Chemistry Research Journal, 2020, 5(2):151-156

Available online www.chemrj.org

Research Article

ISSN: 2455-8990
CODEN(USA): CRJHA5

Reproducibility, Repeatability and Precision analysis of Thyroid function tests (TFT) on two, separately operated-LRS integrated Roche Cobas e411 iECL analyzers

Ishrat Sultana, Junaid Mahmood Alam, Humaira Howrah Ali, Shazia Noureen

Department of Biochemistry lab services and Chemical Pathology, and Liaquat National Hospital and Medical College, Karachi. Pakistan
Corresponding author: Dr Junaid Mahmood Alam, dr_jmalam@hotmail.com

Abstract *Background:* Accuracy, reproducibility, analytical precision and standardization of techniques for analysis of TFTs are some of factors that are essential for better patient's care. *Aim:* Therefore, current study was performed to assess reproducibility (two same instruments, two different groups of technologists), repeatability (same instruments, same controls) and precision (same instruments, same patients samples, multiple runs) of TFTs on two similar iECL instruments (Cobas e411-Roche-Basil), operated by two different sets of technologists at one of the largest private-tertiary care hospital, Clinical Biochemistry Lab services. *Materials and Methods*: Tri-iodothyronine (T3), tetra-iodothyronine (T4) Free- Tri-iodothyronine (FT3), Free tetra-iodothyronine (FT4) and Thyroid Stimulating Hormone (TSH) were run 25 times simultaneously, using electro-chemiluminescence technology on two separately operated Cobas e411 (Roche Diagnostics, Basil) with normal references ranges of 0.8-2.00 ng/ml, 5.1-14.1 µg/ml, 1.9-5.1 pg/ml, 0.9-1.7 ng/ml, 0.27-4.2 µlU/ml, respectively. *Results*: Performance of two separately run analyzers were also excellent, exhibited through R2 of 0.99 throughout for all parameters T3 (R2 = 0.9991), T4 (R2 = 0.9966), TSH (R2 = 0.9952), FT3 (R2 = 0.9971) and FT4 (R2 = 0.9905), manifesting 99% accuracy and precision. *Conclusion*: Collective emphasize needed by all primary and tertiary care hospitals-associated laboratories and even standalone laboratories, that each should cooperatively ensures availability of best possible services (regarding analysis and coverage) to patients with speedy, accurate, inexpensive, consistent data and reporting

Keywords Thyroid function tests, iECL technology

Introduction

Thyroid function tests (TFTs) inclusive of Thyroid hormones (T3, T4, FT3, FT4) and one pituitary hormone TSH (thyroid stimulating hormone) are one of the most frequently and regularly requested tests combo [1-5]. Thus accuracy, reproducibility, analytical precision and standardization of techniques for analysis of TFTs are some of factors that needed attention and without it, patient's care and reliability of results remains questionable [1,5-7]. The technology most commonly used now days for assessment of TFTs is iECL-electro chemiluminescence immunoassay, which is highly sensitive and with excellent throughput. Previously RIA (radio immunoassay), ELISA (enzyme linked immune sorbent assay) and MSP-ELISA (magnetic solid phase-ELISA) were some of the techniques used to analyze TFTs [1,8].

Currently, fully automated, LRS integrated iECL systems are available all around the world, with advantages of accuracy, precision, sensitivity and reproducibility [5,9], however data of such was not readily available for the unit one is about to install for their own laboratory. Nonetheless, if data is available for the same by the manufacturer, working attributes of technologists, analysis and reporting regiments of instruments and services requirements (12 hr cycle or 24/7) does make a an impact and might induce deviation and divergence [6,7,9]. Therefore, current study was performed to assess reproducibility (two same instruments, two different groups of technologists), repeatability (same instruments, same controls) and precision (same instruments, same patients samples, multiple runs) of TFTs on two similar iECL instruments (Cobas e411-Roche-Basil), operated by two different sets of technologists at one of the largest private-tertiary care hospital, Clinical Biochemistry Lab services.

Materials and Methods

Study Design and patients samples: All samples of patients within normal reference were analyzed separately on two Cobas e411 analyzers. Thyroid hormones (T3, T4, FT3, FT4) and TSH were determined in 25 individuals, either gender. The study period was Dec 2019 at Department of Clinical Biochemistry Lab services and Chemical Pathology, Liaquat National Hospital and Medical College. Average age of patients was 40.25 ± 9.20 yrs. All of the individuals were either confirmed cases of thyroid disorders, or under-treatment, recently diagnosed cases, as well as those with overt/sub-clinical thyroid anomalies. Care was taken that samples were that of thyroid diseases and none of the patients had any history of operations, malignancies, liver or renal disease, interferon therapies or β-blockers usage.

Blood collection: Four milliliters whole blood was collected from each patient (n = 25) in Clot-activated tubes (Red Top). Serum was separated and stored at -20^{o}C. Where needed, dilution and aliquots were prepared to get actual quantization of all parameters.

Analytical determinations: Tri-iodothyronine (T3), tetra-iodothyronine (T4) Free- Tri-iodothyronine (FT3), Free tetra-iodothyronine (FT4) and Thyroid Stimulating Hormone (TSH) were run 25 times simultaneously [5,6,9], using electro-chemiluminescence technology on two separately operated Cobas e411 (Roche Diagnostics, Basil) with normal references ranges of 0.8-2.00 ng/ml, 5.1-14.1 μg/ml, 1.9-5.1 pg/ml, 0.9-1.7 ng/ml, 0.27-4.2 μlU/ml, respectively.

Statistical Analysis

All data was statistically analyzed by SPSS ver 20 (USA) through regression correlation analysis R 2 among thyroid hormones and thyroid stimulating hormone.

Results

Current study described comparative precision analysis of T3, T4, TSH, FT3 and FT4 on two similar iECL immunoassay analyzers Cobas e411 (Roche-Basil). Data showed significant precision performance as plotted by R2 regression analyses (Fig 1 to Fig 5). Samples from normal patients were run parallel, 25 times each, on two separately operated analyzers. Both analyzers run 24/7 to provide round the clock services to 700 plus admitted patients and 230 plus OPD patients. Both set of analyzers are operated by three sets of different, trained and skilled technologist in 3 shifts. Data, however, shows excellent precision, reproducibility and performance by different sets of technologists, manifesting same level of skills, understanding and performance. Similarly, performance of two separately run analyzers were also very good, exhibited through R^2 of 0.99 throughout for all parameters T3 (R^2 = 0.9991; Fig 1), T4 (R^2 = 0.9966; Fig 2), TSH (R^2 = 0.9952; Fig 3), FT3 (R^2 = 0.9971; Fig 4) and FT4 (R^2 = 0.9905; Fig 5), manifesting 99% accuracy and precision.

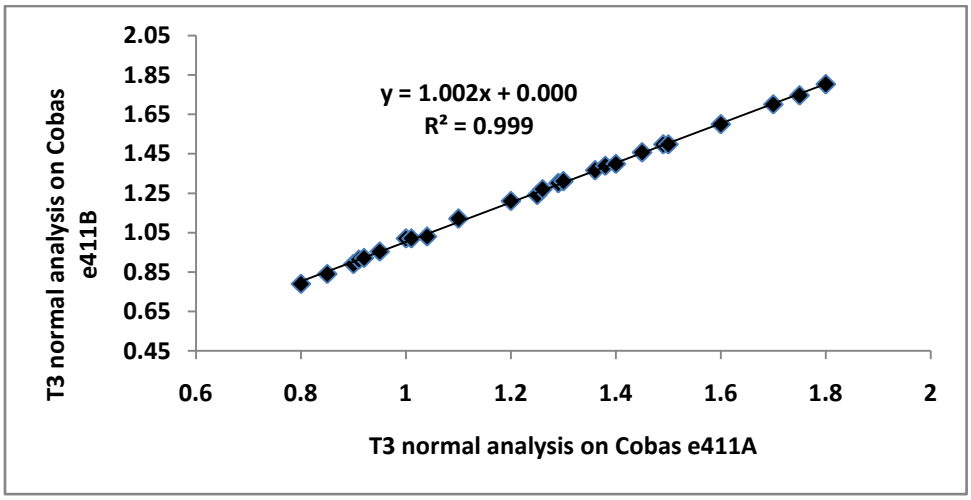

Figure 1: Comparative Precision analysis of TFT (T3) on two immunoassay analyzers Cobas e411 A & B

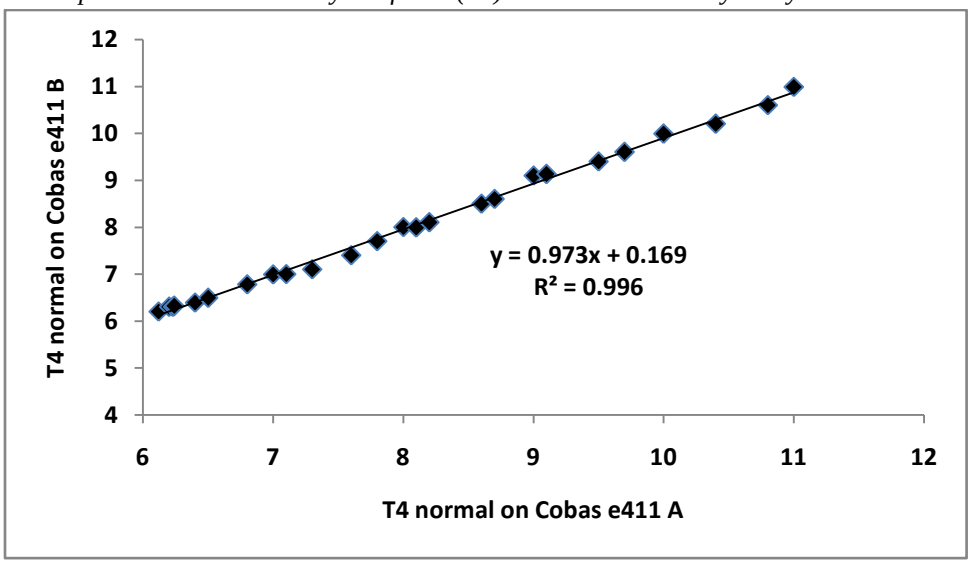

Figure 2: Comparative precision analysis of TFT (T4) on two Immunoassay analyzers Cobas e411 A & B

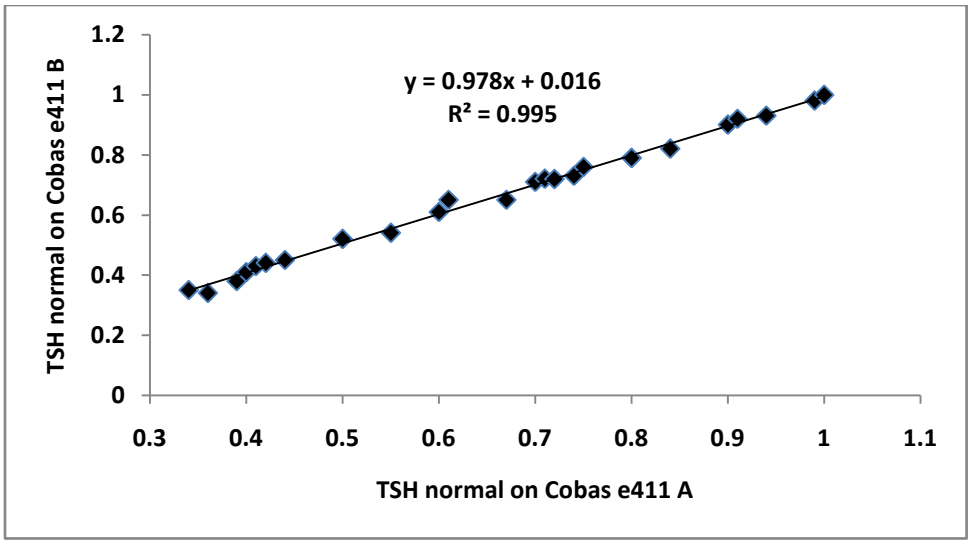

Figure 3: Comparative Precision analysis of TFT (TSH) on two Immunoassay analyzers Cobas e411 A & B

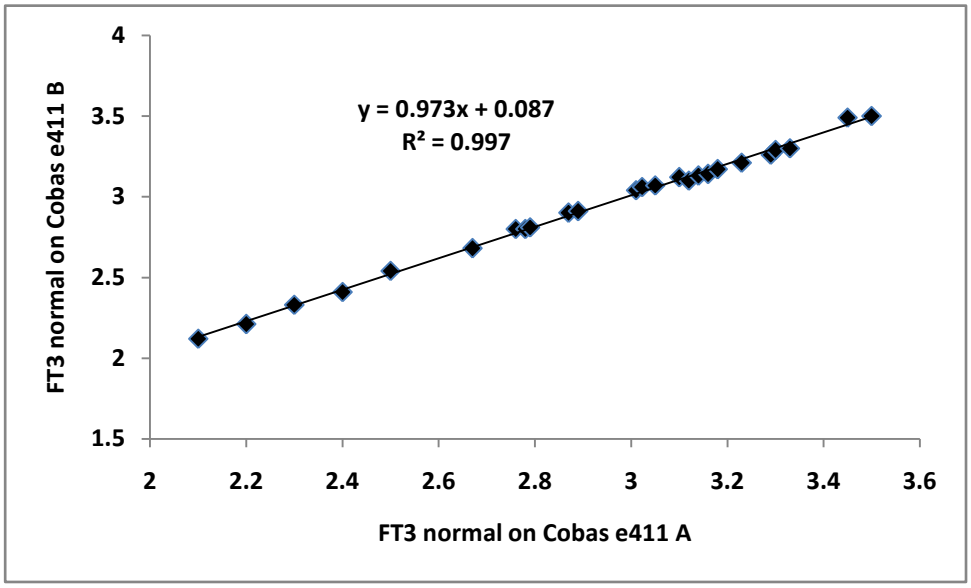

Figure 4: Comparative precision analysi of TFT (FT3) on two Immunoassay analyzers Cobas e411 A & B

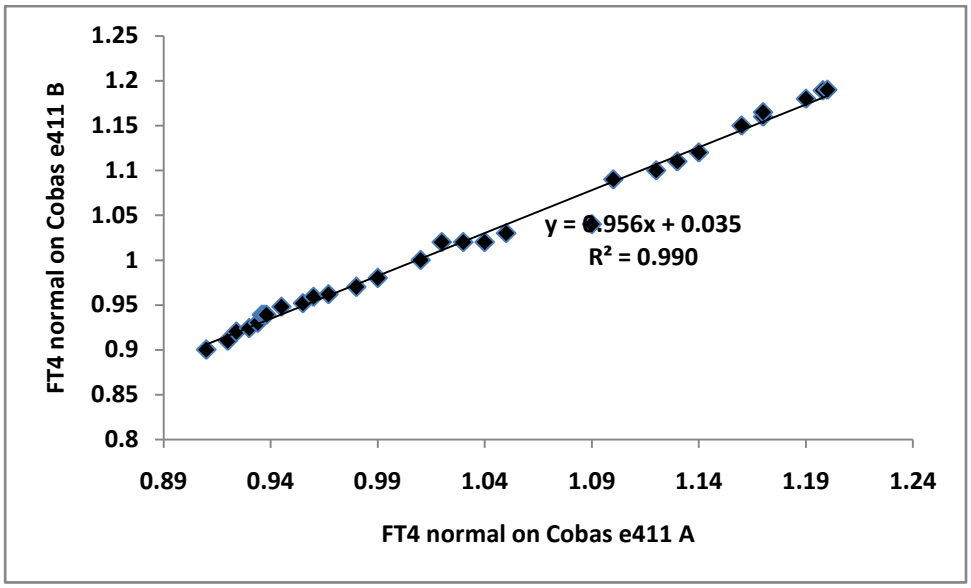

Figure 5: Comparative Precision analysis of TFT (FT4) on two Immunoassay analyzers Cobas e411 A & B

Discussion

Present study described comparative reproducibility, repeatability and precision analysis of Thyroid function tests on two, separately operated-Laboratory Reporting System (LRS) integrated Roche Cobas e411 iECL analyzers. Both analyzers remains operational 24/7 to proved much needed hormonal, tumor markers, cardiac marker services to around 700+ admitted patients and in day times to around 230 plus OPD patients as well. Both immunoassay analyzers are operated by three sets of different, trained and skilled technologist shift-wise. Comparison and analyses in presented study manifested precision, reproducibility and performance by technologists and instruments, corroborating their skills, understanding, performance and accuracy-repeatability of analyzers.

Most commonly used technology for assessment of TFTs is iECL-electro chemiluminescence immunoassay, which is highly sensitive and with excellent throughput [1] and acceptable all around the world as one of the best.

Therefore its accuracy, reproducibility, analytical precision and standardized diagnostic principles for analysis of TFTs are some of feature that considered necessary attention and since this is customer based-activity, patient's care and reliability of results remains a priority [1,5-7]. Nonetheless, thyroid hormones are the most recurrently requested endocrine tests and thus it is imperative and very important to control and manage reliability and accuracy of its iECL analyses [1,10,11]. Previously, study conducted on comparison of three techniques reported and reiterated precision and accuracy of the same iECL technology analyzer Elecsys 2010, a pre-model of currently available e411 Cobas immunoassay analyzers [8].

Few past studies also empathized that earlier available technologies, such as RIA, LC/GC/MASS although more reliable and precise in its determination upto picogram levels, but very expensive, laborious, and with higher machine cost, therefore attention shifted from these orthodox techniques towards more swift, easy to manage, readily available analyzers and techniques such as iECL [5,12-14]. It was also argued that interference in analyses of thyroid function test parameters, either by chemical particulate, human error, and/or analytical mishap, are some factors that shall remain relevant and needed to be controlled or to be avoided at any cost [5,15]. Such interference in analysis and reporting might be hazardous and could compromise clinical decisions, treatment management and resultant outcome. Thus clinicians, scientists, lab pathologists are keen to procure instruments with techniques that are standardized, reliable, reproducible, accurate and precise [1,5-7]. It is collectively empathized that primary and tertiary care hospitals-associated laboratories and even standalone laboratories, should cooperatively ensures availability of best possible services (regarding analysis and coverage) to patients with speedy, accurate, inexpensive, consistent data and reporting [1,2,5-7].

Conclusion

Recent study was performed to assess reproducibility, repeatability and precision of TFTs on two similar iECL instruments (Cobas e411-Roche-Basil), operated by two different sets of technologists at one of the largest private-tertiary care hospital, Clinical Biochemistry Lab services. Data showed significant precision upto 99.0% performance as plotted by R^2 regression analyses and reiterated that iECL technology and e411 is reliable equipment for assessment of complete TFT profile. Furthermore, it has been empathized many times that primary and tertiary care hospitals-associated laboratories and even standalone laboratories, should cooperatively ensures availability of best possible services (regarding analysis and coverage) to patients with speedy, accurate, inexpensive, consistent data and reporting.

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