A comparison of laboratory values in pediatric hemodialysis patients: does day of the week matter?

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Abstract
Background. The National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF-K/DOQI) guidelines recommend the delivered dose of hemodialysis (HD) be measured no less than monthly by checking \( Kt/V \) (\( K \) is effective urea clearance, t is minute and V is urea distribution). To date, no studies have explored whether the day of the week for checking maintenance HD laboratory studies impacts dialysis dosing.

Methods. Data were collected at two HD facilities on 19 patients, ages \( \leq 21 \) years receiving maintenance HD thrice weekly over a consecutive 6-month period. Data obtained from the Monday and Wednesday of each full third week of the month included dialysis vintage, ultrafiltration volume, serum electrolytes, hemoglobin and clearances.

Result. \( Kt/V \) and K+ were significantly different between Monday and Wednesday (\( P = 0.013 \) and \( P = 0.047 \), respectively).

Conclusions. Due to variability in values based on the day of laboratory evaluations, the dialysis provider must consider the impact of this on the quality of patient care when prescribing dialysis. Research on a larger scale needs to be conducted to allow for better decision-making capabilities in the chronic HD population.

Keywords: adequacy; electrolytes; hemodialysis; \( Kt/V \)

Introduction
The concept of hemodialysis (HD) adequacy was established nearly 35 years ago when nephrologists began to quantify the HD dose based on the clearance of toxins through modifying dialyzer type, pump flow rates and treatment time [1]. In 1985, Gotch and Sargent [2] reported a significant difference in mortality based on dialysis dose as assessed by \( Kt/V \). Since then, additional variables have been identified as contributors to mortality in patients receiving HD. Some of these factors include anemia control, nutritional status, electrolyte management and volume status [3].

The National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF-K/DOQI) guidelines recommend the delivered dose of HD be measured no less than monthly by checking \( Kt/V \) (\( K \) is effective urea clearance, t is in minutes of dialysis and V is urea distribution) or urea kinetic modeling (UKM) [3]. Similarly, laboratories are usually obtained monthly to assess anemia control and adequate levels of serum electrolytes. The guidelines...
fail to delineate the best day of the week to obtain lab work. Generally, dialysis is performed thrice weekly (e.g., Monday–Wednesday–Friday), with an extended interdialytic time interval of 3 days between treatments each week. Theoretically, the day of the week for checking \( Kt/V \) should be irrelevant as the patient should be in a steady state. However, no evidence is available to validate this premise in adults or children receiving HD. This is particularly noteworthy in pediatric patients who have metabolic variability and growth velocity as opposed to their adult counterparts. Furthermore, it is not known whether other parameters evaluated during dialysis vary depending on the day of monitoring. Specifically, if interdialytic electrolyte variances are present based on laboratory values, perhaps children need to be monitored differently than adults.

Two additional considerations include serum potassium and hemoglobin levels. Serum potassium levels are critical in managing dialysis patients as of the risk of sudden cardiac death associated with arrhythmias. Similarly, hemodilution may play a role in the management of anemia. As such, we pose the question ‘Does the day of the week labs are drawn matter in pediatric patients undergoing maintenance HD’?

Numerous outcome studies have demonstrated a correlation between delivered dose of HD and patient mortality and morbidity [4]. However, to our knowledge, this is the first report that examines whether clearances [as measured by \( Kt/V \) and urea reduction rates (URR)], anemia control [as measured by pre-dialysis hemoglobin (Hb)] and electrolytes [serum potassium (K+) levels] vary depending on the day of the week labs are obtained.

**Materials and methods**

After obtaining Institutional Review Board approval at each center, pediatric patients undergoing maintenance HD over a consecutive 6-month period were prospectively monitored at Akron Children’s Hospital and Cleveland Clinic Children’s Hospital. All patients received HD every Monday, Wednesday and Friday. Dry weight was determined and achieved using the CritLine®/C210. Specifically, ultrafiltration was adjusted based on if the child demonstrated vascular fluid refill on the monitor. No patients received extra dialysis during the study period: time was not extended nor were additional treatments provided. Each patient received nutritional counseling monthly. Each patient’s iron studies were obtained monthly and iron supplementation was provided in the form of intravenous iron sucrose to maintain an iron saturation >20%. Recombinant human erythropoietin was prescribed in accordance with NKF-K/DOQI guidelines to maintain a hemoglobin of 11–13 g/dL. The patient’s baseline dialysis prescription was determined by his/her pediatric nephrologist as per usual care. All children were under the care of one of two pediatric nephrologists for the duration of the study.

During the study period, each patient underwent laboratory collections at two points monthly: the Monday and Wednesday of the third full week. Based on the assumption that the time interval between Monday and Wednesday and Wednesday and Friday is constant, each patient’s data were collected on Monday and Wednesday; and Friday’s labs were not obtained. The following data were obtained: age, race, gender, dialysis vintage, underlying renal disorder, interdialytic weight gain, ultrafiltration volume, presence or absence of urine production, K+ and Hb.

\( Kt/V \) was calculated using the Daugirdas II method based on a single-pool kinetic model: 
\[
spKt/V = -La \left( R - 0.0088t \right) + 4.35 R^{0.7} UF/W \]  
\( R \) is the rate of change in K+ and Hb. Pre-dialysis labs were collected from the dialysis access immediately prior to the start of dialysis, before there bloodlines are connected to the system. For patients with catheters, 3 mL of blood was drawn and discarded, the sample to be analyzed was drawn and the catheter was flushed with normal saline prior to connection to HD lines. For patients with fistulas, blood was directly collected from fistula and then flushed with saline immediately prior to line connection. Post-dialysis labs were collected 3 min after the conclusion of the treatment from the venous port.

Data on the six measured variables were analyzed using a repeated measures analysis in SPSS® version 11 for interdialytic weight gain, Hb, K+, \( Kt/V \) and URR. Comparisons were based on the difference in the measure for the first dialysis session versus the second dialysis session by subject. Because the number of observations (months) was different between subjects, the mean for each patient was used in the comparisons. The primary comparison of interest was the effect of timing (first versus second treatment of the week) on the measured parameters. Covariates were introduced into the model to look for differences due to gender, age and ability to make urine. Data were censored if each subject did not have complete data.

**Results**

Demographics of the study population are shown in Table 1. The mean age of the study population was 14.1 ± 4.1 years of age and included 10 males and 9 females. Complete data for all 6 months were available in 10 patients, with 3 patients having 5 months of complete data. The remainder of the patients had complete data: four with 4 months and one each with 2 and 3 months of data. Of note, 13 subjects were anuric, while 6 retained some residual renal function. Of note, all patients received thrice weekly treatments (Monday, Wednesday and Friday) in this population. Each patient’s dialysis prescription was not changed for the duration of the study. Specifically, each patient utilized the same brand and size dialyzer for all treatments; prescribed blood flow rates remained constant (actual blood flow rates varied 30 mL/min maximum during treatments) and treatment times were constant. When evaluating for differences in dialysis clearance, \( Kt/V \) and URR were evaluated (Table 2). There was a significant difference in \( Kt/V \) between Monday and Wednesday of each month (\( P = 0.013 \)), while there was no difference between months, Monday to Monday and Wednesday to Wednesday (\( P = 0.5 \)). No significant interactions were observed between treatment day and sex (\( P = 0.986 \)), age (\( P = 0.095 \)) or residual renal function (\( P = 0.431 \)). The effect of time on URR was not statistically different in those who did and did not produce urine (\( P = 0.899 \)).

A significant difference in URR between Monday and Wednesday of each month (\( P = 0.08 \)) was not reached. Adequate anemia control was defined by measuring serum Hb levels. The effect of time on Hb is shown in Table 2. There was no significant difference in Hb between Monday and Wednesday of each month (\( P = 0.198 \)).

Serum K+ levels were used as a measure of electrolyte balance. There was a significant difference in K+ between Monday and Wednesday of each month (\( P = 0.047 \)), while there was no difference between months (\( P = 0.721 \) (Table 2).

A comparison of interdialytic weight gain showed significant differences between Monday and Wednesday of each month (\( P = 0.003 \)), but no difference between months (\( P = 0.721 \) (Table 2).

**Discussion**

This study is the first to evaluate the impact of laboratory measurement techniques, specifically daily lab variability
in children receiving HD. Specifically, we found that $Kt/V$ and K+ were significantly different between Monday and Wednesday each month in all patients. Interdialytic weight gains were significantly different between each patient and treatments; however, this factor was adjusted for when calculating clearances. Hence, it is critical to have a consensus of when to obtain laboratories in chronic HD patients to optimize dialysis delivery.

Although no large-scale studies are in existence, single-center studies support the validity of $Kt/V$ as adequate for pediatric HD monitoring [6, 7]. Some would argue that UKM remains the gold standard of measuring dialysis dosing, but many now agree that $Kt/V$ is the preferred method because it accurately reflects urea removal and can be used to modify dialysis prescriptions for those with residual kidney function [5].

Gotch and Sargent performed a mechanistic analysis of the National Cooperative Dialysis Study (NCDS) and found a non-linear relationship between dialysis dose and outcome but did not examine whether the day of laboratory collection impacted the calculated dose [2, 8]. More specifically, they found that patients receiving a $Kt/V < 1.0$ had a 4-fold increase in hospitalization/death rates when compared to those receiving a $Kt/V > 1.0$. In addition, a more recent study revealed that pediatric patients achieving a $Kt/V$ of 2 with 150% of protein allowances were able to demonstrate catch-up growth without growth hormone supplementation, implying that higher values of $Kt/V$ are needed in children compared to the adult standard of 1.2 [9]. This has led to many discussions of optimal dialysis dosing [2, 10, 11]. To date, a consensus of optimal dosing in children receiving HD has not been established, the NKF-K/DOQI guidelines from 2006 have gone on to recommend that monthly solute clearance and nutrition status measurements are essential to assess dialysis dosing, including dialyzer size, blood flow and treatment time [3]. Prior to establishing adequate dialysis dosing guidelines, one must first establish what variability exists in measurement techniques.

The value of urea kinetic models was validated by Gotch and Sargent’s mechanistic analysis of the NCDS where urea clearance as assessed by the model correlated with patient outcome [1]. The fractional urea mass removed through HD is affected by the dialyzer urea clearance coefficient ($K$), pre- and post-dialysis BUN (milligrams per deciliter) values, duration of treatment (hour), total body water (milliliter), the difference between pre- and post-dialysis weights as a reflection of ultrafiltration volume (kilogram). The urea kinetic models that are the mainstay of HD dosing rely heavily on $Kt/V$, where $K$ is the urea

### Table 1. Demographic data

<table>
<thead>
<tr>
<th>Patient</th>
<th>Disease</th>
<th>Weight (kg)</th>
<th>Age</th>
<th>Residual renal function</th>
<th>Sex</th>
<th>Race</th>
<th>Time</th>
<th>Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Anti-GBM</td>
<td>49</td>
<td>15</td>
<td>Yes</td>
<td>Male</td>
<td>Race</td>
<td>210</td>
<td>300</td>
</tr>
<tr>
<td>2</td>
<td>Dysplasia</td>
<td>37</td>
<td>19</td>
<td>Yes</td>
<td>Male</td>
<td>Black</td>
<td>210</td>
<td>300</td>
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<tr>
<td>3</td>
<td>Juvenile nephronophthisis</td>
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<td>16</td>
<td>No</td>
<td>Female</td>
<td>Caucasian</td>
<td>210</td>
<td>250</td>
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<tr>
<td>4</td>
<td>Dysplasia</td>
<td>52</td>
<td>19</td>
<td>Yes</td>
<td>Male</td>
<td>Other</td>
<td>210</td>
<td>310</td>
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<tr>
<td>5</td>
<td>Dysplasia</td>
<td>51</td>
<td>16</td>
<td>Yes</td>
<td>Female</td>
<td>Caucasian</td>
<td>210</td>
<td>250</td>
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<tr>
<td>6</td>
<td>Dysplasia</td>
<td>82</td>
<td>19</td>
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<td>Female</td>
<td>Other</td>
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<td>350</td>
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<tr>
<td>7</td>
<td>Dysplasia</td>
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<td>Caucasian</td>
<td>150</td>
<td>200</td>
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<tr>
<td>8</td>
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<td>18</td>
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<td>Male</td>
<td>Black</td>
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<td>350</td>
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<tr>
<td>9</td>
<td>FSGS</td>
<td>69</td>
<td>18</td>
<td>Yes</td>
<td>Male</td>
<td>Black</td>
<td>210</td>
<td>270</td>
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<tr>
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<td>Dysplasia</td>
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<td>Caucasian</td>
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<td>300</td>
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<tr>
<td>11</td>
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</tr>
<tr>
<td>12</td>
<td>Atypical HUS</td>
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<td>No</td>
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<td>250</td>
</tr>
<tr>
<td>13</td>
<td>Dysplasia</td>
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<td>Yes</td>
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<td>Caucasian</td>
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<td>300</td>
</tr>
<tr>
<td>14</td>
<td>Dysplasia</td>
<td>83</td>
<td>19</td>
<td>Yes</td>
<td>Female</td>
<td>Caucasian</td>
<td>210</td>
<td>380</td>
</tr>
<tr>
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<td>Dysplasia</td>
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<td>12</td>
<td>No</td>
<td>Male</td>
<td>Other</td>
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<td>400</td>
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<tr>
<td>16</td>
<td>VATER/dysplasia</td>
<td>15</td>
<td>7</td>
<td>No</td>
<td>Female</td>
<td>Caucasian</td>
<td>180</td>
<td>150</td>
</tr>
<tr>
<td>17</td>
<td>FSGS</td>
<td>70</td>
<td>20</td>
<td>Yes</td>
<td>Female</td>
<td>Caucasian</td>
<td>240</td>
<td>300</td>
</tr>
<tr>
<td>18</td>
<td>Fibrillary GN</td>
<td>64</td>
<td>15</td>
<td>No</td>
<td>Female</td>
<td>Caucasian</td>
<td>210</td>
<td>350</td>
</tr>
<tr>
<td>19</td>
<td>FSGS</td>
<td>72</td>
<td>20</td>
<td>No</td>
<td>Female</td>
<td>Caucasian</td>
<td>250</td>
<td>400</td>
</tr>
</tbody>
</table>

aAnti-GBM, antiglomerular basement membrane disease; FSGS, focal segmental glomerulosclerosis; HUS, hemolytic uremic syndrome; GN, glomerulonephritis.

### Table 2. Comparison between groups

<table>
<thead>
<tr>
<th></th>
<th>URR Monday</th>
<th>URR Wednesday</th>
<th>$Kt/V$ Monday</th>
<th>$Kt/V$ Wednesday</th>
<th>Hb Monday</th>
<th>Hb Wednesday</th>
<th>K+ Monday</th>
<th>K+ Wednesday</th>
<th>Weight gain Monday</th>
<th>Weight gain Wednesday</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>0.76</td>
<td>0.77</td>
<td>1.60</td>
<td>1.70</td>
<td>11.48</td>
<td>11.05</td>
<td>4.50</td>
<td>4.30</td>
<td>2.00</td>
<td>1.46</td>
</tr>
<tr>
<td>SD</td>
<td>0.06</td>
<td>0.06</td>
<td>0.28</td>
<td>0.31</td>
<td>1.29</td>
<td>1.40</td>
<td>0.58</td>
<td>0.65</td>
<td>1.60</td>
<td>1.24</td>
</tr>
<tr>
<td>P-value</td>
<td>0.09</td>
<td>0.01</td>
<td>0.20</td>
<td>0.05</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

$(n = 19)$
clearance coefficient, $t$ is time and $V$ is the volume of distribution. Of the variables of $Kt/V$, the volume of distribution is the least studied, particularly in the pediatric population. Despite attempts to validate dialysis dosing, no large-scale studies exist to validate target $Kt/V$ values in children. The target $Kt/V$ recommended in adults is 1.3, although a higher target range of 1.5 is generally recommended for women and small children [12].

The URR has been shown to be successful predictors of mortality in end-stage renal disease, but it is known to have limitations. Urea reduction ratios do not account for the ultrafiltration contribution to the final delivered HD dose, making it less accurate than the urea kinetic model of $Kt/V$. Another shortcoming of the URR is the inability to assess a patient’s nutritional status [12]. Although the true volume of distribution in children remains debatable, the Daugirdas logarithmic formula for UKM is generally accepted. Decisions regarding dialysis dosing are made based on laboratory values and as such, it is critical to know that the laboratory values one uses are valid.

We would argue that in children, the day of measurement is a critical factor in determining dialysis dosing. It is safe to say that children require higher nutrient allotments than adults to allow for adequate linear growth and as a consequence, children may require more frequent modification of dialysis prescription. This leads to the question, if laboratory values are obtained at the worst possible point (i.e. on a Monday pre-dialysis), should dialysis prescriptions be altered to achieve optimum growth and nutrition? Alternatively, if decisions are made based on midweek values, deficiencies may go unnoticed. Similarly, elevations in serum $K^+$ levels can lead to arrhythmias. If dialyzate concentrations of electrolytes are not adjusted, is the patient at risk for arrhythmia during the prolonged interdialytic interval?

Given that most HD patients undergo thrice weekly treatments, there will be an extended interdialytic time interval of 3 days during the week. This can be especially important in the management of the pediatric HD patient because children are expected to grow and gain weight. The variability in $Kt/V$ may be a reflection of how difficult it is to assess the volume of distribution in a growing child and measurement of ultrafiltration may not be the best standard of determining volume status when calculating $Kt/V$. Perhaps, the metabolic variability of a pre-pubertal patient does not allow for the patient to reach a steady state as seen in adults and post-pubertal populations.

Based on the results, pediatric nephrologists need to consider interdialytic variability in laboratory values, ultrafiltration and adequacy when determining individual prescriptions. This is particularly true in the pediatric HD population, in whom the goals of adequate nutrition, growth and development are heavily dependent on appropriate metabolic homeostasis. In some instances, prescriptions may need to be varied more frequently to meet the needs of the pediatric HD patients.

There are certain limitations to this study including the small number of participants. Also, the residual renal function was ascertained; however, urine volume was not measured in this study. However, when the residual urine output was factored as a variable, no statistically significant differences were found. If this study was to be conducted on a larger scale, urine quantification should be considered.

In conclusion, due to variability in values based on the day of lab work, the dialysis provider must consider the impact of this on the quality of patient care when prescribing dialysis. Hence, research on a larger scale needs to be conducted to allow for better decision-making capabilities in the chronic HD population.

Conflict of interest statement. None declared.

References

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