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Original Research Article

Comparison of TSH, Free T3 and Free T4 between different Equipments and its Clinical Implication

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Abstract

Introduction: All major thyroid disorders are chronic, requiring laboratory evaluations for years together. Laboratory reports are likely to be obtained from various laboratories. Unless results are comparative across laboratories, clinician is faced with dilemma as to weather the serial change in reports represent change in clinical condition or not.

Method: Serum samples were analyzed in Beckman Coulter Dxi600 and Vitros 3600 for TSH (n=33), Free T4 (n=35) and Free T3 (n=36). Results were analyzed by linear regression and Bland Altman Plot.

Results: Linear regression plots found slop=1.07 and intercept=-0.11 for TSH, slope=2.07 and intercept=-0.51 for Free T4 , slope=0.71 and intercept=-0.93 for free T3

Conclusion: Although TSH results between Beckman Coulter Dxi600 and Vitros 3600 are comparable, there is lack of comparability among these equipments for Free T4 and Free T3 results. Clinicians evaluating serial Free T4 and Free T3 results in a patient must take in to consideration such variation while making clinical decision on treatment strategy.

Keywords: Thyroid; TSH, Free T4, Free T3, Inter equipment comparison.

Introduction

It is estimated that almost 42 million people in India have one or the other type of thyroid disorders[1]. Most common thyroid diseases in India are hypothyroidism, hyperthyroidism, goiter and iodine deficiency disorders, thyroiditis, and thyroid cancer. They require quarterly or biannual measurement of TSH, Free T3 and Free T4 to monitor progression of disease, modification of treatment modalities and drug dosages. As the treatment and monitoring of thyroid disorder is a lifelong requirement, particularly for hypothyroidism patients who needs to be laboratory evaluated on development of newer conditions (e.g wait gain, hypertension, diabetes mellitus, infertility, pregnancy complications, psychiatric illness, neuromuscular symptoms, cardiac dysfunction)[2] for possible interaction with newer diseases. Patients treated for thyroid cancer poses even greater challenge as their TSH needs to be maintained in almost undetectable range for the life. Thyroid hormones are measured by variety of technique; chief among them, now a days are enzyme linked immunosorbent assay (ELISA), immunofluorescence assay and chemiluminescence assay [2]. For each assay principles, there are plethora of different equipments available in the market, each having their own modifications. Due to fierce market competition, older players in laboratory testing loose out and newer players with newer technology emerge. All such methods needs to give uniformity in their results to be useful to clinicians for evaluating thyroid disorders across the multiple decades of patient life.

This study evaluates two commonly used equipments in Indian market for measurement of TSH, Free T4 and Free T3 in thyroid disorder patients.

Methodology

Fresh leftover serum samples were analyzed in Beckman Coulter Dxi600 (equipment A) and Vitros 3600 (equipment B). Both equipments use chemiluminescence immunoassay technology for measurement of TSH, Free T3 and Free T4.

33 samples were analyzed for TSH, 35 samples were analyzed for Free T4 and 36 samples were analyzed for Free T3 in spreadsheet software. Results were

analyzed by linear regression and Bland Altman Plot for each of TSH, Free T4 and Free T3. The resultant linear regression plots were evaluated for regression coefficient, slope, intercept[5].

The resultant Bland Altman Plot were analyzed for systemic bias sign and nature (constant vs proportional). Correlation between Manufactures' reference ranges were evaluated with respect to observed bias in the methods[5]. As both equipment are used in field and none of the two is reference method, Bland Altman Plots were made against mean of two equipment on X-Axis.

Results

The results of linear regression and Bland Altman Plot for Free T3 are as follows.

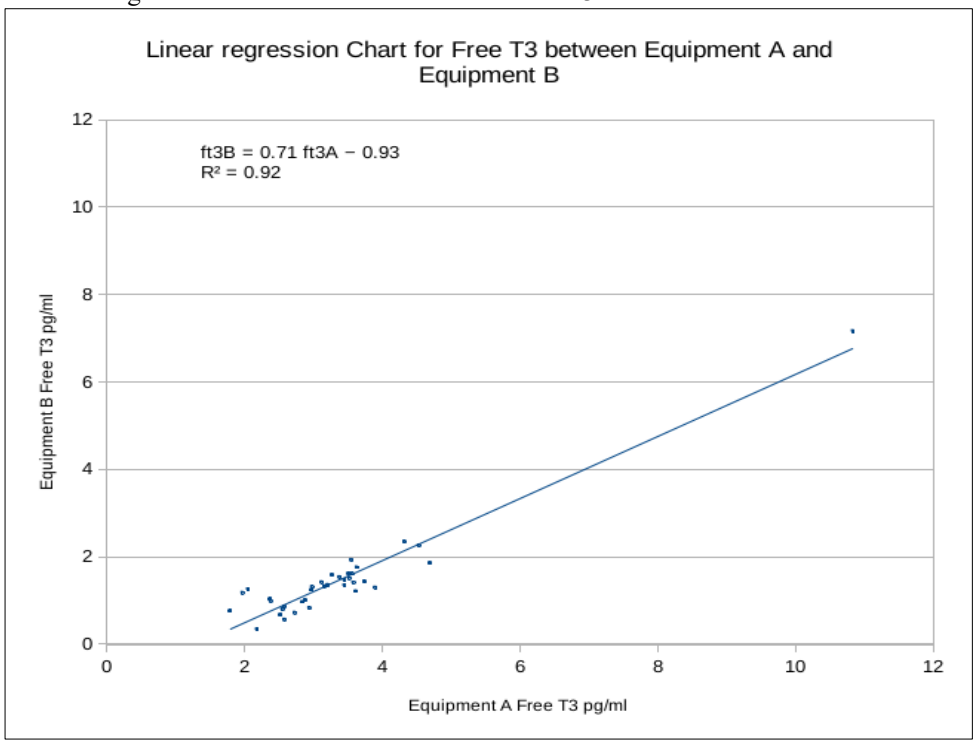

Figure 1:

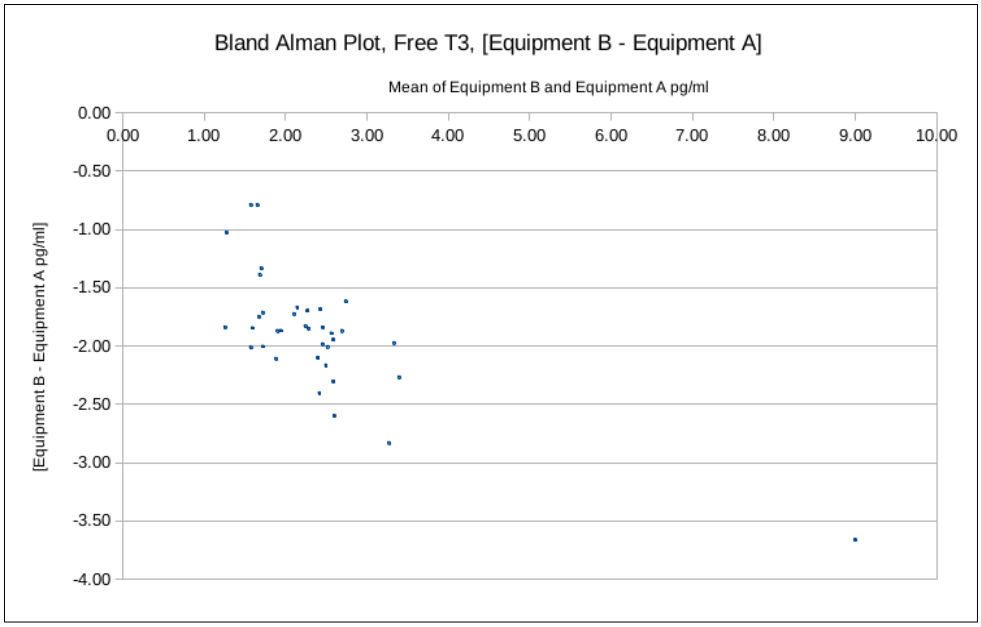

Figure 2:

The results of linear regression and Bland Altman Plot for Free T4 are as follows.

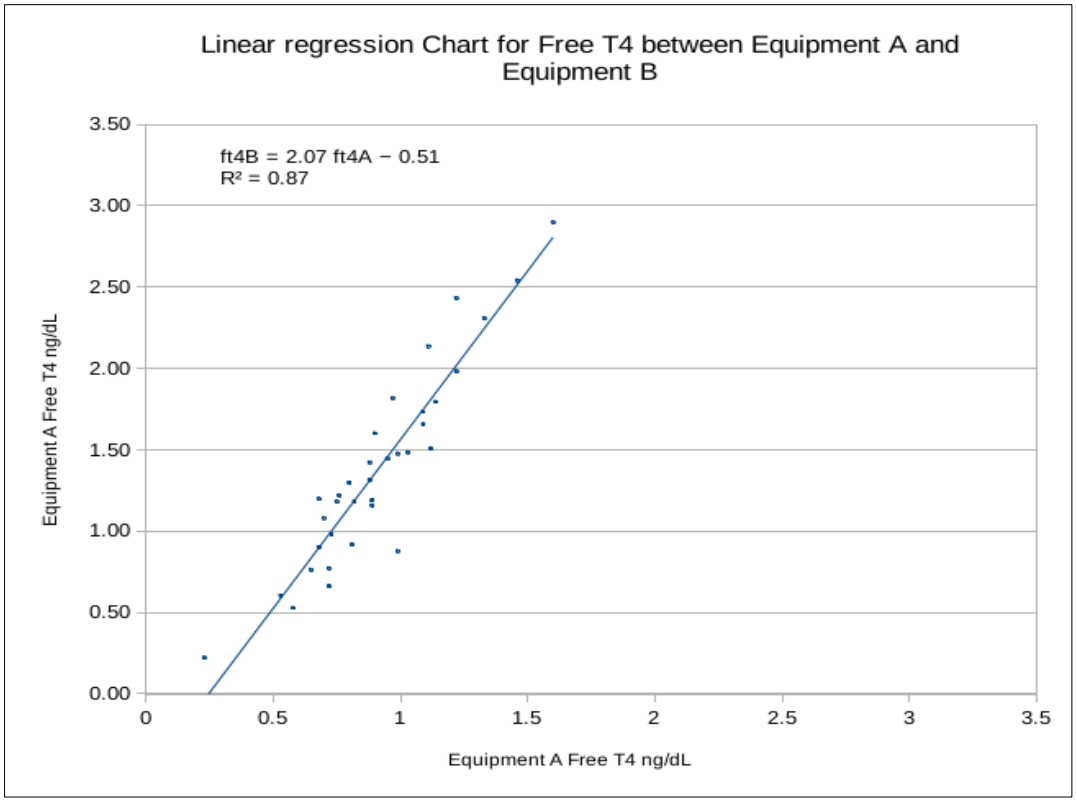

Figure 3:

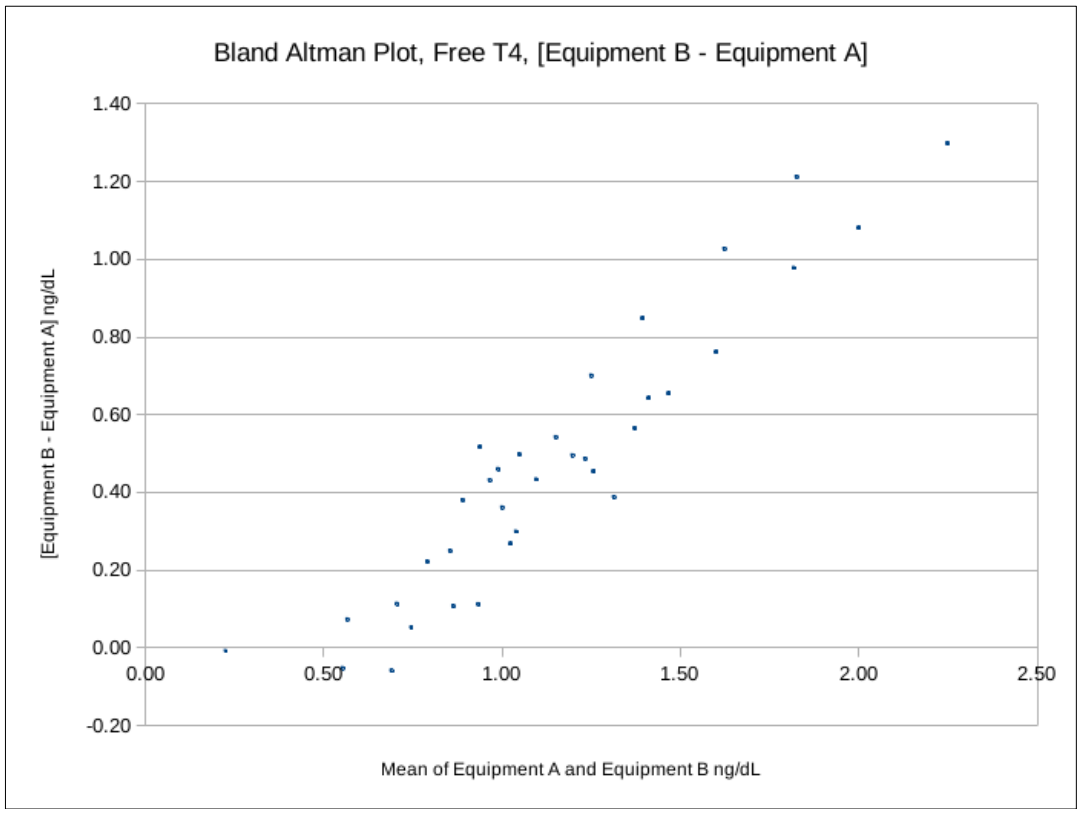

Figure 2:

The results of linear regression and Bland Altman Plot for TSH are as follows.

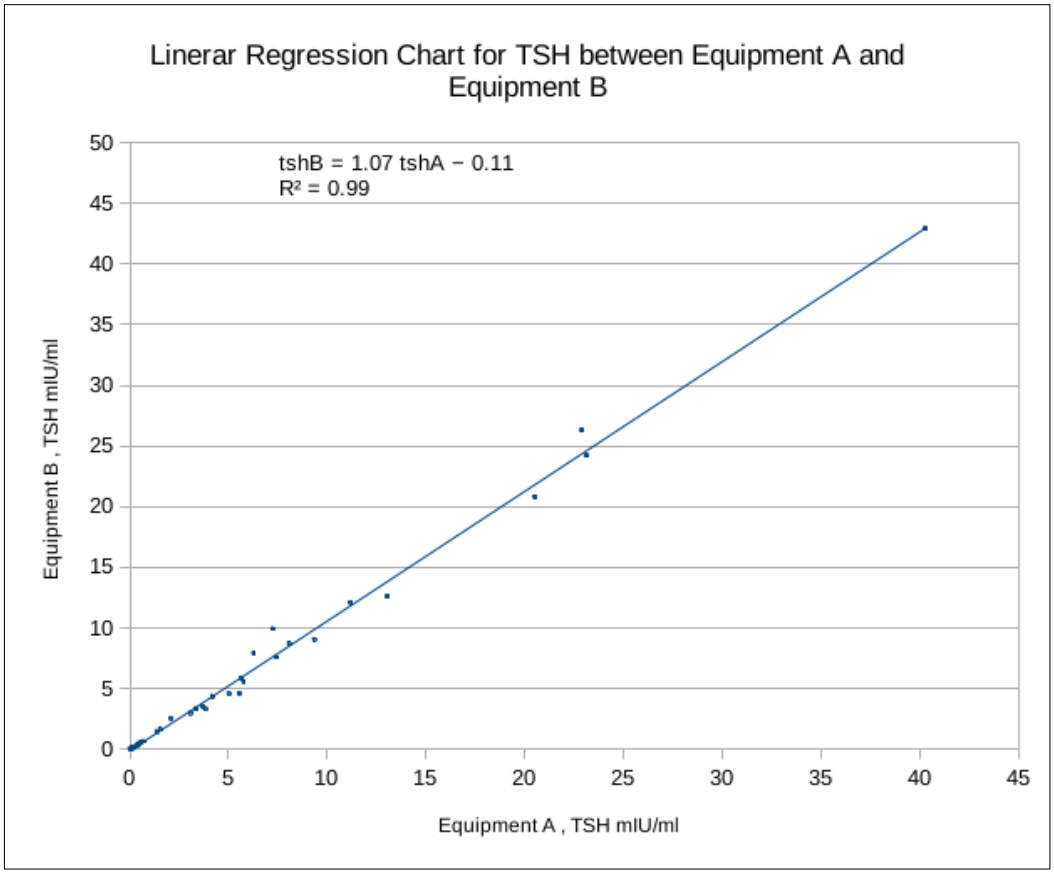

Figure 5:

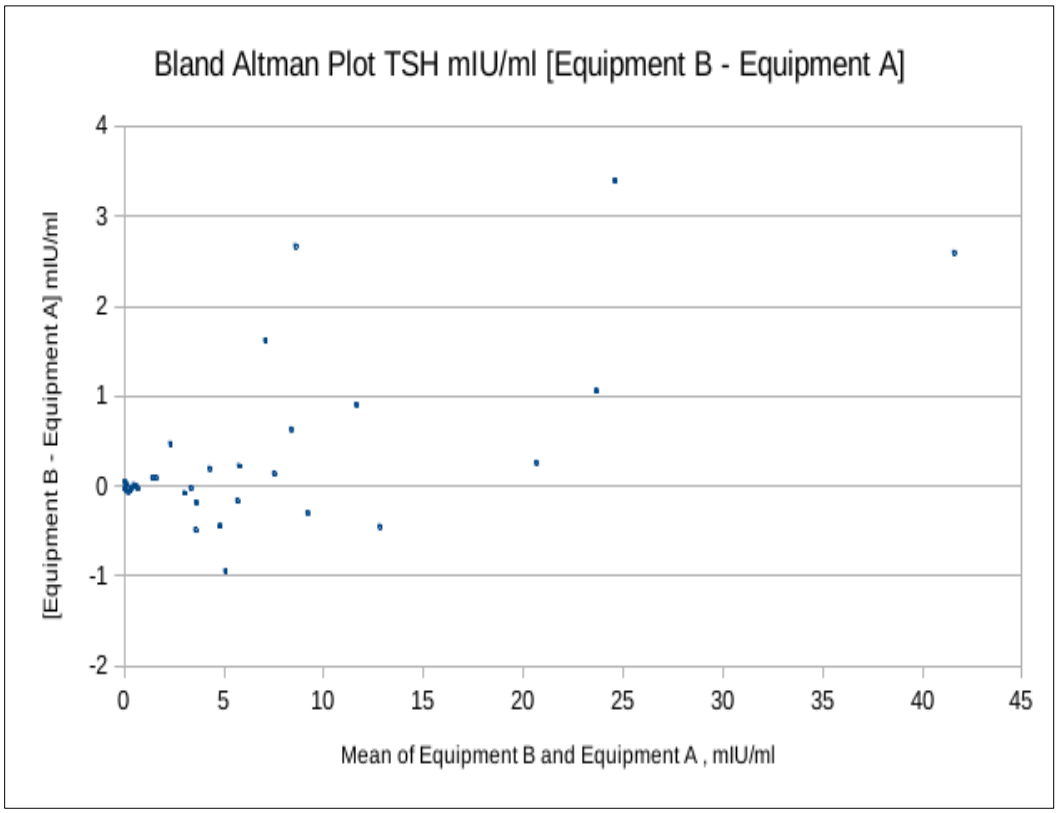

Figure 6:

Discussion

Figure 1 and 2, Linear regression plot and Bland Altman plot respectively for Free T3 shows that there is correlation between Equipment A and Equipment B reported results of Free T3 (R2 = 0.92). However, slope of 0.71 and intercept of (-0.93) indicate that Equipment B consistently gives lower Free T3 result as compared to Equipment A.

The negative bias in equipment B is also evident in Bland Altman plot. As Free T3 value increases, there is proportionate increase in Bias in Bland Altman plot. The slope and intercept can be used in patients where Free T3 results measured over the years include both these equipments. Figure 3 and 4, Linear regression plot and Bland Altman plot respectively for Free T4 shows that there is correlation between Equipment A and Equipment B reported results of Free T4 (R2 = 0.87). However, slope of 2.07 and intercept of (-0.51) indicate that Equipment B consistently gives higher free T4 result as compared to Equipment A. The positive bias in equipment B is also evident in Bland Altman plot. As Free T4 value increases, there is proportionate increase in Bias in Bland Altman plot. The slope and intercept can be used in patients where Free T4 results measured over the years include both these equipments. Figure 5 and 6, Linear regression plot and Bland Altman plot respectively for TSH shows that there is very good correlation between Equipment A and Equipment B reported results of Free T4 (R2 = 0.99). Slope of 1.07 (~1.0) with intercept of -0.11(~0) indicate that Equipment B result are comparable to Equipment A for TSH. Bias spread equally around X-axis evident in Bland Altman plot further support the interference that both equipments have very good correlation of TSH measurement. TSH results measured over the years between equipment A and B can be reliably used for comparison and clinical decision making.

Table 1:

Equipment	TSH mIU/ml	Free T4 ng/dL	Free T3 pg/ml
A	0.38 – 5.33	0.61 – 1.12	2.5 – 3.9
B	0.465 – 4.68	0.78 – 2.19	2.77 – 5.27
Slope	1.07	2.07	0.71
Intercept	-0.11	-0.51	-0.93
R2	0.99	0.87	0.92
Comparability	Correlated	B have Positive bias	B have Negative bias

Table 1 shows that amount of bias far exceed variations in manufacture's reference range for Free T4. In case of Free T3, while B have higher reference ranges, the patient results are almost 30% lower.

International Federation of Clinical Chemistry (IFCC) committee for the standardization of thyroid function tests as well as manufacturers have made efforts to harmonize TSH as well as Free T4 and Free T3 results across the equipments and methods available in market[6]. However, result of present study shows that, although efforts are highly successful for TSH, a lot of work remains to be done for Free T3 and Free T4 harmonization across manufactures. Unlike TSH, considerable variability is also observed for free T4 by Thienpont, L et.al.[7]

Giorgio Iervasi et. al. also have expressed difficulties in harmonization of free thyroid hormone tests and labeled it as mission impossible[8] . It was concluded that more research are necessary to say whether harmonization of the Free T3 and Free T4 assay is an impossible mission (or not).

Conclusion

Beckman Coulter Dxi600 and Vitros 3600 have good correlation for TSH.

Vitros 3600 shows negative bias for Free T3 as compared to Beckman Coulter Dxi600.

Vitros 3600 shows positive bias for Free T4 as compared to Beckman Coulter Dxi600.

Clinicians working with thyroid disorders, i.e Physicians, Otorhinolaryngologist and endocrinologist can reliably interpret TSH results across Beckman Coulter Dxi600 and Vitros 3600 when their patient's serial results are from one of the two equipments.

However, clinicians must refer to equipment used for measurement of Free T4 and Free T3 when interpreting result when source of results Beckman Coulter Dxi600 and Vitros 3600. In such cases, careful interpretation of serial measurements and changes in results observed needs to be made.

References

1. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab. 2011 Jul;15(Suppl 2):S78-81.
2. Welsh KJ, Soldin SJ. DIAGNOSIS OF ENDOCRINE DISEASE: How reliable are free thyroid and total T3 hormone assays? Eur J Endocrinol. 2016 Dec;175(6):R255-R263.
3. Serdar, Muhittin & İspir, Emre & Ozgurtas, Taner & Gulbahar, Ozlem & Ciraci, Zahid & Kurt, Ismail. (2015). Comparison of four immunoassay analyzers for relationship between thyroid stimulating hormone (TSH)

and free thyroxine (FT4). Turkish Journal of Biochemistry. 40. 88-91.
4. Spencer CA. Assay of Thyroid Hormones and Related Substances. [Updated 2017 Feb 20]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279113/
5. Bland JM, Altman DR. Statistical methods for assessing agreement between measurements. Biochim Clin 1987;11:300-404.
6. Araque KA, Klubo-Gwiezdzinska J, Nieman LK, Welsh K, Soldin SJ. Assessment of thyroid function tests and harmonization: opinion on thyroid hormone harmonization. Ther Adv Endocrinol Metab. 2019 Dec 24; 10: 2042018819897049.
7. Thienpont, L. M., Faix, J. D., & Beastall, G. H. (2015). Standardization of Free T4 and Harmonization of TSH Measurements: A Request for Input from Endocrinologists and Other Physicians. European Thyroid Journal, 4(4), 271–272.
8. Iervasi G, Clerico A. Harmonization of free thyroid hormone tests: a mission impossible? Clin Chem Lab Med. 2011 Jan;49(1):43-8.