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Original Article

Diet and estradiol level in adolescent girls

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Abstract

Background Nutritional intake in adolescent girls in Indonesia has been well studied, but there has been little study on its influence on serum estradiol levels. A high estradiol level has been associated with higher risk of breast carcinogenesis.

Objective To evaluate the influence of dietary factors on serum estradiol concentration in adolescent girls.

Methods A community-based survey was conducted in female junior high school students in Jakarta from January 2014 to January 2015. Nutritional intake was assessed by semi-quantitative food frequency questionnaires (FFQ), which included the intake of total energy (kcal), carbohydrate (g), protein (g), fat (g), fiber (g), and phytoestrogen (g). Based on the Indonesian recommended daily allowance (RDA), energy and nutrient intakes were categorized as minimal (<70%), low (70-99.9%), normal (100-129.9%), and high (≥130%). Serum estradiol levels were measured during the follicular phase using an enzyme-linked immunosorbent assay (ELISA).

Results A total of 189 girls aged 13-15 years were enrolled from 8 junior high schools across the municipalities of Jakarta. Twenty-eight (14.8%) subjects were overweight or obese. Median estradiol level was 41.83 (range 13.14-136.5) pg/mL. Serum estradiol level was significantly correlated with energy, protein, and fat intake. Estradiol level was also significantly associated with carbohydrate (P=0.030) and fat (P=0.036) intake status. Multivariate analysis revealed that intake of energy, protein, and fat, as well as body mass index (BMI) were independent predictors of estradiol levels. However, due to its importance as energy source, we included carbohydrate intake in the final equation to predict estradiol level as follows: E_2 = 60.723 – 0.053 (energy) + 0.185 (carbohydrate) + 0.483 (protein) + 0.491 (fat) – 1.081 (BMI).

Conclusion Serum estradiol levels in adolescent girls aged 13-15 years are influenced by diet, especially fat intake. Estradiol levels can be predicted from energy, carbohydrate, protein, and fat intake, as well as BMI. **[Paediatr Indones. 2016;56:134-8.]**

Keywords: *dietary intake; fat intake; estradiol level; adolescent girls; breast carcinogenesis*

Estradiol level in pre-menarchal girls is low and increases to 15-35 pg/mL as they approach puberty.[1] Girls who experience early menarche have higher estradiol levels throughout the menstrual cycle.[2] Consequently, they are at risk to accumulate higher estrogen levels during adulthood which increases the risk of breast cancer.[3,4]

Dietary factors during the adolescent period have been postulated to affect the risk of developing breast cancer in a women's lifetime.[5,6] High levels of serum 17β-estradiol (E_2) have been associated with breast carcinogenesis.[7,8] Estrogen production is influenced by many factors, including diet and lifestyle. Nutritional components, such as carbohydrate, fat, protein, fiber, and phytoestrogen affect estrogen synthesis.[9,10]Although nutritional intake has been well studied in adolescent girls in Indonesia, its effect on estradiol level has not gained much attention. As such, we aimed to evaluate

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the influence of dietary factors on serum estradiol concentration in adolescent girls.

Methods

This cross-sectional study was undertaken in adolescent girls aged 13-15 years in Jakarta. Subjects were recruited by systematic, random sampling from junior high schools in all five Jakarta municipalities from January 2014 to January 2015. This study was approved by the Ethics Committee for Medical Research at the University of Indonesia. Subjects' parents provided written informed consent.

Nutritional intake was assessed using semi-quantitative food frequency questionnaires, which included the intake of total energy (kcal), carbohydrate (g), protein (g), fat (g), fiber (g), and phytoestrogen (g). Interviews were done by experienced nutritionists. Based on the Indonesian recommended daily allowance (RDA), energy and nutritional intakes were categorized as minimal (<70%), low (70-99.9%), normal (100-129.9%), and high (≥130%).

Subjects were asked to report the first day of their next menstrual cycle. They were then scheduled to provide a blood specimen, to be collected between day 7 and day 11 after the onset of menstruation (the follicular phase), between 7:00-10:00 am. A total of 7 mL of blood was drawn from the cubital vein. Estradiol levels were measured using an electrochemiluminescence immunoassay (*Elecsys 2010/Cobas e601*, Roche Diagnostics).[11] The minimum level of detection was 8 pg/mL. The intra-assay coefficient of variability (CV) was 10%, and the inter-assay CV was 8%.

Skewed data were expressed as median and range. Differences among groups were tested using the Mann-Whitney U test. A P value of less than 0.05 was considered to be statistically significant. All analyses were performed using *SPSS version 17.0* (SPSS Inc., Chicago, Illinois, USA) software.

Results

A total of 189 adolescent girls were enrolled from 8 junior high schools across Jakarta. Most girls came from low-income families. Other subject characteristics are given in **Table 1**. Pearson's correlation test revealed that serum estradiol level was significantly correlated with energy, protein, and fat intake (**Table 2**). **Table 3** shows that carbohydrate and fat intake statuses were significantly correlated to estrogen level. Normal carbohydrate intake status was associated with higher estrodiol level, while low or high carbohydrate intake status was assoicated with lower estradiol level (P=0.030). As for fat intake status, higher fat intake was significantly associated with higher estradiol levels (P=0.036). Moreover, estradiol level consistently increased as fat intake increased.

Multivariate analysis revealed that intakes of energy, protein, and fat and BMI were independent

Table 1. Characteristics of the study subjects

Characteristics	(N=189)
Age, n (%)	
13 years	98 (51.9)
14 years	80 (42.5)
15 years	11 (5.8)
School type, n (%)	
Government (public)	97 (51.3)
Private	92 (48.7)
Age at menarche, n (%)	
< 12 years	43 (22.8)
> 12 years	146 (77.2)
Family monthly income, n (%)	
< IDR 1 million	75 (45.5)
IDR 1 – 3 million	84 (44.4)
IDR 3.1 -5 million	19 (10.1)
IDR 5.1 – 10 million	9 (4.8)
> IDR 10 million	2 (1.1)
Nutritional status, n (%)	
Normal	161 (85.2)
Overweight	21 (11.1)
Obese	7 (3.7)
Median BMI (range), kg/m^2	19.91 (12.96-32.25)
Median body fat (range), %	26.07 (14.70-31.51)
Median estradiol levels (range), pg/mL	41.83 (13.14-136.5)

Table 2. Correlation between estradiol level and nutritional intake (n=189)

Nutritional intake	r[a]	P value
Energy	0.168	0.021
Carbohydrate	0.136	0.062
Protein	0.198	0.006
Fat	0.150	0.036
Fiber	0.058	0.425
Phytoestrogen	0.032	0.662

[a] Pearson's correlation test

Table 3. Association between nutritional component status and serum estradiol level (N=189)

Nutritional component	n	Median estradiol level (range), pg/mL	P value*
Energy (kcal)			
Minimal (<70%)	75	38.21 (13.14-136.50)	0.288
Low (70-99.9%)	87	43.24 (15.54-124.70)	
Normal (100-129.9%)	24	45.88 (20.74-106.10)	
High (≥130%)	3	45.28 (36.82-48.77)	
Carbohydrate			
Minimal (<70%)	112	38.78 (13.14-136.50)	0.030
Low (70-99.9%)	42	43.00 (22.97-97.99)	
Normal (100-129.9%)	24	52.44 (23.05-114.20)	
High (≥130%)	11	35.21 (20.74-73.61)	
Protein			
Minimal (<70%)	132	38.48 (13.14-136.50)	0.116
Low (70-99.9%)	35	43.88 (20.14-114.10)	
Normal (100-129.9%)	6	51.35 (25.72-97.99)	
High (≥130%)	16	47.71 (28.25-106.10)	
Fat			
Minimal (<70%)	99	38.21 (13.14-136.50)	0.036
Low (70-99.9%)	38	41.25 (15.54-114.20)	
Normal (100-129.9%)	30	42.79 (18.20-114.10)	
High (≥130%)	22	48.46 (28.40-106.10)	

*Mann-Whitney U test

Table 4. Multivariate analysis to predict estradiol level (N=189)

Variables	B	SE	95% CI	P value
Energy intake	-0.053	0.027	-0.106 to -0.001	0.047
Carbohydrate	0.185	0.109	-0.031 to 0.400	0.092
Protein	0.483	0.194	0.101 to 0.865	0.013
Fat	0.491	0.235	0.027 to 0.955	0.038
BMI	-1.081	0.417	-1.903 to -0.259	0.010
Constant	60.723	9.912		

$R^2 = 0.101$

predictors of estradiol levels. However, since carbohydrate is also an important nutritional component and the main source of energy, we included carbohydrate intake in the final equation to predict estradiol level as follows:

$$E_2 = 60.723 - 0.053(energy) + 0.185\ (carbohydrate) + 0.483\ (protein) + 0.491\ (fat) - 1.081\ BMI)$$

Discussion

Our study showed that serum estradiol was significantly associated with higher fat intakes. Estrogen is synthesized from cholesterol which is obtained from animal products. Cholesterol is synthesized from its precursor, acetyl coenzyme A (acetyl coA).[12] Acetyl coA is the key molecule entering the citric acid cycle to produce energy which may be delivered from the glycolysis of glucose, oxidation of fatty acids, or amino acid deamination. Therefore, adequate intake of carbohydrates and fat is needed for estrogen synthesis. Furthermore, fat is thought to affect estrogen

reabsorption by increasing deconjugation, thereby increasing the estrogen level in the blood.[13] Besides being a cholesterol precursor, glucose can also influence insulin release that eventually affects sex hormone balance. Increased insulin levels leads to an ovarian increase in testosterone production and reduced sex-hormone binding globulin (SHBG), which may increase estradiol.[14] Subjects with higher estradiol levels tended to have higher category of protein intake. Protein is a precursor of cholesterol and is needed in estrogen synthesis. In addition, protein can affect SHBG levels, which in turn, may affect estradiol levels, though the mechanism is not clear.[15]

A previous study on fiber intake showed that estradiol level was higher in girls with low fiber intake.[16] A meta-analysis showed that intervention with a low fat and high fiber diet can reduce estradiol level by as much as 7.4% in pre-menopausal women.[17] Estradiol can be reduced by fiber in two ways. Firstly, unconjugated estrogen may bind to lignin in the digestive tract and then be excreted in stool. Secondly, fiber can modulate gut flora composition, thereby reducing pathogenic bacteria that produce □-glucuronidase and estrogen absorption.[18,19] But in our study, fiber intake was not significantly associated with estradiol levels.

Studies have indicated that phytoestrogen intake can reduce estradiol level. Phytoestrogen is usually present in food which is also rich in fiber, so phytoestrogen and fiber intake tend to correspond.[20,10] In this study, almost all subjects had very low phytoestrogen, therefore, it could not be analyzed further. Phytoestrogen intake can influence estrogen synthesis and metabolism due to phytoestrogen's structural similarity to estradiol. It, too, can bind to estrogen receptors.[9]

In this community-based survey, estradiol was measured once during the follicular phase. This phase may reflect of estradiol level which is cyclically changing according to her menstrual cycle. On the other hand, nutritional intake was assessed by semi-quantitative FFQ, which reflects subjects' daily nutritional intake and food pattern. During perimenarchal period, intake of carbohydrate, protein and fat were not significantly different.[21] Some studies have shown that dietary intervention can alter estradiol levels,[22,23] but this may not reflect the true eating pattern and daily nutritional intake. By performing a cross-sectional study, we could measure the real association between estradiol level and nutritional intake in the population.

There were some limitations of the study. First, although subjects were selected systematically, we failed to include adolescent girls from middle-to-high income families. However, the demographic characteristics of subjects might more suitably represent adolescent girls in suburban societies in Indonesia, which are predominated by middle-to-low income families. Second, we did not count the variation or regularity of subjects' menstrual cycles. Since estradiol level does not fluctuate on a daily basis, specimens taken from the long follicular phase should be sufficiently representive of estradiol levels. Soon after menstruation, estradiol level increases again as the cycle continues to the ovulation and luteal phases.

Estrogen in pre-menopausal women is synthesized mainly by the ovaries, whereas in post-menopausal women, the primary source of estrogen biosyntesis is the adipose tissue.[24] In this study, we found a consistent association between fat intake and estradiol levels, which might be an additional risk factor for future breast carcinogenesis. Therefore, dietary education program is urgently needed, not only for the girls, but also for their parents.

In conclusion, fat intake is significantly associated with serum estradiol levels of adolescent girls aged 13-15 years. Higher fat intake is consistently associated with higher estradiol levels. Estradiol levels can be predicted from energy, carbohydrate, protein, and fat intake, as well as body mass index.

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