Serum Thyroglobulin Concentration in Normal Pregnancy

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Abstract

We measured the levels of serum thyroglobulin (Tg) in 52 pregnant females at various stages and compared them with those of 15 age-matched nonpregnant females. Serum Tg was measured by a solid-phase immunoradiometric assay. In pregnant females, mean serum Tg levels at the first, second, early third, and late third trimesters were 8.4 (range; 1.3-18.0), 9.2 (1.7-25.6), 10.1 (1.8-22.8), and 12.1 ng/ml (5.3-25.2), respectively. The statistical comparison was made after logarithmic transformation of the data. The mean value only at the late third trimester was significantly higher than that of controls (mean; 6.0 ng/ml, range; 1.5-23.6), but each value was within the normal range. Although serum Tg levels have been reported to be high at the end of pregnancy, our results indicate that the Tg levels in females could be clinically interpreted without regard to the coexistence of pregnancy.

Recent progress in radioimmunoassay (RIA) technology has shown that thyroglobulin (Tg) is a protein normally secreted by the thyroid gland (Van Herle et al., 1979) and can be detected in the serum of virtually all normal subjects (Roitt and Torrigiani, 1967; Van Herle et al., 1973; Pezzino et al., 1977; Bodlaender et al., 1978; Roti et al., 1981). The clinical usefulness of measuring serum Tg levels in thyroidal and nonthyroidal disorders has been pointed out by many workers. For example, high levels of serum Tg have been reported in patients with Graves’ disease (Van Herle et al., 1973; Izumi and Larsen, 1978; Gardner et al., 1979; Pacini et al., 1980), and differentiated thyroid carcinoma (Van Herle and Uller, 1975; Shlossberg et al., 1979; Pacini et al., 1980), whereas the suppression of serum Tg levels in thyrotoxicosis factitia has been reported (Mariotti et al., 1982).

Elevated levels of serum Tg have also been reported in normal pregnant women at the third trimester (Torrigiani et al., 1969) and at delivery (Van Herle et al., 1973; Pacini et al., 1980; Roti et al., 1981). However, there has been little information concerning the level of serum Tg in each trimester of normal pregnancy. Therefore, it is not clear whether the levels of serum Tg in pregnant women can be used in the assessment of the clinical states of thyroidal disorders.

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The purpose of this study is to examine the concentrations of serum Tg at various stages of normal pregnancy and to compare them with those of nonpregnant controls.

**Materials and Methods**

1) **Subjects and Tg assay**

Serum samples were obtained from 52 normal pregnant females who were clinically in a euthyroid state and had no history of any thyroid disease. Their mean age was $27.8 \pm 3.5$ (SD) years with a range of 22 to 36 years old. They were divided into four groups according to the stage of pregnancy [the first trimester (8–13 weeks): n=6, the second trimester (14–26 weeks): n=16, the early third trimester (27–33 weeks): n=16, and the late third trimester (34–39 weeks): n=14]. Sera from 15 healthy nonpregnant females who showed normal blood chemistry and normal levels of T3, T4, TSH, and TBG served as controls. Their mean age was $29.1 \pm 3.7$ years with a range of 23 to 36 years. Serum samples from pregnant and nonpregnant women were obtained in the morning and stored at $-20^\circ$C until assayed.

All serum samples were tested for the presence of Tg-autoantibodies and antimicrosomal antibodies by the tanned red cell hemagglutination method using commercial kits (Thyroid test and Microsome test, Fuji Zoki, Japan). Samples with a titer of 1 : 20 or more in either test were not included in the present study.

All samples were analyzed in duplicate in the same assay. Serum Tg was measured by a solid-phase, sandwich-type, immunoradiometric assay (Human Thyroglobulin Immunoradiometric Assay Kit, CIS) (Nakamura et al., 1984). The normal adult reference range was $1.0-26.6$ ng/ml.

2) **Statistical analysis**

Statistical analysis was performed using Student’s t-test after logarithmic transformation of the Tg levels, since the Tg values for healthy

![Fig. 1. Serum concentrations of Tg in 52 pregnant and 15 nonpregnant females. Serum Tg levels of nonpregnant females are noted at “0” week.](image-url)
subjects showed an approximately normal distribution in the logarithmic scale (Van Herle et al., 1976; Nakamura et al., 1984). The Mann and Whitney U test was performed using the native values for Tg (Pezzino et al., 1977; Nakamura et al., 1984). Differences were considered to be significant if p was less than 0.05. Mean values in the results were calculated from the levels of log Tg.

Results

Figure 1 shows the concentrations of serum Tg obtained from 52 pregnant and 15 nonpregnant females. Table 1 shows the mean logarithms for serum Tg and the range. The mean serum Tg concentration calculated from the logarithms for serum Tg of nonpregnant control females was 6.0 ng/ml with a range of 1.5 to 23.6 ng/ml. For pregnant women, the mean serum Tg levels at the first, second, early third, and the late third trimesters were 8.4 (range; 1.3—18.0), 9.2 (1.7—25.6), 10.1 (1.8—22.8), and 12.1 ng/ml (5.3—25.2), respectively. The variation of log Tg levels in the control group was not significantly different from that of the 4 pregnant groups.

The mean value at the late third trimester was significantly higher (p<0.05 in both statistical analyses) than that of the controls. On the other hand, each mean value at the first, second, and early third trimesters was not significantly different from that of the controls when estimated by either Student's t-test or the Mann and Whitney U test.

Discussion

Virtually all aspects of thyroid hormone economy are affected by pregnancy. For example, it is well known that T3 and T4 steadily increase during the first trimester and remain at high levels thereafter (Chan et al., 1975; Yamamoto et al., 1979; Skjöldebrand et al., 1982).

Concerning the values for serum Tg in normal pregnant women, only a few reports have been published. An earlier report by Hjort and Pedersen (1962) using a semiquantitative hemagglutination-inhibition technique showed that serum Tg was not detected in nonpregnant women but was detected in 3, 11, and 50% of pregnant women at the end of the first trimester, at six weeks before delivery, and at delivery, respectively. Torrigiani et al. (1969), using RIA, compared the serum Tg levels of nonpregnant women with those of pregnant women at the first and third trimesters. In their study, there was no significant rise in Tg at the first trimester, but at the third trimester a significant rise in serum Tg levels was observed.

<table>
<thead>
<tr>
<th>Trimester</th>
<th>n</th>
<th>log Tg (mean ± SD)</th>
<th>Range (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pregnant women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>first</td>
<td>6</td>
<td>0.926±0.422</td>
<td>1.3—18.0</td>
</tr>
<tr>
<td>second</td>
<td>16</td>
<td>0.962±0.340</td>
<td>1.7—25.6</td>
</tr>
<tr>
<td>early third</td>
<td>16</td>
<td>1.005±0.325</td>
<td>1.8—22.8</td>
</tr>
<tr>
<td>late third</td>
<td>14</td>
<td>1.084±0.238*</td>
<td>5.3—25.2</td>
</tr>
<tr>
<td>nonpregnant controls</td>
<td>15</td>
<td>0.778±0.384</td>
<td>1.5—23.6</td>
</tr>
</tbody>
</table>

*: p<0.05 vs. controls (Student's t-test)
In our study, the mean serum Tg concentration was significantly higher only at the late third trimester of pregnancy than that of controls. The fact that serum Tg levels rise toward the end of pregnancy is supported by the studies of Van Herle et al. (1973), Pacini et al. (1980), and Roti et al. (1981).

Concerning the degree of rise in Tg at the end of the pregnancy, controversy still exists. Roti et al. (1981) reported that Tg levels of term pregnant women were about 4 times higher than those of controls. On the other hand, Van Herle et al. (1973) reported that the difference was slight.

We could not find any significant change in Tg levels at the first and second trimester. This is apparently in contrast with the report of Hjort and Pedersen (1962). However, their method was a semiquantitative hemagglutination method and less precise than the present method.

Van Herle et al. (1973) reported that the elevated serum Tg levels in pregnant women at delivery might be related to human chorionic thyrotropin (hCT) in the maternal circulation. Recent data (Harada et al., 1978 and 1979), however, do not support the view because the thyrotropic activity of so-called hCT is questionable. At present, the mechanism(s) that causes the elevation of the serum Tg concentration in pregnant women at the late third trimester is still obscure.

Recently, it has been shown that determinations of serum Tg concentrations could provide useful information concerning the recurrence of thyroid carcinoma (Van Herle and Uller, 1975; Shlossberg et al., 1979; Pacini et al., 1980) and the decision to discontinue antithyroid drug in the treatment of Graves' disease (Kawamura et al., 1983). From the results of the present study, it is concluded that pregnancy per se does not likely cause misinterpretation of the evaluation of the Tg level in patients with thyroid disease, since (1) the serum Tg level in pregnant females at the first, second, and early third trimesters is not different from that of controls and (2) the mean serum Tg level in pregnant females at the late third trimester is only slightly higher than that of controls when compared with the clearly elevated Tg level in patients with thyroid disease (Van Herle et al., 1973 and 1975; Izumi and Laysen 1978; Gardner et al., 1979; Shlossberg et al., 1979; Pacini et al., 1980).

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References


in pregnant and parturient women and in newborn infants. *Lancet* ii, 259–263.


