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Original Research Article

Dietary intake of mother in childbearing age with BMI <18.5 kg/m^2 and has heterozygous variant D327N SHBG genotype (w/v)

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ABSTRACT

Background: Body mass index (BMI) determined by genetic and environmental factors. One of the genetic factors that determine the BMI is a genetic polymorphism of sex hormone binding globulin (SHBG), whereas the intake of nutrients is one of the environmental factors. The objective: investigate to macronutrient intake of mother in childbearing age with BMI <18.5 kg/m^2 and has heterozygous variant D327N SHBG genotype (W/v).
Methods: Anthropometric measurement, genotyping of D327N SHBG gen exon 8, and three days repeated food recall and record was done for all subjects. BMI in the group I 16 to <17 kg/m^2 and group II 17 to <18.5 kg/m^2. For all subjects in both groups has heterozygous variant D327N SHBG genotype (W/v).
Results: mother in chieldbearing age with BMI <18.5 kg/m^2 and has heterozygous variant SHBG genotype (W/v) is undernutrition. Seventy two percent of the total subjects including type I of chronic energy deficiency (CED), and 28% as type II of CED. Protein, fat and carbohydrate intake and mid-upper arm circumference (MUAC) in the group I was lower than group II ($p<0.05$), while muscle mass in the group I did not different compare to group II ($p>0.097$).
Conclusions: Mother in childbearing age with BMI <18.5 kg/m^2 and has heterozygous variant D327N SHBG genotypes (W/v) shows that the lower of protein, fat and carbohydrate intake then CED status is getting low.

Keywords: BMI, Bbs-I enzyme, CED, Dietary intake, SHBG genetic polymorphism

INTRODUCTION

Body mass index (BMI) is determined by genetic and environmental factors.[1] One of the genetic factors that determine the BMI is a genetic polymorphism of sex hormone binding globulin (SHBG), whereas the intake of nutrients is one of the environmental factors. Results of previous studies show that the lower of lipid-protein intake also lower the BMI, and it is also shown that human with a low-protein diet had the levels of SHBG serum is higher.[2] Genetics factor appears to play an important role in explaining the variability in BMI in the adolescence, with slight variations between boys and girls.[3] SHBG genetic polymorphisms may occur due to a point mutation of exon 8. The missense mutation in exon 8 causing transition of guanin to adenin (1066 G→A = GAC→AAC), that causing the amino acid exchange aspartate (asp) to asparagine (asn) in codon 327 (D327N)(rs6259).[4]

Genetic polymorphism in the SHBG gene, altering production and/or metabolism, may also contribute to

individual SHBG concentration variation. In the circulation, steroid bind to albumin, SHBG, cortisol-binding globulin (CBG) and as free testosterone.[5-7] Only free testosterone will be use on target cell.[8] In women, the serum levels of SHBG influence free estrogen levels and activity on target tissues.[9] Genetic polymorphisms of D327N SHBG showed that the half-life of SHBG molecule in variant SHBG genotypes (heterozygote variant SHBG and homozygote variant SHBG) was higher than normal SHBG genotype.[10] It increases SHBG levels in the circulation, so that more free testosterone binding, that is causing free testosterone less be used by the target cells, including muscle and bone. Futher more, result of the other research show that testosterone increases mass and strength muscle.[11] In human, the response to steroid at several junctures regulated by SHBG.[12] Beside that, nutrient content (isoflavone) in the diet effect to SHBG levels in the circulation.[13] We suspect that D327N SHBG genetic polymorphism had correlation to muscle and bone formation. Reduction in the formation of muscle and bone mass certainly BMI would decrease.

Result of research show that common environmental factors exert their influence on BMI only in girls.[3] One of the enviromental factors to influence on BMI is chronic energy deficiency (CED). CED status if BMI <18.5 kg/m^2 while a BMI 18.5 kg/m^2 or over as not CED. More over, the risk of CED if mid-upper arm circumference (MUAC) <23.5 cm.[14] Additional research shows that mothers who CED so BMI is low, are at risk of having a baby with low birth weight (LBW). A fact generally indicates that LBW infants was associated with a lower BMI mother.[15]

Indonesian population in 2010 amounted to 237.55 million, which is experiencing stunting (chronic malnutrition) 35.6% and wasting (acute malnutrition) 13.3%.[16] Until now, the problem of malnutrition is still a major problem in Indonesia. Futhermore, characteristic of Indonesian diet where as high carbohydrate and low lipid-protein intake. This fact coresponds to statement that the consumption of foods higher in nutrient-dense carbohydrate and lower in animal protein and saturated fat is associated with lower total energy intakes, more favorable micronutrient intakes, and lower BMI.[17]

Allegedly, mother in chieldbearing age with BMI <18.5 kg/m^2 have characteristics that low nutrient intake and genetic polymorphisms of SHBG is specific. Aims of this study to investigate dietary intake of mother in chieldbearing age with BMI <18.5kg/m^2 and has heterozygous variant D327N SHBG genotype (W/v).

METHODS

Research design

It is a cross-sectional study design

Ethical clearance

This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, University of Indonesia. Before participating in this study, all subjects gave written informed consent.

Sample size

Number of samples for each group have been calculated. The minimum amount for each group of 26 subjects. In this study, in the groups I using 56 subjects while in the group II using 144 subjects.

Study subjects

Two hundred subjects were Indonesian mother residing in West-Jakarta as participants in this study. Inclussion criteria as follow: age 18 - 35 years, BMI 16 to <18.5 kg/m^2, healthy represented by physical examination by doctor, blood serum fasting glucose 70 - 105 mg/dL, triglyceride 40 - 160 mg/dL and albumin 3.5 - 5.3 g/dL. Three days repeated foord recall & record was done to all subjects. For all subjects has heterozygous variant D327N SHBG genotype.

Exclusion criteria include poly-cistic ovary syndrome (PCOS), liver cirrhosis, drugs such as: diazoxide, epinephrine, cortisol, progestin and sulfonylureas. The subject will be exclude in this study if subject is not present during the retrieval of research data and lysis blood samples. Collection of blood samples from August - November 2014.

Blood analysis

Fasting blood collected in the morning from all subjects. Venous blood drawn from vena cubiti. Ten milli-liters venous blood divided into 2 tubes. First tube collected of 8 milli-liters venous blood, and the second tube is EDTA tube + 2 milli-liters venous blood. Serum from 8 milli-liters venous blood was isolated by centrifugation at 15.000 rotation per minute (rpm) for 20 minutes and stored at -20 °C. Measurement of glucose, triglyceride and albumin levels in the blood serum were carried out at the Laboratory of Medika Prima, Jakarta, Indonesia. Blood in the EDTA tube to determine SHBG genotyping. SHBG genotyping was done in Laboratory of Molecular Biology, Faculty of Medicine, University of Gajah Mada, Yogyakarta, Indonesia. SHBG gen exon 8 sequencing to confirmation of missene mutation 1066 G→A.

Measurement of glucose

The glucose levels in the blood serum performed with Glucose GOD-PAP Single Reagent (DIALAB Produktion und Vertrieb von chemisch-technischen Produkten und Laborinstrumenten Gesellschaft mbH). Humalyzer 2000 (Human) photometer as an instrument used to measure of glucose levels in the blood serum.

Coefisient of variation (CV) intra assay in this study 2.4% and CV inter assay 1.3%.

Measurement of triglyceride

The triglyceride levels in the blood serum performed with triglyceride-GPO-PAP with Advanced Turbidity Clearing System (ATCS) Single Reagent (DIALAB Produktion und Vertrieb von chemisch–technischen Produkten und Laborinstrumenten Gesellschaft mbH A-2351 Wiener Neudorf, Austria). Humalyzer 2000 (Human) photometer as an instrument used to measure of triglyceride levels in the blood serum. CV intra-assay in this study 1.78% and CV inter assay 1.26%.

Measurement of albumin

The albumin levels in the blood serum performed with albumin liquicolor, photometric colorimetric test bromcresol green (BCG) method (Human Gesellschaft für Biochemica und Diagnostica mbH Max-Plack-Ring 21-D-65205 Weiesbaden-Germany). Humalyzer 2000 (Human) photometer as an instrument used to measure of albumin levels in the blood serum. CV intra assay in this study 2.92% and CV inter assay 1.31%.

DNA integrity

Blood samples in EDTA tubes of 0.1 mmol/L were stored at -20° C, acclimatized beforehand at room temperature for 15 minutes. Test the integrity of DNA from each sample was performed using Genomic DNA Mini Kit (Blood/Cultured Cell) GB100/GB300. After extraction, measurement of DNA purified using a spectrophotometer at a wavelength (λ) 260 nm and DNA integrity test using gel electrophoresis 2%.

Analysis of SHBG gene exon 8

Two milli-liters (mL) blood sample was done from each subject. Blood colected into EDTA tube 0.1 mmol/L. DNA from each sample extracted using Genomic DNA Mini Kit (Blood/Cultured Cell) GB100/GB300. After extracted, purified DNA amplification using primers 5'-CTG GAT CCG AGC CAC CTT AA-3' (forward) and 5'-GCC TGG TAC ATT GCT AGT GC-3' (reverse). KAPA Taq Ready Mix PCR Kit KR0354-v5.13 reagent used in the study. Mix PCR composition as follow 7.4 µL dH_2O, 10 µL KAPA Tag, 0.8 µL primer of SHBG forward (10 µM), 0.8 µL primer of SHBG reverse (10 µM) and 1 µL sample of DNA. PCR machine Biorad C1000 program as follow: 95°C 3 minute 1 cycle; 95°C 30 second, 60,1°C 30 second, 72°C 1 minute 35 cycle and 4°C -1 cycle.

SHBG gen exon 8 analyzis by RFLP with Bbs-I enzyme. Mix digestive composition as follow 7.8 µL dH_2O, 2 µL 10 XNE buffer, 0.2 µL Bbs-I enzyme and 5 µL PCR product. Incubation at 37°C for 1 hour and then were done gel electrophoresis 3% for 45 minutes.

RESULTS

Subjects characteristic

Subjects residing in Tegal Alur Village, Kalideres District, West Jakarta, Special Capital Region of Jakarta, Indonesia (map in Figure 1). Characteristics of the subjects are presented in Table 1.

Table 1: Characteristics of the subjects.

Variable	Mean±SD
Age (years)	25.90±5.66
Body weight (kg)	40.30±3.13
Body high (cm)	151.79±5.79
BMI (kg/m^2)	17.50±1.02
MUAC (cm)	23.25±1.79
Muscle mass (kg)	30.63±8.74
Glucose (mg/dL)	72.39±9.57
Triglyceride (mg/dL)	75.36±16.46
Albumin (g/dL)	4.5±0.37

Abbreviations: BMI = body mass index; MUAC = mid-upper arm circumference; kg = kilo gram; cm = centi meter; kg/m^2 = kilo gram per meter square; mg/dL = milli gram per deci liter; SD = standard of deviation.

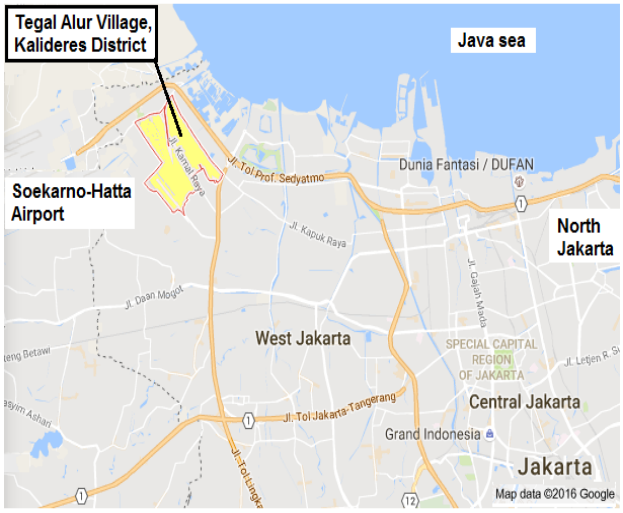


Figure 1: Map of Tegal Alur Village, Kalideres District, West Jakarta, Special Capital Region of Jakarta, Indonesia (Source: Map data 2016 Google with modification).

DNA integrity

DNA intergrity by electrophoresis show in Figure 2. DNA and protein levels in the sample show in Table 2. DNA integrity of the samples was quite nice, it is seen on electrophoresis and measurements of DNA content. The higher levels of DNA (Table 2) than the thick band on electrophoresis (Figure 2). The results of DNA integrity in the form of purified DNA to be used for the genotyping of SHBG gene exons 8.

Table 2: DNA and protein levels.

	Absorbance	Ratio	DNA concentration (µg/ml)	Protein concentration (µg/ml)
19	0.018	0.433	2	0.9
20	0.021	0.493	2.3	0.9
22	0.027	0.86	5.6	1
23	0.016	0.316	1.3	0.9
24	0.013	0.39	1.8	0.9
25	0.013	0.056	0.2	0.8
26	0.02	0.549	2.9	1

Abbreviations: DNA = deoxyribo nucleic acid; µg/mL = micro gram per milli liter.

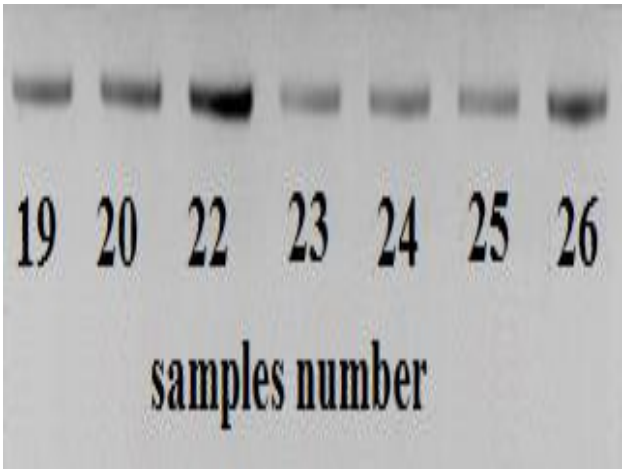
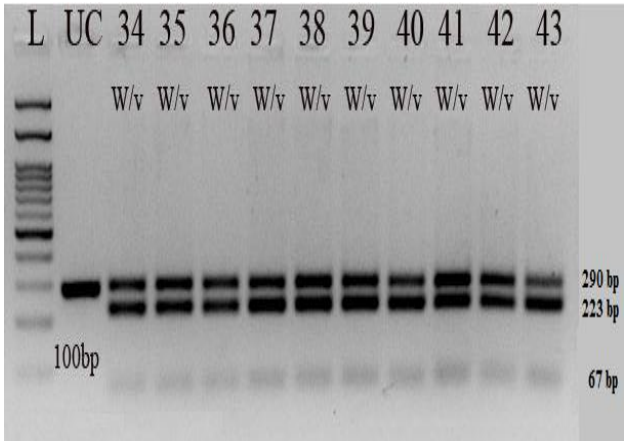


Figure 3: DNA integrity by electrophoresis.

Genotyping of SHBG gen, exon 8 by Bbs-I enzyme show in Figure 3. PCR product of human SHBG gen exon 8 (290 base pair) was digestive by Bbs-I enzyme that result 3 fragment of DNA such as 290, 223, and 67 bp. Base on the fact show that genotype of SHBG gen exon 8 is heterozygote variant (W/v). The result of RFLP by Bbs-I enzyme corespons with sequencing result of SHBG gen exon 8 on Figure 4.

Sequencing of SHBG gen exon 8 show that missense mutation [A/G] on rs6259 (*Homo sapiens*). This result of sequencing corespons with RFLP by Bbs-I enzyme to SHBG gen exon 8.



Abbreviations: L = marker; UC= DNA PCR product without Bbs-I enzyme; 34-43 = DNA PCR product with Bbs-I enzyme; W/v = heterozygous variant SHBG genotype; bp = base pair.

Figure 4: Genotyping of SHBG gen exon 8 by Bbs-I enzyme.

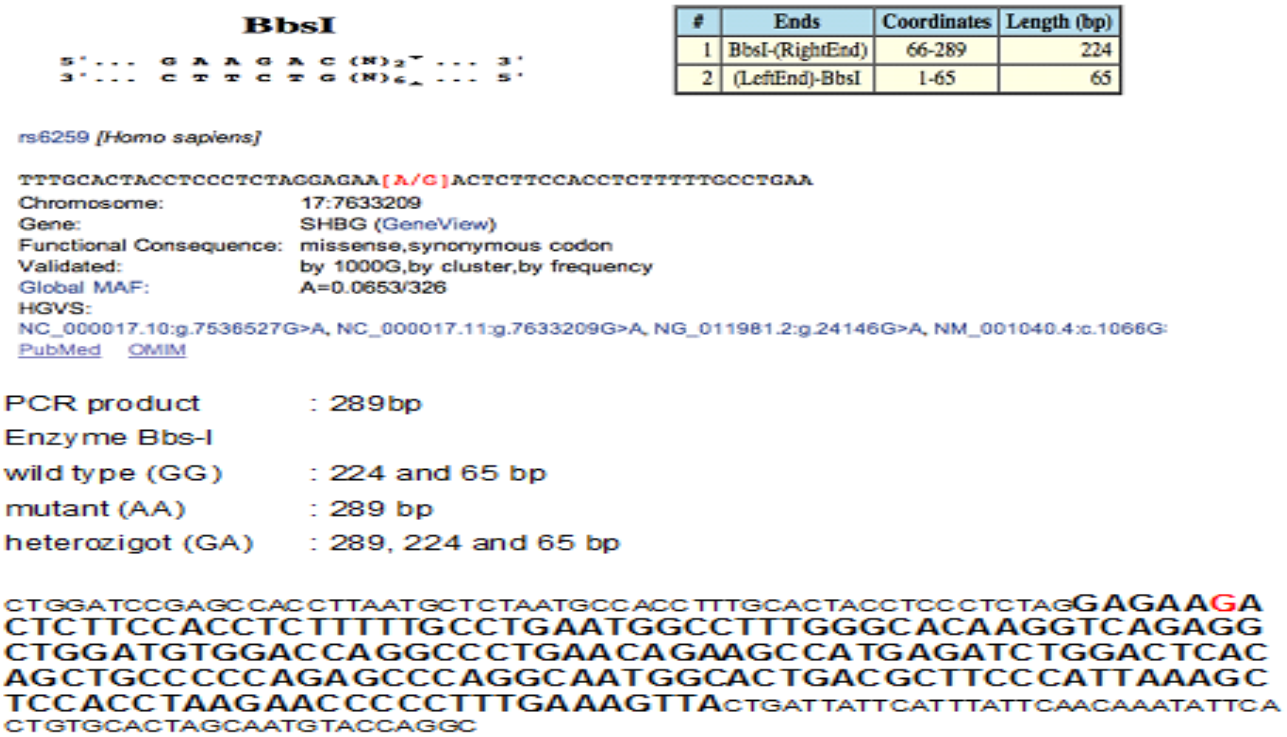
Comparison of antrhopometric between group I and II show in Table 3. Subjects in this study classified as undernutrition with BMI <18.5 kg/m^2. Group I included CED type I with BMI 17 to <18.5 kg/m^2 as much as 72%, while the second group included CED type II with BMI 16 to <17 kg/m^2 as much as 28%. MUAC in the group I was lower compare to group II (p <0.000), while muscle mass in the group I did not different compare to group II (p >0.097).

Table 3: Comparison of anthropometrics between group I and II.

Variables	Group I (mean± SD)	Group II (mean±SD)	p
Height (cm)	155.10 ±4.90	150.65±5.64	0.000
Weight (kg)	38.69±2.78	40.91±3.04	0.000
BMI (kg/m^2)	16.07±0.74	18.00±0.43	0.000
MUAC (cm)	22.28 ±1.30	23.63±1.81	0.000
Muscle mass (kg)	29.54 ± 2.51	31.06±10.16	0.097

Abbreviations: BMI = body mass index; MUAC = mid-upper arm circumference; kg = kilo gram; cm = centi meter; SD = standard of deviation; p = significancy.

Comparison of dietary intake between group I and II show in Table 4. Protein, fat and carbohydrate intake group I was lower than group II ($p<0.05$). The percentage of protein, fat and carbohydrate group I compared to group II did not differ ($p>0.05$), as well as the ratio of protein and carbohydrate, the ratio of fat and carbohydrate, the ratio of protein and fat gorup I compared to group II did not differ ($p>0.05$).



Abbreviations: Bbs-I = restriction endonucleases from *Bacillus laterosporus*; shbg = sex hormone binding globulin; pcr = polymerase chain reaction; bp = base pair; A = adenin; T = timin; C = cytosine; G = guanine.

Figure 5: Sequencing of SHBG gen, exon 8.

Table 4: Comparison of macronutrient intake between group I and II.

Variables	Group I (mean ± SD)	Group II (mean ± SD)	p
Total of energy (kcal)	999.57 ± 134.35	1223.00 ± 242.96	0.000
Protein (gr)	33.64 ± 5.49	42.38 ± 11.8	0.000
Energy of protein (cal)	134.56 ± 21.97	169.53 ± 47.22	0.000
% of protein (%)	13.59 ± 2.32	13.92 ± 3.11	0.412
Fat (gr)	30.14 ± 7.88	39.11 ± 12.58	0.000
Energy of fat (cal)	271.28 ± 70.96	351.95 ± 113.21	0.000
% of fat (%)	27.14 ± 6.01	28.52 ± 6.14	0.150
Carbohydrate (gr)	148.44 ± 28.72	175.49 ± 38.69	0.000
Energy of carbohydrate (cal)	593.73 ± 114.87	701.93 ± 154.76	0.000
% of carbohydrate (%)	59.26 ± 6.87	57.55 ± 7.18	0.122
Ratio of protein-carbohydrate	0.23 ± 0.06	0.23 ± 0.08	0.151
Ratio of fat-carbohydrate	0.47 ± 0.16	0.52 ± 0.18	0.119
Ratio of protein-fat	0.52 ± 0.14	0.51 ± 0.16	0.628

Abbreviations: kcal = kilo calorie; gr = gram; cal = calori; % = percent; SD = standard of deviation; p = significancy.

DISCUSSION

Fasting blood glucose levels in this study included in the range of normal value. Normal value of glucose levels in the blood serum 70 to 115 mg/dL.[18] Fasting blood triglyceride levels in this study included in normal value. Normal value of triglyceride levels in the blood serum <200 mg/dL.[19] Result of the other study show that Indian healthy women with age 25 to 35 years has triglyceride levels 68.90±24.08 mg/dL.[20] The levels of albumin serum in this study included in the normal value and non hypoalbuminemia. Normal value of albumin levels in the blood serum as 3.5 to 5.0 g/dL, while levels <3.5 g/dL is called hypoalbuminemia.[21] The other study in nonpregnant nulliparaus women show that albumin levels 4.0 ± 0.037 g/dL.[22]

In this study area, we are not difficult to find subjects as a mother in childbearing age (MCA) has average 25.9±5.66 years with characteristic of BMI <18.5 kg/m^2. This data shows that a lot of mother in MCA with CED in this study area. This situasion are still a commonly found in the other area in Indonesia. We use BMI as an indicator for the assessment of nutritional status of adults because uses two indicators of growth as follow body weight and height. That is corespons to statement that body weight is a measure of the growth of tissue mass and height is a measure of linear growth.[16] More over, BMI is generally considered a good indicator of not only the nutritional status. Beside that, BMI for adult nutritional status assessment to define of CED status, also define to the poor demographic, socio-economic and environmental conditions of the population, especially adult population of developing countries.[23]

For all subject in this study has heterozygote variant D327N SHBG genotype (W/v). PCR product of human SHBG gen exson 8 were 290 base pair (bp) in this study was digest by Bbs-I enzyme to detect D327N mutation. Genotyping result of D327N SHBG gen exon 8 in this study corespons with the other study.[5, 11] We suspect that the number of individuals in the population who have a heterozygote variant D327N SHBG genotype much more than the homozygote variant D327N SHBG genotype. Our guess is consistent with the results of the study stating that women, allele frequency for W = 0918, v = 0082 and the distribution of phenotype W/W = 233, W/v = 41, and v/v = 2 (p =0.031).[11]

Individuals with homozygote and heterozygote variant D327N SHBG genotype produce variant SHBG molecule as phenotype. Two form of SHBG molecule phenotype were as normal and variant SHBG molecule. Although the variant SHBG molecule does not influence to SHBG levels, but the levels of insulin in individuals with variant SHBG phenotype was higher than normal SHBG phenotype.[24] This fact could be an early indication to the action mechanism abnormality of insulin. Therefore it is necessary to examine the levels of SHBG, tetosterone and insulin in Indonesian mother in childbearing age with BMI <18.5 kg/m^2.

Subjects in this study included underweight thinnes mild group. BMI in the group I was lower compare to group II. We following cut-off points of BMI for thinnes mild underweight were used 17 to 18.49 kg/m^2 (WHO, 1995).[25] Result of the other study showe that the women with low BMI had given birth to about 10% of severe wasting children.[15]

Undernutrition for all subjects in this study generally as a problem in among rural women of reproductive age in Indonesia. As in other countries, the current study showed high prevalence of CED among women of reproductive age. CED in women of reproductive age were found to have associated with factors such as age at first marriage, meal frequency, household food insecurity, dietary intake, and time to fetch drinking water collection.[26] More over, the recent research indicates that 60% of deaths of children under age 5 years are associated with malnutrition, and children's malnutrition is strongly correlated with mothers poor nutritional status.[27]

All subjects in this study is low MUAC base on the guidelines with cut-off point <23.5 cm. Another study in Tanzania using a cut-off point for low MUAC ≤25 cm,[28] while in Malawi using a cut-off point <23 cm.[29] In this study, MUAC in group I was lower compare to group II (p=0.000) (Table 3). Subjects in both groups are certainly at risk of SGA, LBW and preterm birth. We suspect that subjects at group I have a higher risk for SGA, LBW and preterm birth than in group II. In addition, low MUAC associated with BMI <18.5 kg/m^2. Moreover, there was a significant positive association between MUAC and BMI.[30] The research was supported by the results of other studies stating that MUAC has a positive correlation with BMI.[31]

In this study, muscle mass in group I compare to group II was not different (p = 0.097). The other research show that BMI greatly increases with their muscle mass.[32] Moreover, nutrients in the diet, such as protein are associated with muscle mass.[33] A positive correlation was determined between total energy intake and muscle mass (r=0.384; p=0.003). Furthermore, protein and leucine intake positively correlated with muscle mass (r = 0.367 and 0.311, respectively; p = 0.005 for both).[34]

Protein, fat and carbohydrate intake in the group I was lower than group II, because that BMI and MUAC in the group I was lower than group II. Protein intake recommended for adults as part of a complete diet that is 1.5 to 2.2 g/(kg•day).[35] The other research show that mean daily intake of energy, protein and fat of non-vegetarians had higher compare to vegetarians, while mean daily carbohydrate consumption of non-vegetarians was lower compare to vegetarians. Because that BMI and MUAC of non-vegetarians more than vegetarians.[36] Due

to these conditions, low protein intake decrease BMI, according to the results of our research.[2]

Base on the data, Subjects in this study is undernutrition, then it should be performed of nutritional treatment in order to become a normal nutritional status. These recommendations in accordance with the statement of the researchers who suggest that mother in chieldbearing age get adequate levels of nutrient intake during pregnancy to reduce the risk of LBW.[37] The other study show that teenage girls are markedly underweight with little adipose tissue and depleted muscle mass. Furthermore, it was reported that this phenomena of high prevalence of adolescence pregnancy had resulted in increased risk of spontaneous abortion, a combination of fetal death and infant mortality in Saudi Arabia.[38]

Result of research showed that dietary intake of energy, fat, and protein may affect serum concentrations of sex hormone-binding globulin and testosterone.[39] Substitution of saturated fat (animal fats) by unsaturated fat (vegetable and fish fats) may also reduce serum testosterone concentration.[40] Excessive protein intake can lead to a lowered serum concentration of testosterone, especially when a low-fat diet is consumed.[31] We suggest that mother in childbearing age to be considered in terms of dietary intake so the metabolic processes involving SHBG and testosterone to normal, so the individual will have a normal BMI.

Limitations of this study include not assess lifestyle and socioeconomic status. Both of these may affect the dietary intake of the subject. This study also can not compare the dietary intake in the group of BMI <18.5 kg/m^2 with a normal BMI. We also did not know the percentage of subjects with a normal SHBG genotype, heterozygous and homozygous variant D327N SHBG genotype in the population at this area.

Based on the data that the mother in childbearing age in this study included undernutrition with BMI <18.5 kg/m^2 and has heterozygous variant D327N SHBG genotype. Seventy-two percent of the total subjects including type I of CED, while 28% as type II of CED. Protein, fat and carbohydrate intake and MUAC in the group I was lower than group II ($p < 0.05$), while muscle mass in the group I did not different compare to group II ($p > 0.097$).

CONCLUSION

Base on the fact we concluded that differences of dietary intake at mother in childbearing age with BMI <18.5 kg/m^2 and has heterozygous variant SHBG genotype (W/v) determine to status of CED, therefore that low protein, fat and carbohydrate intake then getting low of CED status.

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REFERENCES

1. Segal NL, Feng R, McGuire SA, Allison DB, Miller S. Genetic and environmental contributions to body mass index: comparative analysis of monozygotic twins, dizygotic twins and same-age unrelated siblings. Int J Obes (Lond). 2009;33(1):37-41.
2. Parwanto E. The influence of lipid-protein intake and sex hormone binding globulin (SHBG) polymorphism on the levels of SHBG at Indonesian and Caucasian men (in Indonesian language). Disertation, Faculty of Medicine, University of Indonesia. 2004.
3. Iranzo-Tatay C, Gimeno-Clemente N, Livianos-Aldana L, Rojo-Moreno L. Genetic and environmental contributions to body mass index in a Spanish adolescent twin sample. Med Clin (Barc). 2014;pii: S0025-7753(14)00467-9. doi: 10.1016/j.medcli.2014.05.039.
4. Power SG, Bocchimfuso WP, Pallesen M, Warmeis-Rodenhiser S, Van Baelen H and Hammond GL. Molecular analysis of human sex hormone-binding globulin variant: evidence for an additional carbohydrate chain. J Clin Endocrinol Metab. 1992;75:1066-70.
5. Klee GG, Heser DW. Techniques to Measure Testosterone in the Elderly. Mayo Clin Proc. 2000;75(Suppl):S19-S25.
6. Delehanty B, Hossain S, Jen CC, Crawshaw GJ, Boonstra R. Measurement of free glucocorticoids: quantifying corticosteroid-binding globulin binding affinity and its variation within and among mammalian species. Conserv Phys. 2015;3:1-13.
7. Brand JS, van der Tweel I, Grobbee DE, Emmelot-Vonk MH and van der Schouw YT. Testosterone, sex hormone-binding globulin and the metabolic syndrome: a systematic review and meta-analysis of observational studies. Int J Epid. 2011;40:189-207.
8. Hryb DJ, Khan MS, Romas NA and Rosner W. The control of the interaction of sex hormone-binding globulin with its receptor by steroid hormones. J Biol Chem. 1990;265:6048-54.
9. Riancho JA, Valero C, Zarrabeitia MT, García-Unzueta MT, Amado JA and González-Macías J. Genetic polymorphisms are associated with serum levels of sex hormone binding globulin in postmenopausal women. BMC Med Gen. 2008;9(112):1-6.

10. Cousin P, DéChaud H, Grenot C, Lejeune H, Pugeat M. Human variant sex hormone-binding globulin (SHBG) with an additional carbohydrate chain has a reduced clearance rate in rabbit. J Clin Endocrinol Metab. 1998;83(1):235-40.
11. Basaria S, Coviello AD, Travison TG, Storer TW, Farwell WR, Jette AM, et al. Adverse events associated with testosterone administration. N Engl J Med. 2010;363(2):109-122.
12. Kahn SM, Hryb DJ, Nakhla AM, Romas NA and Rosner W. Beyond carrier proteins: Sex hormone-binding globulin is synthesized in target cells. J Endocrinol. 2002;175:113-20.
13. Parwanto E, Indrawati Y, Setiawan H. Isoflavone supplementation reduced serum sex hormone binding globulin concentration in postmenopausal women. Univ Med. 2012;31(1):52-62.
14. Kalsum U, Sutrisna B, Djuwita R, Achadi EL, Jahari AB. A new alternative indicator for chronic energy deficiency in women of childbearing age in Indonesia. Health Sci Indones. 2014;2:54-9.
15. Kulasekaran RA. Influence of mothers' chronic energy deficiency on the nutritional status of preschool children in Empowered Action Group states in India. Int J Nutr Pharmacol Neurol Dis. 2012;2(3):198-209.
16. Balitbangkes (Badan Penelitian dan Pengembangan Kesehatan) Kementrian Kesehatan RI. Riset Kesehatan dasar (RISKESDAS). 2010.
17. Shay CM, Van Horn L, Stamler J, Dyer AR, Brown IJ, Chan Q et al. Food and nutrient intakes and their associations with lower BMI in middle-aged US adults: the International Study of Macro-/Micronutrients and Blood Pressure (INTERMAP). Am J Clin Nutr. 2012;96:483-91.
18. Thomas L. Clinical Laboratory Diagnostics. 1st ed. Frankfurt: TH-Books Verlagsgesellschaft. 1998:131-7.
19. NCEP (National Cholesterol Education Program), National Heart, Lung, and Blood Institute National Institutes of Health. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. NIH Publication, 2002; Sept No. 02-5215.
20. Deepti GI, Shetty S, Rao AV, Ahmad S. Age related difference in the lipid profile in normal healthy women. Nitte University J Health Sci. 2014;4(2):94-7.
21. Ishizuka M, Nagata H, Takagi K, Horie T, Kubota K: Inflammation-based prognostic score is a novel predictor of postoperative outcome in patients with colorectal cancer. Ann Surg. 2007;246:1047-51.
22. Begum JA, Sultana R and Naher S. Serum levels of total protein, albumin and globulin in women with hyperemisis gravidarum. J Dhaka Med Coll. 2010;19(1):58-60.
23. Pryer JA, Rogers S. Epidemiology of undernutrition in adults in Dhaka slum households, Bangladesh. Eur J Clin Nutr. 2006;60:815-22.
24. Parwanto MLE, Suweino S, Tjahjadi D, Senjaya H, Edy HJ, Pakpahan A. The effect of sex hormone binding globulin (SHBG) protein polymorphism on the levels of SHBG, testosterone, and insulin in healthy Indonesian men. Int J Med Sci Public Health. 2016;5:799-806.
25. WHO (World Health Organization). Physical status: The use and interpretation of anthropometry. Technical Report Series No. 854. Geneva 1995.
26. Abraham S, Miruts G and Shumye A. Magnitude of chronic energy deficiency and its associated factors among women of reproductive age in the Kunama population, Tigray, Ethiopia, in 2014. BMC Nutr 2015;1(12):1-9.
27. Pelletier DL, Frongillo EA. Changes in child survival are strongly associated with changes in malnutrition in developing countries. J Nutr. 2003;133:107-19.
28. Villamor E, Msamanga G, Spiegelman D, Peterson KE, Antelman G, Fawzi WW. Pattern and Predictors of Weight Gain during Pregnancy among HIV-1-Infected Women from Tanzania. JAIDS: J Acq Imm Def Syndr. 2003;32(5):560-9.
29. Verhoeff FH, Brabin BJ, van Buuren S, Chimsuku L, Kazembe P, Wit JM, et al. An analysis of intra-uterine growth retardation in rural Malawi. Eur J Clin Nutr. 2001;55(8):682-9.
30. Chakraborty R, Bose K, Bisai S. Mid-Upper Arm Circumference as a Measure of Nutritional Status among Adult Bengalee Male Slum Dwellers of Kolkata, India: Relationship with Self-Reported Morbidity. Anthropol Anz. 2009;67(2):129-37.
31. Abrhame T, Haidar J. The sensitivity and specificity of mid-upper arm circumference compared to body mass index in screening malnutrition of adult HIV patients taking ART; evidence from selected facilities of Addis Ababa, Ethiopia. Sci J Publ Health. 2014;3(1):19-24.
32. Jelena J, Baltic ZM, Milica G, Jelena I, Marija B, Milka P, Mirjana L. Relationship between Body Mass Index and Body Fat Percentage among Adolescents from Serbian Republic. J Childhood Obes. 2016;1(2):1-5.
33. Scott D, Blizzard L, Fell J, Giles G and Jones G. Associations between dietary nutrient intake and muscle mass and strength in community-dwelling older adults: the Tasmanian Older Adult Cohort Study. J Am Geriatr Soc. 2010;58(11):2129-34.
34. Calvani R, Martone AM, Marzetti E, Onder G, Savera G, Lorenzi M, et al. Pre-hospital dietary intake correlates with muscle mass at the time of fracture in older hip-fractured patients. Front Aging Neurosci. 2014;6(269):1-6.
35. Pencharz PB, Elango R, Wolfe RR. Recent developments in understanding protein needs – How much and what kind should we eat? Appl Physiol Nutr Metab. 2016;41:577-80.

36. Nande PJ. Anthropometric measurements, dietary intake and lipid profile of hypertensive young adults (25-35 years): a comparison between vegetarians and non vegetarians. Curr Res Nutr Food Sci. 2014;2(3):122-30.
37. Ramakrishnan U. Nutrition and low birth weight: from research to practice. Am J Clin Nutr. 2004;79(1):17-21.
38. Shawky S, Milaat W. Early teenage marriage and subsequent pregnancy outcome. East Mediterr Health J. 2000;6(1):46-54.
39. Sallinen J, Pakarinen A, Ahtiainen J, Kraemer WJ, Volek JS, Häkkinen K. Relationship between diet and serum anabolic hormone responses to heavy resistance exercise in strength athletes and physically active males. Int J Sports Med. 2004;25:627-33.
40. Berrino F, Bellati C, Secreto G, Camerini E, Pala V, Panico S et al. Reducing bioavailable sex hormones through a comprehensive change in diet: the diet and androgens (DIANA) randomized trial. Cancer Epidemiol Biomarkers Prev. 2001;10(1):25-33.

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