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Research Article

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Quality check, comparative precision and standardization of liver function test (LFTs) parameters on two identical standalone Cobas c501 analyzers, organized 24/7 and operated by different sets of lab technologists

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Abstract *Background:* Liver function tests (e,g enzymes and/or Bilirubin+ enzyme) components, either of a pair or all can be found elevated, which provide information of area of damages or to a malfunction that in turn facilitate differential diagnosis and clinical decision. *Aim:* In this regard present study illustrates quality check, comparative precision analyses and evaluation of standardized SOPs of liver function test parameters, Total Bil, ALT, AST, ALP, gGT on two identical standalone Cobas c501 analyzers, function 24/7 and operated by different sets of lab technologists. *Materials and Methods*: Controls Precinorm PNU, Precipath PPU (Roche, Basil) were analyzed 25 times each on cobas c501 A and c501 B, both operated by separated group of trained Lab technologists. All five LFTs analytes were determined by standard established methods as per documented protocols. The data was compared statistically by using SPSS ver 20.0 (USA), regression correlation analysis and considered significant when $P < 0.05$. *Results:* Precinorm PPU precisions was in the range of $R^2 = 0.958$ (with accuracy and precision of 95.8%) in Total Bilirubin and $R^2 = 0.997$ (accuracy and precision of 99.7%) in AST. Similarly Precipath was in the range $R^2 = 0.989$ (with accuracy and precision of 98.9%) in Total Bilirubin and $R^2 = 0.996$ (with accuracy and precision of 99.6%) in both ALT and gGT. *Conclusion:* Our study illustrated that strict adherence to analytical and quality assurance SOPs, international guidelines, instrument systems checking, initial and periodic trainings and refreshers, and administrative control are some of the measures that ensured precision and accuracy of LFTs profile.

Keywords Transaminases, Liver Function Tests, LFTs, Precision, Accuracy

Introduction

It's a known fact that reports of clinical laboratories are essential part of patients diagnosis and most of the time, clinical decisions are solely dependent on lab results [1-7]. Most of the large clinical laboratories are associated with tertiary care hospitals with advanced, state of art instruments, specialty educated skilled technologists, postgraduate Pathologists and support staff [1-3, 7].

One of the best and most discussed, reviewed attribute of Clinical Labs is their internationally approved and professionally guided analytical performance [8,9]. Whether, pre-analytical, analytical or/and post-analytical, ever step works through written/approved/internationally guided Standard Operating Procedures (SOPs), manuals and worksheets. However, still, besides all these state of art facilities and highly skilled professional, sole reliance on

both attributes is not enough, as the quality and standardization experts says, because of inherent, systemic and/or random errors [1-3].

In this regard some tests seems to be very significant as clinical diagnosis is dependent on it such as Liver Function Test (LFTs), Renal function tests, cardiac Markers, Endocrine and Infertility testing etc. Liver function test comprised of chemistries inclusive of enzymatic components and coagulation factors, viz alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), Total bilirubin, albumin, prothrombin time (PT) and international normalized ratio (INR) [10]. Pair of two (e,g enzymes and/or Bilirubin+ enzyme) or all can be found elevated, which provide information of area of damages or to a malfunction that in turn facilitate differential diagnosis and clinical decision [11,12]. Therefore, precision, standardization, analytical quality, instrument to instrument/staff to staff reproducibility and compatibility is of significant importance.

In this regard present study illustrates quality check, comparative precision analyses and evaluation of standardized SOPs of liver function test parameters, Total Bil, ALT, AST, ALP, gGT on two identical standalone Cobas c501 analyzers, function 24/7 and operated by different sets of lab technologists.

Materials and Methods

Selection of Controls

Previously described protocol was followed for standardization and precision analyses [1-3]. Precinorm (PNU-PCCC1, Lot # 32420900) and Precipath (PPU-PCCC2, Lot # 32434500) controls of Bilirubin total, ALT, AST, gGT and ALP (Roche Diagnsotic, Basil) were used. Reference ranges for PNU PCCC1 were; Bilirubin Total = 0.93-1.17 mg/dl (mean = 1.05); AST = 41.90-53.10 IU/L (mean = 47.50), ALT = 38.6-49.01 IU/L (mean 43.80), ALP = 91-115 IU/L (mean 103) and gGT = 36.7-46.70 (mean 41.70). Reference ranges for PPU PCCC2 were Bilirubin Total = 3.35-4.27 mg/dl (mean = 3.81); AST = 126-162 IU/L (mean = 144), ALT = 100-128 IU/L (mean 114), ALP = 199-255 IU/L (mean 227) and gGT = 152-192 (mean 172).

Instrumental Analysis

Controls were analyzed 25 times each on cobas c501 A and c501 B, both operated by separated group of trained Lab technologists. All five analytes were determined by standard established methods as per documented protocols [1-3].

Statistical Analysis

The data was compared statistically by using SPSS ver 20.0 (USA), regression correlation analysis and considered significant when $P < 0.05$.

Results

Present study depicted comparative precision analysis and standardization of five LFTs components, ALT, AST, ALP, Total Bilrubin and gGT were performed on two stand-alone automated chemistry analyzers Cobas c501 to assess precision, standardization, analytical quality, instrument to instrument/staff to staff reproducibility and compatibility.

These c501 are dedicated as A and B, operated by separate groups of skilled Lab technologists in a 8 hours shift, 24/7. Comparative analyses was performed by both normal (Precinorm-PNU) and pathological (Precipath-PPU) controls. Highly significant regression correlation was depicted when multiple runs of all five LFTs parameters were analyzed. Statistical evaluation was done, relating performance of one analyzer, operated by group of lab technologists, with another similar analyzer, operated by a separate group of lab technologists using organic and enzymatic parameters as precision indicators. Notably 360^{O} evaluation of analyzers, kits, mechanics and system checks, staff and analyses principles was done with significant correlation outcome (Figs 1 to Fig 10). Data of our study showed marked precision of instruments working, its efficiency and reliability of various groups of technologists. In addition their compatibility was also been proven that different groups of technologists can operate with comparable analytical skills on two similar but separately operating instrument. Regression correlation data of

Precinorm PPU precisions was in the range of R2 = 0.958 (with accuracy and precision of 95.8%) in Total Bilirubin and R2 = 0.997 (accuracy and precision of 99.7%) in AST (Fig 1 and Fig 3 respectively). Similarly Precipath was in the range R2 = 0.989 (with accuracy and precision of 98.9%) in Total Bilirubin (Fig 2) and R2 = 0.996 (with accuracy and precision of 99.6%) in both ALT and gGT (Figs 6 and 10). Regression analyses of rest of LFTs parameters are Precinorm of ALT, ALP gGT showed R2 of 0.964 (Fig 5), 0.985 (Fig 7) and 0.987 (Fig 9), respectively where as Precipath for Total Biliribun, AST, ALP showed regression correlation of R2 = 0.989 (Fig 2), 0.992 (Fig 4) and 0.993 (Fig 8), respectively, thus depicting precision of 96.4%, 98.5%, 98.7%, 98.9%, 99.2% and 99.3%, accordingly. Strict adherence to analytical and quality assurance SOPs, international guidelines for reagents, instrument systems, proper trainings and refreshers, and administrative control are some of the parameters that ensured precision and accuracy of LFts profile.

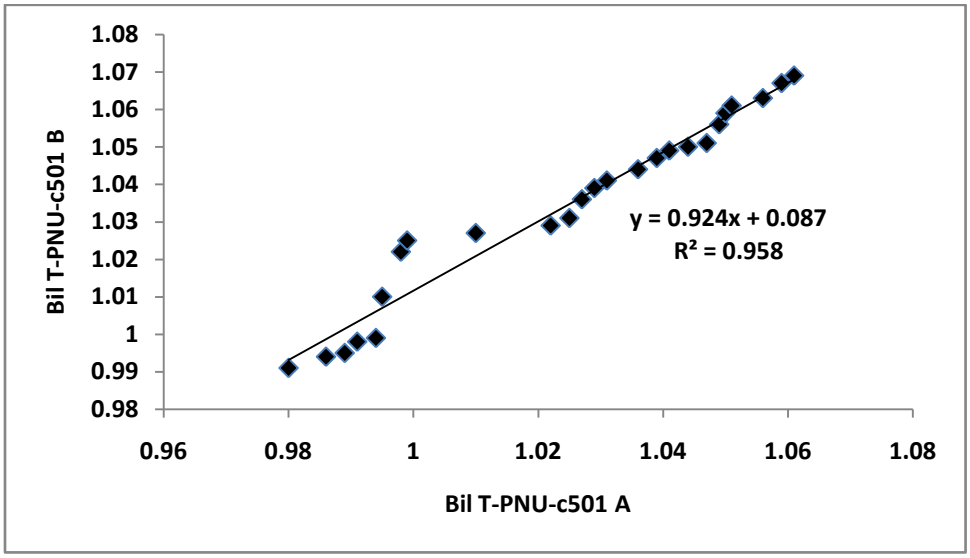

Figure 1: Comparative Precision analysis of LFT parameters "Bilirubin Total" (Precinorm-PNU) on Cobas c501 A and Cobas c501 B

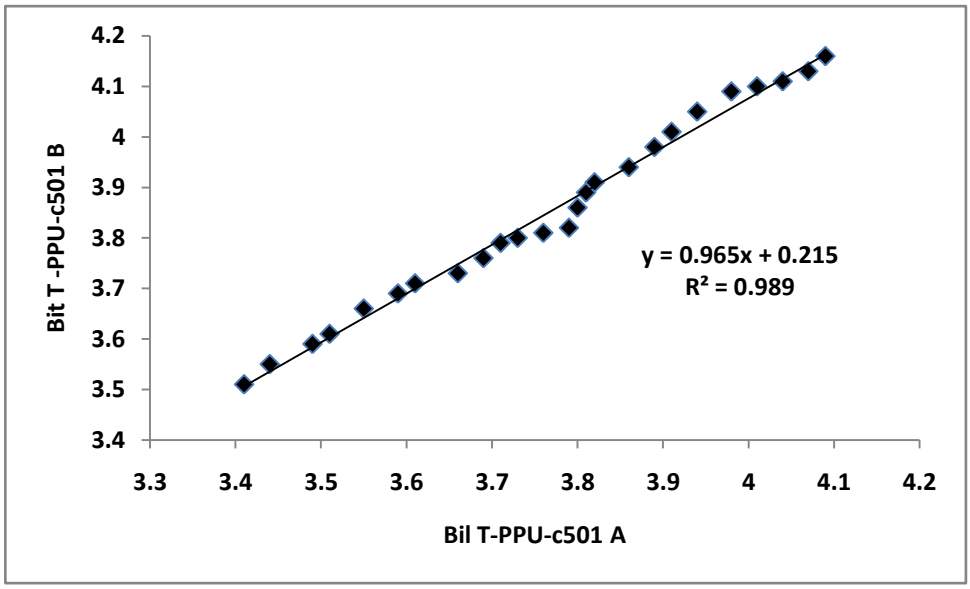

Figure 2: Comparative precision of LFT parameters "Bilirubin Total" (Precipath-PPU) on Cobas c501 A and Cobas c501B

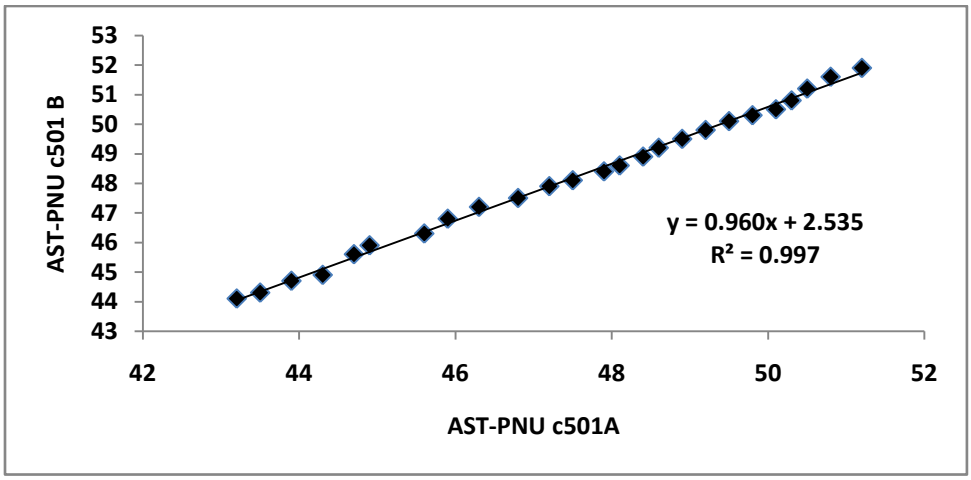

Figure 3: Comparative Precision analysis for LFT parameters "AST" (Precinrom-PNU) on Cobas c501 A and Cobas c501B

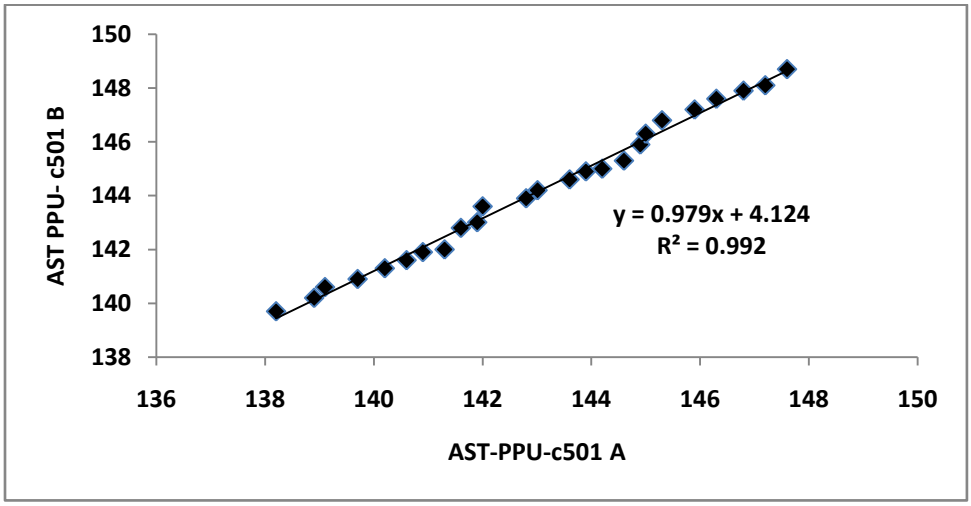

Figure 4: Comparative Precision analyis of LFT parameter "AST" (Precipath-PPU) on Cobas c501 A and C501 B

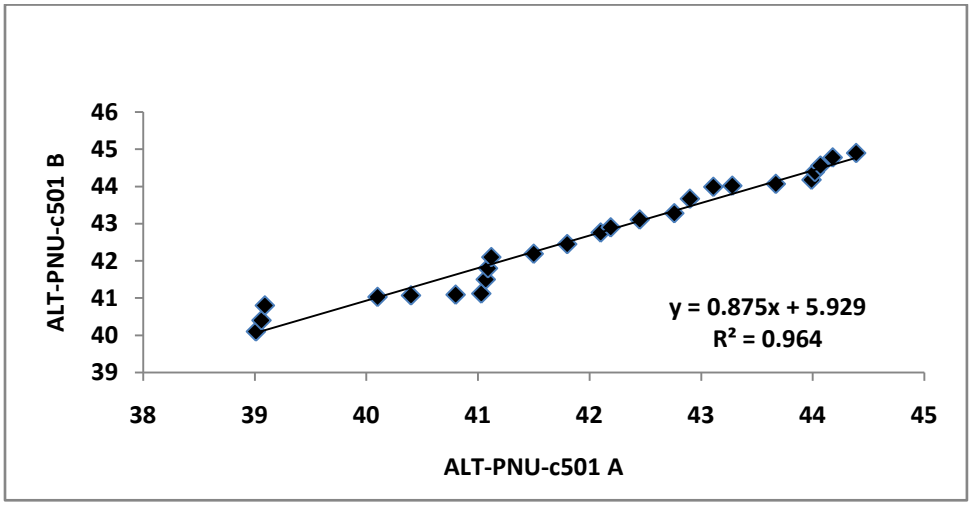

Figure 5: Comparative precision analysis of LFT parameters "ALT" (Precinorm-PNU) on Cobas c501 A and Cobas c501 B

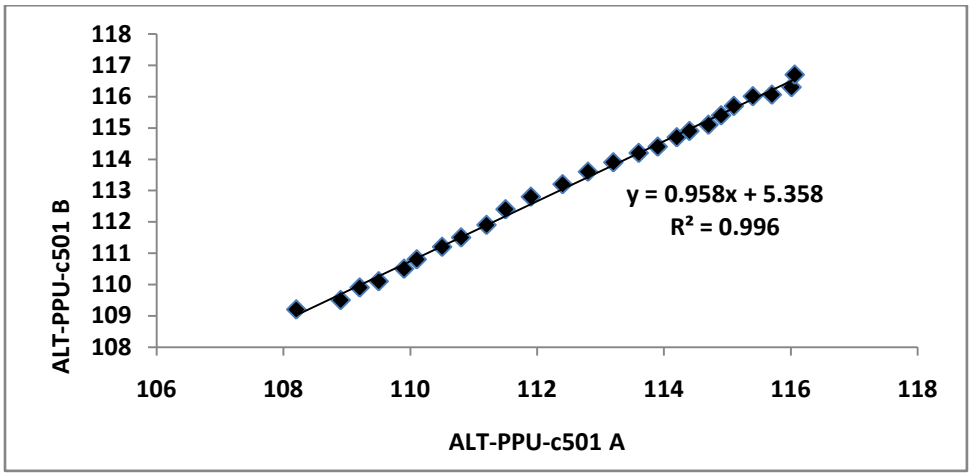

Figure 6: Comparative Precision analysis of LFT parameters "ALT" (Precipath-PPU) on Cobas c501 A and Cobas c501 B

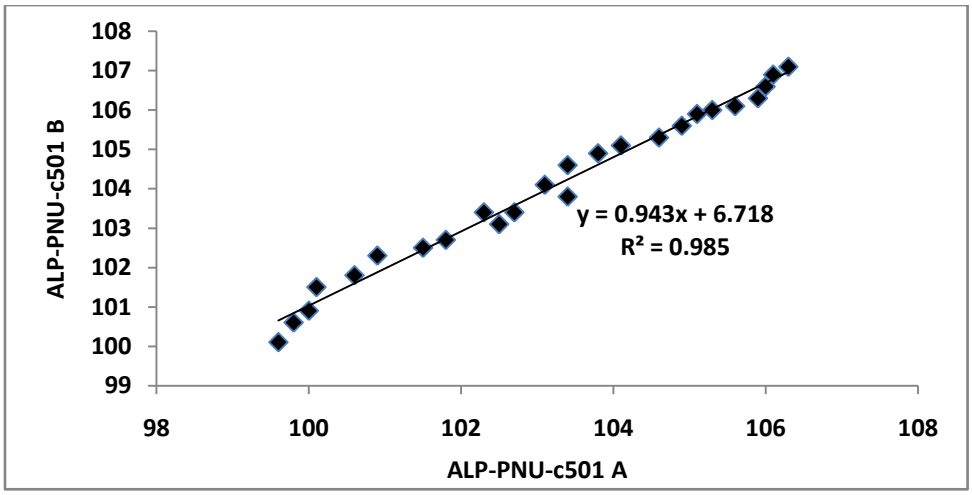

Figure 7: Comparative Precision analysis of LFT parameters "ALP" (Precinorm-PNU) on Cobas c501 A and Cobas c501B

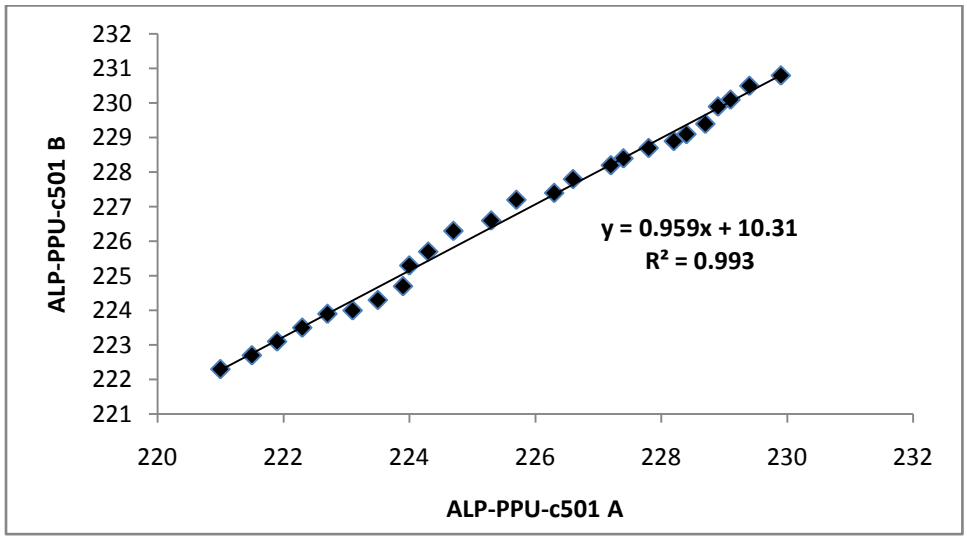

Figure 8: Comparative Precision analysis of LFT parameters "ALP" (Precipath-PPU) on Cobas c501 A and Cobas c501B

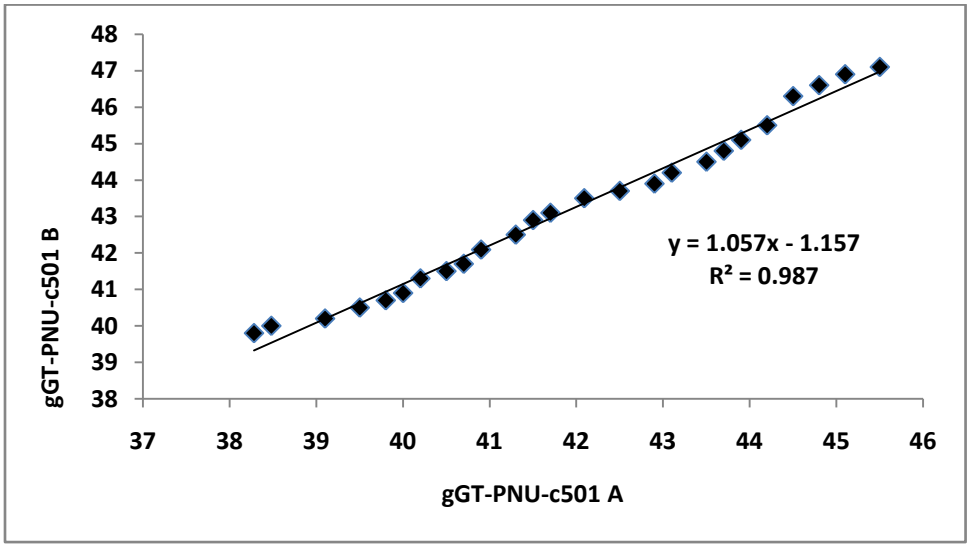

Figure 9: Comparative Precision analysis of LFT parameters "gGT" (Precinorm-PNU) on Cobas c501A and Cobas c501 B

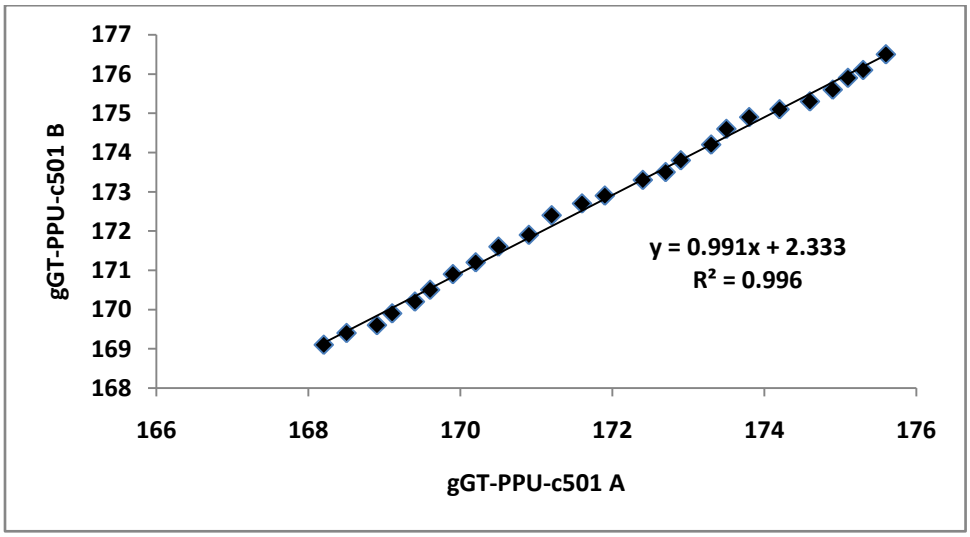

Figure 10: Comparative Precision analysis of LFT parameters "gGT" (Precipath-PPU) on Cobas c501 A and Cobas c501B

Discussion

Clinical significance of LFTs is imperative, helpful in a number of medical conditions and diseases such as Alcoholics, Viral hepatitis, Autoimmune, over-medications, Hepatic Steatosis hemochromatosis and Wilson's disease [10-14].. Several previous studies reported assessment of accuracy and precision of LFTs [4, 9,10,14,15]. Almost all reported precision and accuracy upto 93-97% with only 7% falling outside the permissible limits. It was factually documented that a clinical lab performance is deemed satisfactory when less than 10% of quality control assays falls out of permissible limits [4, 10]. Therefore, precision, accuracy, reproducibility, standardization, thus became not only mandatory but essential pre-requisite for reliable reporting by a clinical laboratory and ensure clinicians and patients trust [15].

Our presented study was done by 360^{O} evaluation of analyzers, kits, mechanics and system checks, technical staff and analytical principles. Hence data of our study showed significant precision of instrumentation outcome,

accuracy/efficiency and reliability of various groups of technologists. Moreover, compatibility of different groups of technologists was also proved that they can operate with comparable analytical skills on two similar but separately operating instruments. Regression correlation data of Precinorm PNU precisions was in the range of marked 95.8% to 99.7% compatibility. Likewise Precipath PPU was in the range of excellent 98.9% to 99.6%, advocating the fact that strict adherence to analytical and quality assurance SOPs, following international guidelines for reagents, instrument systems, providing initial and periodic trainings and refreshers, and administrative control are some of the parameters that ensured precision and accuracy of LFts profile.

To provide quality assured, standardized, precision equated, accuracy guaranteed clinical lab services are now the main goal of all hospital based or individually operating labs. To sustain and uphold this task needs continual assessments, evaluations, trainings, upgrading, advancement (where applicable), planning and budgeting, continued supply chain and management [7]. World health organization (WHO) now enlisted Essential Diagnostic List in 2018, which is referred to for supporting the accessibility and availability of quality and standard assured clinical laboratories services to all, especially resource-limited zones, such as ours [16].. In our setting, that performs around 6500 parametric tests per 24 hours, amounting upto 2.3 million tests per year, inclusive of LFTs, standardization, accuracy, reproducibility, precision are some of the important tools, tasks, needs that we keep updating, executing, implementing and practicing. Such strict measures 24/7 warranted our clinicians and patients to keep relying on us with confidence for quality assured timely reports.

Conclusion

Present study regression correlation data of Precinorm PNU and Precipath PPU precisions was in the range of marked 95.8% to 99.7% and 98.9% to 99.6% compatibility, respectively. This advocates the fact that strict adherence to analytical and quality assurance SOPs, international guidelines, instrument systems checking,, initial and periodic trainings and refreshers, and administrative control are some of the measures that ensured precision and accuracy of LFTs profile.

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