


A New Equation in the Calculation of Osmolality Before and After Hemodialysis Session

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ABSTRACT

Objective: In this study, in hemodialysis patients, we aimed to compare the osmolality values calculated by the equations that are frequently used in the literature and the values measured on the osmometer device, and also to present new equations that are obtained from regression analysis for calculating serum osmolality. In addition, in the evaluation of hemodialysis adequacy of patients, we aimed to evaluate the effectiveness of our equations by comparing the osmolality values calculated with our equations and the measured osmolality values.

Methods: New equations for pre- and posthemodialysis were obtained by linear regression analysis from the pre- and posthemodialysis examination parameters that were analyzed for hemodialysis adequacy assessment:

For prehemodialysis serum osmolality = $1.37 \times ([Na^+] + [K^+]) + 1.1 \times BUN + Glucose + 85$

For posthemodialysis serum osmolality = $1.2 \times ([Na^+] + [K^+]) + BUN + Glucose + 110$

Comparison and correlation of measured and calculated osmolality values were carried out with statistical tests, separately for before and after hemodialysis.

Results: Considering the high correlation strength, low osmolal gap mean and standard deviation, and the lack of significant difference between the measured and calculated osmolality in the selection of the equation with the best results, it is seen that the best results were obtained using our equations and the " $2 \times ([Na^+] + [K^+]) + Glucose + BUN$ " equation.

Conclusion: We suggest using our equations and the equation " $2 \times ([Na^+] + [K^+]) + Glucose + BUN$," which are evaluated as better performing equations according to the results of our study.

Keywords: Osmolality, osmolal gap, hemodialysis.

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INTRODUCTION

Osmolality is the measure of the number of osmoles dissolved per kilogram of water. Usually, the osmolal concentration is expressed in milliosmoles per kilogram of water (mOsm/kg H₂O).^{1,2}

The use of mathematical equations for calculating serum osmolality is beneficial when a specific measurement is not available or a calculation of osmolal gap (OG) is required. Osmolal gap is the difference between measured and calculated osmolality.³⁻⁶ Osmolal gap

specifically indicates the presence of unknown solutes measured by osmometer but not included in the calculation. The optimal equation for calculating osmolality requires that the OG must be zero or near zero.¹ The most desirable range for OG is expressed as <2 mOsm/kg H₂O.⁷

Many equations have been developed to calculate serum or plasma osmolality. Most of these are usually determined by linear regression analysis.^{1,8-11} Although a wide variety of equations have been proposed for osmolality calculation, a few studies have determined which



of them work best. The reason for the lack of consensus on the most effective equations is probably due to the fact that the fitting of any regression equation to a new dataset will almost always produce a lower estimate. The real usefulness of any regression equation depends on how well it predicts data other than the data on which it is developed.

Osmolal gap and serum osmolality levels are important in patients with chronic kidney disease (CKD). Chronic kidney disease patients on hemodialysis (HD) may develop a “dialysis disequilibrium syndrome” when their blood urea levels drop suddenly and significantly.¹² Before and after the HD session, there are changes in analyte concentrations that contribute to serum osmolality. Therefore, we think that the pre- and post-session effectiveness of the equations used in osmolality calculation should be evaluated separately.

60 In this study, in HD patients, we aimed to compare the osmolality values calculated by the equations that are frequently used in the literature and the values measured on the osmometer device, and also to present new equations that are obtained from regression analysis for calculating serum osmolality in HD patients. In addition, in the evaluation of hemodialysis adequacy of patients (validating group), we aimed to evaluate the effectiveness of our equations by comparing the osmolality values calculated with our equations and the measured osmolality values.

METHODS

Volunteers aged 18 years and over who received HD treatment in the Hemodialysis Unit of the Third Stage Health Practice and Research Hospital were included in the study. Routine blood tests were performed once a month for hemodialysis adequacy assessment in the hemodialysis unit. Blood samples were collected during the hemodialysis adequacy assessment for 2 consecutive months and routine analysis data were used for the patients who were a part of our study. Our data for the first month formed our data series (training group), which we used to generate our new equations. Our data for the second month (validating group) was used to evaluate the performance of our equations in general. All procedures performed in this study involving human participants were in accordance with the ethical standards of the Institutional Research Committee and with

the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the local ethics committee (Decision No: 2022/19), and informed consent was obtained from all volunteers.

Blood samples taken during hemodialysis adequacy assessment were allowed to clot at room temperature, then centrifuged at 4000 rpm and serum was obtained. Routine analyses were performed on a Cobas 8000 autoanalyzer (Roche Diagnostics GmbH, Mannheim, Germany) on the obtained patient sera. Glucose and blood urea nitrogen (BUN) measurements were carried out spectrophotometrically in the c702 module of the autoanalyzer, and $[\text{Na}^+]$, $[\text{K}^+]$ measurements were carried out in the ion-selective electrode module of the autoanalyzer. All parameters were expressed in mmol/L. In the remaining serum samples after routine analysis, osmolality was measured on a Osmomat 3000 osmometer device (Gonotec, Berlin, Germany) based on the freezing point measurement principle. The osmolality values that were measured before and after HD were compared. Separately, new equations for pre-HD and post-HD were obtained by linear regression analysis using $[\text{Na}^+]$, $[\text{K}^+]$, glucose, and BUN concentrations from the pre-HD and post-HD examination parameters that were analyzed for hemodialysis adequacy assessment. Equations were optimized by making minor modifications to the coefficients obtained by regression analysis. The osmolality values were calculated with 4 different equations frequently used in the literature⁸⁻¹¹ and our equations. The OG was calculated from the measured and calculated osmolality values with the following formula:

Osmolal gap = measured osmolality – calculated osmolality

Measured and calculated osmolality values were compared and correlation analysis was performed, separately before and after HD session.

Statistical Analysis

All data analyses were performed with IBM SPSS 22 Statistics package programs (IBM SPSS, Armonk, NY, USA). Shapiro–Wilk tests were used to analyze the normality distributions of all values. The Wilcoxon signed-rank test was used to evaluate the differences in measured osmolality pre-HD and post-HD. The correlation of measured and calculated osmolality values was evaluated with the Pearson’s correlation test in normally distributed data and with the Spearman’s correlation test in non-normally distributed data. In addition, Bland–Altman plots were used to compare the osmolality calculated with our equations and the measured osmolality. Bland–Altman plots show a random distribution of points with most observations falling within confidence intervals. The relationship between the osmolality gap (y-axis) and the mean of the calculated and measured osmolality (x-axis) is evaluated with the Bland–Altman plots. The differences between measured and calculated osmolality were assessed using the Student’s *t*-test for data with normal

MAIN POINTS

- For calculating osmolality, we do not recommend the use of the equation proposed by Dorwart and Chalmers.
- In our study, we observed that the correlation coefficients in the equations with $[\text{Na}^+] + [\text{K}^+]$ as the independent variable are slightly higher than that in the equations with only $[\text{Na}^+]$.
- We suggest using our equations and the equation “ $2 \times ([\text{Na}^+] + [\text{K}^+]) + \text{Glucose} + \text{BUN}$,” which have been evaluated as better-performing equations according to the results of our study.
- Our study sheds light on future research for the use of different formulas before and after the hemodialysis session.

Table 1. Correlation of Measured and Calculated Osmolality (Training Group)							
Equations	Ref	OG	SD	Upper LoA	Lower LoA	r	P
Pre-hemodialysis (pre-HD)							
1.86 × [Na ⁺] + Glucose + BUN + 9	8	18.14	4.04	26.06	10.22	0.833	<.001
1.9 × ([Na ⁺] + [K ⁺]) + Glucose + BUN + 5	9	6.88	3.73	14.19	−0.43	0.861	<.001
2 × [Na ⁺] + Glucose + BUN	10	7.95	4.25	16.28	−0.38	0.825	<.001
2 × ([Na ⁺] + [K ⁺]) + Glucose + BUN	11	−2.34	3.84	5.19	−9.87	0.855	<.001
1.37 × ([Na ⁺] + [K ⁺]) + 1.1 × BUN + Glucose + 85	Ours	0.14	3.39	6.78	−6.50	0.884	<.001
Post-hemodialysis (post-HD)							
1.86 × [Na ⁺] + Glucose + BUN + 9	8	15.69	4.41	24.33	7.05	0.630	<.001
1.9 × ([Na ⁺] + [K ⁺]) + Glucose + BUN + 5	9	7.30	4.16	15.45	−0.85	0.668	<.001
2 × [Na ⁺] + Glucose + BUN	10	5.65	4.57	14.61	−3.31	0.614	<.001
2 × ([Na ⁺] + [K ⁺]) + Glucose + BUN	11	−1.66	4.26	6.69	−10.01	0.663	<.001
1.2 × ([Na ⁺] + [K ⁺]) + BUN + Glucose + 110	Ours	0.06	3.81	7.53	−7.41	0.703	<.001
In the prehemodialysis data series, Spearman's correlation test was applied in the third equation and Pearson's correlation test was applied in the other equations. In the posthemodialysis data series, Spearman's correlation test was applied in the all equations. [K ⁺], potassium (mmol/L); [Na ⁺], sodium (mmol/L); BUN, blood urea nitrogen (mmol/L); LoA, Limit of agreement; OG, osmolal gap; SD, standard deviation.							

distribution and the Mann–Whitney *U*-test for data with non-normal distribution. Linear regression analysis was performed to determine the coefficients of the our equations. *P*-values less than .05 were considered significant.

RESULTS

Fifty-two volunteers were included in the study. Pre-HD osmolality values of the volunteers were 310.1 ± 7.26 and post-HD osmolality values were 290.08 ± 5.86. Pre-HD osmolality values were significantly higher than post-HD osmolality values (*P* <.001).

The mean and standard deviation of the osmolal gap values are presented in Table 1. There was a significant positive correlation between the measured and calculated osmolality values. While there was a very strong positive correlation in the pre-HD data, there was a strong positive correlation in the post-HD data (Table 1). The results of the comparison of the measured osmolality values with the calculated osmolality values are presented in Table 2.

Linear regression analysis results of pre-HD and post-HD data are presented in Tables 3 and 4. Minor modifications were

Table 2. Evaluation of Differences in Measured and Calculated Osmolality (Training Group)				
Equations	Ref	Measured Osmolality	Calculated Osmolality	P
Pre-hemodialysis (pre-HD)				
1.86 × [Na ⁺] + Glucose + BUN + 9	8	310.10 ± 7.26*	291.96 ± 6.54	<.001
1.9 × ([Na ⁺] + [K ⁺]) + Glucose + BUN + 5	9	310.10 ± 7.26*	303.21 ± 6.78	<.001
2 × [Na ⁺] + Glucose + BUN	10	311.00** (295.00-325.00)	302.37 (282.50-315.63)	<.001
2 × ([Na ⁺] + [K ⁺]) + Glucose + BUN	11	310.10 ± 7.26*	312.44 ± 6.95	.096
1.37 × ([Na ⁺] + [K ⁺]) + 1.1 × BUN + Glucose + 85	Ours	310.10 ± 7.26*	309.95 ± 6.44	.916
Post-hemodialysis (post-HD)				
1.86 × [Na ⁺] + Glucose + BUN + 9	8	290.50** (268.00-301.00)	274.57 (258.84-285.47)	<.001
1.9 × ([Na ⁺] + [K ⁺]) + Glucose + BUN + 5	9	290.50** (268.00-301.00)	283.47 (266.65-294.17)	<.001
2 × [Na ⁺] + Glucose + BUN	10	290.50** (268.00-301.00)	284.60 (267.90-295.65)	<.001
2 × ([Na ⁺] + [K ⁺]) + Glucose + BUN	11	290.50** (268.00-301.00)	292.29 (274.90-303.25)	.121
1.2 × ([Na ⁺] + [K ⁺]) + BUN + Glucose + 110	Ours	290.50** (268.00-301.00)	290.54 (278.90-300.61)	.696
[K ⁺], potassium (mmol/L); [Na ⁺], sodium (mmol/L); BUN, blood urea nitrogen (mmol/L). *Values were expressed as means ± SD. Student's <i>t</i> -test was applied. **Values were expressed as median (min-max). Mann–Whitney <i>U</i> test was applied. Bold values indicate not statistical significance.				

Table 3. Linear Regression Analysis of Prehemodialysis Data (Training Group)						
Model	Unstandardized Coefficients		Standardized Coefficients	P	95% Confidence Interval for B	
	B	Std. Error	Beta		Lower Bound	Upper Bound
(Constant)	85.58	28.67		.004	27.94	143.22
([Na ⁺] + [K ⁺])	1.37	0.20	0.53	<.001	0.97	1.76
BUN	1.10	0.10	0.77	<.001	0.90	1.29
Glucose	0.98	0.20	0.38	<.001	0.59	1.38
[K ⁺], potassium (mmol/L); [Na ⁺], sodium (mmol/L); BUN, blood urea nitrogen (mmol/L); Std, standard.						

Table 4. Linear Regression Analysis of Posthemodialysis Data (Training Group)						
Model	Unstandardized Coefficients		Standardized Coefficients	P	95% Confidence Interval for B	
	B	Std. Error	Beta		Lower Bound	Upper Bound
(Constant)	110.56	32.52		.001	45.18	175.95
([Na ⁺] + [K ⁺])	1.20	0.23	0.48	<.001	0.73	1.66
BUN	1.03	0.23	0.41	<.001	0.56	1.50
Glucose	0.99	0.21	0.43	<.001	0.56	1.42
[K ⁺], potassium (mmol/L); [Na ⁺], sodium (mmol/L); BUN, blood urea nitrogen (mmol/L); Std, standard.						

made to the coefficients obtained by linear regression analysis, and new equations were presented separately for pre-HD and post-HD.

Our equation for pre-HD = 1.37 × ([Na⁺] + [K⁺]) + 1.1 × BUN + Glucose + 85

Our equation for post-HD = 1.2 × ([Na⁺] + [K⁺]) + BUN + Glucose + 110

Blood samples taken during the next evaluation of the HD adequacy of the patients (validating group) were used to evaluate performance of our equations. For the validating group, the mean and standard deviation of the osmolal gap values are presented in Table 5. There was a significant positive correlation between the measured and calculated osmolality values. In the pre-HD samples, “2 × ([Na⁺] + [K⁺]) + Glucose + BUN” and our equations had very strong positive correlation, and these equations had the highest correlation coefficients. The

Table 5. Correlation of Measured and Calculated Osmolality (Validating Group)							
Equations	Ref	OG	SD	Upper LoA	Lower LoA	r	P
Pre-hemodialysis (pre-HD)							
1.86 × [Na ⁺] + Glucose + BUN + 9	8	20.81	4.53	29.69	11,93	0.539	<.001
1.9 × ([Na ⁺] + [K ⁺]) + Glucose + BUN + 5	9	9.53	4.43	18.22	0.85	0.786	<.001
2 × [Na ⁺] + Glucose + BUN	10	10.60	4.64	19.70	1.50	0.751	<.001
2 × ([Na ⁺] + [K ⁺]) + Glucose + BUN	11	0.30	4.51	9.14	−8.55	0.921	<.001
1.37 × ([Na ⁺] + [K ⁺]) + 1.1 × BUN + Glucose + 85	Ours	3.04	4.13	11.14	−5.06	0.916	<.001
Post-hemodialysis (post-HD)							
1.86 × [Na ⁺] + Glucose + BUN + 9	8	17.03	5.91	28.60	5.45	0.649	<.001
1.9 × ([Na ⁺] + [K ⁺]) + Glucose + BUN + 5	9	8.37	5.54	19,23	−2.48	0.713	<.001
2 × [Na ⁺] + Glucose + BUN	10	6.90	6.01	18,68	−4.89	0.635	<.001
2 × ([Na ⁺] + [K ⁺]) + Glucose + BUN	11	−0.67	5.60	10.30	−11.64	0.700	<.001
1.2 × ([Na ⁺] + [K ⁺]) + BUN + Glucose + 110	Ours	1.67	5.53	12.52	−9.17	0.845	<.001
In the prehemodialysis data series, Pearson's correlation test was used in all equations. In the posthemodialysis data series, Pearson's correlation test was used in our equation and Spearman's correlation test was used in other equations. [K ⁺], potassium (mmol/L); [Na ⁺], sodium (mmol/L); BUN, blood urea nitrogen (mmol/L); LoA, limit of agreement; OG, osmolal gap; SD, standard deviation;							

Table 6. Evaluation of Differences in Measured and Calculated Osmolality (Validating Group)				
Equations	Ref	Measured Osmolality	Calculated Osmolality	P
Pre-hemodialysis (pre-HD)				
1.86 × [Na ⁺] + Glucose + BUN + 9	8	312.02 ± 8.16*	291.21 ± 7.04	<.001
1.9 × ([Na ⁺] + [K ⁺]) + Glucose + BUN + 5	9	312.02 ± 8.16*	302.49 ± 7.41	<.001
2 × [Na ⁺] + Glucose + BUN	10	312.02 ± 8.16*	301.42 ± 7.17	<.001
2 × ([Na ⁺] + [K ⁺]) + Glucose + BUN	11	312.02 ± 8.16*	311.72 ± 7.52	.858
1.37 × ([Na ⁺] + [K ⁺]) + 1.1 × BUN + Glucose + 85	Ours	312.02 ± 8.16*	308.98 ± 7.29	.066
Post-hemodialysis (post-HD)				
1.86 × [Na ⁺] + Glucose + BUN + 9	8	293.00** (270.00-316.00)	276.20 (257.02-288.30)	<.001
1.9 × ([Na ⁺] + [K ⁺]) + Glucose + BUN + 5	9	293.00** (270.00-316.00)	284.21 (266.69-297.69)	<.001
2 × [Na ⁺] + Glucose + BUN	10	293.00** (270.00-316.00)	286.52 (265.94-299.18)	<.001
2 × ([Na ⁺] + [K ⁺]) + Glucose + BUN	11	293.00** (270.00-316.00)	293.32 (274.94-306.79)	.493
1.2 × ([Na ⁺] + [K ⁺]) + BUN + Glucose + 110	Ours	292.33 ± 9.20*	290.66 ± 5.26	.293
[K ⁺], potassium (mmol/L); [Na ⁺], sodium (mmol/L); BUN, blood urea nitrogen (mmol/L). *Values were expressed as means ± SD. Student's t-test was applied. **Values were expressed as median (min-max). Mann-Whitney U test was applied. Bold values indicate not statistical significance.				

correlation coefficient of the “2 × ([Na⁺] + [K⁺]) + Glucose + BUN” equation is slightly higher than the correlation coefficient of our equation. In the post-HD samples, only our equation had very strong positive correlation and the highest correlation coefficient (Table 5). In the validating group, the measured osmolality values were compared to the calculated osmolality values using our equations and 4 different equations frequently used in the literature. The osmolality values calculated with the “2 × ([Na⁺] + [K⁺]) + Glucose + BUN” equation and our equations were not statistically different from the measured osmolality values (Table 6).

In addition, the Bland–Altman plots of our equation and the “2 × ([Na⁺] + [K⁺]) + Glucose + BUN” equation comparing the measured and calculated osmolality are presented in Figures 1-4. The distribution of measured and calculated osmolality values is shown in these graphs.

DISCUSSION

Numerous different equations have been created using regression analyses for serum osmolality calculations.^{1,8-11,13} Although there are many equations for calculating plasma or serum osmolality, there is no consensus on the best equation. The Dorwart–Chalmers equation “1.86 × [Na⁺] + Glucose + BUN + 9,” published in 1975, has been widely used.⁸ However, some reports have suggested that the use of this equation tends to underestimate the true osmolality of the sample.^{1,9} However, this formula is still accepted in textbooks and is included in commercial osmolality measuring devices.¹⁴ In the study by Rasouli et al, it was found that the measured osmolality was greater than the calculated osmolality in almost all cases when the Dorwart–Chalmers formula was used. Rasouli et al⁹ proposed

a new equation “1.9 × ([Na⁺] + [K⁺]) + Glucose + BUN + 5” from their own data and osmolality calculations were made with this equation in our study. In his study published in 2016, Rasouli¹ strongly recommends withdrawing the Dorwart–Chalmers formula from textbooks and autoanalyzers and using Worthley et al’s simpler equation. In a study by Calderon et al on the comparison of several equations, the use of the Dorwart–Chalmers formula is not recommended. In addition, among the equations they examined in their study, it was found that the 2 best equations were those proposed by Khajuria and Krahn, “1.86 × ([Na⁺] + [K⁺]) + 1.15 × Glucose + BUN + 14” and “2 × [Na⁺] + 1.15 × Glucose + BUN,” and the equation proposed by Worthley “2 × [Na⁺] + Glucose + BUN” was acceptable as an alternative due to its simplicity of use.¹³ Vareesangthip et al¹⁵ compared the osmolality calculated with 14 different equations with the measured osmolality. The 4 equations used in our study are also included in this study. Vareesangthip et al found that out of 14 equations, 2 equations outperformed the other equations. One of these equations is the “2 × ([Na⁺] + [K⁺]) + Glucose + BUN” equation, which we also used in our study, and the other is the “1.86 × ([Na⁺] + [K⁺]) + 1.15 × Glucose + BUN + 14” equation proposed by Khajuria and Krahn.¹⁵ In a study published in 2020, it was reported that there was a statistically significant difference between the measured osmolality values and the osmolality values calculated with the “2 × ([Na⁺] + [K⁺]) + Glucose + BUN” formula, and the calculated osmolality values were significantly higher than the measured osmolality values. A significant positive correlation was reported between the osmolality values measured and calculated according to the results of this study.¹⁶

In the validating group of our study, there was a significant positive correlation between the measured and

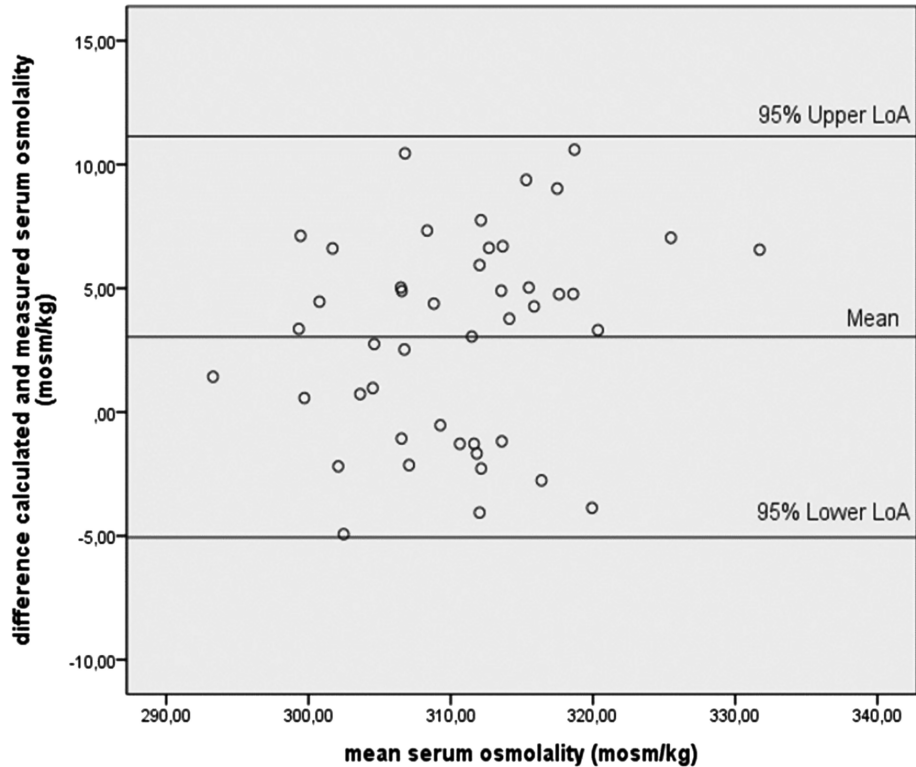


Figure 1. Bland–Altman plots of osmolality measured with osmolality calculated from our equation for pre-hemodialysis (validating group). Bland–Altman mean bias: 3.04 (95% limits of agreement [LoA]: –5.06-11.14).

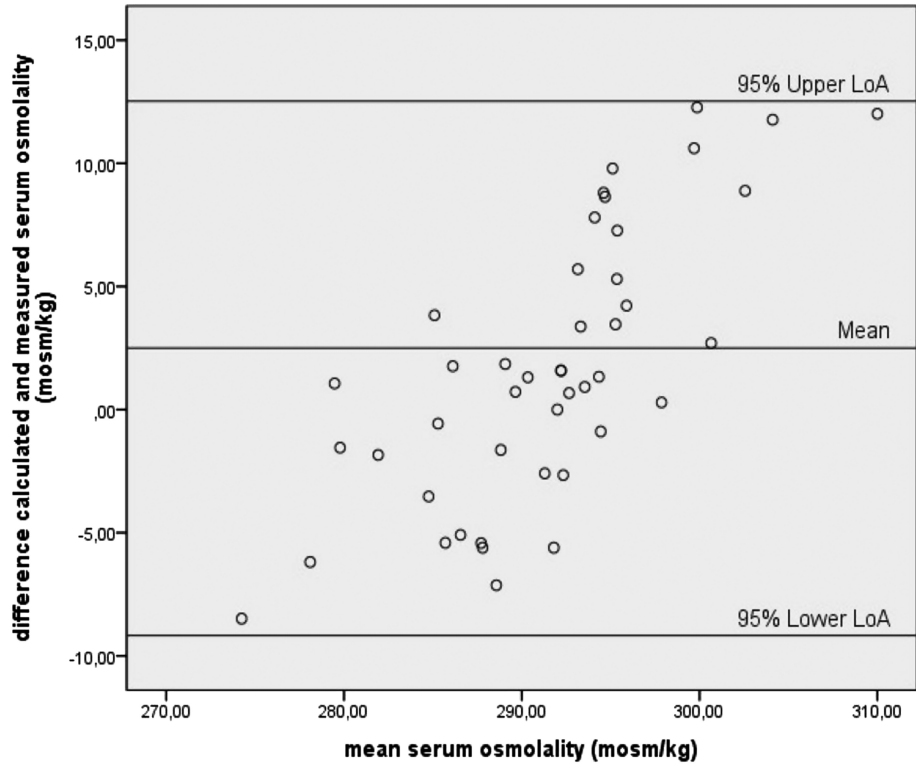


Figure 2. Bland–Altman plots of osmolality measured with osmolality calculated from our equation for post-hemodialysis (validating group). Bland–Altman mean bias: 1.67 (95% limits of agreement [LoA]: –9.17-12.52).

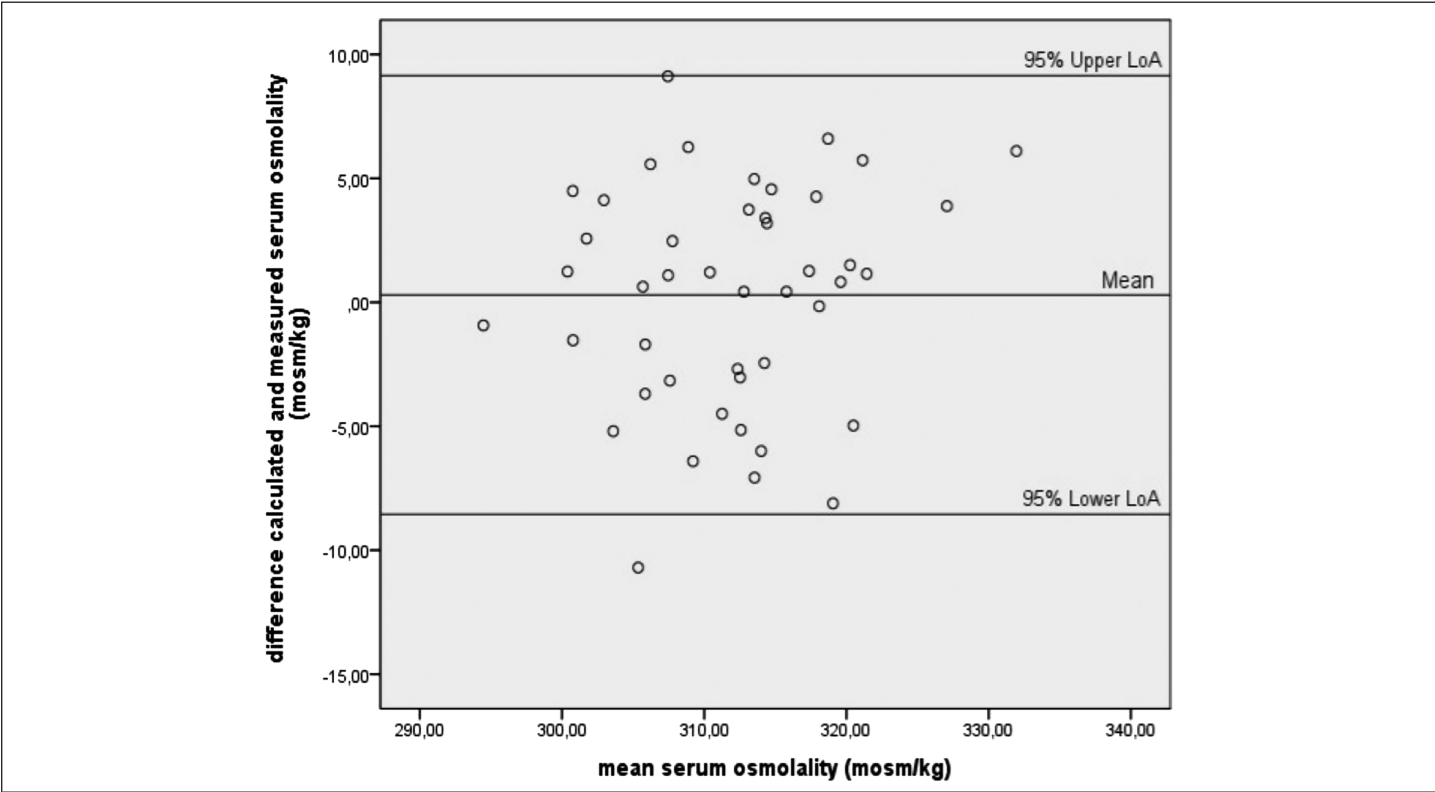


Figure 3. Bland–Altman plots of osmolality measured with osmolality calculated from “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$ ” equation for pre-hemodiaysis (validating group). Bland–Altman mean bias: 0.30 (95% limits of agreement [LoA]: -8.55 – 9.14).

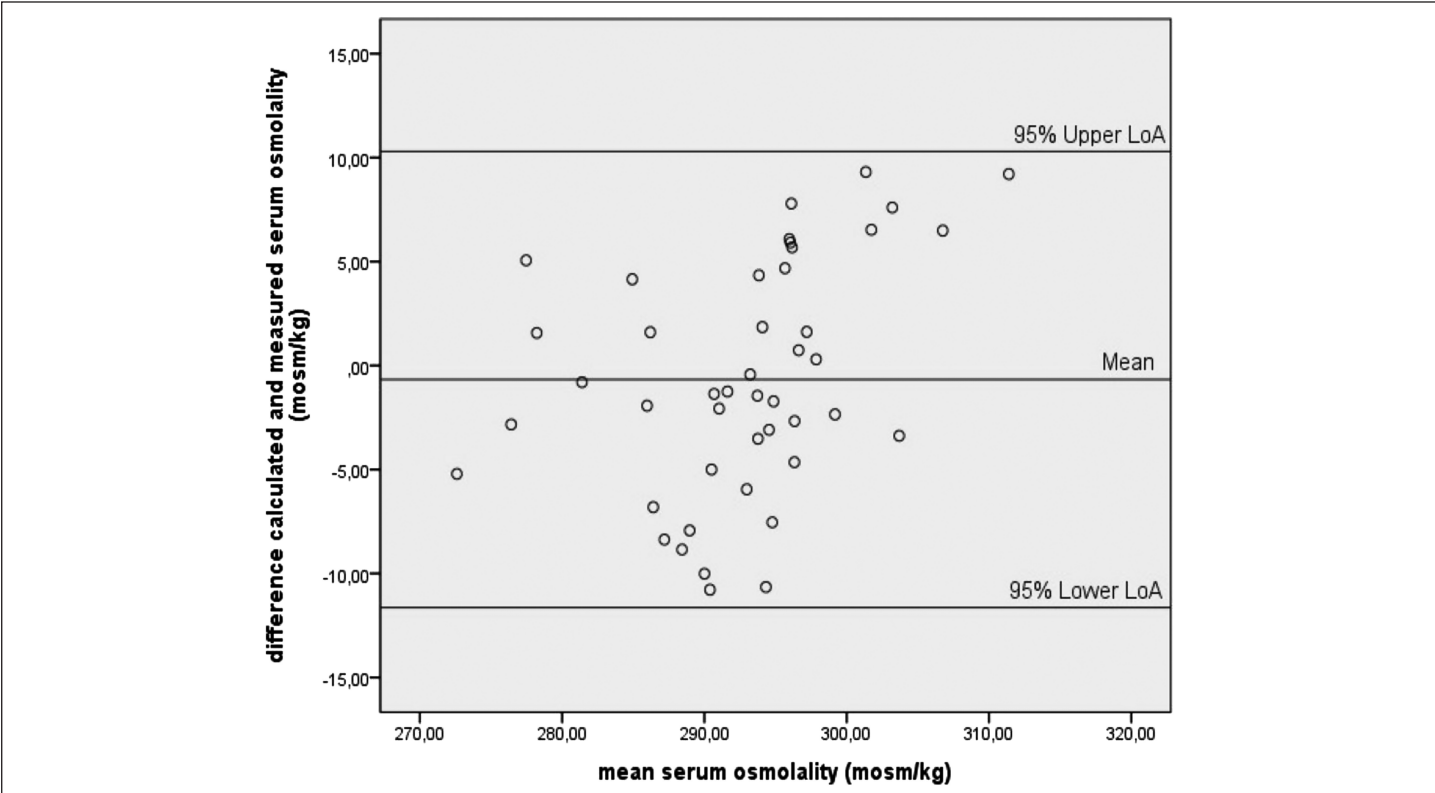


Figure 4. Bland–Altman plots of osmolality measured with osmolality calculated from “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$ ” equation for post-hemodialysis (validating group). Bland–Altman mean bias: -0.67 (95% limits of agreement [LoA]: -11.64 – 10.30).

calculated osmolality values. In the pre-HD samples, the “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$ ” equation and our equation had very strong positive correlation, and these equations had the highest correlation coefficients. In the post-HD samples, only our equation had very strong positive correlation and the highest correlation coefficient (Table 5). In the comparison of the measured and calculated osmolality, the osmolality calculated by our equations and the “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$ ” equation did not differ statistically from the measured osmolality. Taking into account that Fazekas et al⁷ consider a mean osmolal gap of <5 mosm/kg as desirable (preferably <2 mosm/kg), our equations and the equation “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$ ” appear to produce a satisfactory osmolal gap. Considering these results, it is seen that the best results were obtained using our equations and to the “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$ ” equation, and the worst results were obtained with the Dorwart–Chalmers formula. In the selection of the equation with the best results, high correlation strength, low osmolal gap mean and SD, and no significant difference between the measured and calculated osmolality were taken into account. Similar to Calderon et al, we do not recommend using the Dorwart–Chalmers formula. Also, the “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$ ” equation is the same as 1 of the 2 equations that Vareesangthip et al found to perform better.

In addition, the osmolality values calculated by our equation and the “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$ ” equation were compared with the measured osmolality values by Bland–Altman plots. Based on this graphical analysis, all cases fall within the confidence interval ($\text{mean} \pm 1.96$). When we examine the graph of our equation for post-HD, we observe that there is a systematic change in the difference with increasing mean values. Although our equation is one of the equations that gives the best results as a result of statistical evaluations, we think that this systematic change is caused by the tendency to underestimate the true osmolality of the sample as the osmolality value increases.

When we examine Worthley’s equation and the “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$ ” equation, we see that the inclusion of $[Na^+] + [K^+]$ as the variable in the “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$ ” equation, and the inclusion of $[Na^+]$ in Worthley’s equation make a difference. In our study, it is seen that the correlation coefficients in the equations with $[Na^+] + [K^+]$ as the independent variable are slightly higher than the equations with only $[Na^+]$. In a study by Calderon et al, a statistically significant relationship was found between potassium and measured osmolality, even though the correlation coefficient was low. However, they found that only potassium was not a significant predictor in the regression analysis, but potassium became a significant predictor when it was included as a composite variable along with sodium.¹⁷ These results of Calderon et al may explain why some published equations do not include potassium. In addition, in the study of Calderon et al, it was found that the correlation coefficient of the equations involving the $([Na^+] + [K^+])$ variable was slightly higher than that of the equations involving only the sodium variable.¹⁷

These results were similar to the results of our study. Rasoulis et al^{1,9} confirm that addition of potassium to equation increases the correlation, brings the mean osmolal gap closer to zero, and the potassium concentration stabilizes with constant values.

In the training group, while there was a very strong correlation in the pre-HD samples, there was a strong correlation in the post-HD samples. Also, only our equation had very strong correlation in post-HD samples in the validating group. Considering these results, we recommend making calculations with separate equations for before and after hemodialysis.

CONCLUSION

In conclusion, our study contributed to the literature by discussing the effectiveness of the equations in pre-HD and post-HD data of the HD patient group, and by introducing and verifying new equations. Considering the results of our study and that of other studies in the literature, we do not recommend the use of the equation proposed by Dorwart and Chalmers. We suggest using our equations and the equation “ $2 \times ([Na^+] + [K^+]) + \text{Glucose} + \text{BUN}$,” which are evaluated as better performing equations according to the results of our study. Our study sheds light on future research for the use of different formulas before and after the hemodialysis session.

The real usefulness of any regression equation depends on its ability to predict data other than the data on which it was developed. The small sample size and the fact that our equations were not used for other patient populations are the study’s limitations. Further studies in larger data series are needed to evaluate the effectiveness of our equations.

Data Availability Statement

The data generated and analysed in the presented study are available from the corresponding author on request.

Ethics Committee Approval: This study was approved by the Medical Ethics Committee of Kahramanmaraş Sütçü İmam University (Decision number: 2022/19).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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REFERENCES

1. Rasouli M. Basic concepts and practical equations on osmolality: biochemical approach. *Clin Biochem.* 2016;49(12):936-941. [\[CrossRef\]](#)
2. Nelson PH. Osmosis and thermodynamics explained by solute blocking. *Eur Biophys J.* 2017;46(1):59-64. [\[CrossRef\]](#)
3. Berend K, de Vries AP, Gans RO. Physiological approach to assessment of acid-base disturbances. *N Engl J Med.* 2014;371(15):1434-1445. [\[CrossRef\]](#)
4. Arora A. The 'gap' in the 'plasma osmolar gap'. *BMJ Case Rep.* 2013;2013. [\[CrossRef\]](#)
5. Wu AH, Yang HS, Thoren K. Biological variation of the osmolality and the osmolal gap. *Clin Biochem.* 2014;47(15):130-131. [\[CrossRef\]](#)
6. Rondon-Berrios H, Agaba EI, Tzamaloukas AH. Hyponatremia: pathophysiology, classification, manifestations and management. *Int Urol Nephrol.* 2014;46(11):2153-2165. [\[CrossRef\]](#)
7. Fazekas AS, Funk GC, Klobassa DS, et al. Evaluation of 36 formulas for calculating plasma osmolality. *Intensive Care Med.* 2013;39(2):302-308. [\[CrossRef\]](#)
8. Dorwart WV, Chalmers L. Comparison of methods for calculating serum osmolality from chemical concentrations, and the prognostic value of such calculations. *Clin Chem.* 1975;21(2):190-194. [\[CrossRef\]](#)
9. Rasouli M, Kalantari KR. Comparison of methods for calculating serum osmolality: multivariate linear regression analysis. *Clin Chem Lab Med.* 2005;43(6):635-640. [\[CrossRef\]](#)
10. Worthley LI, Guerin M, Pain RW. For calculating osmolality, the simplest formula is the best. *Anaesth Intensive Care.* 1987;15(2):199-202. [\[CrossRef\]](#)
11. Gerich JE, Martin MM, Recant L. Clinical and metabolic characteristics of hyperosmolar nonketotic coma. *Diabetes.* 1971;20(4):228-238. [\[CrossRef\]](#)
12. Mistry K. Dialysis disequilibrium syndrome prevention and management. *Int J Nephrol Renovasc Dis.* 2019;12:69-77. [\[CrossRef\]](#)
13. Martín-Calderón JL, Bustos F, Tuesta-Reina LR, Varona JM, Caballero L, Solano F. Choice of the best equation for plasma osmolality calculation: comparison of fourteen formulae. *Clin Biochem.* 2015;48(7-8):529-533. [\[CrossRef\]](#)
14. Scott MG, LeGrys VA, Hood JH. Electrolytes and blood gases. In: Burtis CA, Ashwood ER, Bruns DE, eds. *Tietz Textbook of Clinical Chemistry and Molecular Diagnosis.* 5th ed. Philadelphia: WB Saunders; 2012:807-849.
15. Vareesangthip K, Davenport A. Comparison of measuring serum osmolality and equations estimating osmolality in peritoneal dialysis patients. *Perit Dial Int.* 2020;40(5):509-512. [\[CrossRef\]](#)
16. Kar E, Kocatürk E, Küskü Kiraz Z, Demiryürek B, Alataş İÖ. Comparison of measured and calculated osmolality levels. *Clin Exp Nephrol.* 2020;24(5):444-449. [\[CrossRef\]](#)
17. Martín-Calderón JL, Tuesta-Reina LR. Derivation and validation of a new formula for plasma osmolality estimation. *Clin Biochem.* 2022;105-106:44-48. [\[CrossRef\]](#)