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Original Article

# Agreement of results between dry and wet chemistry system for common clinical chemistry parameters

Saroj Thapa[1], Apeksha Niraula[2], Prabodh Risal[1]

[1]*Department of Clinical Biochemistry, Kathmandu University School of Medical Sciences, Dhulikhel, Nepal*
[2]*Department of Clinical Biochemistry, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal*

**Keywords:**

Agreement; Biochemical parameters; Dry chemistry; Wet chemistry

## ABSTRACT

**Background:** The advancement of analytical chemistry has led to the use of automated systems in clinical laboratories, including liquid-based wet chemistry and film-based dry chemistry systems. Reflectance spectrophotometry-based dry chemistry systems offer a viable alternative to wet chemistry analyzers. This study aimed to compare the agreement of results between the dry chemistry system and the wet chemistry system.

**Materials and Methods:** Secondary data from external quality control samples were analyzed using the Vitros 350 and BA-400 analyzers, over a period of one year (from 1st August 2021 to 31st July 202). A total of 57 samples and 12 biochemical parameters were considered. Statistical analysis, including paired t-tests, Spearman's correlation, Bland-Altman plots, and Intraclass Correlation Coefficient were applied. P-value <0.05 was considered to be statistically significant.

**Results:** The bland-Altman analysis demonstrated that the measurements from both methods fell within the 95% limits of agreement for most of the clinical chemistry parameters like glucose, urea, creatinine, and liver enzymes indicating overall agreement. ICC values indicated excellent reliability for 10 out of 12 parameters, with HDL-C showing moderate reliability and albumin demonstrating good reliability respectively.

**Conclusions:** The findings of the present study suggest a high level of agreement and correlation between dry and wet chemistry systems for common biochemical parameters. However, it is important to consider the specific parameters and limitations of each system. These results have implications for laboratories and healthcare professionals in selecting the most suitable system for as per their needs and resources.

**Correspondence:**
*Dr, Saroj Thapa, MD*
*Department of Biochemistry*
*Kathmandu University School of Medical Sciences, Dhulikhel, Nepal*
*ORCID ID: 0000-0003-1234-644X*
*Email: sarojthapa@kusms.edu.np*

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## INTRODUCTION

Clinical chemistry laboratories are facing an increasing workload, leading to the adoption of different methods for efficient workload management without compromising quality. Reflectance spectrophotometry-based dry chemistry systems have been introduced and are now being utilized in numerous clinical laboratories. These systems offer a viable alternative to wet chemistry analyzers.[1,2] Initially designed as desktop analyzers for point-of-care use by clinicians, dry chemistry analyzers had some drawbacks such as limited test parameters, result reliability, and test cost.[3] However, with the

advancement in technologies and systems, there are notable advantages. One key advantage is the absence of carry-over effects, which ensures accurate and reliable results. Dry chemistry systems also offer excellent precision and high stability of both calibration and reagent lots, contributing to consistent and reproducible measurements. Additionally, the use of very small dead volume in dry chemistry analysis is particularly beneficial for analyzing samples from pediatric or geriatric patients. Notably, microslide assays are available for a range of classic clinical chemical parameters, providing a convenient and efficient testing option within the dry chemistry technology framework.[4]

The majority of analysis systems employed in clinical chemical laboratories rely on traditional wet chemistry analysis. Tests run on wet chemistry analyzers generally have a lower cost compared to those run on dry chemistry analyzers.[5] Currently, we are running both these system side by side in the Department of clinical biochemistry of Dhulikhel Hospital. The present study intends to compare the agreement of results between dry and wet chemistry systems for common clinical chemistry parameters i.e., Glucose, urea, creatinine, total bilirubin, total protein, albumin, total calcium, total cholesterol, triglyceride, HDL-Cholesterol, AST and ALT respectively.

## MATERIALS AND METHODS

This was a prospective cross-sectional study conducted from 1st August 2021 to 31st July 2022, in the Department of clinical biochemistry of Dhulikhel Hospital Kathmandu University Hospital. Permission for the study was obtained from IRC-KUSMS. We analyzed the secondary data generated from testing the external quality control sample across two different systems simultaneously viz. Vitros 350 (Ortho clinical diagnostics) and BA-400 (Biosystem), Both of them are fully automated biochemistry analyzers with Vitros 350 being a dry chemistry system and BA-400 a wet chemistry system In total, we analyzed 57 samples across these two systems. The total number of studied parameters were twelve namely Glucose, Urea. Creatinine, Total bilirubin, Total protein, Albumin, Total Calcium, Total Cholesterol, Triglyceride, HDL-Cholesterol, AST, and ALT.

The wet chemistry system employs various assay principles for different biochemical parameters. In our study, we utilized Glucose oxidase peroxidase (GOD-POD) for glucose estimation, Urease/Glutamate dehydrogenase for urea, Jaffe's alkaline picrate for creatinine, diazotized sulfanilic acid for bilirubin, Biuret for total protein, Bromocresol green (BCG) for albumin, Arsenazo III for total calcium, uricase for uric acid, cholesterol oxidase peroxidase for cholesterol, glycerol phosphate oxidase peroxidase for triglycerides, enzymatic direct method for HDL-C, and UV kinetic method for AST and ALT estimation respectively.

The data obtained from the study were recorded and managed using an Excel sheet. Continuous variables were described as means with standard deviations or as a median with an interquartile range depending on their distribution. Paired t-test and Bland-Altman plot was used for analyzing the agreement between the two systems. Spearman's correlation was used to measure the correlation between the two systems. To analyze the bias and variability of differences in analyte values between the two methods, we followed the Bland and Altman method. The difference between the measurements obtained from the two methods was calculated and plotted against the mean of the two measurements. Subsequently, the 95% limits of agreement were determined by calculating the mean difference ±2 standard deviations (SD) of the paired measurements.[6]

To assess the reliability and reproducibility of the measurements, we employed the Intraclass correlation coefficient (ICC). The ICC estimates and their corresponding 95% confidence intervals (CI) were calculated using SPSS statistical package version 23 (SPSS Inc, Chicago, IL). The ICC was calculated based on a mean rating, absolute agreement, and 2-way mixed-effects model.

**Interpretation of ICC values is as follows[7]:**

| ICC Value | Inference |
|---|---|
| < 0.5 | Poor Reliability |
| 0.5-0.75 | Moderate Reliability |
| 0.75-0.9 | Good Reliability |
| > 0.9 | Excellent Reliability |

By utilizing these thresholds, we assessed the reliability of the measurements obtained in our study.

## RESULTS

A total of 57 samples received for the external quality assurance program was analyzed across the two systems. Table 1 displays the Mean±SD/Median (IQR) of the twelve routine biochemical parameters using both the dry and wet chemistry analyzer. There was a significant difference between the means across the two methods. To observe the correlations between the two methods, Spearman rho correlation was used. There was a strong correlation between the two methods as shown in Table 1.

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**Table 1: Comparison between dry and wet chemistry systems with the correlation coefficient**

| Parameters | Dry Chemistry | Wet Chemistry | Correlation coefficient (r) | p- value |
|---|---|---|---|---|
| **Glucose** | 130.3 (101.5, 251.1) | 140.1 (110, 259.6) | 0.99 | 0.001* |
| **Urea** | 59.1 (36, 113) | 58.8 (33.5, 106.4) | 0.99 | 0.001* |
| **Creatinine** | 2.8 (1.5, 5.2) | 2.8 (1.5, 5.6) | 0.98 | 0.001* |
| **Total Bilirubin** | 2.3 (1.5, 3.2) | 2.4 (1.6, 3.7) | 0.96 | 0.001* |
| **Total Protein** | 5±0.8 | 5.3±0.8 | 0.90 | 0.001* |
| **Albumin** | 2.9±0.6 | 3.2±0.5 | 0.91 | 0.001* |
| **Total Calcium** | 9.3±1.6 | 9.7±1.3 | 0.88 | 0.001* |
| **Total Cholesterol** | 99±27.8 | 111.2±26.4 | 0.96 | 0.001* |
| **Triglyceride** | 166.5±62.1 | 140.9±57 | 0.96 | 0.001* |
| **HDL-Cholesterol** | 20.9±4.2 | 25.8±5 | 0.77 | 0.001* |
| **AST** | 98 (61.5, 207.2) | 96 (56, 179) | 0.99 | 0.001* |
| **ALT** | 90 (55, 169.5) | 70.2 (40, 154.5) | 0.97 | 0.001* |

**Correlation is significant at the 0.01 level (2-tailed)*

To assess the agreement between dry and wet chemistry results, difference between the two methods was calculated (Mean of dry chemistry result-Mean of wet chemistry result). The mean difference for glucose concentrations was calculated as -10.70, with a standard deviation of 12.11. The highest mean difference was observed for triglycerides with a mean difference of 25.6 and a standard deviation of 16.59. Similarly, for AST, the mean difference was 20.46, with a standard deviation of 28.25. The mean difference of other biochemical parameters is shown in Table 2.

**Table 2: Mean difference and Intra-class correlation coefficients between dry chemistry and wet system**

| Parameters | Mean Difference (Dry Chemistry-Wet Chemistry) | ICC (Confidence Interval) |
|---|---|---|
| **Glucose** | -10.70 | 0.99 (0.96-0.99) |
| **Urea** | 3.44 | 0.99 (0.98-0.99) |
| **Creatinine** | -0.30 | 0.98 (0.96-0.98) |
| **Total Bilirubin** | 0.19 | 0.99 (0.97-0.99) |
| **Total Protein** | -0.35 | 0.91 (0.52-0.96) |
| **Albumin** | -0.32 | 0.86 (0.15-0.96) |
| **Total Calcium** | -0.43 | 0.91 (0.78-0.95) |
| **Total Cholesterol** | -12.14 | 0.93 (0.08-0.98) |
| **Triglyceride** | 25.6 | 0.93 (0.11-0.98) |
| **HDL-Cholesterol** | -4.86 | 0.66 (-0.21-0.88) |
| **AST** | 20.46 | 0.98 (0.92-0.99) |
| **ALT** | 14.12 | 0.97 (0.90-0.98) |

The mean difference represents the estimation of bias between the two methods.

To measure reliability that reflects both degree of correlation and agreement between measurements, Intraclass Correlation Coefficient (ICC) was used. Among the total of 12 biochemical parameters, 10 parameters ICC value was above 0.90 as shown in Table 2. ICC value of more than 0.90 indicates excellent reliability. ICC of HDL-C was 0.66 and that of albumin was 0.86, which indicates moderate and good reliability respectively. ICC estimates and their 95% confidence interval (CI) of the biochemical parameters across the two systems is shown in Table 2.

Scatter plots were generated by plotting the differences between the dry chemistry method and the wet chemistry method. The values were then plotted against the mean of the two measurements using the Bland and Altman method. The 95% limits of agreement for glucose values in the given samples were determined to be from 13.03 to -34.43, as shown in Figure 1. Likewise, the 95% limits of agreement for urea were found to be from 14.9 to -8.02, as depicted in Figure 1. Both the dry and wet chemistry methods for determining urea values fall within the upper and lower limits, demonstrating a 95% limit of agreement. Similarly, the 95% limits of agreement for creatinine, total bilirubin, total protein, albumin, total calcium, phosphorus, uric acid, Total cholesterol, triglyceride, HDL-C, AST, and ALT are also shown in Figure 1.

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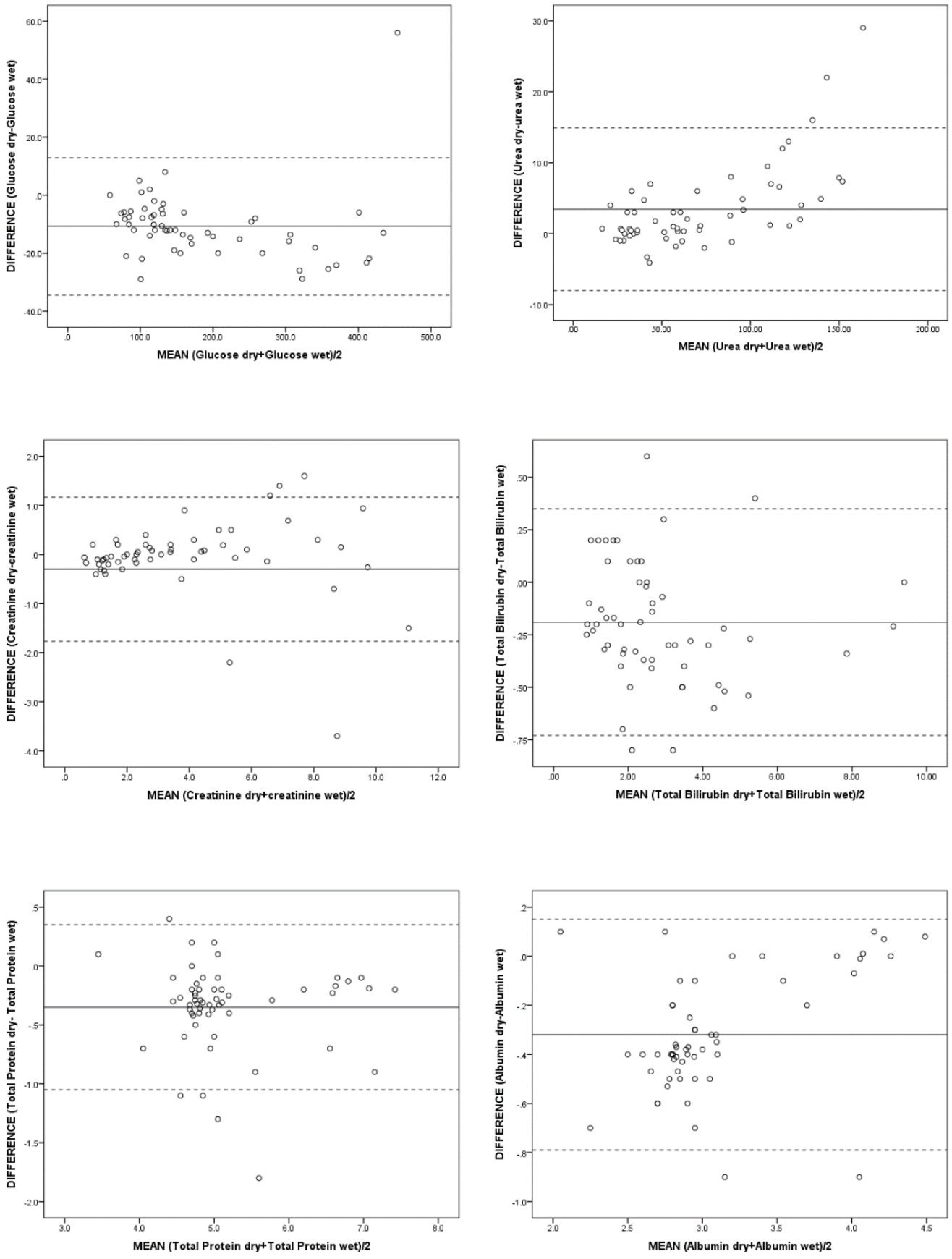


***Figure 1:*** *Bland-Altman plots of dry chemistry parameters against wet Chemistry parameters*

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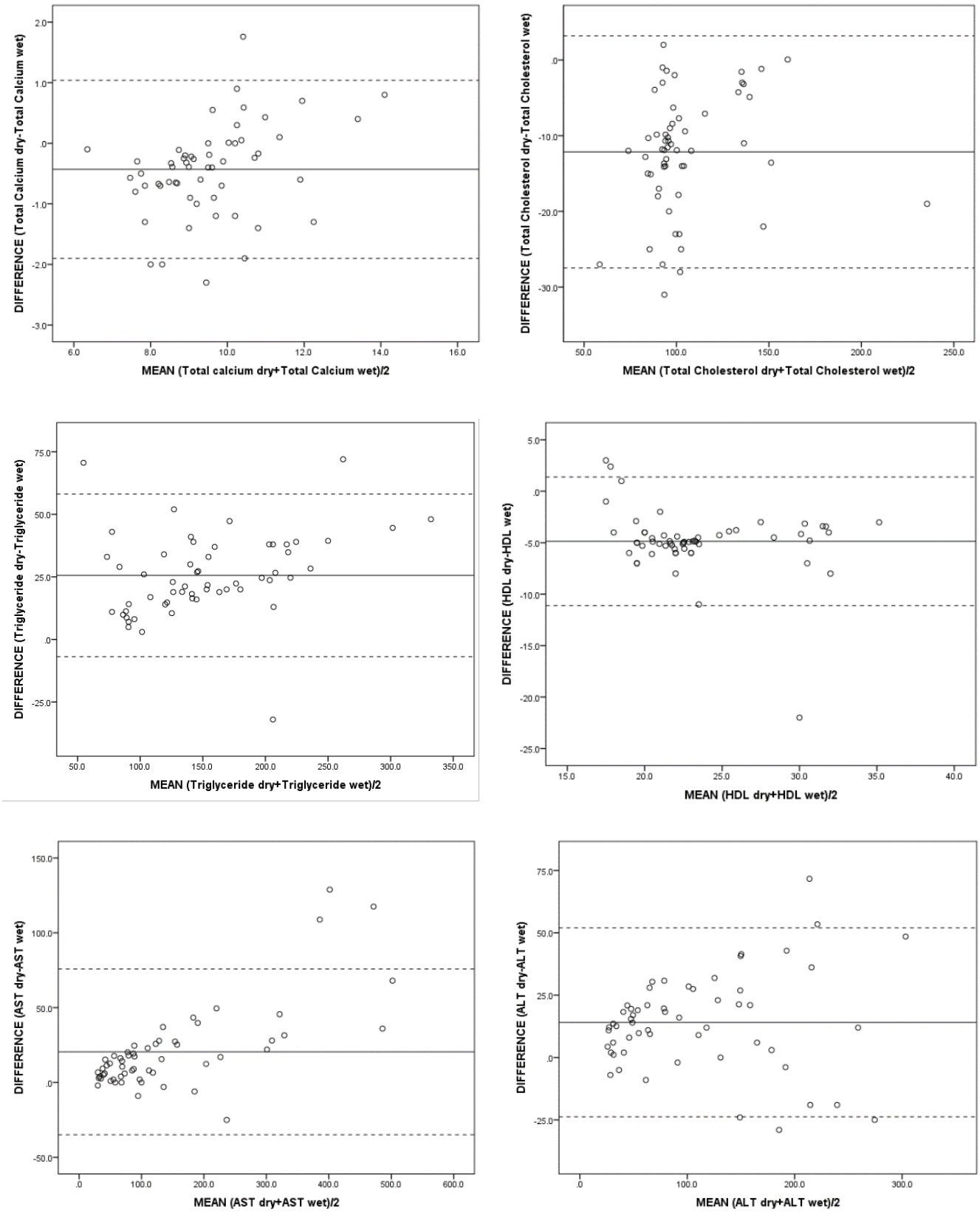


***Figure 1 (Contd.):*** *Bland-Altman plots of dry chemistry parameters against wet Chemistry parameters*

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## DISCUSSION

The present study revealed a high level of agreement between the two systems for most biochemical parameters. While significant differences were observed in means of the biochemical parameters, a strong correlation between two methods indicated overall agreement. Bland-Altman plots showed that for most parameters, the dry and wet chemistry methods fell within the 95% limits of agreement, indicating agreement between the two systems. The reliability of the measurements was also evaluated using the Intraclass Correlation Coefficient (ICC), where 10 out of the 12 biochemical parameters exhibited ICC values above 0.90, indicating excellent reliability. HDL-C showed moderate reliability with an ICC value of 0.66, while albumin demonstrated good reliability with an ICC value of 0.86.

There are limited number of comparative studies available on dry and wet chemistry systems. Our study was comparable with few of those studies. Zipp A[1] in the year 1981, a developer of the dry chemistry system, conducted a comparison with the wet chemistry system, demonstrating a strong correlation between these two methods.[1] However, it is important to note that the number of assays analyzed in this comparison study were limited i.e. LDH, BUN, and cholesterol.[1] Lanevschi and Kramer[8] compared seven chemistry analytes in canine serum on two tabletop clinical dry chemistry analyzers and the results were compared to the wet chemistry analyzer.[8] The study showed acceptable correlations for most of the analyte measurements, but significant differences were observed for certain analytes, likely due to systematic errors occurring at high analyte concentrations.[9] Similarly, Sutton et al conducted a study among 26 feline and 37 canine serum samples and evaluated the agreement between a wet and dry reagent analyzer for thirteen analytes in the respective veterinary serum.[9] The study revealed excellent agreement for eight analytes, but unreliable correlations were found for albumin, potassium, and calcium. The researcher concluded that the methodological variations might be the potential cause for the significant differences in slopes observed between the two analyzers.[9]

A large clinical study evaluated the VITROS 5,1 FS analyzer in a clinical laboratory where the researcher compared the methods using different specimens and chemistry systems.[4] The study depicted good agreement between the microslide assays (used in the Vitros 5.1 FS analyzer) and the wet chemistry methods, with correlation coefficients ranging from 0.872 to 0.998. These findings align with the results of our study, further confirming the agreement between the dry chemistry system and the wet chemistry system.[10] The study outlined a particular observation regarding the microslide assay for direct determination of HDL cholesterol, which showed a shift towards higher values compared to the wet chemistry analysis methods. The author highlighted that this discrepancy may be attributed to the matrix of the quality control samples used, which could have influenced the performance of the multilayer film technology employed in the microslide assay.[11] The similar finding was observed in the present study where we observed a potential impact on the HDL result, which could be attributed to similar factors. Similar to our study, Herkner et al[10] compared the microslide assay with a homogeneous assay using a Roche method. The findings of this study indicated good agreement between these two methods. However, the study also observed a shift towards higher values, particularly in lower concentrations. It is speculated that the deviations observed could be attributed to the different standardization approaches employed by the respective methods.[10]

Wet chemistry analyzers play an indispensable and crucial role in clinical chemistry laboratories. However, the emergence of dry chemistry analyzers has provided a viable alternative, particularly for larger centers with higher workloads. One advantage traditionally associated with wet chemistry analyzers is their lower cost per test (CPT) compared to dry chemistry analyzers. Nonetheless, advancements in dry chemistry technology and improved test parameters are addressing these cost limitations, making dry chemistry analyzers a more feasible option for many laboratories. Mukherjee et al[5] compared the cost between the two systems and delineated that lower costs per test are associated with wet chemistry analyzers. However, when considering high specific workloads, the cost per reporting test (CPRT) of the dry chemistry system was found to be lower than that of the wet chemistry system.[5] Beside the cost factor, dry chemistry analyzer is also believed to enhance performance in external quality assurance schemes (EQAS) as observed by Mukherjee et al.[12]

The high level of correlation and agreement observed suggests that both systems can provide reliable results. However, it is important to consider the specific parameters and limitations of each system when interpreting the results. These findings have practical implications for laboratories and healthcare professionals in selecting the most suitable system based on their specific needs and available resources. It is justified to use both these systems or interchangeably use any of the two methods. Future studies that incorporate patient samples on a larger scale and include comprehensive cost analyses are warranted to further elucidate this topic.

## CONCLUSIONS

There is a strong agreement observed when comparing the dry chemistry system with the wet chemistry system for measuring routine biochemical parameters. Our study depicted that there was moderate reliability with HDL-C and good reliability with albumin and excellent reliability with the rest clinical chemistry parameters. Though the dry chemistry system offers advantages such as reduced external interventions and improved precision and accuracy compared to wet chemistry system, they do not differ significantly enough to create issues in clinical interpretation.

**Conflict of Interest:** None

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