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Precision standardization of Lactate assay on Cobas 6000 c501 and comparative analysis with corresponding Lactate dehydrogenase concentrations

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1. Abstract:

Background: Standardization of technology for introducing new tests or for the transformation from manual to automation is a necessity for analytical precision and accuracy. Aim: Objective of current study is to establish the standardization of lactate assessment on automated analyzer Cobas c501 standalone and its comparative precision evaluations. Material and Methods: Both normal and pathological samples n = 30 each were used to standardized precision of lactate assay on Cobas 6000 c501. Samples were utilized that has already been analyzed on semi-automated Randox Monza Rx instrument (Randox-UK). Lactate dehydrogenase was also assessed in both manual and pathological valued lactate samples on C501 for validation. Data were analyzed through Regression analysis R2 by plotting manual Randox Rx data versus Cobas 6000 c501 for both lactate vs lactate and Lactate vs LDH assays. Results: Regression analysis showed 97.8% to 99.11% linearity and precision standardization of analytical principles and assay on automated c501 instruments when lactate was compared with manual analyses. Similarly, LDH levels corresponded well with its lactate concentration in both control and pathological categories. Conclusion: Regression analyses exhibited significant linear standardization of lactate assay with R^2 0.97 to 0.982. Lactate assay precision was also validated through comparison with corresponding LDH concentration with R^2 outcome of 0.978 to 0.982.

Key Words: Lactate, Cobas 6000 c501, Randox Rx Monza, Regression, validation.

2. Introduction:

Standardization of technology for introducing new tests or for the transformation from manual to automation is a necessity for analytical precision and accuracy [1-4]. Moreover, as advancement in clinical laboratory equipments are more accessible, ability to perform and report a test as per standardization protocol with specific TAT is now a requirement in both independent laboratory and those associated with tertiary care hospital [5-8].

Lactate is a byproduct of anaerobic glycolysis and any change, mostly elevation in its level, cause lactic acidosis, resulting into respiratory or metabolic syndromes. Thus due to its clinical significance, several validation, precision targets and standardization of lactate analysis or point-of-care instruments' reliability assessments has been performed in recent years [9-11].

The current study reports the standardization of lactate assessment on automated analyzer Cobas c501 standalone and comparative precision evaluation of manual Randox Monza Rx (Randox) and automated modular analytical analyzers Cobas 6000 c501.

3. Materials and Methods:

Both normal and pathological samples were used to standardized precision of lactate assay on Cobas 6000 c501. Thirty samples each with normal levels and pathological (elevated) concentrations were utilized that has already been analyzed on semi-automated Randox Monza Rx instrument (Randox-UK). Additionally, lactate dehydrogenase was also assessed in both manual and pathological valued lactate samples on C501 and then compared with corresponding values of Lactate assay. L-lactate was determined at 550 nm by para-amino antipyrine (PAP) assay. In brief, L-lactate oxidized to pyruvate and hydrogen peroxide by lactate oxidase (LOD). A colored product is produced by the reaction of peroxidase (POD), hydrogen peroxide 4-amino antipyrine and hydrogen donor TOOS. The intensity of colored product is directly proportional to the concentration of lactate in the sample [12-14]. Lactate dehydrogenase (LDH) was performed by the methods described earlier [15,16]. Briefly LDH activity was assessed by indirectly measuring NAD conversion to NADH at 340 nm. The increase in absorbance of NADH is directly proportional to LDH activity in samples.

Data were analyzed through Regression analysis R2 by plotting manual Randox Rx data versus Cobas 6000 c501 for both lactate vs lactate and Lactate vs LDH assays.

4. Results:

Standardization of precision assays of lactate was performed with both normal controls (n = 30) and patients (n = 30) who were diagnosed with lactic acidosis, diabetes and respiratory acidosis. All samples that were analyzed for lactate on Randox Monza Rx semi-automated analyzer (both control and pathological) were re-assayed with standardized precision processing on Cobas 6000 c501 auto-analyzer. For further confirmation of analytical precision and clinical reference, LDH was also analyzed in same samples as per corresponding parameter of lactate levels. Regression analysis showed 97.8% to 99.11% linearity and precision standardization of analytical principles and assay on automated c501 instruments when lactate was compared with manual analyses. Similarly, LDH levels corresponded well with its lactate concentration in both control and pathological categories. Results are summarized in Fig 1 to Fig 5. Comparative precision standardization exhibited R^2 value of Y = 1.168 x-2.288 R2 0.991 for control lactate re-analyzed on Cobas 6000 c501; Y = 1.020 x – 0.63 R^2 0.991 for pathological samples; Y = 10.81 x -139.7 R^2= 0.978 for LDH vs lactate

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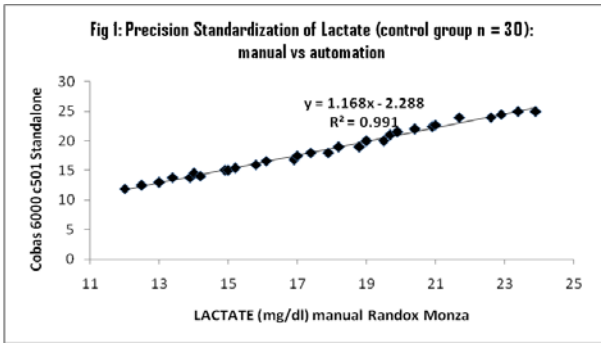
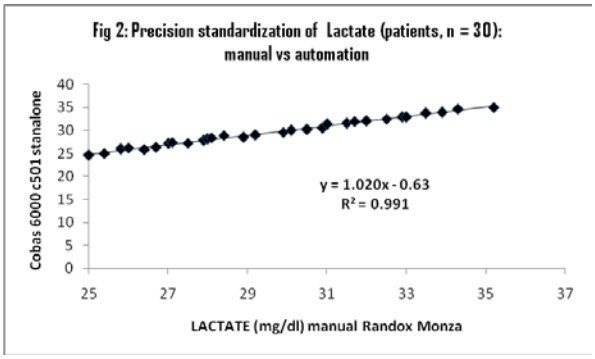
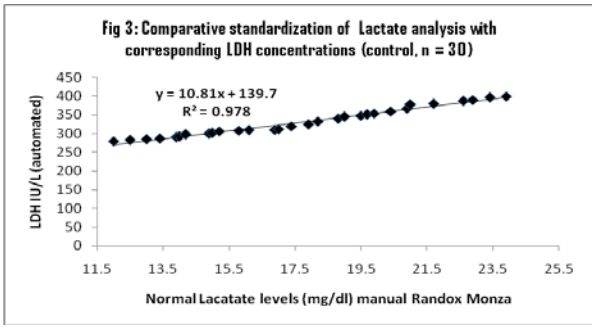
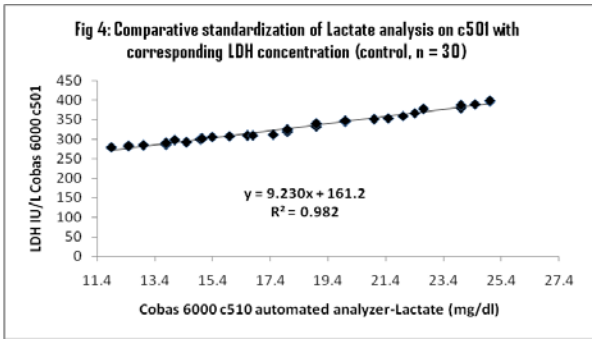
performed on Randox Monza Rx; Y = 9.23 x +161.2 R^2 = 0.982 for LDH vs lactate on c501 and Y = 14.14 x + 99.34 R^2 = 0.981 for LDH pathological on c501 vs lactate pathological on c501, respectively.







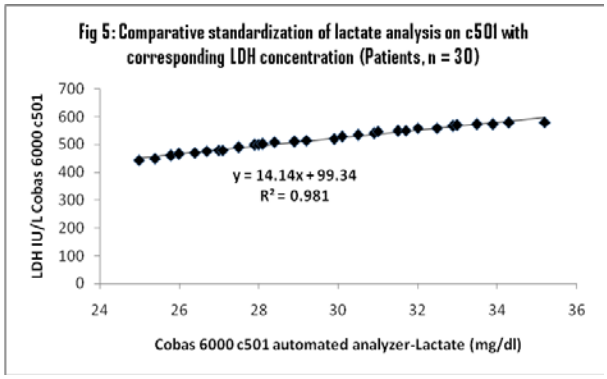


5. Discussion:

Recent studies regarding availability of precision-oriented lactate test in patients with lactic acidosis, reliability of point-of-care instruments and validation of fetal blood sampling instruments for lactate analysis were few significant examples that shows the interest of clinicians, healthcare professional and scientists in standardization of lactate assays [9-11]. It was argued that allowable analytical errors in precision is a fact, however, can be avoided or minimized through controlling the variables [10]. Similarly after validating the components, such as pH, in auto-analyzers specific for lactate analysis, the analyzers can provide precise results with minimal errors and deviations [11].

Previous studies on precision analysis, standardization and performance evaluation showed appreciable similarity and sustainable validated outcomes [1,2,8]. Multiple parameters were evaluated, including cancer antigens CEA, PSA and hormones such as T4, TSH on immunological equipments [6], routine chemistry parameters such as uric acid, cholesterol, calcium, glucose on dry chemistry analyzer [1] with standardized precision and analytical resultant.

Our study presented here have also manifested appreciable precision of R^2 0.976 to R^2 0.991 for lactate analyzed on semi-automated Randox Monza Rx and compared with standardized precision on fully automated dry chemistry analyzer Cobas 6000 c501. The standardization and precision of assay and instrument were also confirmed by R^2 0.97 to R^2 0.982 regression analysis, when lactate levels were compared with corresponding LDH concentrations, both in control and patients samples. In agreement with our studies, recent studies on lactate through analytical outcome and precision target studies showed imprecision lowered to only 13.5% in lactic acidosis patients, R^2 of 0.98 in Scout-POC instrument and fetal lactate precision exhibiting R^2 of 0.977 [9-11].



6. Conclusion:

Present study described standardization of precision analysis of lactate on Cobas 6000 c501 automated analyzer, in comparison with analytical performance on semi-automated Randox Rx Monza both in control and patients' samples. Regression analyses showed significant linearity with R^2 0.97 to 0.982. Lactate precision was also validated through comparison with corresponding LDH concentration with R^2 outcome of 0.978 to 0.982.

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