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Original Article

Effect of iron deficiency anemia during pregnancy on T3, T4 and TSH levels in newborns

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Abstract

Background Iron deficiency anemia (IDA) in infants is associated with maternal iron deficiency anemia during pregnancy. Infants from anemic mothers often have lower hemoglobin levels than those from non-anemic mothers. Several studies have suggested that IDA in infants can impair thyroid peroxidase (TPO) enzyme which is required to produce thyroid hormones.

Objective To determine the effects of IDA during pregnancy on T3, T4, and TSH levels in newborns.

Methods We conducted a cross-sectional study from September to December 2010 in two hospitals. Mothers' blood specimens were examined for IDA. Newborns' hematocrit, hemoglobin, ferritin, T3, T4, and TSH levels were measured in umbilical vein blood specimens taken at 24 hours of life.

Results Mean T3, T4, and TSH levels of 40 newborns whose mothers suffered from IDA were 2.2 nmol/L (SD 1.19), 8.4 ug/dL (SD 6.12), and 15.3 mIU/mL (SD 3.99), respectively. There was no significant relationship between maternal IDA during pregnancy and infant T3 and TSH levels (P=0.96, P=0.29, respectively). However, maternal IDA significantly correlated with infant T4 levels.

Conclusion There was no significant relationship between maternal IDA during pregnancy and levels of T3 and TSH in newborns. However, maternal IDA significantly correlated with lower infant T4 levels. **[Paediatr Indones. 2011;51:178-81]**.

Keywords: *iron deficiency anemia, pregnancy, thyroid hormone*

Iron deficiency anemia (IDA) in infants cannot be separated from maternal IDA during pregnancy. The National Household Health Survey in 2001 showed that the prevalence of IDA in pregnant women was 40.1%. There are many factors affecting IDA in newborns. Newborns from anemic mothers have lower hemoglobin (Hb) levels than newborns from non-anemic mothers.[1-3]

Anemia in pregnancy is defined by Hb levels below 11 g/dL in the first and third trimester or below 10.5 g/dL in the second trimester.[1-3] Sonja *et al*. found that in rats with IDA, thyroid peroxidase enzyme (TPO) activity was reduced, affecting the production of thyroid hormones.[4] Other studies reported that IDA in women impacted the generation of thyroxine (T4), triiodothyronine (T3), as well as hemoglobin levels. Furthermore, maternal IDA affected thyroid function in their newborns.[4-7]

Maternal thyroid hormone metabolism changes significantly in patients with IDA. Newborns from mothers with anemia and low thyroid hormone levels

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may themselves also have low thyroid hormone levels, since the infant thyroid hormone level is partially from the mother through the placenta.[8-10] Our study was designed to determine the effects of maternal IDA during pregnancy on T3, T4, and TSH levels in newborns.

Methods

We conducted a cross-sectional study in Adam Malik and Pirngadi Hospitals from September to December 2010 in cooperation with the Obstetric and Gynecology Department. We included mothers with IDA and their newborns if they met the following newborn inclusion criteria: spontaneous birth, birth weight 2500 - 4000 grams, and Apgar score in first minute ≥7. All parents provided written, informed consent. We excluded mothers with diabetes, preeclampsia or eclampsia, hypertension, hypoalbuminemia and those who received diazepam or oxytocin for induction of labor. Babies with major congenital anomalies, birth trauma, such as cephalohematoma, caput succedaneum, sub-aponeurotic bleeding, and those born from mothers with a history of thyroid dysfunction were also excluded.

From blood specimens collected from brachial veins, we measured hemoglobin, ferritin, T3, T4, and TSH levels from pregnant women who suffered from IDA. We collected newborns' Apgar scores, and gestational age with New Ballard score and birth body weight. Two ml blood samples were drawn from newborns' umbilical veins within 24 hours of birth and placed in EDTA vacutainer tubes for measurement of T3, T4, and TSH levels. All blood tests were measured by commercially available kits and the Cobas 6000 instrument (USA) in Thamrin Laboratory.

Anemia during pregnancy and in neonates was defined by WHO criteria as hemoglobin level below 12 g/dL and 14 g/dL, respectively.[1] We defined hypothyroidism as thyroid hormone indices of T3 < 1.3 nmol/L, T4 < 6.0 ug/dL and TSH > 20 mIU/mL. In addition, hypoalbuminemia in pregnancy was defined as an albumin level < 3.5 g/dL. Ethical approval for this study was obtained from the Research Ethics Committee of the University of Sumatera Utara Medical School.

The collection data was processed, analyzed and presented using the Statistical Package for the Social Sciences (Windows version 15.0; SPSS Inc, Chicago). Statistical comparison between IDA during pregnancy and T3, T4, and TSH levels in newborns were determined using independent t-test. Significance was set with $P<0.05$ and a 95% confidence interval.

Results

During the period of study, we found 198 pregnant women planning to birth spontaneously. One hundred and fifty eight were excluded, leaving only 40 pregnancies that fulfilled the inclusion criteria.

Of 40 newborns, 21 were female (52.5%) and 19 were male (47.5%). Mean birth weight was 3.1 kg (SD 0.29) and mean birth length was 49.1 cm (SD 1.17). Baseline characteristics of subjects is shown in **Table 1**.

Table 1. Baseline characteristics of subjects

Characteristics	Values
Newborns	
Gender, n	
Males	19
Females	21
Mean birth weight, kg (SD)	3.1 (0.29)
Mean birth length, cm (SD)	49.1 (1.17)
Mean hemoglobin level, g/dL (SD)	16.4 (2.43)
Mean hematocrit level, % (SD)	49.8 (5.91)
Mean serum T3, nmol/L (SD)	2.2 (1.19)
Mean serum T4, ug/dL (SD)	8.4 (6.12)
Mean serum TSH, mIU/mL (SD)	15.3 (3.99)
Mothers	
Mean age, years (SD)	25.7 (2.69)
Education level, n	
Primary school	3
Junior high school	10
Senior high school	24
Bachelor's	1
Post-graduate	2
Mean gestational age, weeks (SD)	38.5 (0.82)
Mean hemoglobin level, g/dL (SD)	10.6 (0.83)
Mean serum ferritin, ng/mL (SD)	24.8 (8.49)

Table 2. Correlation of maternal hemoglobin and serum ferritin levels to newborns' serum T3, T4, and TSH levels

Infant hormones	Maternal Hb			Maternal ferritin level		
	r	R2	P	r	R2	P
T3	0.007	0.001	0.96	0.182	0.033	0.268
T4	0.324	0.105	0.04	0.203	0.041	0.215
TSH	0.17	0.209	0.29	0.311	0.097	0.054

Hb and serum ferritin levels of mothers and thyroid function of newborns are shown in **Table 2**. There was a weak association between infants' serum T4 levels and maternal hemoglobin levels (r = 0.324, P=0.042). However, there was no significant associations between infants' serum T3 or TSH levels and maternal Hb levels. Furthermore, infants' T3, T4, and TSH levels were not significantly associated with maternal serum ferritin levels.

Discussion

The Ministry of Health has recommended thyroid screening for newborns. One study reported that thyroid disorders were 4-5 times more frequent in women than men, and mostly occurring during pregnancy due to hormonal and metabolic changes. Thyroid disorders in pregnant women can be either a deficiency or an excess of thyroid hormones, but a deficiency or hypothyroidism is more common.[11-13]

The mechanism by which iron status influences thyroid and iodine metabolism is unclear. IDA may cause impairment in thyroid metabolism through anemia and decreased oxygen transport. IDA may also alter central nervous system control of thyroid metabolism and nuclear T3 binding. Similarly, IDA could lower TPO activity, thereby interfering with iodine metabolism in the thyroid.[4,8] TPO is a 103-kDa iron-dependent enzyme, located at the apical membrane of thyrocytes. TPO catalyzes the first two steps in thyroid hormone synthesis, iodination of thyroglobulin and coupling of the iodotyrosine residues. TPO activity requires a heme protein attached to ferriprotoporphyrin IX or a closely related porphyrin. IDA lowers the activities of other heme-containing enzymes, such as cytochrome oxidase, myeloperoxidase and succinate-ubiquinone oxidoreductase, as all are prone to depletion during iron deficiency.

Pregnant women with IDA may experience disturbances in thyroid hormone production and pregnancy complications, such as fetal death. Iodine deficiency causes hypothyroidism in pregnant women. In addition, approximately 10% of women in early pregnancy can produce antibodies which attack the thyroid gland itself. These antibodies are known as anti-thyroid peroxidase antibodies (anti-TPO-Ab). Some pregnant women who produce anti-TPO-Ab may experience subclinical or asymptomatic hypothyroidism, but their serum TSH tends to increase. Hypothyroidism in pregnancy can be serious for both mother and fetus, especially in the first trimester since during this period the fetus can only obtain thyroid hormone from the mother.[8,14-17]

We took infants' blood specimens through the umbilical vein within 24 hours after birth. In contrast, a study in India reported blood sampling taken from infants' heels to be used for thyroid screening.[18]

Another study showed that diabetic mothers had higher blood volume remaining in the placentae.[19] Therefore, we excluded subjects with maternal diabetes mellitus in our study to avoid bias. In addtion, mothers with preeclampsia, eclampsia, hypertension, and those receiving diazepam or oxytocin to induce labor were excluded as these conditions may also affect placental transfusion and thus placental blood volume. Also, infants with major congenital abnormalities were excluded. Similarly excluded were infants with birth trauma such as cephal hematoma, sub-aponeurotic bleeding, caput succedaneum, and bruising, as these conditions may affect hemoglobin levels due to extravasated blood.[19-24]

Subjects in our study were term babies who were delivered spontaneously and were from single pregnancies. Premature infants were not included as they often experience a lack of enteral intake, slower meconium discharge, and increased enterohepatic circulation, hence may have lower levels of albumin, affecting their T3, T4 and TSH levels.[23] Placenta previa, multiple pregnancies, and Caesarean sections can reduce placental transfusion compared to uncomplicated vaginal labor.[25] In twin pregnancies, twin-to-twin transfusion may also affect placental transfusion.[26]

One method of improving iron status of infants is to delay binding the umbilical cord, affecting TPO levels by decreasing T3 and T4, and increasing TSH. IDA in infants may lead to more serious problems, such as motor disorders, reduced cognitive abilities, behavioral disorders, and irreversible *myelin* disruption.[4-7]

A limitation in our study was the small number of subjects, since most parents did not allow blood specimens to be taken from their babies. There were some factors that were not assessed which may lead

to bias and affect the results of study, such as maternal nutritional status, infant caloric intake and relatively short hospitalization time.

We found no significant correlation between maternal Hb and infant T3 and TSH levels, but maternal Hb had a weak correlation to infant T4 levels. In addition, we found maternal ferritin levels was not correlated to newborn T3, T4 and TSH levels.

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