

A Single Measurement System May Not Be Enough for Questionable High Free T4 Levels

Sir,

The study by Alegre *et al.* is very interesting.¹ The paper reported incongruent free T4 (FT4) levels in relation to the clinical conditions or/and thyroid stimulating hormone (TSH), ruling out familial dysalbuminemic hyperthyroxinemia (FDH) patients and some potential interferences, and concluded that a single alternative method may not be enough to avoid the similar analytical problem.

We fully support the above conclusion. FDH is a rare autosomal dominant genetic disorder (albumin gene variant (R218S)).² There is a pseudo-high FT4 report on laboratory testing and an increased risk of miscarriage for FDH. Recently, we also collected a group of results of high FT4 levels in a 33-year female. Although the test results from the Beckman Coulter and Roche measurement systems showed that FT4 was high (Table I), there was no evidence of abnormal thyroid function. The woman had been trying to conceive without any treatment and drugs. However, there was a normal value of FT4 from the measurement system of Mindray (CL-6000i) for the same patient (Table I).

Table I: The different levels of FT4 for the female patient.

Date	TSH (mIU/L)	FT3 (pmol/L)	FT4 (pmol/L)	Measurement System	Reference intervals
2022/9/22	3.28	5.44	18.39	Mindray CL-6000i	TSH: from 0.35 to 4.94 mIU/L FT3: from 2.43 to 6.01 pmol/L FT4: from 9.30 to 19.00 pmol/L
2022/9/9	5.15	5.31	24.35	Beckman Coulter UniCel Dxl 800 Access	TSH: from 0.34 to 5.60 mIU/L FT3: from 3.80 to 6.00 pmol/L FT4: from 7.89 to 14.41 pmol/L
2022/8/19	4.74	5.23	30.88		TSH: from 0.27 to 4.20 mIU/L FT3: from 3.10 to 6.80 pmol/L FT4: from 12.00 to 22.00 pmol/L
2022/7/29	3.68	6.37	37.93	Cobas 8000 Analyzer Series e602	TSH: from 0.34 to 5.60 mIU/L FT3: from 3.80 to 6.00 pmol/L FT4: from 7.89 to 14.41 pmol/L
2022/5/23	3.03	5.87	33.70	Beckman Coulter UniCel Dxl 800 Access	TSH: from 0.27 to 4.20 mIU/L FT3: from 3.10 to 6.80 pmol/L FT4: from 12.00 to 22.00 pmol/L
2021/8/24	3.01	6.47	20.66		TSH: from 0.27 to 4.20 mIU/L FT3: from 3.10 to 6.80 pmol/L FT4: from 12.00 to 22.00 pmol/L
2021/5/23	2.37	6.47	31.26		TSH: from 0.27 to 4.20 mIU/L FT3: from 3.10 to 6.80 pmol/L FT4: from 12.00 to 22.00 pmol/L
2021/5/17	2.66	6.36	32.15		TSH: from 0.27 to 4.20 mIU/L FT3: from 3.10 to 6.80 pmol/L FT4: from 12.00 to 22.00 pmol/L
2021/1/15	5.40	6.34	32.52	Cobas 8000 Analyzer Series e602	TSH: from 0.27 to 4.20 mIU/L FT3: from 3.10 to 6.80 pmol/L FT4: from 12.00 to 22.00 pmol/L

TSH, Thyrotropin; FT3, Free triiodothyronine; FT4, Free thyroxine.

Gene sequencing showed support for FDH diagnosis. To avoid the pseudo-high FT4 reports from a laboratory, we propose the following methods:

1. The doctors should be aware of FDH and ask whether the patient has FDH.
2. There may be a high FT4 result in FDH patients using the Beckman Coulter (the immunoassay system), Elecsys (Roche), and Centaur (Siemens) measurement systems but not on the Vitros (Ortho) and Mindray (CL-6000i) measurement systems.¹
3. Laboratory technologists and pathologists should be aware of FDH to avoid reporting erroneous reports.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

GMZ: Designed the report and revised the manuscript.
QJZ: Collected the case data and drafted the main part of the manuscript.
All authors approved the final version of the manuscript to be published.

REFERENCES

1. Alegre E, Casal H, Galofré JC, González Á. Questionable high free T4 concentrations: When confirming against an alternative method is not enough. *Clin Chem* 2022; **68**(9): 1128-32. doi:10.1093/clinchem/hvac114.

2. Abali S, Yavas Abali Z, Yararbas K, Semiz S. Rapid molecular diagnosis of ALB gene variants prevents unnecessary interventions in familial dysalbuminemic hyperthyroxinemia. *J Pediatr Endocrinol Metab* 2021; **34**(9):1201-05. doi: 10.1515/jpem-2021-0087.

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