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Research Article

STUDY OF PERFORMANCE CHARACTERISTICS OF TSH ON FINECARE™ POCT DEVICE

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ABSTRACT

Objective: Thyroid diseases can be diagnosed and monitored by serum thyroid stimulating hormone (TSH) measurement along with serum T_3 and T_4 (both free and total). However, TSH is used to distinguish between euthyroid and hyperthyroid patients. Hence, analysis sensitivity of the TSH assay plays a very significant role. Aims and objectives – The aim of the study was to perform the precision study, calculate the randomerror and analytical measurement rangeverification, as well as verify the accuracy of TSH estimation on Finecare™ point of care testing (POCT).

Methods: The experimental evaluation was done in preliminary and final parts. The preliminary part calculates random errors, systemic errors, and recovery whereas the final evaluation comprises the implementation of the method comparison between chemiluminescence and immunofluorescence assay (CLIA).

Results: In the preliminary evaluation, the inter-assay-high-value sample had CV% was 15 whereas the low-value sample has 13, and the intra-assay had a CV% of 5.8. The recovery test shows 22.22% CV. The final evaluation of the new method Immuno Fluorescence Assay and reference method (CLIA) has a correlation of coefficient 0.9937.

Conclusion: POCT reduces pre-analytical error by reducing misidentification of the patient, specimen, and sample handling. This reduces the turn-around time. It helps to improve the quality of care, healthy outcomes, and affordability.

Keyword: Immunofluorescence assay, Preliminary evaluation, Final evaluation, TSH.

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INTRODUCTION

The most common endocrine disorder is thyroid dysfunction [1]. Thyroid diseases can be diagnosed and monitored by serum thyrotropin thyroid stimulating hormone (TSH) measurement along with serum T4 and T3 (both free and total) [2]. TSH assay is used to distinguish between euthyroid and hyperthyroid patients, especially in subclinical cases where T3 and T4 levels are normal. Hence, the analytical sensitivity of the TSH assay plays a very important role [3]. Initially, radioimmunoassay was used to measure serum TSH. This was considered a first-generation method with a functional sensitivity of 1 mIU/L, immuno-radiometric (IRMA) has functional sensitivity of 0.1 mIU/L which was the second-generation method from the 1990s, whereas the third-generation methodology was electrochemiluminescence assay with improved sensitivity [4]. Point of Care Testing (POCT) assay for TSH is a rapid quantitative method based on fluorescence immunoassay technology. It is a patient-centered care approach that is generally utilized outside the lab to directly evaluate the number of clinical parameters [5,6].

POCT is a rapid analysis that takes few seconds to minutes and is useful in emergencies. Our present study aims to compare serum concentration of TSH, measured using the available POCT method (Finecare™) and conventional lab-based Chemiluminescence and immunofluorescence assay (CLIA) methods in Cohorts of patients. To validate the procedure, we perform the intra- and inter-assay procedures according to CLSI guidelines. The recovery experiment for testing linearity will also be performed.

Today's laboratory medicine is facing a challenge of quality standards while reporting results on the newly established system of POCT devices. These POCT devices are usually installed in small to mid-cap laboratory segments and due to monetary constraints rarely, Quality material procured for POCT devices. This creates an enigmatic state during reporting of laboratory results, especially for the abnormal values and values above clinical decision points. Finecare™ is securing its place in the POCT segment in many laboratories. There is scarcely any independent literature available related to performance specifications of various parameters on this instrument and their comparison with set standard methods by IFCC.

METHODS

The study was carried out at Noida International institute of medical sciences by the department of biochemistry. Serum samples (n=20) were collected from unselected patients either attending OPD or admitted to the hospital. The informed consent was taken from the patient after institutional ethical committee approval. The patients suffering from ischemic heart disease, liver disease, tuberculosis, cancer, and rheumatoid arthritis were excluded from the study.

Methodology

The serum TSH level was determined through the immunofluorescence (Sandwich Immunodetection method) technique for Finecare™ TSH Rapid Quantitative Test and the same sample were sent for CLIA (Sandwich Chemiluminescence Immunoassay), the reference method, on the same day to a NABL accredited lab. This was done for verification of analytical accuracy. The agreement between the result and the true result was verified through a comparison of results between the new method and the reference method.

Statistical analysis

All statistical analysis was performed using SPSS 13. The slope and intercept of the linear regression equation describe the constant and proportional error of the method. Relationships between parameters

were determined by Pearson's correlation coefficient. The values of ($p<0.005$) were considered significant.

RESULTS

In the present work, we have taken TSH processed during the installation of the POCT instrument in our central biochemistry laboratory. We performed the preliminary and final steps to validate the result of this test.

For preliminary evaluation

The preliminary evaluation was done for verification of Precision.

Precision was tested by

1. Repeatability (Intra assay variation)
2. Reproducibility (Inter-assay variation).

Pool samples (n=5) of the two chosen TSH serum concentrations, one in the normal range and one in the high range (above 6) were taken. The inter-assay testing was performed according to CLSI protocol over the course of 5 days. In the morning and evening respectively adding up to 20 test runs each (n=40). For intra-assay evaluation, one sample was run 20 times on the same day. For the recovery experiment, a high serum sample was taken to test the linearity. 11 dilutions were prepared using normal saline as a diluent.

The diluted samples were tested and the result was compared with the target values. The difference between the two values was noted.

Verification of precision

Intra-assay evaluation

The intra-assay evaluation had a mean of 8.87, SD of 0.51, and CV% of 5.8% which is also in an acceptable range comparable to the manufactures claim (<15%) (Table 1).

Inter-assay evaluation

The inter-assay evaluation had high and low-value samples, high-value samples had a mean of 37.93, SD of 5.61, and CV% of 15% whereas low-value samples had a mean of 3.18, SD of 0.41, and CV% of 13% which is acceptable comparable by the manufactured claim (<15%) (Table 2).

Verification of linearity and recovery

For the linearity check, we selected an abnormal sample above the linearity range (264 mIU/L) and serial dilutions were done up to 1:512 (expected value 0.51mIU/L). The recovery test showed a mean % recovery of 187.08, a % recovery range of 41.68, and CV% 22.22% (Table 3).

For final evaluation

Verification of analytical accuracy

The comparison of results between the new method Immuno Fluorescence Assay (IFA) and the reference method (CLIA) correlates with the coefficient (R^2) was 0.9937 (Table 4 and Fig. 1).

The cause of deviation or increased recovery of diluted sample showing non-linearity may be indicative of macro TSH presence. Lack of parallelism can be due to other interfering antibodies (e.g., -heterophilic antibodies, rheumatoid factor, and anti-Ru antibodies). Random inherent error at each dilution point can cause a 10% error [7].

DISCUSSION

Thyroid gland disorders are very commonly seen worldwide [8]. Now autoimmune disorders and thyroid nodules represent the common causes of thyroid dysfunction, as iodine deficiencies are less concern now. Thyroid dysfunction ranges from biochemical, subclinical, hypo, or hyper thyroids to symptomatic hypo-hyperthyroidism. The measurement of TSH level is the first-line assay for the assessment of thyroid function; hence, rapid diagnosis and treatment are required. Hence, the POCT is an important milestone for the rapid estimation of TSH levels. However, TSH assays should be standardized, quality control study should be implicated and repeatability and accuracy should be ensured [9]. Many methodologies have been utilized for the measurement of TSH levels since the 1950s. In 1965, radioimmunoassay was used to evaluate TSH levels [10]. It had low sensitivity (not able to detect <0.1 mIU/L) and cross-reactivity with LH, FSH, and hCG interfered with the results. The third generation method had higher sensitivity (up to ≤0.01–≤0.001 mIU/L). These were isotopic (immune radiometric IRMA, Immuno-enzymatic) and no-isotopic methods (such as ELISA, IF, FIA, and CLA) [11]. Immunoassay platforms are hence the current method of choice in the clinical lab for measurement of Thyroid Function Tests. However, they face a different type of interference that causes erroneous clinical decisions. CLIA has higher sensitivity, low background signal, and automatic and faster sample processing time, the only disadvantage is the high cost of instrumentation [9]. In standard protocol for lab analysis, the test is requested, and the specimen is obtained, processed, and analyzed after which therapy is prescribed by the clinician. Whereas in POCT analysis, the test is

Table 1: Intra-assay variation

Sample 1	7.66
Sample 2	8.94
Sample 3	8.94
Sample 4	9.06
Sample 5	9.05
Sample 6	9.58
Sample 7	8.50
Sample 8	8.93
Sample 9	8.43
Sample 10	9.89
Sample 11	8.42
Sample 12	9.32
Sample 13	8.97
Sample 14	8.61
Sample 15	9.67
Sample 16	8.79
Sample 17	8.63
Sample 18	9.07
Sample 19	8.53
Sample 20	8.42
Mean	8.87
SD	0.51
CV	5.8%

Table 2: Inter-assay variation

???	High-value sample	Low-value sample
Day 1		
Morning	39.75	3.73
Evening	37.77	3.27
Day 2		
Morning	34.5	3.44
Evening	31.07	3.59
Day 3		
Morning	39.37	3.21
Evening	34.20	2.80
Day 4		
Morning	38.55	2.49
Evening	38.31	2.90
Day 5		
Morning	34.09	2.80
Evening	51.72	3.53
Mean	37.93	3.18
SD	5.61	0.41
CV	15%	13%

Table 3: Linearity check and recovery of TSH

Serial number	Dilution	Expected value	Observed value	Recovery %
1	Undiluted	264.0	>100	
2	1:2	132.0	>100	
3	1:4	66	87.68	132.85
4	1:8	33	53.57	162.33
5	1:16	16.5	38.36	232.48
6	1:32	8.25	16.77	203.27
7	1:64	4.125	9.66	234.18
8	1:128	2.06	4.68	227.18
9	1:256	1.03	1.60	155.34
10	1:512	0.51	0.76	149.02
Mean percentage recovery				187.08
Percent recovery range				187.08±83.36
SD				41.68
CV%				22.22%

Table 4: Interlab comparison study

Chemilumenence (CLIA) Assay Range: 0.01–100 mIU/L	Immuno Fluorescence Assay (IFA) Assay Range: 0.1–100 mIU/L
1.5	1.69
5.41	5.9
4.15	4.74
1.4	1.47
2.7	3.42
3.7	4
3.3	3.68
1.8	2.01
28.3	32.8
3.1	3.42
1.6	1.7
1.8	2.16
1.8	2.22
1.2	1.29
1.5	2.2
0.8	0.49
4.9	5.57
3.5	3.82

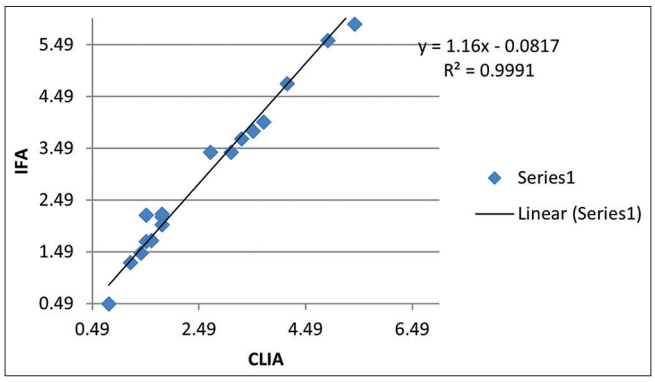

Fig. 1: Coefficient of correlation

ordered, the specimen is obtained, analyzed, and then therapy is prescribed by the clinician.

In our study, we have used the Finecare™ FIA system to quantitatively determine TSH in human whole blood, serum, or plasma. It is a point-of-care tool that is cost-effective it uses disposable chips and the calibrator chip is provided along with LOT. We have performed the preliminary and final evaluation.

CONCLUSION

The pivotal role of any clinical laboratory is the desire to report accurate patient results. The validation of methods is an imperative part of that process. The Finecare™ POCT system has been validated by verification of intra-assay variation, and inter-assay variation which shows an acceptable level of impression. The verification of analytical accuracy by comparing IFA with CLIA showed an accuracy of 0.9937. Hence, the POCT is acceptable, cost-effective, and reduces turnaround time. It can be used for emergency setup and small diagnostic laboratories.

AUTHORS CONTRIBUTIONS

The manuscript writing had accomplished by Jaspreet Kaur and the data collection and analysis were done by Mithilesh Kumar Singhand Amit Samadhiya. The research was reviewed and edited by Gitanjali Guptaand statistical analysis was done by Renu Chane. The manuscript was finalized and submitted for publication by Jaspreet Kaur and Jaswant Kaur.

CONFLICTS OF INTEREST

The authors affirm no conflicts of interest.

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None.

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