# SERUM LEVEL OF BIOTIN RATHER THAN THE DAILY DOSE IS THE MAIN DETERMINANT OF THE INTERFERENCE ON THYROID FUNCTION ASSAYS IN PATIENTS WITH BIOTINIDASE DEFICIENCY

Ahu Paketçi[1], Engin Köse[2], Özlem Gürsoy Çalan[3], Sezer Acar[1], Pelin Teke[2], Ferhat Demirci[3], Ayhan Abacı[1], Korcan Demir[1], Nur Arslan[2], Ece Böber[1]
Dokuz Eylül University, [1]Pediatric Endocrinology, [2]Pediatric Metabolism and Nutrition, [3]Biochemistry, İzmir, Turkey

**Introduction:** High doses of biotin are reported to cause incorrect results in various immunoassays in some patients. However, there is no systematic study regarding biotin interference in childhood.

**Aim:** To assess thyroid function with different methods in subjects with biotinidase deficiency. to determine the factors causing interference. and to investigate the efficiency of the methods for overcoming interference.

**Subjects:**

- **Group 1:** Children with biotinidase deficiency who were regularly treated with biotin
  - Blood samples were obtained two hours after the morning biotin dose.
- **Group 2:** Healthy subjects

**Methods:**

- fT3. fT4. and TSH levels were measured using both biotin-containing (Beckman Coulter) and biotin-free methods (Siemens Advia Centaur XP).
- Serum biotin levels were measured (in duplicate) with an ELISA-based kit.
- Streptavidin coated magnetic particles were used to remove biotin for serum samples of cases with biotin interference.

**Table 1.** Age, gender, weight, and height were similar between two groups (All *p* values >0.05)

| | Group 1 (n=44) | Group 2 (n=30) |
|---|---|---|
| **Age (year)** | 1.83 (1.04 – 2.9) | 1.05 (0.37 – 3.37) |
| **Gender (female/male)** | 26/18 | 16/14 |
| **Weight SDS** | 0.12 (-0.46 – 0.60) | 0.26 (-0.66 – 1.01) |
| **Height SDS** | -0.20 (-1.03 – 0.56) | 0.38 (-0.65 – 1.01) |

**Figure 1.** Nearly two thirds of the patients in Group 1 had high levels of fT3 and fT4 as measured by Beckman Coulter. TSH measurements were all normal (Not shown).

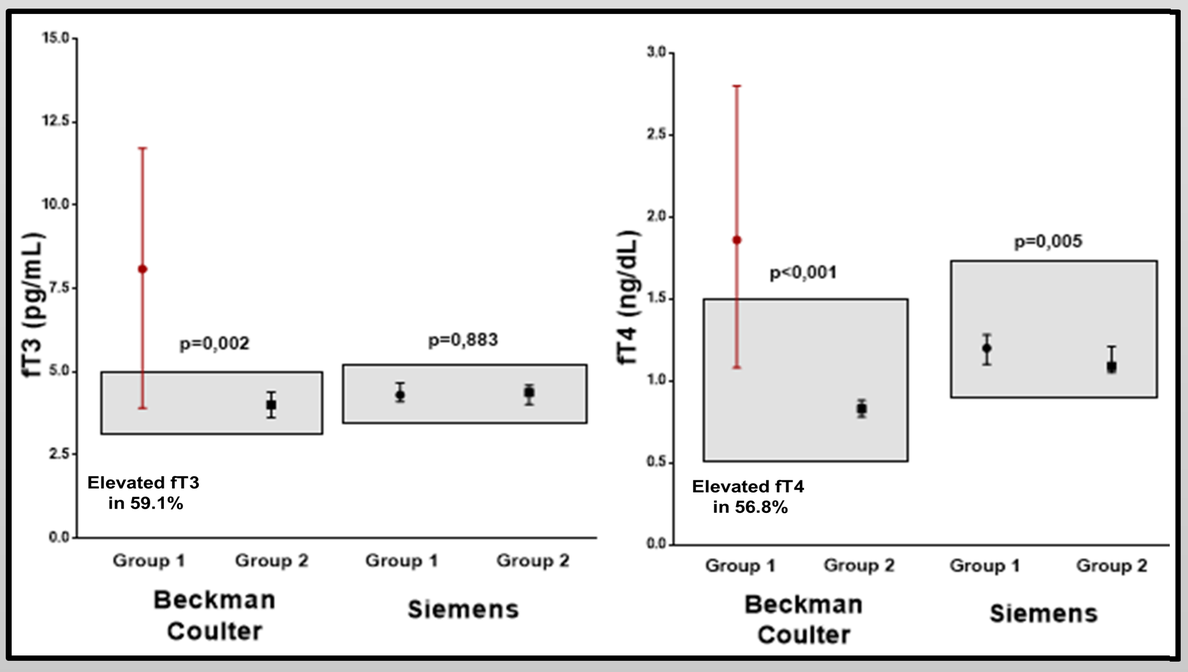



**Figure 2.** The serum biotin level of 80.35 µg/L was found to be the best cut-off value for predicting interference (96.2% sensitivity and 94.4% specificity) with a discriminative ability of 0.987±0.01 (95% CI: 0.962–1.000, p<0.001**).**

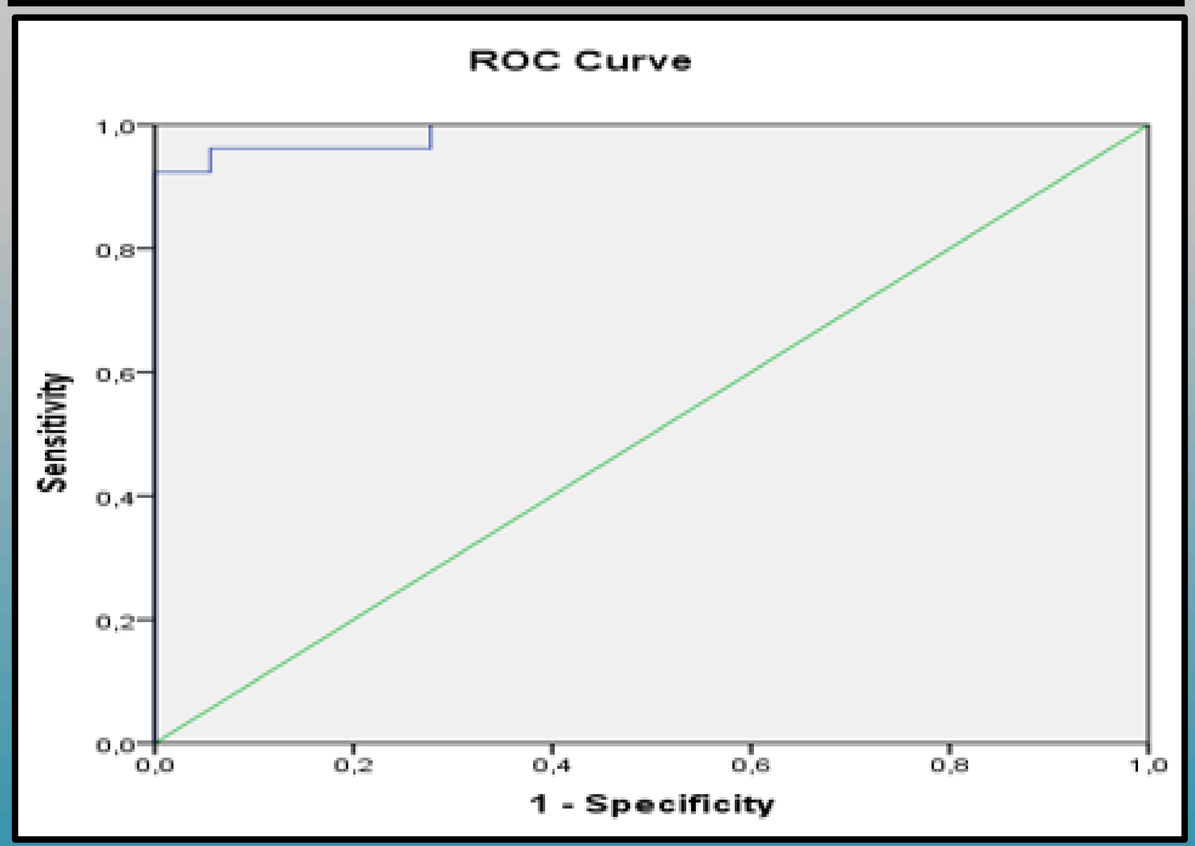


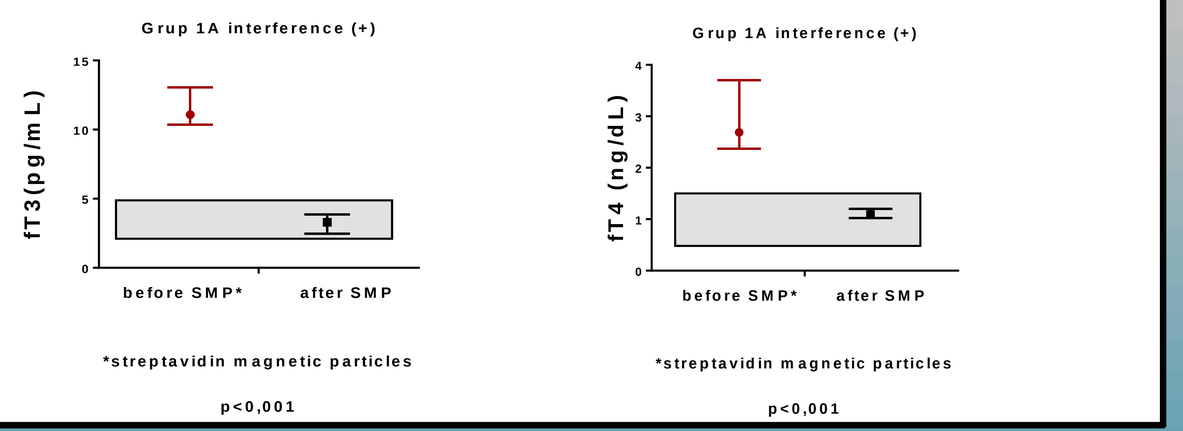

**Table 2.** Other baseline features of the two groups. Biotin levels were significantly higher in Group 1 (p <0.001 ).

| | Group 1 (n=44) | Group 2 (n=30) |
|---|---|---|
| **Partial deficiency** | 32 (%72.7) | - |
| **Duration of treatment (month)** | 20 (11.5-38.8) | - |
| **Dose (mg/day)** | 10 (10-10) | - |
| **Dose (mg/kg/day)** | 0.83 (0.74 – 0.83) | - |
| **Serum biotin (µg/L)** | 136.78 (52.15 – 261.70) | 0.30 (0.17-0.39) |

**Table 3.** Characteristics of patients with (Group 1A) and without interference (Group 1B) in Group 1, where serum biotin levels showed a strong positive correlation with fT3 (r=0.867) and fT4 levels (r=0.905).

| | Group 1A (n=26) | Group 1B (n=18) | *p* |
|---|---|---|---|
| **Age** | 1.83 (1.18-2.49) | 2.07 (0.96-6.22) | 0.759 |
| **Gender (female)** | 14 (%53.8) | 9 (%50) | 0.802 |
| **Partial deficiency** | 20 (%76.9) | 12 (%66.7) | 0.453 |
| **Duration of treatment** | 19.50 (12.50-33.25) | 21 (9.75-69.75) | 0.577 |
| **Dose (mg/day)** | 10.00 (10.00-10.00) | 10 (10.00-11.25) | 0.594 |
| **Dose (mg/kg/day)** | 0.83 (0.74-1.05) | 0.84 (0.63-1.05) | 0.955 |
| **Biotin level (microgram/L)** | 221.08 (144.83-348.75) | 48.58 (37.79-71.24) | **<0.001** |

**Figure 3.** Repeated tests with Beckman Coulter revealed no interference after neutralization of biotin with streptavidin magnetic particles (SMP) in serum samples of the cases in Group 1A**.**




**Conclusion:** Interference is an important problem in thyroid function tests in children receiving biotin treatment for biotinidase deficiency. Serum levels of biotin rather than the dose are the main determinant of interference, which can be eliminated by choosing appropriate laboratory methods.