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Hormonal Contraception, Nutritional Status and Thyroid Function's Women in an Iodine Replete Area

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ABSTRACT
Hormonal contraception is one of the most popular method to prevent the pregnancy. Several studies have reported a significant increase in body weight during hormonal contraception. It can also affect thyroid hormone which plays a role in basal metabolism, energy expenditure and weight. This study aims to analyse the relationship between hormonal contraception and nutritional status with thyroid function in child bearing ages women in an iodine replete area. 171 CBAW (47 taking hormonal contraception (HC), 124 non HC) in Bener Purworejo were examined serum TSH and fT4 levels. Interviews conducted for the characteristics of the subjects and measurement of nutritional status. The body weight (49.2 ± 8.88 vs 51,7 ± 8,86, p=0,096) and BMI (22,9 ± 3,42 vs 23,6 ± 3,73, p=0,220) were lower in women taking hormonal contraception, but statistically not significant. There were no difference in TSH (2,99 ± 3,73 vs 3,03 ± 3,73 µIU/ml, p=0,752) and free T4 (1,36 ± 0,32 vs 1,30 ± 0,34 ng/L, p=0,068). Women who taking hormonal contraception has significantly increased BMI (1,266) compared the non-hormonal contraception group after controlling years of age, level ot TSH and level of fT4. In this study, hormonal contraception is not related to thyroid functions.
Keywords: *hormonal contraception, nutritional status, thyroid function, iodine replete area*

1. INTRODUCTION

Hormonal contraception is one of the most popular method to prevent pregnancy because of its high efficacy, safety, low cost and easiness to use [1]. The most widely used contraceptive method in Indonesia is the hormonal contraceptive method (51,6%) [2]. The use of hormonal contraception can affect a variety of side effects, including the addition of a user's weight gain. Several studies have reported a significant increase in weight gain in hormonal contraception [3, 4] users, both in pill [5], injection [5-7] and implant [5,8] contraception. However the etiology of the weight gain seen in some women after starting the use of hormonal contraception is still unclear.

The weight gain mechanism in hormonal contraception users is related to anabolic effect and fluid retention in the appetite control center in the hypothalamus. Progesterone if used in the long term can have effect of stimulating weight gain, because progesterone activating conversion of carbohydrates and glucose into fat, resulting in the accumulation of subcutaneous fat. Progesterone can stimulate the central control of appetite in the hypothalamus, resulting in increased appetite and decreased physical activities [9]. Other explanation is through the failure of inhibiting hipofise process in hormone secretion causing increased appetite. In addition, progesterone ease the process of changing carbohydrate into triglyceride that only could breaks down with heavy physical activity [10].

On the other hand, hormonal contraception can affect thyroid hormone which play role in basal metabolism, energy expenditure and weight [11]. Treatment with estrogens can increase thyroxine (T4) and triiodothyronine (T3) caused by an increase in the serum-binding capacity of thyroxine-binding globulin (TBG). Therefore, change in circulating hormonal parameters may differ. It cannot be excluded that hormonal contraception may directly affect synthesis and release of thyroid hormones [12]. This study aims to analyze the relationship between hormonal contraception and nutritional status with thyroid function in childbearing age women in the replete area of iodine deficiency disorders (IDD).

2. METHODS

2.1. Design of The Study

We conducted a cross sectional study at the replete iodine deficiency disorders area in Bener Purworejo. The project was nested within a principal study focused on intervention iodized salt [13]. This study was approved by the Ethics Committee of National Health Research and Development of the Ministry of Health Republic Indonesia. All volunteers signed an informed consent form prior to enrolment. We selected women 17-45 years of age, married, lived in the study area for more than 3 years and passing the screening for clinical examination. We exclude women if they were pregnant, have a chronic disease, and/ or currently undergoing treatment. The estimation minimum sample required is 115 child bearing ages women, using two population means with 95% of CI and 90% power the test [6].

2.2. Data Collection

The participants' sociodemographic characteristics were collected through interviews. Body weight was measured using an AMP mechanical scale with 100 g precision and 200 kg capacity. Height was measured using Microtoise stature meter with 1 millimeter precision. Nutritional status was calculated by body mass index (BMI). For the thyroid parameters, the blood was centrifuged and the serum was stored at 20°C until analysis. In this study, the serum parameters were determined in the biochemical laboratories of the Magelang Health Research and Development Center, Central Java, Indonesia. The Enzyme Linked Immunosorbent Assay (ELISA) method was used to measure thyroid stimulating hormone (TSH) level (reference value (Human) 0,4 – 4,0 µIU/ml) with Human TSH ELISA kit and free thyroxine (fT4) level, Human 0,8 – 2,0 ng/L) with Human thyroxine ELISA kit.

Table 1 Characteristics of subjects based on contraceptive methods

Variable	Hormonal Contraception (124)	Non Hormonal Contraception (47)	P value
Characteristic subject			
Years of age, mean±SD	31.4 ± 6.84	34.2 ± 6.82	0.018
Age categories			
< 25 years	23 (18.5)	6 (12.8)	
25 – 35 years	66 53.2)	19 (40.4)	0.070
> 35 years	35 (28.2)	22 (46.8)	
Education			
Primary education	83 (66.9)	34 (72.3)	0.497
Secondary education	41 (33.1)	13 (27.7)	
Job categories			
Private sector	7 (5.6)	5 (10.6)	
Trading	4 (3.2)	3 (6,4)	
Former	15 (12.1)	9 (19.1)	0.312
Labor	23 (18.5)	9 (19.1)	
Housewife	75 (60.5)	21 (44.7)	
Weight, kg, mean±SD	51.7 ± 8.86	49.2 ± 8.88	0.096
BMI, kg/m², mean±SD	23.6 ± 3.73	22.9 ± 3.42	0.220
Categories of BMI			
Underweight	2 (1.6)	2 (4.3)	
Normalweight	92 (74.2)	37 (78.7)	0.387
Overweight	30 (24.2)	8 (17.0)	
Biochemistry			
TSH, µIU/ ml,mean±SD	2.99 ± 3.73	3.03 ± 3.73	0.752
TSH, median(min-max)	2.74 (0.28 – 8.12)	2.71 (0.29 – 7.57)	
fT_4, ng/L, mean±SD	1.36 ± 0.32	1.30 ± 0.34	0.068
fT_4, median median(min-max)	1.30 (0.87 – 2.83)	1.17 (0.88 – 2.30)	

2.3. Statistical Analysis

We used Pearson's chi-square test, or Fisher's exact test when necessary (age categories, education, job categories, categories of BMI) to compare the categorical variables and the Mann–Whitney test to compare the numerical variables non normally distribution (TSH and fT4), and Independent T test to compare the normally variables normally distribution (years of age, weight, BMI). Spearman's correlation coefficient was used to evaluate the correlations between thyroid hormone levels, years of age, BMI and contraceptive methods. Adjustment for differences in covariates and variables during the study were performed by linear regression. The significance level of 0,05 was used for these analysis

Table 2 Relationship between hormonal contraception, BMI and thyroid function

Variable	Multivariable linear regression estimates				
	Coefficient	Standard Error	β	95% (CI)	
				Lower	Upper
Constant	18.715	1.902		14.961	22.470
Contraceptive methods (1=HC, 0=NHC)	1.266	0.617	0.154	0.049	2.484
Years of age	0.159	0.040	0.302	0.081	0.238
TSH level	0.056	0.165	0.025	-0.269	0.382
fT_4 level	-1.110	0.833	-0.099	-2.754	0.535

3. RESULTS

Of the 183 women who responded to the study, 171 met inclusion criteria. The final analysis used data from 171 women: 47 in the hormonal contraception group and 124 in the non-hormonal contraception group. The hormonal contraception group had significantly younger than the non-hormonal contraception group. No systematic differences in education and occupation were found between the groups (Table 1). Weight and BMI were lower in the hormonal contraception group than in the non-hormonal contraception group, but not statistically significant. Free T4 level were lower in the hormonal contraception group than in the non-hormonal contraception group, but not statistically significant. There were no differences between the groups in any of the biochemical and anthropometric variables evaluated. Analysis of the correlation between thyroid hormone level and the other variables showed a direct correlation between years of ages and BMI and an inverse correlation between TSH and fT4, years of ages and contraceptive methods.

Multiple linear regression analysis showed that participants who taking hormonal contraception has increased BMI (1,266) compared the non-hormonal contraception group after controlling years of age, fT4 level and TSH level. Factors that significantly affect BMI are hormonal contraception and years of age, while other factors are not significant. Effective contribution of these factors to increase BMI are 10.7%.

Table 3 Relationship between hormonal contraception, BMI and thyroid function

Constant	Years of age	Contraceptives method	TSH	fT_4
BMI	0.306**	0.098	0.039	-0.056
Years of age		-0.182*	0.046	-0.019
TSH		0.024		-0.154*
fT_4		0.140		

** correlation is significant at the 0.01
* correlation significant at the 0.05

4. DISCUSSION

Most study on the effects of hormonal contraception increases weight. This study found that participants who taking hormonal contraception has increased BMI compared the non-hormonal contraception group after controlling years of age, level ot TSH and level of fT4, consistence with previous studies. But we found no relationship with thyroid hormone. This finding was in accordance with Moro which proves the existence of weight gain in DMPA users but did not find changes in thyroid hormones that could explain this weight gain [6]. Weight gain could be explained by factors already known, such as age, or change in appetite and energy expenditure. In this study, the hormonal contraception group had significantly younger than the non-hormonal contraception group and significantly direct correlation with BMI. This is in accordance with the basic health research (RISKESDAS) data, the proportion of hormonal contraception users is highest in the age group of 25-29 years, while long-term contraceptive users are widely used by the age group of 40-44 years [2].

Participant of hormonal contraception users showed an increase in fT4 level, but not statistically significant. This findings is in accordance with the previous study that treatment with oral contraceptives (levonorgestrel or desogestrel) did not significantly change fT4 and TSH levels [14]. In this study, this increased production of fT4 was due to compensation from depot medroxyprogesterone acetate (DMPA) which inhibited peripheral conversion from fT4 to fT3 [6]. An increased serum binding leads to a reduction of the free proportion of these hormones, while total T4 was increased [12]. Most studies on the effect of hormonal contraception revealed an increase the levels of T4, while T3 and TSH were increased or unchanged. In women using hormonal contraception's, the rise in the levels of total T3 and T4 is caused by an increase in the serum-binding capacity of thyroxine-binding globulin (TBG), which reduces the clearance of these hormones. An increased serum binding leads to a reduction of the free proportion of these hormones. Therefore, the resulting amount of free T3 (FT3) and free T4 in the circulation may be unchanged. The rise in TBG levels is due to the pronounced effect of ethinylestradiol (EE) on hepatic globulin synthesis, which is dose-dependent and, to a certain degree, can be modulated by the progestogen component [12]. Therefore, according to the composition of the preparations, changes in circulating hormonal parameters may differ. In addition, it cannot be excluded that hormonal contraception may directly affect synthesis and release of thyroid hormones.

The elevation of thyroid hormones may be appearing after a long time of using the hormonal contraceptive as the results of the present study showed, and this corresponding with previous study [6], [12], [15]. In the bloodstream, T4 is the principal product secreted by the thyroid gland and must be activated through the process of deiodination to T3. Free T4 and free T3 not bound to transport proteins, and its this form that is available to the cell receptors and that therefore is hormonally active [16], [17]. Unfortunately, levels of Total T3 and T4 in this study were not measured. In that study, the TSH levels were not significantly increased, which is in accordance with the effects of hormonal contraception in the present study [12].

Hormonal contraceptives may positively or negatively influence the course of a thyroid disease depending on the type of immune mechanism involved in its pathogenesis [18]. In the patient with autoimmune thyroid disease, found

that estrogen use was associated with a lower rate of hyperthyroidism [RR 0.169; (95% CI) 0.06-0.52]; in addition, estrogen use was negatively correlated with the presence of thyroid peroxidase auto-antibodies [19]. According to Williams, there is no published evidence of any significant effect of combined oral contraceptive on the subsequent development of hypothyroidism [20]. In the healthy women, combined oral contraceptive use do not influence the size and function of thyroid gland, thyroid-stimulating hormone levels were not significantly modified and free thyroxin levels did not change [21].

5. CONCLUSION

In this study involving child bearing age women, using hormonal contraception, there was a higher BMI than non-hormonal contraception groups; however there was no relationship between thyroid function and BMI.

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