

THYROID FUNCTION DISORDER AND QUALITY OF LIFE ON CHILDBEARING WOMEN IN ENDEMIC AREAS OF IODINE DEFICIENCY

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Abstract

Indonesia has not been free from iodine deficiency, new problems that occur in endemic areas of iodine deficiency is the presence of iodine excessive. Both deficiency and excessive of iodine can result in thyroid dysfunction. Impaired thyroid function is manifest broadly on biopsychosocial aspects, which is detrimental especially for childbearing women, as a determinant of survival and quality of life for future generations.

Participants included 50 childbearing women who living in endemic areas such as in subdistrict Cangkringan Sleman, Yogyakarta and Selo Boyolali, Central Java. We measured two thyroid hormones, TSH and FT4 and we also administered biopsychosocial test by iodine disorder questionnaire (IDQ). We then described result of biochemical measurement with result of biopsychosocial test, and explained the mechanism of the thyroid disorder and quality of life changes.

Based on the measurement of TSH and FT4, found childbearing women who suffer subclinical hypothyroidism 2%, subclinical hyperthyroidism 26% and euthyroid 76%. Biopsychosocial characteristics that represented quality of life can be described from hypothyroid subjects is visible goiter, puffy face, dry skin, fatigue, decreased concentration, menorrhagia, easily upset, depressed, apathetic and withdrawn. Meanwhile, the varying percentage of subjects with subclinical hyperthyroidism showed signs and symptoms include a palpable goiter, heat intolerance, exophthalmos, tiredness, pritibial edema, muscle weakness, delicated skin, poor memory, decreased concentration, menstrual disorders, anxiety, sleep disturbances, irritability, decreased motivation and decreased social activity.

Thyroid function disorder caused quality of life changes on childbearing women in endemic area of iodine deficiency .

Keywords: thyroid function disorder, quality of life, childbearing women

A. Introduction

Due to iodine deficiency disorders (IDD) is one of the serious public health problem, because a very large impact on the survival and quality of human resources. The cause of IDD is inadequate intake of iodine in the body, known as iodine deficiency disorder (IDD)^(1,2). Indonesia make IDD as one of the major nutritional problems, as some 42 million people living in IDD endemic areas, 10 million suffer from goiter and 750 thousand suffer cretins. The survey results across Indonesia showed an increased

prevalence of total goitre rate (TGR) of 9.8% in 1998, increased to of 11.1% in 2003⁽³⁾.

Iodine deficiency is closely related to geographical factors, such as mountainous regions humus layer of soil as the persistence of iodine is not there, due to continuous soil erosion, eroded by the floods, lava, tropical rain on sloping lands, calcareous soil and water-soluble iodine is brought up to the estuary and the sea, the burning forest also cause lost the iodine. Some geographical conditions led to a state of the soil, water and food ingredients

contain less iodine. An area that has a characteristic that reduces the iodine content in soil is known as endemic areas of IDD ⁽⁴⁾.

The endemic areas of IDD at risk of iodine deficiency causes in all age groups, ranging from fetal, neonatal, children, adolescents, adults and elderly. The impact of iodine deficiency include a very wide spectrum, such as: miscarriage, stillbirth, congenital malformations, perinatal mortality, infant mortality, cretins, goiter, hypothyroidism, decreased IQ, impaired mental function, impaired muscle function, stunted growth and iodine induced hyperthyroidism or IIH ⁽⁵⁾.

New problems that occur in endemic areas of IDD is the presence of excess iodine, as a result of iodine deficiency elimination program of universal salt iodization (USI) and iodol supplementation within a relatively at along time ^(6,7). It's not different from iodine deficiency, iodine excess also have several risks to health, such as lead thyroiditis, hyperthyroidism, hypothyroidism, goiter and the effects of IIH with various manifestations, such as increased heart rate, weight loss, excessive sweating and tremors. IIH is also an increased risk of autoimmune thyroid disease (AITD) ^(6,7).

Several studies have found cases of excess iodine in endemic areas, such as Alsayed et al. (2008) found 54.8% of women in Egypt have excess iodine and correlated with subclinical hypothyroidism ⁽⁸⁾. Mutalazimah and Asyanti (2010), found 10% cases of excess iodine on elementary school children in the Cangkringan Sleman, Yogyakarta, Indonesia ⁽⁹⁾. Henjum et al. (2010) showed results that are very extreme, which found 84% of children in endemic areas Saharawi Algeria have excess iodine ⁽⁷⁾. Hermann et al. (2004) and Lamfon (2008) also found a tendency for subclinical hyperthyroidism, which is a decrease in serum thyroid stimulating hormone (TSH) in subjects in endemic areas of iodine deficiency, while levels of free T4 (FT4) or the hormone thyroxine is still in normal threshold ^(10,11).

Various problems related to iodine and thyroid dysfunction in women, there was 4-10 times more frequently than in men, particularly

in childbearing women of ^(6,11,12). Without early warning for screen of childbearing women who suffer from iodine deficiency, would pose a risk pregnancy associated with fetal death, with a prevalence of up to 79%. In addition, an increase in congenital hypothyroidism, cretinism, mental retardation, impaired psychomotor development, and decreased intelligence in children, up to 4 to 7 point ^(13,14).

The recent study of the effects of iodine deficiency and excess have been widespread, not only the impact on biological aspects (clinical and physical), but also on the psychosocial aspect is related to the condition of iodine metabolism disorder. Thus, the signs and symptoms caused by iodine deficiency and excess, is the result of the interaction of biological, psychological and social, or well known as the biopsychosocial model approach. Biopsychosocial model states that health, illness and disease is the result of the interaction between biological, psychological and social differences between the pathophysiological mechanisms that cause disease and one's perception of health and its consequences, called diseases ^(15,16).

Biopsychosocial model also explains psychological and social effects of disease risk, prevention, treatment compliance, morbidity, quality of life and survival. Biopsychosocial model of the iodine disorder, based on a variety of signs and symptoms of iodine deficiency and excess that manifests on the biological aspects, which are related to the physical, clinical and psychological aspect, which is related to psychological conditions, and social aspects, which are related to the interaction individuals with social environmental ⁽¹⁷⁾.

Biopsychosocial approach is based on several studies that found an association between the results of clinical examination, psychological and biochemical test results in children and adults who suffer from a deficiency. Iodine and hypothyroidism. Including among others, found 28% of children in Cangkringan Sleman, Yogyakarta, Indonesia with low iodine status, it has also impaired the biological and psychosocial status. Thus there is a significant relationship

between status of iodine in urine and biological-
psychosocial status on children ⁽⁹⁾.

Brown et al. (2005) found several domains of the biopsychosocial model associated with hypothyroidism, namely: biological aspects, including the central nervous system (CNS), musculoskeletal, cardiovascular, gastrointestinal, eye-ear-nose-throat (EENT), genito urinary, general and radiology; psychological aspects, including mood and stress disorder with various symptoms of depression such as sleep disturbances, decreased activity, lack of energy, decreased concentration, appetite disorders and other psychological disorders, such as easy to panic, anxiety, depression, phobias, irritability and irritability; and social aspects, including low self-esteem, easily come into conflict with others, less able to understand others, to limit interaction with the other persons ^(12,15). This study to identify any cases of thyroid dysfunction, either due to iodine deficiency or excess by measuring levels of TSH and FT4 and explore biopsychosocial characteristics related to the impact of thyroid dysfunction, on childbearing women in endemic areas of iodine deficiency. In addition, this study also discusses the pathophysiological mechanisms of biopsychosocial characteristic caused by thyroid dysfunction.

B. Method

The study is a descriptive study, with the target population is women childbearing aged 20-35 years, who live in endemic areas of iodine deficiency. Source population is of reproductive age women aged 20-35 years in Cangkringan Sleman, Yogyakarta and Selo Boyolali, Central Java, Indonesia. Fifty participants, drawn by simple random sampling technique. Identification of thyroid dysfunction, whether caused by iodine deficiency or excess, by performing measurements of thyroid hormones, TSH and FT4, using the ELISA method performed at the Laboratory of Clinical Pathology of Sardjito hospital in Yogyakarta. Meanwhile, the biopsychosocial characteristics as a result of thyroid dysfunction, measured using a iodine disorder questionnaire that had design before,

that containing items that represent the signs and symptoms domains of biological and psychosocial, which are referred from the results of a literature review. Data analysis was done by presenting a descriptive. Furthermore thoroughly reviewed by the theories and previous research results, through various mechanisms underlying the association of thyroid function disorders and biopsychosocial changes.

C. Result and discussion

Measurement of TSH and FT4 levels in all women, as an indicator for the presence of thyroid dysfunction, showed an average yield of 1.10 ± 1.02 TSH $\mu\text{U} / \text{l}$, while the average levels of FT4 of 0.85 ± 0.271 ng / dl. This study found there are three criteria for thyroid dysfunction in childbearing women, the majority of the normal thyroid function (euthyroid) of 72%, subclinical hypothyroidism 2% and subclinical hyperthyroidism 26%. Quality of life characteristics as a result of thyroid dysfunction are explored in this study, the domain of each item is represented by the signs and symptoms of thyroid dysfunction is the manifestation of biological and psychosocial aspects.

There are at least three main reasons for TSH be a good indicator for detecting disorders of thyroid function, namely the log-linear inverse relationship between TSH and FT4 concentrations. Almost all cases of hypothyroidism and hyperthyroidism are commonly encountered in medical practice of diseases caused by primary (thyroid gland), so associated with the thyroid hormone that stimulates the activity of TSH. A further reason, tests for TSH immunometric test is highly sensitive and specific, with a sensitivity and specificity higher than 99% ⁽¹⁷⁾.

Interpretation of the serum TSH levels, usually defined by the normal reference interval of about 0.4 to 4.0 $\mu\text{U} / \text{l}$, while the normal reference intervals for FT4 levels ranged from 0.7 to 2.1 ng/dl [18]. Iodine deficiency that occurs in the long length will increase the levels of TSH, but the production of the hormone thyroxine in normal levels constant, the condition is known

as subclinical hypothyroidism. Conversely, if the TSH level decreased but the production of normal levels of the hormone thyroxine, referred to as subclinical hyperthyroidism. If the two conditions FT4 levels are too low and too high, then it is referred to as clinically hypothyroidism and hyperthyroidism^(15,19).

This study found a case of hypothyroid subjects with subclinical, ie, with normal TSH levels exceeding the limit, though not so extreme (4.90 μ U/l). Meanwhile, on 13 subjects (26%) with subclinical hyperthyroidism (TSH <0.4 μ U/l), a total of 8 subjects showed very low levels of TSH (<0.004 μ U/l). The discovery of subclinical hyperthyroid subjects by 26% this reinforces some research on the phenomenon of excess iodine which affects the trend of decreased levels of TSH in subjects in endemic areas of deficiency yodium [8,12]. Even Hermann et al. (2004), found that extreme numbers, the incidence of excess iodine in school children reached 84%⁽¹⁰⁾.

Iodine deficiency is a major cause of hypothyroidism and hyperthyroidism, with the largest percentage of their respective 30.9% and 19.3%, compared the other causes⁽¹¹⁾. Hypothyroidism occurs as the first functional consequences of iodine deficiency, through enhancing iodida by the thyroid's absorption of the trans-membrane proteins is mediated through the sodium iodide symporter (NIS). Iodida absorption is increased, most probably accompanied by, and as a result of an increase in serum TSH⁽¹⁹⁾. Iodine deficiency can also cause hyperthyroidism, iodine-induced hyperthyroidism via mechanisms, such as iodine supplementation in endemic areas are not monitored well, excess iodine as antithyroid drug therapy, the excesses of drugs that contain high levels of iodine such as amiodarone and expectorant including glycerol and organidin, contrast media such as tomography or arteriography, drinking water with excess iodine, the use of antiseptics in food and beverage industry, especially dairy products, food and beverage industry with raw materials rich in iodine such as seaweed or the iodine fortification⁽²⁰⁾.

Excess of iodine as a cause of hypothyroidism is much explained by the mechanism of the Wolff-Chaikoff effect, namely an excessive amount of iodine in the thyroid gland to iodine deficiency condition, it will inhibit thyroid hormone synthesis. As an adaptation of Wolff-Chaikoff effect, which increases the concentration of iodine intratiroid, causing decreased thyroid iodida trapping, then lower and lower intratiroid iodida NIS mRNA and protein expression. Iodine excess also decreases the release of T4 and T3 from the thyroid, with a slightly decreased levels of T4 and T3 and TSH increased compensation. In contrast, excess iodine as a cause of hyperthyroidism is explained through the mechanism of thyroid autoimmunity through JOD Basedow effect. Autoimmune thyroid disease occurs because the body produces antibodies that works similarly to TSH, which is able to stimulate the TSH receptor (thyrotropin receptor antibody = Trab) to produce T4 (thyroxine) and T3 (triiodothyronine) is excessive, so the impact hipertiroidisme^(19,20,21).

Related to the biopsychosocial aspects, thyroid dysfunction has many underlying pathophysiological mechanisms, of any signs and symptoms that accompany. Hypothyroidism due to iodine deficiency causes goiter, because the absolute decision iodida reduced and decreased levels of iodine in the thyroid. Below the critical level of iodine intake, an increase iodide clearance, to maintain a normal absolute uptake by the thyroid iodida. Consequences for organic iodine in thyroid levels remain within normal limits, the onset of goitre. Goitre also arise in cases of hyperthyroidism, basically due to the activity of the thyroid gland in secreting excess thyroid hormone. Can occur due to excessive iodine intake or because of the increased metabolism of all nutrients have an impact on increased glomerular filtration rate (GFR), thereby increasing the iodine that comes out through the kidneys. This condition will reduce the iodine in the plasma, leading to compensation in the thyroid gland to make ends meet by increasing the activity of thyroid hormone, causing goitre⁽¹⁹⁾.

Subjects with hypothyroidism showed a swollen face (face puffiness), due to a decrease in metabolism of carbohydrates and protein, leading to increased water binding glycosaminoglycans and increased transcapillary escape of albumin (increased extravascular albumin), but it decreased GFR, creatinine clearance will decrease so that there was edema. On the subject of hyperthyroidism, the edema that occurs in the lower legs (pretibial edema), caused by increased thyroid hormone increases the glycosaminoglycan deposits, thereby increasing the osmotic pressure and increase the accumulation of fluids, especially in the low extremities⁽²²⁾. Dry and scaly skin, and felt very cold in hypothyroid subjects, as a result of a decreased metabolism and skin vasoconstriction. Dryness of the skin due to reduced secretion of the sweat glands and sebaceous. Changes in the characteristics of the skin is caused also by an increase in the number of glycosaminoglycan, as a result of the catabolism of mucopolysaccharide and collagen by skin fibroblasts. While the symptoms are very soft skin and always wet on the subject of hyperthyroidism, caused by an increase in the amount of compensation hypothalamic sweat to lower body temperature because of the increased heat production caused by an increase in basal metabolic rate (BMR)⁽²²⁾.

Tiredness complaints, in hypothyroidism is caused by a decrease in mitochondrial oxidative metabolism, as reflected in an increase in the ratio of inorganic phosphate to ATP in the muscle at rest and a sharp decline in phosphocreatine in active muscle. Reduction of calcium ATPases also appear to explain one of the most obvious clinical manifestations of hypothyroidism, namely: the slow relaxation of deep tendon reflexes, myalgia, muscle weakness, stiffness, cramps, fatigue, arthralgias, joint stiffness, joint effusion and bone, pseudogout, as well as carpal tunnel syndrome⁽²²⁾.

Fatigue that occurs in hyperthyroidism, caused an increase in metabolism that lead to rapid energy consumption, thereby decreasing energy sources quickly. In addition to increasing metabolism, the increased heat production, stimulate perspiration and dehydration, so prone

to fatigue. The increased heat production in hyperthyroid subjects, will also increase body temperature, making it more sensitive or heat intolerance.

Menstrual disorders arising in hypothyroid subjects, characterized by the amount of blood that comes out and or longer menstrual periods (menorrhagia), due to low activity of the thyroid hormone that causes interference with the pituitary-ovarian axis hypothalamic, causing an imbalance in estrogen and progesterone, as compensation on this imbalance there was heavy bleeding in the endometrium. Hyperthyroid subjects also experienced menstrual disorder, characterized by the least amount of menstrual blood or menstrual irregularities, which can happen 2 or 3 months (hypomenore and amenorrhea). Generally the cause of amenorrhea is primary ovarian failure (hypergonadotropic hypogonad), which can occur due to decreasing levels of TSH, which causes hyperthyroxinemia thereby increasing the gonadotropin releasing hormone (GnRH). Meanwhile, complaints of sexual libido loss in hyperthyroid subjects, in addition to the imbalance of sex hormones, are also explained by a mechanism of anxiety⁽²³⁾.

Decrease in concentration and memory in hypothyroid subjects, through the mechanism of decrease in basal metabolism which causes a decrease in oxygen consumption, thereby reducing the synthesis of neurotransmitters and reduce cytokines release in the brain. The state will lose neuromodulator and disrupt production processes associated with neurochemical, neuroendocrine, neuroimmune, and behavioral change, which affects the psychological conditions including cognitive abilities, such as decreased concentration and memory. Cognitive impairment in hyperthyroid subjects such as difficulty concentrating and forgetfulness, it is caused by a decrease in thyroid releasing hormone (TRH), which leads to increased synthesis and release of acetylcholine, thereby disrupting the brain function⁽²⁴⁾.

Muscle weakness experienced on hyperthyroid subjects, starting from the increased metabolism due to an increase in thyroid hormone activity, then an increase in protein

breakdown and reduce the capacity function in skeletal muscle contraction. Muscle weakness is often caused subjects to lose motivation and reluctant to interact with the surrounding environment, as well as trying to reduce their daily activities ⁽²²⁾. Hyperthyroid subjects with exophthalmos, caused by the presence of edema and fatty infiltration of the dystrophy causes the muscles outside the eye, causing progressive protrusion of eyeball. Another mechanism associated with autoantibodies that cause autoimmune reactions and cause infiltration of lymphocytes, mast cells and plasma cells, which further inflammation and retro orbita tissue swelling ⁽²⁵⁾.

Psychosocial symptoms in hypothyroid subjects, such as easily upset, depressed, dispirited, apathetic and limited interaction, caused by a mechanism related to the biological aspects of hypothyroidism to depression, a series of processes associated with CSF CCK-4, which is cholecystokinin peptides in cerebrospinal fluid and triptophan (serotonin precursor), which decreased the levels are increasing levels of TSH. Depression is also associated with low serotonergic (5-HT) in the brain, resulting from a disruption in thyroid-pituitary hypothalamic axis ⁽¹⁵⁾.

Anxiety experienced by the subject of hyperthyroidism, can be explained through a mechanism that makes the proliferation of adrenergic receptors of target cells more sensitive to catecholamines, thereby increasing the components that create anxiety. In addition, the increase in thyroid hormone increases the activity of the CNS, stimulates the sympathetic nerves and epinephrine and cortisol to increased the anxiety ⁽¹⁵⁾. Not much different, the mechanism of the hyperthyroid subjects are easily angered, caused by excessive thyroid gland activity will spur the proliferation of β -adrenergic receptors, and enhance the effects of catecholamines so that the subject is relaxed and more sensitive. In the meantime, sleep disturbances experienced by the subject of hyperthyroidism, occurs through the mechanism of increased metabolism, oxygen consumption rapidly, increased cardiac output, feeling excited,

and less relaxation, so difficulty to sleep. Another mechanism of sleep disturbance is increased production of heat and sweat that cause restlessness and wake up frequently when sleeping (26).

D. Conclusion

Based on the levels of TSH and FT4, thyroid dysfunction on childbearing women in endemic areas of iodine deficiency, can be categorized by 2% subclinical hypothyroidism, subclinical hyperthyroidism 26% and euthyroid 76%. Thus it can be found the fact that there is a tendency of cases of subclinical hyperthyroidism in endemic areas of iodine deficiency. This study found a variety of signs and symptoms that includes biopsychosocial aspects, as the impact of thyroid dysfunction that could explain the interaction, through the mechanisms of interaction between biological and psychosocial aspects that represented of quality of life.

E. References

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