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Revalidation of Existing IFCC Standardized Hepatic and Thyroid Function Tests by Precision Optimization and External Quality Assurance Programs

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Abstract: Revalidating and harmonizing clinical chemistry analytical principles and optimizing methods through quality control programs and assessments is the preeminent means to attain optimal outcome within the clinical laboratory services. Aim: Present study reports revalidation of our existing IFCC regularized analytical methods, particularly hepatic and thyroid function tests, by optimization of precision analyses and processing through external and internal quality assessments and regression determination. Materials and Parametric components of hepatic (Bilirubin ALT, ?GT, ALP) and thyroid/pituitary (T3, T4, TSH, FT3, FT4) function tests were used to validate analytical techniques on automated chemistry and immunological analyzers namely Hitachi 912, Cobas 6000 e601, Cobas c501, Cobas e411 with UV kinetic, colorimetric dry chemistry principles and Electro-Chemiluminescence immunoassay (ECLi) techniques. Process of validation and revalidation was completed with evaluating and assessing the precision analyzed Preci-control data of various instruments plotting against each other with regression analyses R^2. Results showed that: Revalidation and optimization of respective parameters that were accredited through CAP, CLSI and NEQAPP assessments depicted 99.0% to 99.8% optimization, in addition to the methodology and instruments used for analyses. Regression R^2 analysis of BilT was 0.996, whereas that of ALT, ALP, ?GT, T3, T4, TSH, FT3 and FT4 exhibited R^2 0.998, 0.997, 0.993, 0.976, 0.996, 0.997, 0.997 and R^2 0.990, respectively. This confirmed marked harmonization of analytical methods and instrumentations thus revalidating optimized precision standardization as per IFCC recommended guidelines. inConclusion: It is concluded that practices of revalidating and harmonizing the existing or any new services should be followed by all clinical laboratories, especially those associated with tertiary care hospital. This is will ensure deliverance of standardized, proficiency tested, optimized services for prompt and better patient care that will guarantee maximum patients' confidence.

Key words: Revalidation · Standardized · IFCC · CAP · Harmonized

INTRODUCTION

It is not only the necessity and requirement but also logical and ethical to continue focusing on improving standardized analytical practices in clinical laboratories services [1-3]. Revalidating and harmonizing clinical chemistry analytical principles and optimizing methods through external and internal quality control programs and assessments, regularized by international standardization bodies such as Internal Federation of Clinical Chemists (IFCC), Clinical Laboratories Standard Institute (CLSI) and College of American pathology (CAP), is the best way to achieve optimal outcome within the clinical laboratory services [2,3]. This enables lab services to obtain maximal level of data and prompt patient's care [3,4].

Present study reports revalidation of our existing IFCC regularized analytical methods, particularly hepatic and thyroid function tests, by optimization of precision analyses and routine processing through external (CAP, NEQAPP) and internal (Preci-controls) quality assessments.

MATERIALS AND METHODS

Study Period and Protocols: The study was carried out at Department of Biochemistry Lab services and Chemical Pathology, Liaquat National Hospital and Medical College. Retrospective data was collected for the period Jan 2013 to Jan 2015. Parametric components of hepatic (Bilirubin TBil, alanine aminotransferase ALT, ?-glutamyl

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transpeptidase ?GT, alkaline phosphatase ALP) and thyroid/pituitary (triiodothyronine T3, Tetraiodo thyronine T4, thyroid stimulating hormone TSH, Free triiodothyronine FT3, free Tetraiodo thyronine FT4) function tests were used to validate our existing standardized IFCC regulated analytical techniques on several automated chemistry and immunological analyzers namely Hitachi 912, Cobas 6000 e601, Cobas c501, Cobas e411 with UV kinetic, colorimetric dry chemistry principles and Electro-Chemiluminescence immunoassay (ECLi) techniques. Process of validation and revalidation was completed with evaluating and assessing the precision analyzed Preci-control data of various instruments (modular or standalone, conventional or advanced) and plotting against each other with regression analyses R^2

Analytical Methods: Analytical methods that were used to process and examine parametric components of hepatic and thyroid function tests were also CAP, IFCC and CLSI accredited and regularized inclusive of instruments. Precision data were retrieved for all individual parameters determination that was optimized through 30 consecutive run on respective instruments. All blood parameters were analyzed by standard methods as established earlier for BilT [5], ALT [6]; ?GT [7]; ALP [8]; T3 and FT4 [9]; T4 [10]; FT3 [11] and TSH [12]. Normal reference ranges of BilT, ALT, ?GT, ALP, T3, T4, FT3, FT4 and TSH were < 1.0 mg/dl, < 31-41 U/L, 32-49 U/L, 187-390 U/L, 0.80-2.00 ng/ml, 5.1-14.1 ?g/dl, 1.9-5.1 pg/ml, 0.90-1.7 ng/dl and 0.27-4.2 uIU/ml, respectively.

Statistical and Regression Analysis: For re-validation, precision analytical methods were used as confirmatory tools, where data resulting either from patient's samples or Preci-controls analyzed on various instruments were plotted as Regression analysis R^2. R^2 that showed values greater than 0.90 or 90% was considered as satisfactory.

RESULTS

All parametric data shows optimized results when plotted through regression correlation after analyses of internal quality assurance controls (Fig 1 to 9). Revalidation and optimization of respective parameters that were accredited through CAP, CLSI and NEQAPP assessments depicted 99.0% to 99.8% equivalency, in addition to the methodology and instruments used for analyses. Regression analysis of BilT of normal-valued Preci-control, analyzed on two separate instruments, resulted in R2 of 0.996, manifesting precision, revalidation and harmonization upto 99.6% (Fig. 1).

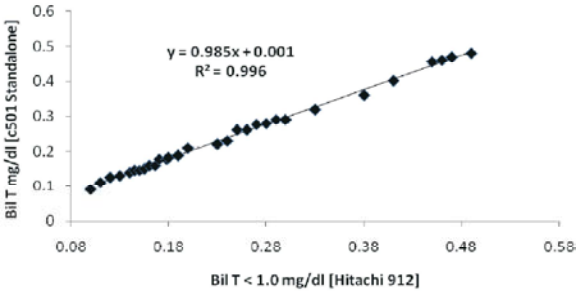

Fig. 1: Precision standardization of total Bilirubin (n=30)

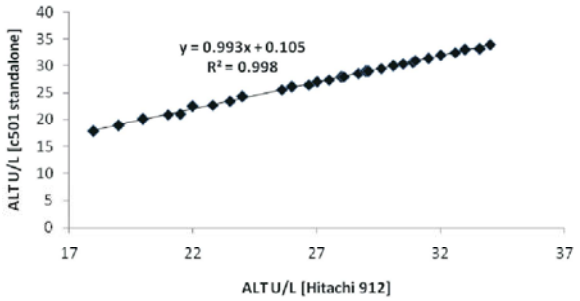

Fig. 2: Precision standardization of ALT (n=30)

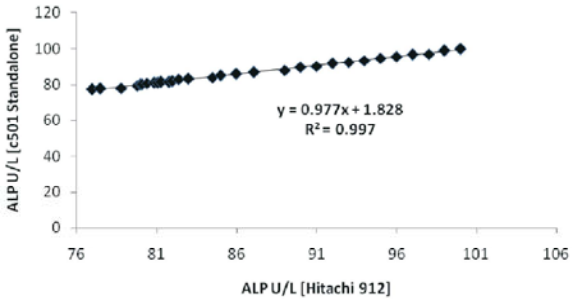

Fig. 3: Precision standardization of ALP (n=30)

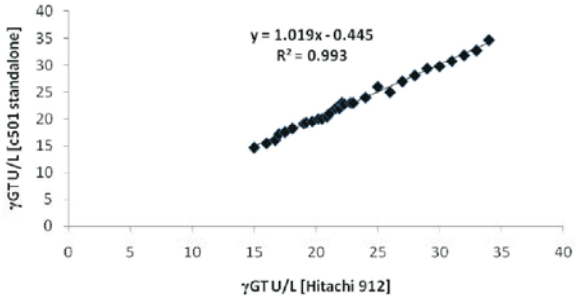

Fig. 4: Precision standardization of gGT (n=30)

Similarly ALT, ALP and ?GT regression analyses depicted R^2 of 0.998 (Fig 2), 0.997 (Fig 3) and 0.993 (Fig 4), respectively, confirming marked harmonization of analytical methods and instrumentations thus revalidating optimized precision standardization as per IFCC recommended guidelines. Revalidation and standardization of thyroid and pituitary hormones parameters also showed synchronized precisions from

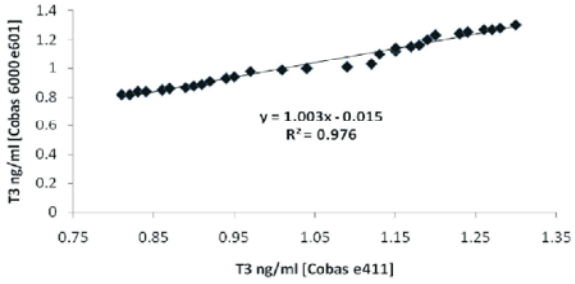

Fig. 5: Precision standardization of T3 (n=30)

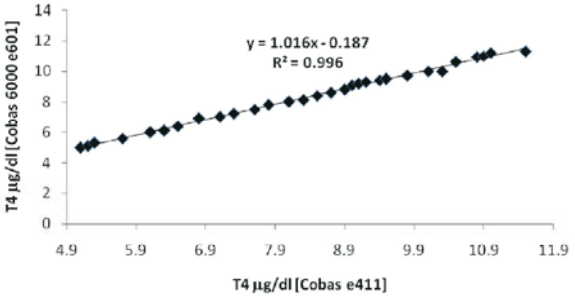

Fig. 6: Precision standardization of T4 (n=30)

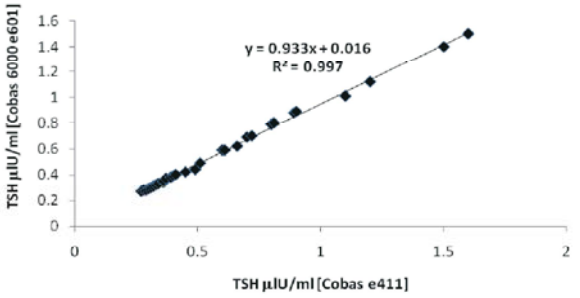

Fig. 7: Precision standardization of TSH (n=30)

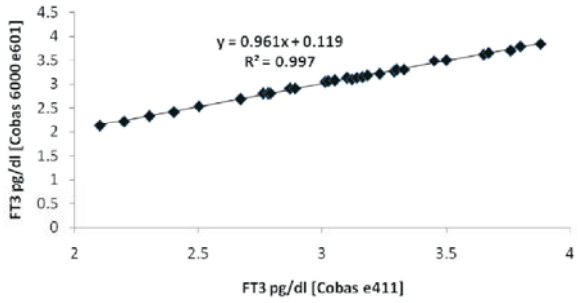

Fig. 8: Precision standardization of FT3 (n=30)

R^2 0.976 to R^2 0.990. Hormonal profile parameter of T3 exhibited R^2 0.976 (Fig 5), T4 R^2 0.996 (Fig 6), TSH 0.997 (Fig 7), FT3 R^2 0.997 (Fig 8) and FT4 R^2 0.990 (Fig 9). Moreover, current study also concomitantly provided revalidation and standardization of instruments, with optimal output, both standalone (Hitachi 912, Cobas e411, c501) and modular (Cobas 6000 e601) as revalidation and standardization was overtly done through precision

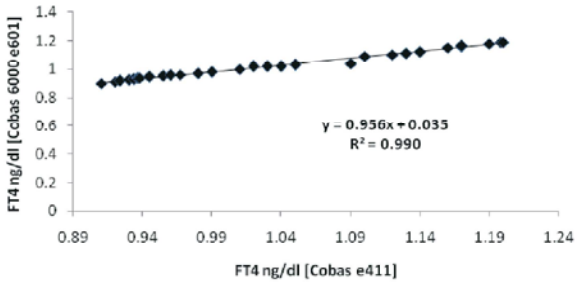

Fig. 9: Precision standardization of FT4 (n=30)

analyses of hepatic and thyroid parameters, through various analytical techniques and that manifested marked conformity of results evident by R^2 of 0.990 to 0.998.

DISCUSSION

Present study described the revalidation and standardization of our existing IFCC recommended analytical methods for BilT, ALT, gGT, ALP, T3, T4, FT3, FT4 and TSH through precision assessments and regression correlation analyses. All parameters were presently accredited with CAP, CLSI and NEQAPP certification surveys conducted thrice per year cycle. Regression correlation analyses depicted marked precision and optimization upto 99.8%, thus exhibiting conformity standardization of analytical methods, reagents and instrumentations. Previous studies showed immense interest and work such as perceived by IFCC committee for androgen and thyroid function tests, that aimed to provide equivalent level of analytical methods for T3, T4, FT3 and FT4 parameters [1,13,14]. The resultant outcome and recommendation were made based on feasibility of standardization and harmonization of endocrine parameters with in-vitro diagnostics (IVD) instruments [1], such as used in our laboratory as well, ensuring minimal deviation from assay to assay or avoiding intra-assay bias [15]. A recent study reported harmonization of several enzymes including hepatic-origin such as ALP, ALT and ?GT [3]. Scientists used multiple instruments and methodologies to equate the analytical processes, thus obtaining successful outcome of 96% to 100% recovery of designated enzymatic levels. More recently it was emphasized that several guidelines are to be followed if any clinical laboratory requires certain improvements in patients' confidence [4,16,17]. Our clinical laboratory not only focused on all aforementioned guidelines, but also participates in external proficiency testing and quality assurance surveys such as CAP, NEQAPP and yearly cycle of ISO 9001 quality management system auditing of all of our processes, instruments, reagents, control of services and validation systems.

CONCLUSION

Present study described the harmonization and revalidation of our existing IFCC regularized and CAP/NEQAPP/CLSI/ISO certified/accredited services of hepatic and thyroid function tests that includes several parametric components. Precision analyses and its optimization exhibited linear correlation and standardization of methods upto 99% assessed through regression methods. It is recommended that practices of revalidating and harmonizing the existing or any new services should be followed by all clinical laboratories of medium to large size, especially those associated with tertiary care hospital. This is will ensure deliverance and availability of standardized, proficiency tested, optimized services for prompt and better patient care that will guarantee maximum patients' confidence.

REFERENCES

1. Thienpont, L.M., K.V. Uytfanghe, S.V. Houcke, B. Das, J.D. Faix., F. MacKenzie., F.A. Qninn, M. Rottmann and A.V. den Bruel, 2014. IFCC working group on standardization of thyroid function tests. A progress report of the IFCC committee for standardization of Thyroid function tests. Eur Thyroid J., 3: 109-116.
2. Miller, W.G., G.R.D. Jones, G.L. Horowitz and C. Weykamp, 2011. Proficiency testing /External quality assessment: Current challenges and future directions. Clin Chem., 57(12): 1670-1680.
3. Wekamp, C., P. Franck., J.K. Gunnewick., R. de Jonge, A. Kuypers, D. van Loon, H. Steigstra and C. Cobbaert, 2014. General Chemistry Division of the SKML (Foundation for the quality assessment in Medical laboratories, The Netherlands). Harmonization of seven common enzyme results through EQA. Clin Chem Lab Med., 52(11): 549-555.
4. Gruver, A.M. and A.E. Schade, 2015. Advanced companion diagnostics facilities: Opportunity favors the prepared laboratory. Arc Pathol Lab Med., 139(10): 1201-1202
5. Wahlefeld, A.W., G. Herz and E. Bernt, 1972. Modification of the Malloy-Evelyn method for a simple, reliable determination of total bilirubin in serum. Scand J Clin Lab Invest., 29: 11-12.
6. Bergmeyer, H.U., M. Horder and R. Rej, 1986. Approved recommendation (1985) on IFCC methods for the measurement of catalytic concentration of enzymes. Part 3. IFCC method for alanine aminotransferase. J Clin Chem Clin Biochem., 24(7): 481-495.
7. Szasz, G., 1974. New substrates for measuring gamma-glutamyl transpeptidase activity. Z Klin Chem Klin Biochem., 12(5): 228.
8. Tietz, N.W., A.D. Rinker and L.M. Shaw, 1983. IFCC method for alkaline phosphatase. J Clin Chem Clin Biochem., 21: 731-748.
9. Klee, G.G., 1996. Clinical usage recommendations and analytical performance goals for total and free triiodothyronine measurements. Clin Chem., 42: 155-159.
10. Nelson, J.C. and R.B. Wilcox, 1996. Analytical performance of free and total thyroxine assays. Clin Chem., 42(1): 146-154.
11. Ekins, R.P., 1990. Measurement of free hormones in blood. Endocr Rev., 11: 5.
12. Surks, M.I., I.J. Chopra, C.N. Mariash, J.T. Nicoloff and D.H. Solomon, 1990. American Thyroid disorders. JAMA, 263: 1529-1532.
13. Thienpont, L.M., K.V. Uytfanghe, G. Beastall, J.D. Faix., T. Ieiri, W.G. Miller, J.C. Nelson, C. Ronin, H.A. Ross, J.H. Thijssen and B. Toussaint, 2010a. IFCC working group on standardization of thyroid function tests. Report of the IFCC working group for standardization of thyroid function tests, part 1: thyroid-stimulating hormone. Clin Chem., 56: 901-911.
14. Thienpont, L.M., K.V. Uytfanghe, G. Beastall, J.D. Faix., T. Ieiri, W.G. Miller, J.C. Nelson, C. Ronin, H.A. Ross, J.H. Thijssen and B. Toussaint, 2010b. IFCC working group on standardization of thyroid function tests. Report of the IFCC working group for standardization of thyroid function tests, part 2: free thyroxine and free triiodothyronine. Clin Chem., 56: 912-920.
15. International Federation of Clinical Chemistry; Laboratory Medicine Working group for standardization of thyroid function tests, S.K. Van Houcke., K.V. Uytfanghe., E. Shimizu., W. Tani., M. Umemoto and L.M. Thienpont. 2011. IFCC international conventional reference procedure for the measurement of free thyroxine in serum: International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Working group for standardization of thyroid function tests (WG-STFT)(1). Clin Chem., 49: 1275-1281.
16. Khoury, J.D. and D.V. Catenacci, 2015. Next generation companion diagnostics: promises, challenges and solutions. Arch Pathol Lab Med., 139(1): 11-13.
17. Allen, T.C., 2013. Food and Drug administration approval of laboratory tests. Arch Pathol Lab Med., 137(1): 13-18.