

## **Difference of thyroid hormone reference ranges in diagnosis of thyroid functions between normal pregnant women in the early, middle and late pregnancy and normal adults.**

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### **Abstract**

**Objective:** To discuss and analyze the difference in thyroid hormone reference ranges between normal pregnant women and normal adults, and study the thyroid dysfunction in pregnant women during pregnancy.

**Methods:** Blood samples of 166 pregnant women and 50 non-pregnant women were randomly collected, to detect Thyroid Stimulating Hormone (TSH), Free Triiodothyronine (FT3), Free Thyroxine (FT4), Total Triiodothyronine (TT3) and Total Thyroxine (TT4).

**Results:** The ratio of thyroid dysfunction was 9.64% (16/166) by using normal thyroid hormone reference ranges of pregnant women as an index, while the ratio of thyroid dysfunction was 1.20% (2/166) by using the normal thyroid hormone reference ranges of non-pregnant women as an index. The difference in thyroid hormone reference ranges between the two methods was statistically significant ( $P<0.05$ ).

**Conclusions:** There were significant differences in thyroid hormone levels between pregnant women and non-pregnant women, and between women during different stages of pregnancy, and the ratio of thyroid dysfunction during pregnancy was 9.64%; therefore, thyroid function screening is necessary in all pregnant women.

**Keywords:** Pregnancy, Thyroid hormone, Reference ranges, Thyroid dysfunction.

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### **Introduction**

Iodine is a necessary trace element in the human body to synthesize thyroid hormone, and thyroid hormone plays an important role in human growth and development stages [1]. Since pregnant women are a special group and pregnancy is also a special physiological process, the changes in thyroid hormone metabolism, elevated plasma volume, estrogen secretion changes and changes in maternal immune status in pregnant women would cause abnormal changes in thyroid functions [2]. The demands for iodine during pregnancy will be significantly increased, so iodine deficiency may occur [3]. Excessive iodine intake can cause abnormal thyroid function, seriously affecting pregnant women and fetuses [4]. Studies have shown that, insufficient iodine intake will lead to miscarriage, stillbirth, premature birth, foetal malformations

and other pathological pregnancy responses, hinder the normal physical and physical developments of the next generation of children, cause iodine-deficiency thyroid dysfunction, which will seriously the safety of pregnant women and fetuses, therefore, a timely diagnosis and treatment of pregnant women's thyroid disease can prevent the harms [5,6]. The thyroid dysfunction disease has mild symptoms which are often neglected, but its adverse effects on pregnancy should attracted attentions [7]. Domestic and foreign relevant studies indicate that clinical abnormal thyroid gland during the pregnancy may largely increase the risk of adverse pregnancy, resulting in such sequences as abortion, miscarriage and so on. However, the studies also indicate that adverse consequence may not occur and intelligence development of the foetal may not be endangered after the patient with clinical abnormal thyroid gland during the pregnancy has been treated effectively

[8]. Clinically, the thyroid hormone reference ranges of healthy non-pregnant adults are used to compare with that of pregnant women, to judge if the pregnant women's thyroid functions are normal, which will increase the probability of misdiagnosis of thyroid dysfunction in pregnant women [9]. Race is also an important factor affecting thyroid functions and even for the same race in different regions, the thyroid hormone levels of pregnant women may be abnormal due to different iodine intakes. Therefore, it is extremely important to establish the thyroid hormone reference ranges of pregnant women in the same race and race region, and analyze their changes and differences [10]. In this study, using the normal pregnant women in early, middle and late pregnancy as subjects, we compared the thyroid hormone changes between the pregnant women and non-pregnant women in Anshun city, and conducted difference analysis, to provide accurate and reliable experimental basis for the thyroid dysfunction screening of pregnant women.

## Data and Methods

### General data

The thyroid hormone level of pregnant women aged between 20 and 45 y were collected in Anshun City from June 2012 to June 2016, including 60 cases of early pregnancy (0~13 weeks), 56 cases of mid-pregnancy (14~27 weeks) and 50 cases of late pregnancy (28~40 weeks) and 50 cases of non-pregnancy (control group), 216 cases in total. All subjects screened were healthy, without history of thyroid diseases and without hyperthyroidism or hypothyroidism signs or symptoms. They had no touchable goiter and did not take anti-thyroid, estrogen or iodine-containing drugs in recent 6 months. All subjects voluntarily participated in this study and carefully read and signed the informed consent.

### Experimental methods

**Sampling:** For all pregnancy women in early, middle and late pregnancy and non-pregnant women, 3 mL of non-anticoagulant blood was collected from elbow vein in fasting condition in the morning; then the blood was placed in tubes, after centrifugal separation, the serum was reserved at -70°C for standby.

### Instruments and reagents

Use the automated chemiluminescence immunoassay instrument (model: DX2800) imported from the agent production country. The diagnostic reagents, calibrators and QC substances were Beckman's original products.

### Experimental methods

The TSH, FT3, FT4, TT3 and TT4 of serum samples were determined by US. Beckman automated chemiluminescence immunoassay instrument and its kits. The intra-batch CV of serum indexes was <5% and the inter-batch CV was <10%.

## Diagnostic indexes (Table 1)

Table 1. Diagnostic indexes.

Thyroid dysfunction status	TSH	FT4	TT4
Clinical hypothyroidism	Elevated	Decreased	Decreased
Subclinical hypothyroidism	Elevated	Normal	Normal
Simple low T4 syndrome	Normal	Decreased	Decreased

### Quality control

Professionals were responsible for sample collection, laboratory testing and quality control. The TSH, FT3, FT4, TT3 and TT4 were determined by specially-assigned staffs of the Special Inspection Center of Anshun Hospital.

### Statistical analysis

Data processing and statistical analysis was performed using SPSS17.0 software. TSH level was in skewed distribution, expressed by the median; non-parametric test was carried out for the comparison between groups. FT3, FT4, TT3, TT4 were in symmetrical distribution, expressed by mean. The ANOVA was performed for the comparison between groups, and the chi-square test was performed for the comparison of rates between groups.  $P < 0.05$  was considered statically significant difference.

## Results

### The thyroid functions of pregnant women in early, middle and late pregnancy and non-pregnant women

The thyroid hormone levels of pregnant women in early, middle and late pregnancy and non-pregnant women were shown in Table 2. As shown from Table 2, TSH level tended to decline, more apparently in early pregnancy, and in the middle and late pregnancy, TSH level was rebounded, but still lower than that of the non-pregnancy stage. FT3 and FT4 levels were decreased with the pregnancy stage. The TT3 and TT4 levels showed a trend opposite to the FT3 and FT4 levels. The TT3 and TT4 levels in pregnant women were significantly higher than those in control group; TT3 reached the peak in late pregnancy, while TT4 reached the peak in mid-pregnancy.

### Thyroid dysfunction status of pregnant women in early, middle and late pregnancy

The thyroid dysfunction status of pregnant women in early, middle and late pregnancy was shown in Table 3. When the normal thyroid hormone reference ranges of pregnant women were used as an index, the test results showed that no clinical hypothyroidism occurred in pregnant women, but the subclinical hypothyroidism occurred, with a ratio of 3.01% (5/166), of which, 5.36% in mid-pregnancy, 4.00% in late pregnancy [10]; and low T4 syndrome occurred, with a ratio of

*Difference of thyroid hormone reference ranges in diagnosis of thyroid functions between normal pregnant women in the early, middle and late pregnancy and normal adults*

6.63% (11/166), of which 10.00% in early pregnancy, 5.36% in mid-pregnancy and 4.00% in late pregnancy.

**Table 2.** The pregnancy-pregnant and non-pregnant women with thyroid hormone reference ranges.

Group	Number cases (n)	of Median	Inter-quartile range	FT3 (pmol/L)	FT4 (pmol/L)	TT3 (nmol/L)	TT4 (nmol/L)
Control group	50	2.17	1.6	5.32 ± 1.76	16.30 ± 3.36	1.41 ± 0.78	101.97 ± 22.73
Early pregnancy	60	1.50**	2.71	4.75 ± 0.63**	15.76 ± 1.98	2.04 ± 0.73**	127.91 ± 24.05**
Mid-pregnancy	56	1.72*	1.32	4.66 ± 0.47**	13.93 ± 1.54***##	2.17 ± 0.69**	140.74 ± 24.08**
Late pregnancy	50	2.17	1.6	5.32 ± 1.76	16.30 ± 3.36	1.41 ± 0.78	101.97 ± 22.73

Note: Compared with the control group, \*P<0.05, \*\*P<0.01; Compared with early pregnancy, ##P<0.01.

When the normal thyroid hormone reference ranges of non-pregnant women were used as an index, the test results showed that no clinical hypothyroidism or low T4 syndrome occurred in pregnant women, but the subclinical hypothyroidism occurred, with a ratio of 1.20% (2/166), of which, the abnormal ratios in mid-pregnancy and late pregnancy were 1.78% and 2.00% respectively [10]. The difference in thyroid hormone reference ranges was statistically significant in judging thyroid dysfunctions of pregnant women (P<0.05).

**Table 3.** Each pregnant woman thyroid dysfunction status during pregnancy (n, (%)).

Group	Number of cases (n)	Clinical hypothyroidism		Subclinical hypothyroidism		Low T4 syndrome	
		S1	S2	S1	S2	S1	S2
Early pregnancy	60	0 (0)	0 (0)	0 (0)	0 (0)	6 (10)	0 (0)
Mid-pregnancy	56	0 (0)	0 (0)	3 (5.36)	1 (1.78)	3 (5.36)	0 (0)
Late pregnancy	50	0 (0)	0 (0)	2 (4)	1 (2)	2 (4)	0 (0)
Total	166	0 (0)	0 (0)	5 (3.01)	2 (1.2)	11 (6.63)	0 (0)

Note: S1 represented the normal thyroid hormone reference ranges of pregnant women; S2 represented the normal thyroid hormone reference ranges of non-pregnant women

**Discussion**

At present, the thyroid hormone reference ranges of pregnant women have been established in many countries, but it was rarely reported in china [11-13]. The examination of thyroid for pregnant women should adopt the specific reference ranges of each pregnancy stage [14]. In this study, we screened 166 pregnant women at different pregnancy stages and 50 non-pregnant women, and determined their TSH, FT3, FT4, TT3 and TT4 levels using automated chemiluminescence immunoassay instruments and compared them. The results showed that, TSH, FT3 and FT4 was in a decline trend during pregnancy, while TT3 and TT4 was in a rising trend during pregnancy, to establish the local thyroid hormone reference

ranges. In addition, we conducted analysis on their thyroid dysfunctions. The pregnant women had a high ratio of subclinical thyroid dysfunction. Results showed that the pregnant woman did not catch clinical hypothyroidism at each pregnant stage and the sub-clinical hypothyroidism rate is 3.01% (5/166), of which the abnormal rate is 5.36% during middle pregnancy and 4.00% during later pregnancy. The rate of low T4 symptom is 6.63% (11/166), of which the abnormal rate is 10.00% during early pregnancy, 5.36% during middle pregnancy and 4.00% during later pregnancy. The normal thyroid hormone reference range of the women out of pregnancy is adopted as the test indicates and it is found that the pregnant woman does not have clinical hypothyroidism and low T4 symptom during each pregnancy stage [10]. The sub-clinical hypothyroidism rate is 1.20% (2/166), of which the abnormal rate is 1.78% and 2.00% during the middle and later pregnancy stages, respectively. In judging the abnormality of thyroid gland functions of pregnant women during pregnancy, the differences of two thyroid hormone reference ranges are significant statistically (P<0.05). The thyroid hormone levels of normal pregnant women of different races in different regions were varied, and its changes in various pregnancy stages were varied, which were possibly associated with the races, regions and detection reagents. Therefore, it is required to establish the local thyroid hormone reference ranges of pregnant women.

The thyroid hormones of pregnant women are very important for the development of cerebral cortex responsible for intelligence, hearing and language. The thyroid hormones secreted by mothers will always influence the foetal development [15]. Iodine intake also affects the function of the thyroid, and inadequate iodine intake will directly lead to hypothyroidism, and further lead to mother's subclinical hypothyroidism and low T4 syndrome [16]. In about 20 weeks after pregnancy, the foetus's thyroid can be basically formed to play its role in the synthesis and secretion of thyroid hormones, but before that, the thyroid hormones that foetus needs is dependent on the mother, especially in the early pregnancy, it is totally from maternal secretion [17].

In conclusion, in this study, we established the thyroid hormone reference ranges of normal pregnant women in all pregnancy stages in Anshun City, revealed the range of thyroid

hormone levels of the local pregnant women, and conducted statistical analysis of thyroid dysfunctions, which can provide valuable basis for the clinical diagnosis, detection and treatment of thyroid dysfunction of pregnant women.

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