral fat obesity. Overall, the prevalence of deficiencies of all minerals examined did not differ significantly between the obese and non-obese patients.

Of eight patients with BMIs of < 25, five with VFA

of ≥ 100 cm² had hypertriglyceridemia, hyper-LDL cholesterolemia, and/or hypo-HDL cholesterolemia. Accordingly, in contrast to when we classified them by VFA, we found no significant differences in terms of serum levels of total cholesterol, HDL-C, and the prevalence hypo-HDL cholesterolemia between patients with BMIs of ≥ 25 and < 25 (data not shown). We found similar results for serum mineral levels and the prevalence of mineral deficiencies whether the patients were classified by VFA or BMI.

Association of serum or blood levels of constituents related to obesity and minerals with VFA in patients with mental illness

Except for HDL-C, the serum or blood levels of all constituents related to obesity were significantly and positively associated with the increase of VFA

Table 3 Association of serum or blood levels of constituents related to obesity and micronutrients with visceral fat area (VFA) and body mass index (BMI) in patients with mental illness.

	Patients with mental illness (50 men and 27 women)			
	Comparison with VFA		Comparison with BMI	
	$\rho =$	Significance	$\rho =$	Significance
Constituents related to obesity				
FPG	0.329	$p < 0.01$	0.361	$p < 0.01$
HbA1c	0.335	$p < 0.01$	0.301	$p < 0.01$
IRI	0.338	$p < 0.01$	0.412	$p < 0.01$
TG	0.363	$p < 0.01$	0.340	$p < 0.01$
TC	0.266	$p < 0.05$	0.292	$p < 0.05$
LDL-C	0.302	$p < 0.01$	0.297	$p < 0.01$
HDL-C	-0.502	$p < 0.01$	-0.340	$p < 0.01$
Minerals				
Iron (Men)	-0.145	ns	-0.013	ns
Iron (Women)	0.140	ns	-0.051	ns
Zinc	0.078	ns	0.116	ns
Magnesium	0.006	ns	0.054	ns
Sodium	0.037	ns	0.033	ns
Potassium	0.066	ns	0.087	ns
Calcium	0.115	ns	0.075	ns
Phosphorus	-0.249	$p < 0.05$	-0.060	ns

ρ : Spearman's Rank correlation coefficient. ns: not significant ($p > 0.05$).

FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; IRI, immunoreactive insulin; TG, triglyceride; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

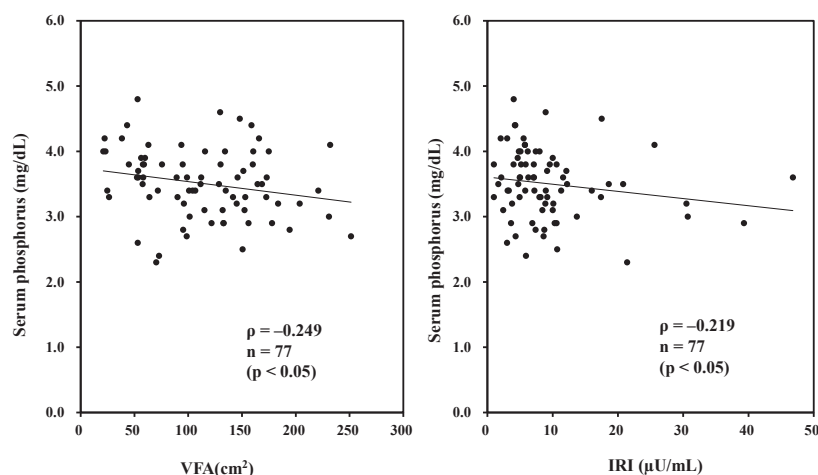


Fig. 1 Association between serum phosphorus concentration and VFA (visceral fat area: left) and IRI (immunoreactive insulin: right) in patients with mental illness. The line of best fit on the scatterplot was calculated using the Passing–Bablok procedure.

(Table 3) in patients with mental illness. HDL-C levels were significantly and negatively associated with VFA. Regarding minerals, a significant association was found for phosphorous ($\rho = -0.249$, $p < 0.05$). Phosphorus levels (Fig. 1) showed that VFA increased as the serum concentrations of phosphorus decreased. No significant or negative associations were observed for the other minerals. Serum levels of all of the components associated with obesity were found to be significantly associated with BMI; however, serum levels of minerals—including phosphorus—were not.

4. Discussion

In this study, visceral fat obesity was observed in 57.1% of hospitalized patients with mental illness. Since they were provided hospital meals that met RDAs, the causes for obesity were not due to overeating of high-calorie foods; instead, the causes were attributed to reduced physical activity, side effects of antipsychotic drugs, and eating many snacks not provided by hospital meals. Moreover, since individuals with obesity typically have a greater basal metabolic rate^{28,29}, this study is essential to determine whether the increased body size in these patients leads to greater mineral usage, potentially resulting in mineral deficiencies. Accordingly, mineral deficiencies have been reported to be associated with obesity across different reports⁴⁻¹⁰. We compared our results with those reported by Suman et al.⁴ and McKay et al.⁷ in cross-sectional studies conducted on individuals with obesity caused by unbalanced diets and overeating.

Serum levels of iron⁴ and several minerals (magnesium, potassium, zinc, sodium, and calcium)⁷ have been reported to decrease with obesity; however, they did not differ significantly in our patients with mental illness having VFA ≥ 100 cm² and < 100 cm². Suman et al.⁴ reported significant decreases in serum iron levels in participants who were overweight and obese compared with those in participants without obesity. However, we suspected that their results would be affected by the number of women increasing from 7 in “normal” to 9 in “overweight” and 11 in

“obese” out of each 30 participants, as serum iron levels in women were usually 70% to 80% of that in men. Although inflammation during obesity can decrease serum iron levels^{4,27}, other reports have indicated that serum iron levels are maintained within the reference range^{5,7}. The same authors⁴ also reported that serum copper concentrations were elevated in individuals with obesity; thus, we did not examine whether serum copper concentrations were reduced in our patients as a result of visceral fat accumulation.

McKay et al.⁷ reported significant negative associations of serum levels of magnesium and potassium with BMI, along with a very high prevalence of deficiency (100% both for magnesium and potassium), which is inconsistent with our results. In our patients, the prevalence of deficiency was 0.0% both for magnesium and potassium. Their dietary records⁷ showed lower intakes of magnesium and potassium, which vegetables are rich in. People with obesity in Australia may consume significantly fewer vegetables^{7,30}, whereas our patients consumed sufficient amounts of these minerals based on RDAs. We opined that mineral nutrition could be maintained at normal levels in our patients through pre-obese to obese class I in the obesity classification as long as they eat hospital meals containing sufficient nutrients following RDAs. However, in individuals with obesity greater than Class I, further studies are required to determine the changes in nutritional needs with respect to increasing body mass. McKay et al.⁷ could not account for the negative associations observed between BMI and serum levels of magnesium and potassium, while no such associations were found for zinc, sodium, and calcium. Magnesium and potassium are the major intracellular cations, and their extracellular concentrations are maintained by electrolyte balance²⁷. Insulin stimulates glucose transport into tissues along with potassium³¹ and increases renal magnesium excretion³². Therefore, hypokalemia and hypomagnesemia³³ may be induced in individuals with insulin resistance who were obese. However, this hypothesis remains unresolved because serum concentrations of magnesium and potassium are not associated with IRI in our patients.

In patients with mental illness, a higher

prevalence of zinc deficiency was observed regardless of visceral fat obesity (Table 2). Zinc deficiency was common in several psychiatric disorders with a prevalence of 41.0% using cutoff levels of 74 $\mu\text{g}/\text{dL}$ for men and 70 $\mu\text{g}/\text{dL}$ for women³⁴, and it would be driven by psychiatric causes (i.e., a change in diet due to the onset of depressive symptoms) along with low dietary intake of zinc. This notion did not apply to our patients who consumed standard meals prepared by the hospital; however, we did conclude that visceral fat accumulation did not cause zinc deficiency, since marginal levels of zinc deficiency were observed both in patients with VFA of $< 100 \text{ cm}^2$ (63.6%) and those with VFA of $\geq 100 \text{ cm}^2$ (52.3%), at a similar prevalence. One of the current nutritional challenges in Japan is the high prevalence of zinc deficiency, as the prevalence of marginal zinc deficiency in the general Japanese population around 60 years of age is reported to be 46.4% in men and 39.0% in women³⁴. We therefore hypothesized that psychiatric disorders might spur the onset of zinc deficiency.

Serum phosphorus levels in our patients were significantly and negatively associated with VFA (Fig. 1). Although reduced serum phosphorus levels have been reported in patients with metabolic syndrome³⁶⁻³⁸, to the best of our knowledge, our study is the first to report a negative association between serum phosphorus concentrations within the reference range and VFA in patients with normal to pre-obesity BMIs as per the obesity classification. In metabolic syndrome, the decrease in serum phosphorus level is believed to be attributed to increased insulin levels in patients, which facilitates the transfer of phosphorus from extracellular (i.e., serum phosphorus) to intracellular components^{33,39}. In our patients, serum phosphorus levels were significantly associated with IRI level ($\rho = -0.219$, $p < 0.05$; Fig. 1). The lack of association we found between BMI and serum phosphorus level may be because BMI is a measurement of relative body weight, not body composition (i.e., body fat).

The present study has some limitations. First, our study population was small; the sample size of women is too small to reflect the true nutritional

status of women with obesity. Future studies should increase the sample size. Second, the study population comprised participants from only one hospital; therefore, it is uncertain whether these findings can be generalized to other patients with mental illnesses. Our results may serve as a basis for future large-scale studies. Finally, we could not investigate how different types of mental illnesses, food intake habits, patient behaviors, and treatments (including psychiatric medications) affected serum micronutrient levels in this study. For example, in 65 of the patients who had schizophrenia, the association between serum phosphorus and VFA or IRI increased to $\rho = -0.318$ ($p < 0.05$) and $\rho = -0.251$ ($p < 0.05$), respectively—but in another 12 who had mental retardation and manic-depressive illness, this association was not observed, likely because of the small number of cases. All of our patients were fed nutritionally complete meals based on the Japanese RDAs, but individual differences in serum mineral concentrations were nevertheless observed. Snacking may be one possible cause for these variations, but the nutrient levels present in the snacks that some of the patients consumed were not examined. Some patients with mental illness were observed to have water intoxication⁴⁰, also known as dilutional hyponatremia, caused by excessive consumption of soft drinks, in previous studies. Individual differences in the intestinal absorption of nutrients may also be responsible for variations in serum mineral levels, but these were not examined in this study. The prevalence of obesity has been reported to be 48.9% for schizophrenia outpatients in the Japanese population¹². Admission to a mental hospital was reported to decrease this prevalence to 23.1% through lifestyle improvements alongside the administration of appropriate treatments (i.e., psychotherapy and medication). Future studies of the relationship between VFA and serum mineral levels in outpatients with mental illness are warranted. The effects of antipsychotics on serum mineral levels were not examined in this study, except for zinc.

In conclusion, consistent with previous studies, a higher prevalence of visceral fat obesity was found in hospitalized patients with mental illness.

However, in previous studies, mineral deficiencies were more common in obese individuals, whereas in our patients, despite the presence of visceral fat obesity, the prevalence of mineral deficiencies of iron, magnesium, sodium, potassium, calcium, and phosphorus were low. This low prevalence may be explained by the fact that patients consume meals that meet the RDAs.

Conflicts of interests

The authors have declared that no conflict of interest exists.

References

1. Dhurandhar NV: What is obesity? *Int J Obes (Lond)*, 46:1081-1082, 2022.
2. Kansral AR, Sinduja Lakkunarajah S, Jay NS: Childhood and adolescent obesity: A Review. *Front Pediatr*, 8:581461, 2021.
3. García OP, Long KZ, Rosado JL: Impact of micronutrient deficiencies on obesity. *Nutr Rev*, 67:559-572, 2009.
4. Suman SD, Indumati V, Suchetha K: Relationship of obesity with micronutrient status. *Int J Appl Biol Pharm Technol*, 2:280-284, 2011.
5. Madan AK, Orth WS, Tichansky DS, Ternovits CA: Vitamin and trace mineral levels after laparoscopic gastric bypass. *Obes Surg*, 16:603-606, 2006.
6. Ernst B, Thurnheer M, Schmid SM, Schultes B: Evidence for the necessity to systematically assess micronutrient status prior to bariatric surgery. *Obes Surg*, 19:66-73, 2009.
7. McKay J, Ho S, Jane M, Pal S: Overweight & obese Australian adults and micronutrient deficiency. *BMC Nutr*, 6:12.2020.
8. Kimmons JE, Blanck HM, Tohill BC, Zhang J, Khan LK: Associations between body mass index and the prevalence of low micronutrient levels among US adults. *MedGenMed*, 8:59, 2006.
9. Kiani AK, Dhuli K, Donato K, et al: Main nutritional deficiencies. *J Prev Med Hyg*, 63:E93-E101, 2022.
10. Damms-Machado A, Weser G, Bischoff SC: Micronutrient deficiency in obese subjects undergoing low calorie diet. *Nutr J*, 11:34, 2012.
11. Afzal M, Siddiqi N, Ahmad B, et al: Prevalence of overweight and obesity in people with severe mental illness: Systematic review and meta-analysis. *Front Endocrinol*, 12:769309, 2021.
12. Sugai T, Suzuki Y, Yamazaki M, et al: High prevalence of obesity, hypertension, hyperlipidemia, and diabetes mellitus in Japanese outpatients with schizophrenia: A nationwide survey. *PLoS One*, 11:e0166429, 2016.
13. Hagane Y, Kiuchi S, Ihara H, Sihoya N, Hashizume N: Clinical nutritional studies on atherosclerosis risk factors in hospitalized patients with schizophrenia [Jpn]. *New Diet Ther*, 39:3-17, 2023.
14. Correll CU, Lencz T, Malhotra AK: Antipsychotic drugs and obesity. *Trends Mol Med*, 17:97-107, 2010.
15. Smith E, Singh R, Lee J, Colucci L, Graff-Guerrero A, Remington G, Hahn M, Agarwal SM: Adiposity in schizophrenia: A systematic review and meta-analysis. *Acta Psychiatr Scand*, 144:524-536, 2021.
16. Lampl Y, Eshel Y, Rapaport A, Sarova-Pinhas I: Weight gain, increased appetite, and excessive food intake induced by carbamazepine. *Clin Neuropharmacol*, 14:251-255, 1991.
17. Ranganath HN: Carbamazepine and weight gain. *Neurology India*, 48:299, 2000.
18. Dayabandara M, Hanwella R, Ratnatunga S, Seneviratne S, Suraweera C, de Silva VA: Antipsychotic-associated weight gain: management strategies and impact on treatment adherence. *Neuropsychiatr Dis Treat*, 13:2231-2241, 2017.
19. Cohn TA and Sernyak MJ: Metabolic monitoring for patients treated with antipsychotic medications. *Can J Psychiatry*, 51:492-501, 2006.
20. Kodama H Itakura H Ohmori H Sasaki M Sando K Takamura T Fuse Y Hosoi T Yosida H: Practice guideline for zinc deficiency [Jpn]. *J Jpn Soc Clin Nutr*, 40:120-167, 2018.
21. Braun LA and Rosenfeldt F: Pharmaco-nutrient interactions - a systematic review of zinc and antihypertensive therapy. *Review Int J Clin Pract*, 67:717-725, 2013.
22. Japan Society for the Study of Obesity: Guidelines for the management of obesity disease 2022 [Jpn]. 1-27, Life Science Publishing, Tokyo (2022).
23. Ministry of Health, Labour and Welfare of Japan: Overview of the Dietary Reference Intakes for Japanese (2020) [Jpn]. https://www.mhlw.go.jp/stf/newpage_22536.html, accessed Aug 24, 2024.
24. Tanaka S, Horimai C, Katsukawa F: Ethnic differences in abdominal visceral fat accumulation between Japanese, African-Americans, and Caucasians: a meta-analysis. *Acta Diabetol, Suppl 1:S302-S304*, 2003.
25. The Committee of the Japan Diabetes Society on the

- Diagnostic Criteria of Diabetes Mellitus: Report of the committee on the classification and diagnostic criteria of diabetes mellitus. *J Diabetes Investig*, 1:212-228, 2010.
26. Japan Atherosclerosis Society: Japan Atherosclerosis Society (JAS) guidelines for prevention of atherosclerotic cardiovascular diseases 2022 [Jpn]. 19-28, 2022.
 27. Wu AHB: *Tietz Clinical Guide to Laboratory Tests*, 4th ed. Saunders, Elsevier, St. Louis, (2006).
 28. Jéquier E: Energy metabolism in human obesity. *Soz Präventivmed*, 34:58-62, 1989.
 29. James WP, Davies HL, Bailes J, Dauncey MJ: Elevated metabolic rates in obesity. *Lancet*, 27:1122-1125, 1978.
 30. Giskes K, Turrell G, Patterson C, Newman B: Socio-economic differences in fruit and vegetable consumption among Australian adolescents and adults. *Public Health Nutr*, 5:663-669, 2002.
 31. NguyenTQ, Maalouf NM, Sakhaee K, Moe OW: Comparison of insulin action on glucose versus potassium uptake in humans. *Clin J Am Soc Nephrol*, 6:1533-1539, 2011.
 32. Djurhuus MS, Skøtt P, Hother-Nielsen O, Klitgaard NA, Beck-Nielsen H: Insulin increases renal magnesium excretion: a possible cause of magnesium depletion in hyperinsulinaemic states. *Diabet Med*, 12:664-669, 1995.
 33. Kalaitzidis R, Tsimihodimos V, Bairaktari E Siamopoulos KC, Elisaf M: Disturbances of phosphate metabolism: another feature of metabolic syndrome. *Am J Kidney Dis*, 45:851-858, 2005.
 34. Grønli O, Kvamme JM, Friborg O, Wynn R: Zinc deficiency is common in several psychiatric disorders. *PLoS One*. 8:e82793, 2013.
 35. Yokokawa H, Fukuda H, Saita M, Miyagami T, Takahashi Y, Hisaoka T, Naito T: Serum zinc concentrations and characteristics of zinc deficiency/marginal deficiency among Japanese subjects. *J Gen Fam Med*, 21:248-255, 2020.
 36. Shimodaira M, Okaniwa S, Nakayama T: Reduced serum phosphorus levels were associated with metabolic syndrome in men but not in women: A cross-sectional study among the Japanese population. *Ann Nutr Metab*, 71:150-156, 2017.
 37. Stoian M, Stoica V: The role of disturbances of phosphate metabolism in metabolic syndrome. *Maedica*, 9:255-260, 2014.
 38. Hamano T: Kidney diseases and metabolic disorders-basic and applications required for general physicians. Topics: VII. Abnormality in phosphate metabolism [Jpn]. *Nihon Naika Gakkai Zasshi*, 104:953-959, 2015.
 39. Wong SK: A review of current evidence on the relationship between phosphate metabolism and metabolic syndrome. *Nutrients*, 14:4525, 2022.
 40. Singh S, Padi MH, Bullard H, Freeman H: Water intoxication in psychiatric patients. *Br J Psychiatry*. 146:127-311, 1985.