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ORIGINAL ARTICLE

Comparison of Quality Assurance using Six Sigma between Chemiluminescence and Electrochemiluminescence Techniques for Thyroid Function Test

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Abstract

Background: Thyroid function tests are critical for diagnosing and monitoring thyroid disorders. They are usually performed using Electrochemiluminescence Immunoassay (ECLIA) or Chemiluminescence Immunoassay (CLIA). However, variations in test results across different laboratories can impact patient management, particularly in subclinical thyroid dysfunction. To address this, evaluating the Six Sigma performance of both systems using quality control (QC) data can help assess their precision and reliability, ensuring more consistent and accurate results for diagnosis and treatment decisions. **Methods:** The present study was a retrospective study conducted in Hormone lab of Tertiary care Hospital, New Delhi for a period of five months. Thyroid Stimulating Hormone (TSH), free Triiodothyronine (fT3), free Thyroxine (fT4) assays were performed on Beckman Coulter DXI 800 (CLIA) and Elecsys TSH, fT3, Ft4 on Roche cobas e411 (ECLIA). BIAS% was taken from External Quality scheme of Randox and Total Allowable Error (TEa) value was taken from Westgard website. Mean and SD and CV was calculated using excel from Internal Quality Control data. **Results**: For TSH, it was seen for all 3 levels, maximum sigma for CLIA was 5 in the months of April and minimum was 3 in February and May while for ECLIA it was 6 in the month of March and minimum it is 4 in both months of May and June. For fT3, it was found that for all 3 levels, maximum sigma for CLIA was consistently 2 for all 5 months while in ECLIA, the score varied between 2 and 3. For fT4 for all 3 levels, for CLIA sigma was consistently between 1 and 2 for all 5 months while in ECLIA, the score varied between 1-3. **Conclusion:** The present study indicates that ECLIA offers better accuracy and precision for TSH testing compared to CLIA, though both methods need improved standardization and internal quality control for fT3 and free fT4 measurements. ECLIA seems to have better accuracy and precision in comparison to CLIA and it is imperative to follow Westgard's Rules to ensure consistent, high-quality results and minimize variability in thyroid function testing.

Keywords: Electrochemiluminescence Immunoassay (ECLIA), Chemiluminescence Immunoassay (CLIA), Thyroid Stimulating Hormone (TSH), free Triiodothyronine (fT3), free Thyroxine (fT4) assays

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Introduction

Quality or conformance to requirements of a user or customer is the embodiment of a well working medical laboratory. No report is processed or accepted if the analyte and machine do not conform to the quality it is supposed to provide. In a lab, good quality is often detected by reduced number of quality material runs, maintained turn around time, the values matching the diagnosis etc. While running quality control materials to assess the quality of test results is worldwide practise, many times we miss possible biases and errors despite stringent assessment of quality control every run. To over come this, in recent times, the inclusion of six sigma metrics has been a huge game changer [1-2].

Many times, relying on IQC practices and SD, many problems are masked. Six Sigma metrics helps the lab to see the reality and unmask these issues associated with analytical and preanalytical errors. Six sigma metrics also shows IQC rules that need to be followed to improve the sigma and also how we can maintain it and catch bias before it affects patient results. Thus, six sigma is like a microscope to assess quality. For this reason, like CV%, six sigma should also be used as an important attribute when doing intermachine comparison or when comparing two methodologies for starting or verifying the sensitivity and specificity of any analyte [2-3].

With an increase in thetesting of the thyroid function, it has been

important to get as precise and accurate result as possible as drug monitoring and treatment changes are heavily dependent on TSH levels and T3, T4 values to corroborate the diagnosis. Thyroid function test is generally performed on immunoassay with hospitals choosing either Electrochemiluminescence (ECLIA) or Chemiluminescence (CLIA). While the major school of thoughts remain that ECLIA is more sensitive than CLIA, the cost factor and maintenance gives more props to CLIA. This is because, ECLIA combines analytical advantages of chemiluminescent analysis with ease of reaction control by applying electrode potential [4-5].

Both ECLIA and CLIA are considered as 3rd generation testing for TSH. However, this often leads to variations in numerous labs which may impact the patient results. Thus, there is the need for an evaluation of thyroid function tests assay in order to distinguish between euthyroid, hyperthyroid and hypothyroid especially if patient is in subclinical stages. This is particularly important to ensure good quality of the results which corroborate with the diagnosis and treatment monitoring of patients having thyroid disorders [5]. While majority of method comparisons is done using patient sample and consequent comparison, in this study we compare the six sigma of our ECLIA and CLIA machine using their respective QC data.

Materials and Methods

Study was conducted in a tertiary care hospital from North India

Study Design

Retrospective Study

Study Period

Five months

Analytes Studied

Thyroid Stimulating Hormone (TSH), free Triiodothyronine (fT3), free Thyroxine (fT4)

Analyser

Access TSH, fT3, fT4 on Beckman Coulter DXI 800 (CLIA) and Elecsys TSH, fT3, Ft4 on Roche cobas e411 (ECLIA). Manufacturer directions were followed regarding maintenance of machine, reconstitution of Primer, Calibrator and Quality control materials, after which QC and Calibrator were stored according to said instructions.

Statistical Analysis

Three levels and two levels of internal quality controls (Provided by BioRad QC materials & Elecsys QC materials respectively) results over 5 months were compiled and mean was calculated to establish CV%. BIAS% was taken from External Quality scheme of Randox (RIQAS) and Total Allowable Error (TEa) value was taken from Westgard website [6]. Mean and SD was calculated using excel. CV, Coefficient of Variation was determined from calculated laboratory mean and calculated standard deviation, obtained from 5 months of IQC data

$$CV\% = \frac{Standard\ Deviation}{Laboratory\ mean} \times 100$$

Sigma metrics for each parameter was calculated using below formula

$$Sigma = \frac{TEa - Bias}{CV}$$

The minimum acceptable performance of process was 3 sigma and world class performance is 6 sigma or higher.

Using CV%, bias and SD, Method decision chart was plotted for each month to evaluate the imprecision and inaccuracy.

Results

Since our internal quality control was often within acceptable limits, present study it was decided to calculate the Bias from RIQAS values. Mean, SD and CV has been calculated for all parameters per month from the IQC data collected over 5 months. Sigma was calculated for internal QC level 1, 2, 3 of CLIA and Level 1 and 2 of ECLIA using TEa values from CLIA and Westgard website [6].

For TSH, it was seen for all 3 levels, maximum sigma for CLIA is 5 in the months of April and minimum is 3 in February and May while for ECLIA it is 6 in the month of March and minimum it is 4 in both months of May and June. This showed that ECLIA had a better sigma score as not even once the score had gone less than 3 while CLIA has had only once a score of 5 but otherwise maintained the score above 3. [Table 1]

For fT3, it was found that for all 3 levels, maximum sigma for CLIA was consistently 2 for all 5 months while in ECLIA, the score varied between 2 and 3, 3 majority in the months of February, march, and June. While both machines maintained the minimum sigma requirements of a medical testing laboratory, it indicates the need for improvement especially in comparison to TSH. [Table 2]

Table 1: Calculating Sigma for TSH IQC in Dxi 800 and Cobas e411

Chemiluminescence (CLIA)						**Electrochemiluminescence (ECLIA)**				
	Feb	**March**	**April**	**May**	**June**	**Feb**	**March**	**April**	**May**	**June**
Level 01						**Level 01**				
TEa	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7
Sigma	3	4	5	3	4	5	6	5	4	4
Level 02						**Level 02**				
TEa	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7
Sigma	3	4	5	3	4	5	6	5	4	4
Level 03										
TEa	23.7	23.7	23.7	23.7	23.7					
Sigma	3	4	5	3	4					

Table 2: Calculating Sigma for fT3 for IQC in Dxi 800 and Cobas e411

Beckman Coulter DXI 800						Electrochemiluminescence (ECLIA)				
	Feb	March	April	May	June	Feb	March	April	May	June
Level 01						**Level 01**				
TEa	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3
Sigma	2	2	2	2	2	3	3	2	2	3
Level 02						**Level 02**				
TEa	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3
Sigma	2	2	2	2	2	3	3	2	2	3
Level 03										
TEa	11.3	11.3	11.3	11.3	11.3					
Sigma	2	2	2	2	2					

Table 3: Calculating sigma for different fT4 IQC in DXI 800 and Cobas e411

Beckman Coulter DXI 800						Electrochemiluminescence (ECLIA)				
	Feb	March	April	May	June	Feb	March	April	May	June
Level 01						**Level 01**				
TEa	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33
Sigma	1	2	2	2	1	2	3	1	2	1
Level 02						**Level 02**				
TEa	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33
Sigma	1	2	2	2	1	2	3	1	2	1
Level 03										
TEa	8.33	8.33	8.33	8.33	8.33					
Sigma	1	2	2	2	1					

TSH: Thyroid stimulating Hormone; fT: Free Thyroxine; CLIA: Chemiluminescence Immunoassay; ECLIA: Electrochemiluminescence Immunoassay; Tea: Total allowable error

For fT4 for all 3 levels, for CLIA sigma was consistently between 1 and 2 for all 5 months while in ECLIA, the score varied between 1-3, 3 sigma majorities in the months of March. Both machines maintained the show lower than the minimum sigma requirements of a medical testing laboratory; it spectacles the need for improvement and standardization. [Table 3]

These values were plotted on a method decision chart to see how much of the sigma values fell within the acceptable limits [6]. The charts were plotted for all levels of IQC of both machines based on the calculated bias and CV from the TEa given for all three parameters. The sigmas for the graph were plotted based on the

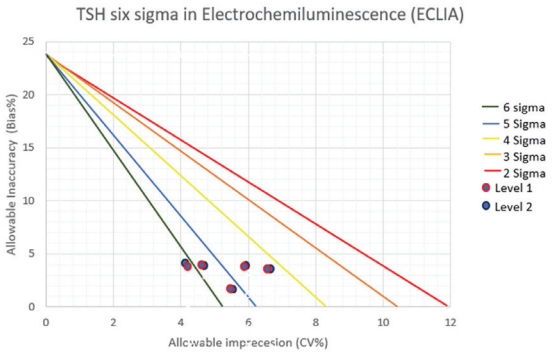

Figure 1: TSH six sigma for ECLIA in method decision chart (TEa-23.7)

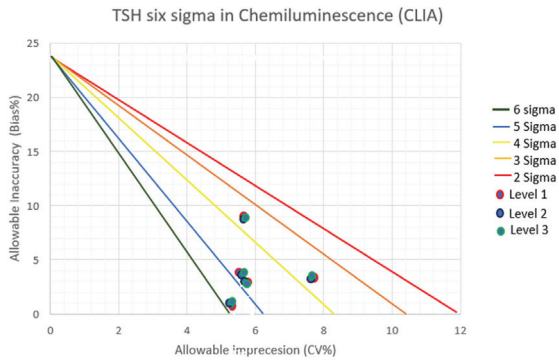

Figure 2: TSH Six Sigma for CLIA in method decision chart (TEa-23.7)

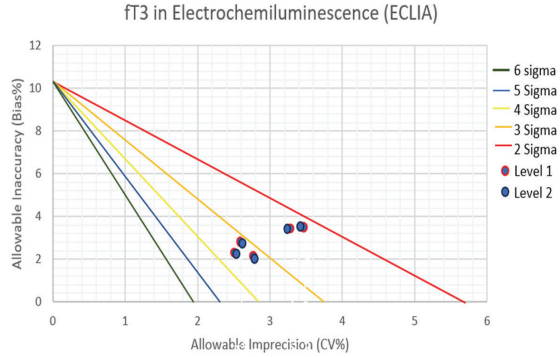

Figure 3: fT3 six sigma in ECLIA in method decision chart (TEa – 11.3)

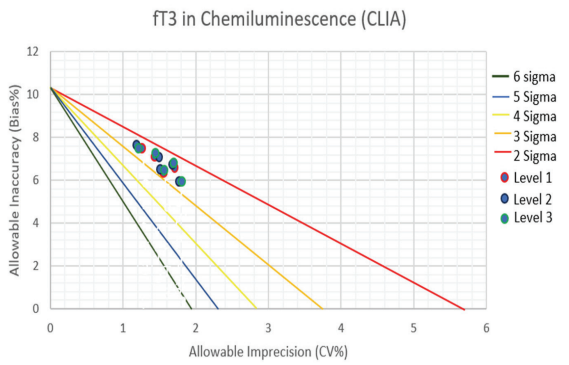

Figure 4: fT3 six sigma in CLIA in method decision chart (TEa – 11.3)

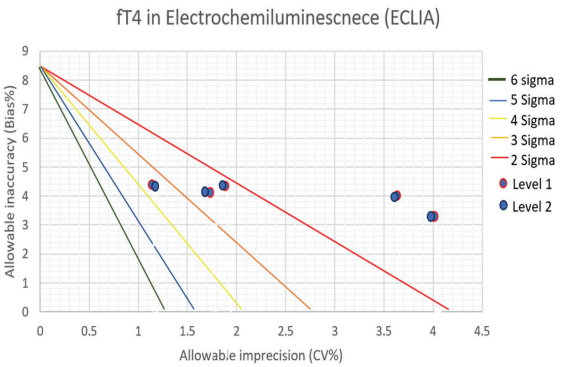

Figure 5: fT4 six sigma in ECLIA in method decision chart (TEa-8.33)

TEa and the CV. [Figure1-6]

Discussion

Six sigma metric analysis is used by many laboratories to assess their quality and results accuracy. It has been noted that six sigma metrics may be a better tool to use being a sensitive marker to a method's performance as six sigma utilizes Coefficient of variation (cv), bias and Standard Deviation (SD) in its calculated. As CV, bias and SD is an indicator of precision and accuracy, however we do not take the total allowable error (TEa) into consideration when looking into the three attributes. As six sigma takes all these into consideration into its calculation, it provides a better outlook to the quality of the lab [1-3].

As per six sigma rules, a sigma e" 6 shows world class performance while <3 sigma shows the need for improvement and is associated with accuracy and precision. Six sigma metrics takes into emphasis how the result of each parameter should be within the designated TEa that has been denoted by CLIA or in Westgard website. Over the years, comparison between methodology and machines, CV% is often taken into consideration to assess if the method or machine is sensitive. However this practise does not take into consideration the standard deviations of the results, nor does it consider the quality control practises being utilized in that lab. Six Sigma, takes all these into consideration and should thus be used when doing method and machine comparison [2-3].

In our study, TSH in Cobas e411, which uses electrochemiluminescence method, was found to have a much better sigma than TSH in Beckman coulter dxi 800 which uses Chemiluminescence. TSH sigma in Cobas e411 varied between 4-6

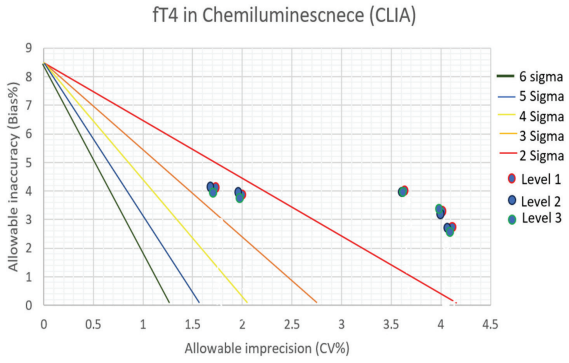

Figure 6: fT4 six sigma in CLIA in method decision chart (TEa - 8.33)

while in DXI 800 it varied between 3-5 over the 5 months it was analysed. It shows that both machines TSH is within acceptable sigma and have a good performance but also indicates that Cobas e411 is more sensitive and more accurate and precise. fT3 and fT4 have shown relatively poor performance in both machines, irrespective of methodology, however it can be noted that fT3 and fT4 had still better sigma in cobas e411 than that of DXI 800 [5-7].

It could be sought that, while the electrochemiluminescence methodology is found to be more sensitive, ECLIA machine uses 2 levels of QC while the chemiluminescence uses 3 levels. Since more QC levels tend to make the values more accurate, it can be noted that along side QC practises, the method through which the parameter is measured, plays an important role in its accuracy and precision as well. When CV of both methods was taken in consideration, the CV for Cobas e411 was lower compared to DXI 800. The six sigma metrics took into consideration both the CV and the QC practise and had established the result [5-9].

While TSH seems to be showing a better sigma for both machines in comparison in fT3 and fT4. fT3 and fT4 have been found to have a poor sensitivity and specificity in many other papers, who found their TSH having acceptable six sigma value but their fT3 and fT4 having just acceptable to poor sigma values. This could because fT3 and fT4 analysis is still to be properly standardized and assessed. However, despite this, in electrochemiluminescence, fT3 and fT4 maintained a minimum of 2 sigma which is accepted for medical laboratories, while in chemiluminescence often dipped down to 1 which is unacceptable [10—11].

Literature reviews have found that electrochemiluminescence techniques had better six sigma values and much better CV%. In chemiluminescence, while TSH is better maintained, there is a reduced sigma for fT3 and fT4 mostly at 1 which is consistent with present study [8-9]. Many labs either have chemiluminescence or electrochemiluminescence, and sometimes this variation in can cause a variation in laboratory results as well. By having both methods in our lab, we were able to compare and assess the quality, accuracy and precision of our results on both machines while taking both advantages to run the sample. There are studies which also show that Electrochemiluminescence methods fared better than Chemiluminescence method. The CV% of ECLIA for TSH was lower in comparison to CLIA, however in either method, fT3 and fT4 had higher in both ECLIA and CLIA methodologies [10-12].

With study, by comparing the sigmas of both machines, it may be established that the ECLIA is good, quite accurate for TSH in comparison to CLIA, however both methods require better standardization and IQC practices for fT3 and fT4. For this, six

sigma rules should be followed if sigma is less than 3, and maximum westgard rules are to be followed till the sigma score improves. As our TSH for both machines is more than 3, it is still imperative that we stick to the westgard rules to ensure accurate and precise TSH levels.

Conclusion

In conclusion, with a better sigma score, ECLIA seems to have better accuracy and precision in comparison to CLIA and it is imperative to follow Westgard rule according to the sigma score calculated to ensure improvement and consistent quality of results.

Conflict of Interest:	Author declare no COI
Ethics:	There is no ethical violation as it is a retrospective study with use of quality control material. no human sample were taken for this study.
Funding:	No external funding
Guarantor:	Dr Preeti Chauhan, will act as guarantor of this article.

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