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Correlation between Neuropeptide Y and Vitamin D: Is It Related to Body Mass Index in Gender Difference?

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Abstract: One's appetite has a role in controlling food intake and maintaining energy balance, but its effect on body metabolism related to obesity is still questionable, especially in the sex difference. This study aimed to determine the correlation between neuropeptide Y and vitamin D and whether it is related to body mass index or not in healthy people and to see differences in gender difference. The goals were to understand orexigenic factors in the brain to be used to understand obesity. The scientific novelty was this study is the first to examine the correlation of brain neuropeptides that affect appetite with vitamin D, see how they are related to obesity, and compare between sexes. This study was a cross-sectional study of healthy males and females aged 18-60 who did not have chronic diseases or metabolic disorders. This research was conducted from April to July 2020 in North Sumatra Province, Indonesia. The parameters examined in this study were 25(OH)D serum levels, neuropeptide Y serum levels, and anthropometric parameters. The statistical analysis performed the correlation was the Spearman test. This study involved 62 study subjects; based on an anthropometric examination, it was found that obesity was more common in the female group than in the male group (p = 0.003). However, serum neuropeptide Y levels were significantly different between male and female groups (p = 0.001). There was also a considerably lower 25(OH)D serum level in the female group than the male group (p = 0.001). There was a positive correlation between neuropeptide Y and 25(OH)D serum levels and a negative correlation between neuropeptide Y and body mass index. The study found significant differences in serum neuropeptide Y levels in male groups but higher body mass index in female groups—many factors affecting obesity in females such as lower 25(OH)D serum level.

Keywords: obesity, appetite, sexes, orexigenic, 25(OH)D serum.

神經肽是和維生素D之間的相關性：它與性別差異中的體重指數有關嗎？

摘要：食慾具有控制食物攝入和維持能量平衡的作用，但其對與肥胖相關的身體代謝的影響仍然值得懷疑，尤其是在性別差異方面。本研究的目的是確定神經肽 Y 和維生素 D 之間的相關性是否與健康人的體重指數有關，並觀察性別差異的差異。目標是了解大腦中的促食慾因素，以便它們可以用於了解肥胖症。科學新穎之處在於，這項研究是第一個檢查影響食慾的腦神經肽與維生素 D 的相關性，了解它們與肥胖的關係並在兩性之間進行比較的研究。本研究是一項橫斷面研究，健康男性和女性，年齡 18-60 歲，沒有慢性疾病或代謝紊亂並發症。這項研究於 2020 年 4 月至 7 月在印度尼西亞北蘇門答臘省進行。本研究中檢查的參數是 25(哦)D

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血清水平、神經肽 Y 血清水平和人體測量參數。執行相關性的統計分析是斯皮尔曼檢驗。本研究涉及 62 名研究對象，根據人體測量學檢查發現，女性組的肥胖率高於男性組（磷=0.003）。然而，發現男性和女性組之間的血清神經肽是水平顯著不同（磷= 0.001）。女性組的 25(哦)D 血清水平也顯著低於男性組（磷=0.001）。神經肽Y與血清25(哦)D水平呈正相關，神經肽Y與體重指數呈負相關。研究發現，男性組血清神經肽 Y 水平存在顯著差異，但女性組的體重指數更高。許多影響女性肥胖的因素，例如較低的 25(哦)D 血清水平。

关键词：肥胖、食慾、性別、促食慾、25(哦)D 血清。

1. Introduction

Motivation and appetite are essential phenomena in maintaining energy balance and body weight [1, 2]. Increased appetite temporarily or permanently leads to weight gain, and thus the risk of obesity is more significant [3, 4]. As the center of hunger and fullness, the hypothalamus produces neuropeptide Y as a potent anabolic peptide that increases appetite and reduces energy consumption [1, 5].

Previous studies have shown no difference in neuropeptide levels in men and women, but some have shown different results [6, 7]. One study linked metabolic parameters, such as body mass index and blood pressure, and found no differences in neuropeptide Y levels between the sexes, which may have been due to a complex mechanism that still needs further research [8, 9].

Neuropeptide Y is a critical orexigenic neuropeptide that regulates adiposity by reducing energy storage and utilization [10]. Fasting conditions or low caloric intake stimulate neuropeptide Y expression, which increases appetite [10]. Neuropeptides are expressed mainly in the hypothalamus and peripheral tissues such as white fat tissue and bone cells, indicating several other physiological functions besides maintaining energy balance [10-12]. After reviewing the relevant research, it is clear that neuropeptide Y research is related to the accumulation and mobilization of lipids. These regulate peroxisome proliferator-activated receptor gamma 2 and hormone sensitive lipase (HSL) [12, 13]. If neuropeptide Y levels are reduced, the factors that cause imbalance age-related adipose tissue metabolism increases, such as decreased increased inflammation, decreased de novo lipogenesis in visceral fat, and decreased thermogenic activity in subcutaneous fat [13]. Low levels of neuropeptide Y did not affect adiposity in mouse studies, whereas some studies have found it humans while some have not [13-15]. For this reason, it is interesting to investigate whether there is a difference in neuropeptide Y levels in the associated factors in male and female groups.

Another factor that affects body mass index is the level of vitamin D in the body [16, 17]. Previous research has suggested that low vitamin D levels lead to obesity in healthy and patients with the infectious disease [18, 19]. However, other studies indicate that obesity causes low vitamin D levels in the body [16, 18, 20]. Research suggests the link between vitamin D deficiency and obesity because the body's deficiency can affect calcium absorption [21, 22]. Low calcium will stimulate the expression and activity of fatty acid synthase enzymes, stimulating lipogenesis and inhibiting lipolysis [23]. So the lower the vitamin D levels, it can lead to obesity. Different lifestyles between men and women make vitamin D levels different, so that this causes differences in the occurrence of obesity between men and women [24].

This study aimed to determine whether there were differences in neuropeptide Y levels in certain groups, namely social factors (age and sex) and metabolic parameters (body mass index, energy intake, and fat intake). This study aimed to determine the correlation between neuropeptide Y and vitamin D and whether it is related to body mass index or not in healthy people and to see differences in gender difference. The results of this study are expected to provide a new understanding of the differences in obesity between men and women.

2. Methods

2.1. Study Design

This study included a cross-sectional design that took sociodemographic data (i.e., age, ethnicity, sex, occupation, history obesity of father and mother), anthropometric examinations (i.e., body mass index and abdominal circumference), examination of daily food intake (i.e., energy, intake fat, protein intake, and carbohydrate intake per day), serum neuropeptide Y levels, and 25(OH)D serum level in the study subjects.

2.2. Participant

All research subjects were collected from areas far from urban areas in North Sumatra, Sumatra Island, Indonesia. We avoided issues from urban areas because they had a diverse diet. This research was conducted from April to July 2020, after the COVID-19 pandemic had spread across the globe, yet the study location has not had any COVID-19 cases. During the data collection period, it was also carried out by implementing strict health protocols.

The included research subjects were healthy men and women aged 18-60 years old. Exclusion criteria were pregnant women, nursing mothers, impaired kidney and liver function, chronic disease, or other metabolic disorders complication. Finding research subjects came by appealing to the local community health center and spreading word of mouth, wherein the subjects came voluntarily. When we selected research subjects, 96 research subjects were enrolled, but only 62 passed the exclusion criteria.

2.3. Anthropometric Examination

Anthropometry included height (to the nearest 0.5 cm), weight (to the nearest 0.1 kg), and body mass index (calculated as kg/m^2). Categorized body mass index (BMI) was based on Asia Pacific, which were <18.5 kg/m^2 classified as underweight, 18.5-22.9 kg/m^2 classified as normoweight, 23-24.9 kg/m^2 classified as overweight/at risk, 25-29.9 kg/m^2 classified as obese I, and >30 kg/m^2 classified as obese II [25].

We examined waist circumference using a standardized measuring tape in centimeters. The category of abdominal circumference was different between men and women. Less than 90 cm was classified as standard for men, and more than 90 cm was classified as central obesity. Less than 80 cm was classified as usual for women, and more than or equal to 80 cm was classified as central obesity [25].

2.4. Nutrient Intake Assessment

Assessment of nutrient intake was based on food recall for two days (one day for weekday and one day for the weekend), including energy, protein intake, fat intake, carbohydrate intake, and percentage of fulfillment according to the Indonesian Recommended Dietary Allowances (RDA) 2019. Calculations were conducted using the Nutrisurvey application (2005), which included Indonesian foods.

The following categorizations were determined: for calorie intake, < 2500 calories per day were low and ≥ 2500 calories per day were average; for protein intake, < 60 grams per day was low and ≥ 60 grams per day was normal; for carbohydrate intake, < 400 grams per day was low and ≥ 400 grams per day was normal; for fat intake, < 65 grams per day was low and ≥ 65 grams per day was normal; for fiber intake, < 25 grams per day was low and ≥ 25 grams per day was normal [26].

2.5. Neuropeptide Y Examination

This examination was conducted by drawing blood serum from research subjects and centrifugation with 2000-3000 revolutions per minute (RPM) for 20 minutes. Furthermore, we carried out blood serum tests to check neuropeptide Y levels using the Human Neuropeptide Y Enzyme-link Immunosorbent Assay (ELISA) kit (Thermo Fisher Scientific brand, Waltham, MA, USA) (Bioassay Technology Laboratory, Shanghai, China).

2.6. Vitamin D Examination

The tests carried out were examinations of 25 (OH) D levels of serum. The study was done by taking 5 mL of blood. The serum 25 (OH) D level is defined as a deficiency if below 10 ng/mL, insufficiency if between 11–20 ng/mL, and sufficiency if ≥20 ng/mL [27]. Examination of 25 (OH) D and 1.25 (OH) D serum and saliva was carried out using the Bio-Rad ELISA technology tool, California, United States of America, using the Enzyme-Linked Immunosorbent Assay (ELISA) kit, Brand Bioassay, Bioassay Technology Laboratory, Shanghai, China.

2.7. Ethics Approval and Consent to Participate

This study was conducted according to the guidelines laid down in the Declaration of Helsinki. All methods/procedures involving research study participants were registered with ClinicalTrials.gov (NCT04650308) with a date of recorded 18 November 2020. The Universitas Sumatera Utara Ethical Committee also approved this study. The Research Ethics Committee approved this research procedure and protocol of the University of North Sumatra, Indonesia, with the certificate number: No. 61/KEP/USU/2020. All participants knowledgeably consented to participate in this study; the research subjects had also read the explanation about the research and were willing to participate in the study by signing the informed consent form.

2.8. Sample Size and Power Calculation

The study sample sizes were chosen to demonstrate a correlation between neuropeptide Y and 25(OH)D serum level, neuropeptide Y and body mass index, and 25(OH)D serum level and body mass index. To determine the minimum sample size in each two-tailed hypothesis test, this study had a significance level of 0.05 (α-value) and 80% power (β-value). This study calculates all hypotheses and takes the largest sample size.

2.9. Statistical Analysis

Data were analyzed using version 11.5 of the IBM-SPSS statistical program (IBM Corp., Chicago, IL). Categorical variables were expressed as percentages. Normally distributed continuous variables were expressed as mean ± SD, whereas non-normally distributed continuous variables were expressed as median (minimum-maximum). To correlate the two parameters, the Pearson statistic test was used if the distribution was normal. Still, most of the data in this study were not a normal distribution, so the Spearman statistic test was used. A weak correlation was determined as 0.2 to <0.4, a moderate correlation was 0.4 to <0.6, and a strong correlation was 0.6 to <0.8. Positive correlation shows the direction of unidirectional correlation. The greater the value of one variable, the greater the value of the other variables. Whereas a negative correlation indicates the direction of the correlation is opposite, namely the greater the value of one variable, the smaller the value of the other variables.

3. Results

3.1. Baseline Characteristics of the Study Population

This oldest population of research subjects was aged 41-50 years old (35.5%). The youngest population was aging 20-30 years old (19.4%). Ethnic groups, namely the Indonesian Malay and Batak tribes, were evenly divided into two groups. These two tribes are the largest ethnic group found in North Sumatra, Indonesia (Table 1).

Table 1 Socio-demographic data of all subjects

Characteristics	N (%)	Mean ± SD
Age (years)		40.48±10.85
20-30	12(19.4)	
31-40	15(24.2)	
41-50	22(35.5)	
51-60	13(20.9)	
Ethnics		
Indonesian	31(50)	
Malay	31(50)	
Bataknese		
Gender		
Male	27(43.5)	
Female	35(56.5)	
Occupation		
Housewife	23(37.1)	
Labour	17(27.5)	
Farmer	9(14.5)	
Government	8(12.9)	
staff	5(8)	
Student		
Father's obesity		
history	52(83.9)	
No	10(16.1)	
Yes		
Mother's obesity		
history	45(72.6)	
No	17(27.4)	
Yes		

Notes:
Age data presented in mean and standard deviation
Others presented in a number of the subject and percentage

Table 1 shows that most subjects were women (56.5 vs. 43.5%), and the most common occupation was housewives (37.1%). The study was located in a rural area, so that the occupation of most adult women were housewives. Most males in this study were laborers (27.5%), an outstanding financial job in this region.

The history of obesity from patients' parents was also asked to see if there was a relationship to obesity in adulthood. Most patients did not have parents with obesity (83.9 vs. 72.6%) (Table 1). The analysis stated no significant relationship between the incidence of obesity and a history of obesity in the father (p = 0.738) and mother (p = 0.581).

3.2. Characteristic Data on Sex Differences Based on Neuropeptide Y, Vitamin D, and BMI

This study compared to age and anthropometric data between men and women, aiming to see differences between these two groups. This study showed that no significant differences were found between men and women in terms of age. In both groups, most patients were in the 41-50 age group (Table 2).

Table 2 Characteristic data of the subjects based on anthropometry status

Characteristics of anthropometry status	Male (mean ± SD)	Female (mean ± SD)	*p*
Age (years)	41.89 ± 10.98	39.40 ± 10.78	0.375
Categorized,			
n(%):	4(6.5)	8(12.9)	0.501
20-30	6(9.7)	9(14.5)	
31-40	9(14.5)	13(21)	
41-50	8(12.9)	5(8.1)	
51-60			
Body mass index (kg/m^2)	28.66 ± 16.31	25.15 ± 4.12	0.793
Categorized,			
n(%):	2 (3.2)	1(1.6)	0.727
Underweight	10(16.1)	13(21)	
Normal	2(3.2)	5(8.1)	
Overweight	13(21.0)	16(25.8)	
Obese			
Waist circumference (cm)	83.67 ± 10.3	82.6 ± 11.92	0.713
Categorized for			
male, n(%):	22(81.5)		
< 90 cm	5(18.5)		
> 90 cm			
Categorized for			
female, n(%):		16(45.7)	
< 80 cm		19(54.3)	
> 80 cm			

Notes:
Numeric data were presented in mean and standard deviation
Categorical data were presented in a number of the subject, and percentage
The analysis test for age and abdominal circumference used an independent t-test
Mann Whitney test was used to analyze body mass index

An anthropometric examination did not show any differences between the two groups of men and women. The obese group was more common in the female group than in the male group, but there was no significant difference (Table 2). Table 2 also shows no abdominal circumference difference between men and women, yet the percentage of abdominal circumference exceeded the standard limit more in the female group (54.3%). There was a difference between serum 25 (OH) D levels in the male and female groups. These results indicate that serum 25 (OH) D levels in women are significantly lower than in men (*p*=0.001). There was also a significant difference between neuropeptide Y serum levels in men and women.

In Table 3, based on food intake for two days, there was no difference between men and women, except in total energy (p = 0.019), wherein the average energy intake for women is higher than that of men. The information on fat, protein, and carbohydrates also showed that the intake of women was higher than men but did not show a significant difference.

Table 3 Characteristic data of the subjects based on food intake

Characteristics of food intake	Male (mean ± SD)	Female (mean ± SD)	*p*
Energy intake	1105.32 ± 577.77	1597.22 ± 939.89	0.019*
Categorized, n(%):	23(37.1)	34(54.8)	0.086
Less than 2500 kcal/day	4(6.5)	1(1.6)	
More than 2500 kcal/day			
Fat intake	39.21 ± 25.56	44.13 ± 41.42	0.809
Categorized, n(%):	4(6.5)	6(9.7)	0.805
Less than 65 gram/day	23(37.1)	29(46.8)	
More than 65 gram/day			
Protein intake	44.91 ± 18.48	56.10 ± 29.73	0.056
Categorized, n(%):	18(29)	29(46.8)	0.12
Less than 60 gram/day	9(14.5)	6(9.7)	
More than 60 gram/day			
Carbohydrate intake	39.21 ± 25.56	44.13 ± 41.42	0.809
Categorized, n(%):	27(100)	27(100)	-
Less than 400 gram/day	-	-	
More than 400 gram/day			

Notes:
*Significant: p < 0.005
Numeric data were presented in mean and standard deviation
Categorical data were presented in a number of the subject, and percentage
The analysis test for age and abdominal circumference used an independent t-test
Mann Whitney test was used to analyze body mass index

Table 4 shows the differences in neuropeptide Y levels in several parameters related to neuropeptide Y activity as orexigenic. The mean neuropeptide Y levels of all study subjects did not have a normal distribution, with the minimum value being 71.5 ng/L, the median value was 173 ng/L, and the maximum value was 846 ng/L. The neuropeptide Y level with the 5th percentile was 80.59 ng/L; the 10th percentile was 82.3 ng/L; the 25th percentile was 99.28 ng/L; the 50th percentile was 173 ng/L; the 75th percentile was 494.33 ng/L; the 90th percentile was 581 ng/L, and the 95th percentile was 668.25 ng/L. Table 4 shows that the differences in neuropeptide Y levels were found in the male and female groups.

Table 4 The difference in mean of Neuropeptide Y in groups

Neuropeptide serum level (ng/L)	N (%)	Median (minimum-maximum)	Mean ± SD	*p*
In:				
Male group	27(43.5)	121(71.5-981)	348.37 ± 330.09	0.036*
Female group	35(56.5)	100(71.5-938)	223.38 ± 244.62	
In:				
Non-obese group	33(53.2)	117(71.5-981)	278.18 ± 301.11	0.447
Obese group	29(46.8)	116(77.8-981)	277.39 ± 52.1	
In:				
Low fat intake group	52(83.9)	116(71.5-981)	270.18 ± 279.98	0.66
High fat intake group	10(16.1)	118.5(80.5-981)	317.45 ± 347.85	

Notes:
Data represented in mean ± standard deviation (SD)
Using Mann-Whitney test
*: significant; p < 0.05

The 25(OH)D serum level with the 5th percentile was 11.66 ng/mL; the 10th percentile was 14.09 ng/mL; the 25th percentile was 17.29 ng/mL; the 50th percentile was 19.3 ng/mL; the 75th percentile was 26.1 ng/mL; the 90th percentile was 28.65 ng/mL, and the 95th percentile was 28.85 ng/mL. There was a difference between serum 25 (OH) D levels in the male and female groups. It shows that the levels of neuropeptide Y differ in the insufficiency group and the vitamin D deficiency group.

This study also shows significant differences in neuropeptide Y serum level between the obese or non-obese groups, but not with the high and low fat intake groups. Based on the results of this study, it can be seen that neuropeptide Y showed significant differences in the male and female groups, vitamin D insufficiency and sufficiency, not obese and obese group, yet not in fat intake groups. This difference requires further discussion.

Table 5 showed that there was there is a strong correlation between serum neuropeptide Y levels and serum 25 (OH) D levels. It indicates a positive correlation. Meanwhile, the correlation between neuropeptide Y levels and body mass index is weak (r = 0.323) and harmful; however, this occurs in gender differences.

Table 5 Correlation among neuropeptide, vitamin D, and body mass index

Parameters	Correlation
Neuropeptide Y and 25(OH)D	r = 0.678 (positive)

serum level	p = 0.001* n = 62
25(OH)D serum level and body mass index	r = –0.279 (negative) p = 0.028* n = 62
Body mass index and neuropeptide Y level	r = –0.323 (negative) p = 0.010* n = 62

Notes:
All the correlation analysis using Spearman test

This result is contradictory because it may be caused by several factors, such as the influence of vitamin D levels, described in the scheme of factors affecting BMI (Fig. 1).

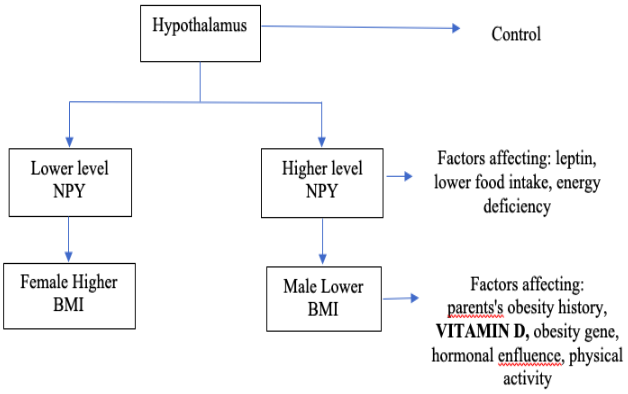

Fig. 1 Scheme of factors that affecting BMI

The scatter-plot graph outputs from Figures 2, 3, and 4 show that the data plot points form a straight line pattern from the bottom left up to the top right, showed a correlation among parameters. It can be concluded that there is a linear and positive relationship between levels of neuropeptide Y and serum 25(OH)D levels. This positive relationship means that if the neuropeptide Y level increases, the serum 25(O)D level will increase.

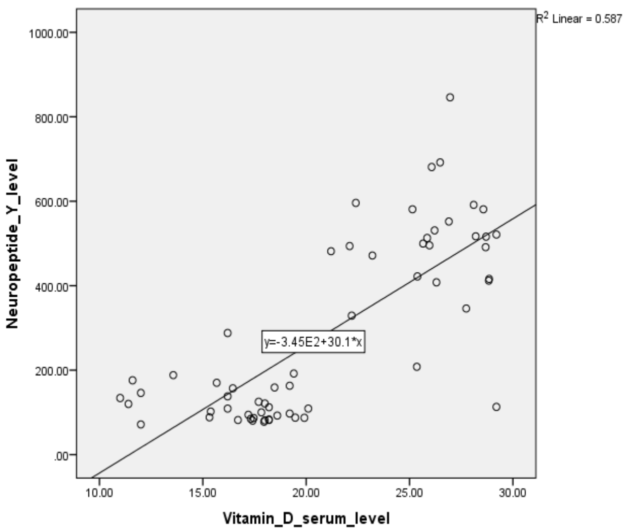

Fig. 2 Scatter plot of Neuropeptide Y and Vitamin D serum level

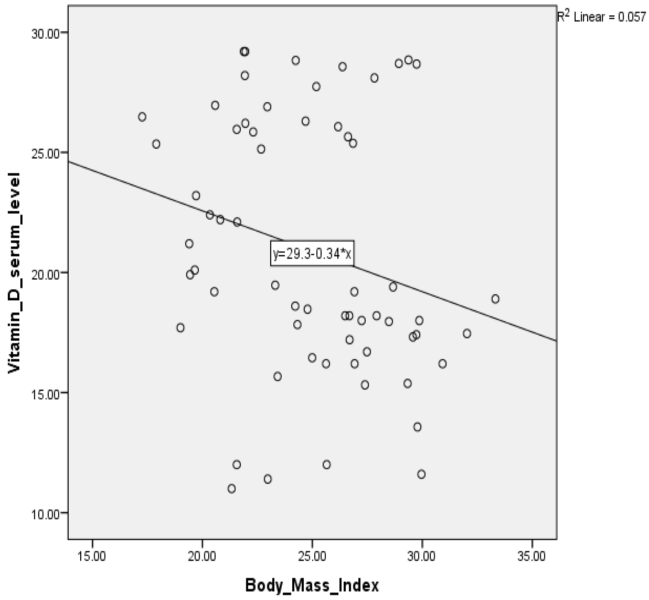

Fig. 3 Scatter plot of Vitamin D serum level and BMI

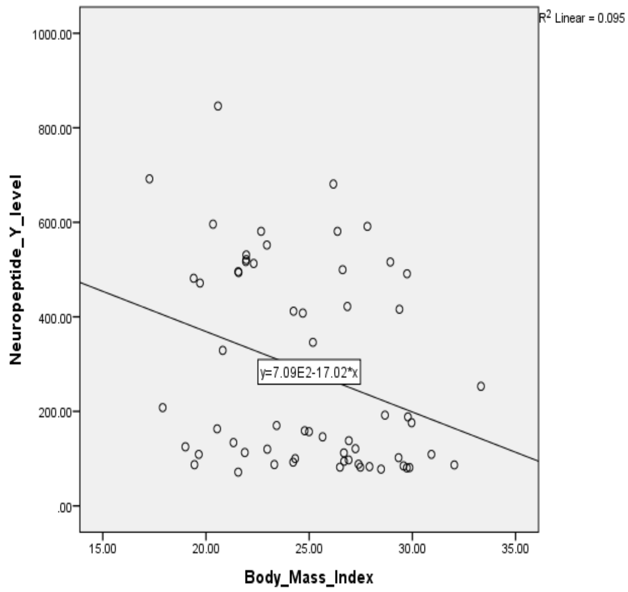

Fig. 4 Scatter plot of Neuropeptide Y and BMI

4. Discussions

Motivation and appetite are the basis for regulating energy balance and weight and can determine whether a person is obese or not [13]. Obesity is caused by consuming energy that exceeds basic needs; however, becoming obese is also influenced by several factors apart from high serum neuropeptide Y levels, including available food ingredients and diet. Residents in rural areas who are far from a high-fat diet will naturally consume the food available to them. It differs from urban areas that have more diverse foods.

High energy intake can be attributed to consuming too much saturated fat from red meat, animal fat, palm oil, or deep-fried foods. High-fat food ingredients are found in fast food, which is generally found in urban areas. However, in locations far from urban areas, excess energy intake comes typically from high carbohydrate consumption, consisting of rice, noodles, or sweet potatoes. Excess glucose is stored in the form of fatty acids. The role of neuropeptide Y does not seem to focus solely on high fat intake, but, in our study, it appeared that higher levels of neuropeptide Y were found in the male group.

Neuropeptide Y is an orexigenic peptide that plays an essential role in life extension. Calories also restrict it, and the mechanism is less clear [13]. Low neuropeptide Y levels combined with calorie restriction lead to the high mortality associated with lipolysis and lipodystrophy. Low levels of neuropeptide Y cause active lipolysis and thermogenic signals, i.e., Beta3 adrenergic receptors and sensitive lipase hormones in white adipose tissue. The result is a negative energy balance [10, 13]. The role of neuropeptide Y includes regulating lipid metabolic homeostasis and survival via lipolysis and thermogenesis control pathways in a negative balance [10].

Neuropeptide Y is an appetite stimulator that increases fat collection through insulin and corticosteroid secretion, increases hepatic glucose utilization, reduces muscle glucose, increases glucose utilization by white fat tissue, activates brown fat tissue metabolism, decreases sympathetic activity, increases parasympathetic activity, and decreases thermogenesis [2, 3]. Neurons containing neuropeptide Y become active during negative energy balance conditions such as hunger, dietary restrictions, breastfeeding, physical exercise, and uncontrolled diabetes [28]. Neuropeptide Y provides changes in eating behavior, but the role of neuropeptide Y receptors and their expression also affect appetite enhancement [29]. Seven subtypes of neuropeptide Y receptors, namely Y_1 to Y_7, are associated with stimulating appetites [30].

Neuropeptide Y changes one’s energy balance positively by increasing food intake, limiting energy expenditure, and reducing thermogenesis in brown fat tissue [31]. In parallel with this process, neuropeptide Y also facilitates fat storage in white fat tissue through increased insulin activity [2, 14]. However, in this study, various factors affect increased food intake. Based on our analysis, high levels of neuropeptide Y in serum did not directly correlate to obesity and fat intake. The condition of food shortages can be a direct cause of this, considering that most research subjects are laborers and housewives who live in rural areas.

Although the age of patients in this study was predominantly older (41–60), the total calorie intake was still low. The female group showed more obesity than the male group, and the female group also had larger abdominal circumferences. For women with hormonal influences, the combination of food availability and inactivity caused more significant obesity than men, even though the serum neuropeptide Y levels were significantly lower than men. It shows several factors that greatly influence the incidence of obesity in a person. In addition, hereditary factors influenced obesity, but this study showed that, when a person entered adulthood, there were multifactorial occurrences that increased their likelihood of becoming obese. High appetite also caused neuropeptide Y to be released by the hypothalamus [5, 32].

The history of obese parents did not correlate with patient obesity, although most patients did not have obese parents [32, 33]. Family history of obesity or metabolic disease played an important role, especially in childhood, associated with obesity [34]. Multifactorial lifestyles that provide the availability to consume high-fat or high-carbohydrate foods encourage a lack of physical activity, breakfast habits, or genetic polymorphisms independent of high and low levels of neuropeptide Y released by the hypothalamus [34-37]. All conditions are related to obesity and primarily impacted children entering adulthood [38]. Various processes can make a person obese, including the role of neuropeptide Y.

In this study, women had lower levels of neuropeptide Y than men, and previous studies suggested that women had lower expressions of neuropeptide Y than men in non-stressed states, significantly when their brains were associated with stress [8]. Further, estrogen levels play a potential role in its regulation [9, 39, 40]. Another possibility for appetite control is related to neuropeptide Y, which regulates depressive-like behavior. The effects of anxiety, however, are more common in men [39, 41]. Therefore, high levels of neuropeptide Y affect appetite if intake is not excessive.

Gender plays an essential role in the development of stress-induced psychological disorders [39]. Stress causes more traumatic disorders in men than in women. However, for other neuropsychiatric disorders, women have twice the vulnerability of men, such as post-traumatic stress disorder, depression, anxiety, and anorexia nervosa [39]. It also triggers the possibility that, in this study, there were no visible increases in body weight or high fat intake in the male group despite higher levels of neuropeptide Y in women.

Vitamin D is a fat-soluble vitamin found in fish oils and mushrooms; however, sunlight can help convert vitamin D under the skin [42]. Vitamin D will go through the hydroxylation process in the liver and kidneys to produce 1α, 25-dihydroxy vitamin D3 (1,25 (OH) D3), also called calcitriol [43]. This form binds to the vitamin D receptor (VDR), which forms a heterodimer with the retinoid X receptor and modulates gene expression [43]. Although vitamin D plays an essential role in calcium/phosphorus regulation and bone health, vitamin D also has important actions in immunity, inflammation, and differentiation [17, 44].

Based on previous research, research on vitamin D is often associated with obesity. These various possibilities include the role of vitamin D in increasing thermogenesis and levels of fat oxidation. This study showed that high levels of neuropeptide Y showed a positive correlation with vitamin D, indicating that if neuropeptide Y levels increased, serum 25 (OH) D levels would also increase. It is what causes a decrease in body mass index and is seen in males. Whereas in women, the neuropeptide levels are seen to be low but accompanied by low serum 25 (OH) D levels so that an increase in body mass index levels occurs. In women, several lifestyle factors that cause obesity are more likely besides hormonal problems and the influence of genes. Lifestyle such as low vitamin D intake, lack of physical activity, and avoiding sunlight are lifestyles that lead to obesity.

Understanding how vitamin D balances body weight is essential for creating effective strategies for using vitamin D in managing obesity and the role of neuropeptide Y. The brain, in particular the hypothalamus, is well known for weight control, especially appetite control, and is associated with neuropeptide Y. Thee results can show the correlation between neuropeptide Y and vitamin D. Still, it has to be better understanding about these results related to gender difference to managing obesity.

5. Conclusion

The study found significant differences in serum neuropeptide Y levels in the male and female groups, with neuropeptide Y levels being higher in men than in women. The study found significant differences in serum neuropeptide Y levels in male groups but higher body mass index in female groups.

The scientific novelty was this study is the first to examine the correlation of brain neuropeptides that affect appetite with vitamin D, see how they are related to obesity, and compare between sexes. This study is the first to look at differences in neuropeptide Y and vitamin D levels in men and women but gave contradictory results. On the one hand, there are high levels of neuropeptide Y correlated with vitamin D levels, which is a natural mechanism for a person to become obese. It occurs in men. However, these results show that it was first discovered that high levels of neuropeptide Y in men with high vitamin D levels did not necessarily indicate obesity.

This study is also the first to show that the results in men differ from those in women, low levels of neuropeptide Y, which of course indicates a low level of appetite, accompanied by low levels of vitamin D in the body. Low levels of vitamin D in the body cause a greater risk of obesity. This understanding should be the basis for handling different obesity management between men and women. Many factors are affecting obesity in females, such as lower 25(OH)D serum levels. It is hoped that by finding these results, there will be a new understanding of appetite in men and women. It will fulfill vitamin D intake, sunlight exposure, and increase physical activities, especially in women regardless of fat intake.

This study has limitations, which is this research subjects do not easily remember what they ate or drank on a given day, and some of the issues are afraid to report what they have consumed, especially in the male group. Another limitation was that we did not give information about vitamin D intake, parathyroid hormon serum levels, and calcium level, so it did not describe the factors affecting vitamin D and neuropeptide Y serum levels.

Future research should attempt to obtain more accurate data. Our findings provide important insights into the role of neuropeptide Y in the occurrence of obesity, especially in sex differences. This study's results can be the basis for further research on obesity management or lifestyle changes related to gender differences.

The research perspective of this study is to understand the differences in the management of obesity based on gender. Additionally, this research, In addition, the study looks at the role of vitamin D in the brain and affects neuropeptide Y.

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