

# Reference Interval of Thyroidal Function of Women in the Early, Middle and Late Pregnancy in Jingzhou City, Hubei Province

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**Abstract** [Objectives] To study the reference value of thyroid function in healthy women of childbearing age during different pregnancies (early, middle and late pregnancy) in Jingzhou City. [Methods] 362 healthy women of childbearing age during different pregnancies (early, middle and late pregnancy) were selected as the study group, and 360 non-pregnant women were selected as the control group. Serum thyroid hormone levels in the two groups were detected, and the reference value was expressed as the median (M) and 95% confidence interval (CI). On this basis, the chart of changing trend of thyroid hormone in the early, middle and late pregnancy were plotted. [Results] Compared with the control group, FT3, TT4, TT3, FT4 and TSH in the early, middle and late pregnancy were significantly different in the study group ( $P < 0.05$ ). In the study group, there were significant differences in the early, middle and late pregnancy ( $P < 0.05$ ). [Conclusions] This trend chart has certain reference value in the screening, diagnosis and treatment of thyroid diseases in healthy women of childbearing age during different pregnancies (early, middle and late pregnancy) in Jingzhou City of Hubei Province.

**Key words** Early, middle and late pregnancy, Thyroid function, Reference value, Thyroid hormone

## 1 Introduction

Thyroid dysfunction is a high risk factor for metabolic syndrome in pregnant women of childbearing age<sup>[1]</sup>. Abnormal iodine intake is the main cause of abnormal thyroid function (including hypothyroidism and hyperthyroidism)<sup>[2]</sup>. Among them, the greatest harm caused by hypothyroidism during pregnancy is fetal neurocognitive dysplasia<sup>[3]</sup>. Hyperthyroidism in women of childbearing age mainly causes high metabolic diseases in pregnant women, but has limited impact on intelligence, growth and development of newborns, mainly showing transient thyroid dysfunction<sup>[4]</sup>. Regular examination of thyroid function during pregnancy is of great significance for the detection and timely treatment of thyroid dysfunction, as well as for the protection of maternal and infant safety and the improvement of birth population quality<sup>[1,5]</sup>.

## 2 Data and methods

**2.1 General information** A total of 362 healthy pregnant women with single or multiple pregnancies who were treated in the outpatient department of Jingzhou First People's Hospital of Hubei Province from March 2021 to February 2024 were selected as the study group, and 360 healthy non-pregnant women (unmarried and non-pregnant healthy women who volunteered to participate in the study) were selected as the control group. In the study group, pregnant women were (22–45) years old, with an average age of (30.27 ± 3.02) years. A total of 1645 subjects were included in the two groups. In the control group, the women were (22–46) years old, and their mean age was (30.54 ± 4.07) years old. The levels of free tetraiodothyronine (FT4), serum total thyroxine (TSH), free triiodothyronine (FT3), total thyroxine (TT4) and total triiodothyronine (TT3) were detected in both groups<sup>[2,6]</sup>. In

the study group, the above indicators were detected in three stages, namely the early (gestational weeks: < 12 weeks), middle (gestational weeks: 13–26 weeks) and late pregnancy (gestational weeks: 27–36 weeks). In the control group, they were randomly tested only once.

**2.2 Inclusion and exclusion criteria** Inclusion criteria: (i) they ate iodized salt for 10 years or more; (ii) they were healthy Han women with single or multiple pregnancies aged 22–46 years; (iii) Their thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TGAb) were negative; (iv) their thyroid gland was normal without enlargement, and there were no symptoms and signs of hyperthyroidism or hypothyroidism; (v) they had no history of thyroid dysfunction, family history of thyroid disease, thyroid surgery history, autoimmune disease history, especially type 1 diabetes, and history of abortion and hyperemesis gravidarum; (vi) none of them had taken iodine and anti-thyroid drugs recently<sup>[2,6–7]</sup>. Exclusion criteria: (i) women with positive thyroid receptor antibody and TGAb and TPOAb; (ii) those who are not living or living in Jingzhou City for a long time were excluded; (iii) pregnant women who took iodine-containing drugs and antithyroid drugs during pregnancy were excluded; (iv) women having family history of thyroid disease, suffering from goiter, hypothyroidism or hyperthyroidism should be excluded; (v) women suffering from serious heart, brain and kidney diseases, gastrointestinal bleeding and moderate-to-severe anemia were excluded; (vi) women suffering from goiter should be excluded<sup>[2,6–7]</sup>.

**2.3 Detection indicators and calculation method of reference value of thyroid hormone** Fasting venous blood of the women in the control group and the study group were collected in the early (gestational weeks: < 12 weeks), middle (gestational weeks: 13–26 weeks) and late pregnancy (gestational weeks: 27–36 weeks). The levels of TT3, TSH, FT3, FT4 and TT4 were detected by immunochemiluminometric assays, and the changing trend chart of thyroid hormone during pregnancy was drawn. The refer-

ence value of thyroid hormone was expressed with 95% confidence interval (CI) and median (M).

**2.4 Statistical treatment** Kmogorov-Smirnov method was used to correct the normal distribution of the measured values of TT3, TSH, FT3, FT4 and TT4. The measured data with normal distribution were represented by " $\bar{x} \pm s$ ", and if they did not follow normal distribution, the range of the reference value was represented by the median (M) and 95% confidence interval (CI). Analysis of variance, *t* test or rank sum test were used, and  $P < 0.01$  and  $P < 0.05$  mean that the difference was statistically significant.

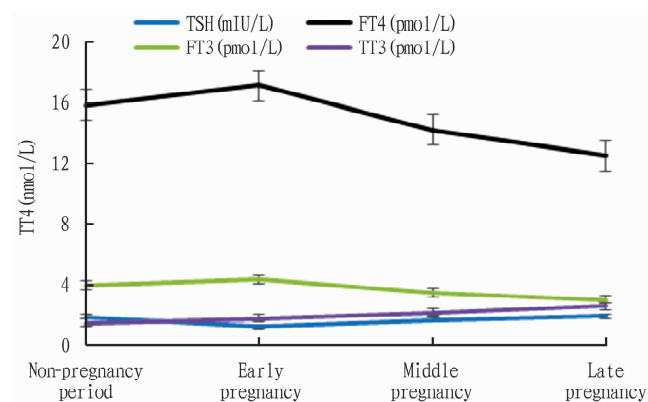
**Table 1** Biological reference intervals of TT3, TSH, FT3, FT4 and TT4 in the two groups [M (P2.5 – P97.5)]

Group	Number of cases ( <i>n</i> )	Time	TT3//nmol/L	TSH//mIU/L	FT3//pmol/L	FT4//pmol/L	TT4//nmol/L
Control	360	Non-pregnancy period	1.53 (0.90 – 2.70)	1.92 (0.30 – 5.21)	3.89 (2.80 – 7.11)	15.27 (9.27 – 24.77)	98.22 (59.63 – 146.24)
Study	362	Early pregnancy	1.76 (1.31 – 5.90) <sup>a</sup>	1.29 (0.04 – 4.27) <sup>a</sup>	4.40 (3.70 – 7.03) <sup>a</sup>	17.05 (10.78 – 26.60) <sup>a</sup>	145.08 (74.7 – 232.15) <sup>a</sup>
	362	Middle pregnancy	2.03 (1.58 – 5.82) <sup>ab</sup>	1.74 (0.14 – 5.02) <sup>ab</sup>	3.60 (2.62 – 6.08) <sup>ab</sup>	14.08 (12.08 – 24.91) <sup>ab</sup>	176.90 (96.95 – 240.94) <sup>ab</sup>
	362	Late pregnancy	2.72 (1.59 – 5.27) <sup>abc</sup>	1.93 (0.19 – 6.17) <sup>bc</sup>	3.1 (12.50 – 4.99) <sup>abc</sup>	12.13 (11.49 – 23.02) <sup>abc</sup>	191.60 (103.90 – 249.33) <sup>abc</sup>

**NOTE** Compared with the control group, <sup>a</sup> $P < 0.05$ ; compared with the early pregnancy, <sup>b</sup> $P < 0.05$ ; compared with the middle pregnancy, <sup>c</sup> $P < 0.05$ .

### 3.2 Changing trend of thyroid hormone levels (M) in the early, middle and late pregnancy

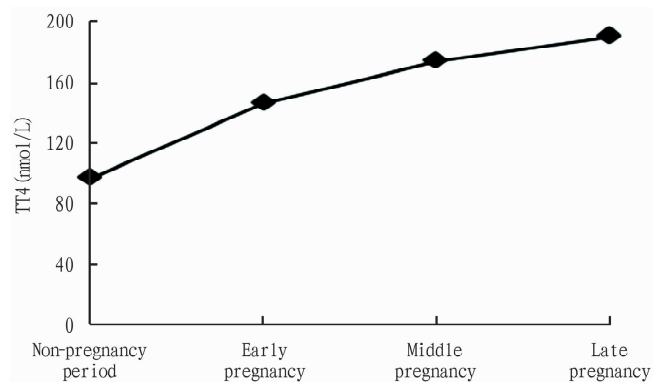
Fig. 1 shows that TSH in the early and middle pregnancy was lower than that in the non-pregnancy period and the late pregnancy, and it higher in the middle pregnancy compared with the early pregnancy. In the late pregnancy, it gradually recovered to that in the non-pregnancy period, and the difference between the groups was statistically significant ( $P < 0.05$ ). The changes of TT3, FT3 and FT4 were opposite to the changes of TSH in different gestational weeks. Compared with the non-pregnancy period, they were high in the early pregnancy, and gradually decreased with the increase of pregnancy. That is, they were low in the middle pregnancy compared with the non-pregnancy period and the early pregnancy, and the minimums appeared in the late pregnancy. The difference between different groups was statistically significant ( $P < 0.05$ ). As shown in Fig. 1 and Fig. 2, TT3 and TT4 gradually rose with the increase of pregnancy, and the difference between various groups was statistically significant ( $P < 0.05$ ).



**Fig. 1** Changing trends of TT3, FT3 and FT4

## 3 Results and analysis

**3.1 Reference value of serum thyroid hormone in the two groups** Compared with the control group, the levels of TT3, TSH, FT3, FT4 and TT4 in the study group were statistically significant in different pregnancies (early, middle and late pregnancy) ( $P < 0.05$ ), and in the study group, there were also statistically significant differences in the early, middle and late pregnancy ( $P < 0.05$ ). Moreover, they were different from the reference values in the guidelines of the American Thyroid association (ATA) (Table 1).



**Fig. 2** Changing trend of TT4 in the early, middle and late pregnancy

## 4 Discussion and conclusions

Thyroid hormone plays an important role in screening, clinical diagnosis and treatment of thyroid diseases, improving maternal and infant outcomes, and avoiding pregnancy-induced hypertension, intrauterine growth retardation, abortion, fetal distress, and long-term fetal intellectual disability<sup>[2,8]</sup>. Studies have shown that maternal hypothyroidism may lead to low weight of a newborn baby<sup>[9]</sup>. In addition, maternal hyperthyroidism can increase the probability of macrogynia, lead to placental abruption, fetal abortion, premature delivery or even stillbirth, significantly increase the incidence of maternal hypertension and diabetes during pregnancy and perinatal fetal mortality. Therefore, it is of great significance to establish the reference value of thyroid hormone during pregnancy for healthy pregnant women in this region and provide guidance for pregnancy health care<sup>[2,10]</sup>.

The *Guidelines for the Diagnosis and Treatment of Thyroid Diseases during Pregnancy and Postpartum Period (2<sup>nd</sup> Edition)* formulated and promulgated in 2019 have played an important role in guiding the diagnosis and treatment of thyroid diseases during

pregnancy and postpartum period. However, due to the differences in iodine intake and thyroid hormone levels in different regions, this standard may be regional differences<sup>[11]</sup>. It is necessary to establish the reference value of serum thyroid hormone in healthy women of childbearing age during the early, middle and late pregnancy in Jingzhou. In this study, TSH in the early and middle pregnancy was lower than that in the non-pregnancy period and the late pregnancy, and it higher in the middle pregnancy compared with the early pregnancy. In the late pregnancy, it gradually recovered to the value in the non-pregnancy period. The variations of TT3, FT3 and FT4 were opposite to the changes of TSH in various gestational weeks. Compared with the non-pregnancy period, they were high in the early pregnancy, and gradually decreased with the increase of pregnancy. That is, they were low in the middle pregnancy compared with the non-pregnancy period and the early pregnancy, and the minimums appeared in the late pregnancy. TT3 and TT4 gradually rose with the increase of pregnancy.

In summary, through the general survey, the reference value of thyroid function in pregnant women of childbearing age during different pregnancies (early, middle and late pregnancy) in Jingzhou City was established, and the chart of their changing trends with gestational weeks was drawn to provide a reference for screening, clinical diagnosis and treatment of thyroid diseases in Jingzhou City. At the same time, this research result is also conducive to the prevention of thyroid diseases in pregnant women and the protection of childbirth and childbearing in pregnant women in Jingzhou City.

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