A new accurate method for predicting lithium clearance and daily dosage requirements in adult psychiatric patients


Objective: The present study aimed to derive new equations for estimating lithium clearance and daily dosage requirements needed to achieve an intended lithium serum level for adult psychiatric inpatients and outpatients.

Methods: Data were retrospectively collected from 60 adult psychiatric patients (34 males and 26 females, aged between 18–80 years) in both inpatient and outpatient settings. All variables that might affect lithium clearance and/or lithium serum concentration were included and analyzed by stepwise multiple linear regression to produce equations describing lithium clearance and daily dosage requirements for these patients. The validation of the developed equations was performed by application to another 60 psychiatric subjects in both the inpatient and outpatient settings. The bias and accuracy of the new methods were also compared to those set forth by the empirical method and the a priori methods developed by Zetin, Pepin, Jermain and Terao and colleagues.

Results: The following prediction equations for lithium clearance (CL\textsubscript{Li}) were obtained: CL\textsubscript{Li} (inpatients) = 0.932 + 0.185CL\textsubscript{Cr} and CL\textsubscript{Li} (outpatients) = 1.021 + 0.141CL\textsubscript{Cr}. The equations derived for daily dosage requirements were: daily dose (inpatients, mg) = 350.15 + 289.92 (desired lithium level, mmol/L) + 0.84 (weight, kg) + 1.76 (age, years) + 34.43 [tricyclic antidepressant (TCA), yes = 1, no = 0] + 62.1(C\textsubscript{CR}, L/h) + 13.1 [blood urea nitrogen (BUN), mmol/L] + 40.9 (sex, male = 1, female = 0) and daily dose (outpatients, mg) = 784.92 + 530.22 (desired lithium level, mmol/L) + 8.61 (weight, kg) – 12.09 (age, years) – 11.14 (TCA, yes = 1, no = 0) – 7.63 (CL\textsubscript{Cr}, L/h) – 42.62 (BUN, mmol/L) – 23.43 (sex, male = 1, female = 0). In the present method, the prediction error for clearance was 10.31% and 6.62% for inpatients and outpatients, respectively, and the prediction error for daily dosage requirements was 3.96% and 2.95% for inpatients and outpatients, respectively.

Conclusions: Compared to previously reported methods, the present method proved to be accurate and can be safely used for the prediction of lithium clearance and daily dosage requirements in psychiatric inpatients and outpatients.

Key words: clearance – dosage requirements – lithium – prediction

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Lithium has been used in the treatment of mania and in the prophylaxis of bipolar disorder (BD) and recurrent depression (1, 2). Despite a growing number of proposed alternatives, including several
The toxicity of lithium is closely related to serum lithium levels, and can occur at doses close to its therapeutic level; therefore, regular clinical and serum level monitoring of lithium is a requirement for good clinical practice (9, 10). In addition, conditions that alter electrolyte balance may affect lithium levels in patients (11). Lithium removal from the body is achieved almost exclusively via the renal route. Concomitant medications with lithium may also contribute to the clinical manifestations of lithium toxicity since its clearance varies proportionally with glomerular filtration rate (GFR) and is usually 20–30% of GFR (12). As a result, any medication that increases GFR or affects electrolyte exchange in the nephron may influence the pharmacokinetic disposition of lithium. It was also found that lithium clearance is usually reduced in elderly subjects (13). Concomitant use of diuretics, angiotensin-converting enzyme inhibitors, calcium channel antagonists, or non-steroid anti-inflammatory drugs have been associated with lithium toxicity through pharmacokinetic interactions (14–17). Viguera et al. (18) analyzed 17 studies on the use of lithium in BD to investigate sex differences in response to lithium. They concluded that women may clear lithium less efficiently than men, or more probably, they vary more in lithium clearance.

Although a number of studies have examined strategies for determining optimal lithium dosages in the treatment of patients with BD based on single-dose plasma concentrations (19–33), none of these studies has exclusively gained recognition as the sole method for lithium monitoring in the routine clinical practice. The purpose of these methods is to eventually maintain steady-state therapeutic levels of 0.6–1.2 mmol/L. The most evaluated methods, both retrospectively and prospectively, were the empirical method (6), and the methods of Pepin et al. (21) and Zetin et al. (24–26). Browne et al. (34) retrospectively compared five of these methods and found significant differences in their accuracy for estimating lithium maintenance dosing requirements in inpatients. When the accuracy of the method of Pepin et al. (21) was tested in 13 healthy volunteers, it was found to be a safe but conservative method for the prediction of the appropriate daily dose of lithium (35). Markoff and King (36) compared the method of Zetin et al. (24–26) in 12 patients versus the empirical dosing method in 21 patients to determine which method would efficiently produce a target concentration predetermined by the clinician. They concluded that 83% of patients had reached the desired lithium blood level with the method of Zetin et al. (24–26), whereas only 38% had done so with the empirical method. Other studies (37–39) found no significant differences between methods or no improvement was noted compared to the empirical method.

Most of the reported predictive a priori methods had never been evaluated in both psychiatric inpatients and outpatients at the same time. Our observations indicated a probable difference in lithium clearance and consequently a difference in the predictability of lithium daily dosage requirements between inpatients and outpatients.

The present study aimed to derive new equations for estimating lithium clearance (CL_{Li}) in inpatients and outpatients. Sex differences in lithium clearance were considered in this derivation. The bias and accuracy of these equations were compared to those set forth by Jermain et al. (31), Pepin et al. (21) and the empirical methods. In addition, new equations for determining lithium daily dosage requirements in adult psychiatric inpatients and outpatients were derived. The bias and accuracy of the derived equations were also compared to the methods of Pepin et al. (21), Zetin et al. (25) and Terao et al. (32).

**Methods**

**Patients**

Data were collected from King Khalid University Hospital (KKUH) medical records at Riyadh, Saudi Arabia. Patients were included in the study if they were adults aged 18–80 years receiving multiple daily doses of lithium carbonate for at least seven consecutive days prior to the commencement of the study. The patients were included if they had no evidence of cardiac, respiratory, hepatic or renal abnormalities. Patients who were on a sodium-restricted diet or taking any other medication that would affect lithium levels were excluded from the study. The period between lithium serum and body weight and renal function measurements did not exceed one month. Serum lithium samples were drawn 12–14 h after the last dose. The study protocol was approved by KKUH,
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College of Medicine Research Center, King Saud University, Riyadh, Saudi Arabia.

A total of 60 patients (34 males and 26 females) met the study criteria. Of these, 53 patients were Saudi nationals (28 males and 25 females). The mean ± SD age was 38.83 ± 9.87 years (range 21–77 years) and the mean ± SD body weight was 71.39 ± 17.04 kg (range 33–120 kg). Only 7 (11.7%) patients were smokers. Fifty-three (88.3%) patients were diagnosed with bipolar affective disorder, 3 (5%) with schizoaffective disorder and the rest were affected by other psychiatric conditions. Only 3 (5%) patients were taking tricyclic antidepressant agents. Twenty-eight (46.7%) patients had a family history of psychiatric illness. Lithium serum levels were measured both as inpatients and outpatients for 47 (78.3%) patients, as outpatients only for 9 (15%), and as inpatients only for the rest. Lithium dose in these patients averaged 1016.7 ± 230.1 mg/day (range 375–1800 mg/day) and lithium serum level was 0.61 ± 0.13 mmol/L (range 0.3–1.0 mmol/L) for the outpatient setting. On the other hand, lithium dose was 1016.2 ± 230.1 mg/day (range 375–1800 mg/day) and lithium serum level was 0.58 ± 0.18 mmol/L (range 0.06–1.21 mmol/L) for these patients in the inpatient setting. Blood urea nitrogen (BUN) averaged 11.36 ± 3.28 mg/dL (range 6.02–22.13 mg/dL) and 10.85 ± 3.13 mg/dL (range 4.76–19.05 mg/dL) for inpatients and outpatients, respectively. The mean serum creatinine level was 0.92 ± 0.17 mg/dL (range 0.63–1.37 mg/dL) and 0.92 ± 0.20 mg/dL (range 0.49–1.86 mg/dL) for inpatients and outpatients, respectively.

Data analysis

Data were collected from patient medical records at KKUH, Riyadh, Saudi Arabia, using a specially designed collection form. The total body clearance (CL) of lithium (L/h) in these patients was estimated from the following relationship:

\[
CL_{Li} = \frac{F \times D}{24C_{ss}} \left( \frac{8.12}{300} \right)
\]

where \( F \) is the oral bioavailability (usually 100%), \( C_{ss} \) is the average steady-state serum concentration of lithium (mmol/L) and \( D \) is the daily dose (mg/day) of lithium carbonate. The creatinine clearance was calculated from Cockcroft and Gault’s equation (40).

Data collected from the 60 patients retrospectively (both in the inpatient and the outpatient settings) were applied to published \emph{a priori} methods either to determine lithium clearance or lithium daily dosage regimen. The methods applied for clearance determination are the empirical method (7), and the methods of Pepin et al. (21) and Jermain et al. (31). The methods applied for daily dosage requirements determinations are those of Pepin et al. (21), Zetin et al. (25) and Terao et al. (32). The calculated daily dose requirement necessary to produce the lithium levels observed in these patients was compared to the daily dose actually used by these patients during the course of the treatment.

The empirical method assumes that lithium clearance (CL\(_{Li}\)) is one-fourth of the creatinine clearance (CL\(_{Cr}\)) and each 300 mg of lithium increases lithium level by 0.3 mmol/L. On the other hand, the equation used by Pepin et al. (21) was \( CL_{Li} = 0.235 \times CL_{Cr} \). The method of Jermain et al. (31) utilized a one-compartment open model equation and population pharmacokinetic modeling to produce the following estimate of CL\(_{Li}\):

\[
CL_{Li} = 0.0093 \times LBW + 0.0885CL_{Cr}
\]

where LBW is the lean body weight and was calculated from the following relationship:

\[
LBW_{Males} = 1.10W - 128 \left( \frac{W}{H} \right)^{2}
\]

\[
LBW_{Females} = 1.07W - 148 \left( \frac{W}{H} \right)^{2}
\]

where \( W \) is the total body weight (kg) and \( H \) is the height (cm). The ideal body weight (IBW) is calculated as: IBW\(_{Males} = 50 + 2.3(H) \) and IBW\(_{Females} = 45.5 + 2.3(H) \) where \( H \) is the height in inches.

The daily dosage requirements and serum concentrations were calculated also by the following formula used by Pepin et al. (21):

\[
D = \left( \frac{300}{8.12} \right) \left( C_{ss}^{min} \times \frac{V_{d}}{F \times e^{-k_{d}t}} \right) \left( 1 - e^{-k_{d}t} \right)
\]

where \( D \) is daily dosage of lithium (mg), \( C_{ss}^{min} \) is the desired steady-state trough concentration (mmol/L), \( V_{d} \) is the apparent volume of distribution (L) (calculated as CL\(_{Li}/k_{d} \)), \( F \) is the oral bioavailability of lithium (1.0), \( \tau \) is dosing interval (24 h), \( k_{d} \) is elimination rate constant (h\(^{-1}\)) [calculated as ln(2)/lithium \( t_{1/2} \)].

The method of Terao et al. (32) was given by the following formula:

\[
\text{Daily lithium dose (mg)} = 100.5 + 752.7(C_{Li}) - 3.6(\text{age}) + 7.2(W) - 13.7(\text{BUN})
\]
where $C_L$ is the expected lithium concentration in mg/L, age is in years, $W$ is weight in kg and BUN is the blood urea nitrogen in mg/dL.

### Validation of Equations

For validation of the equations, the predicted clearance and daily dosage requirements were correlated with the observed clearance and dosage in another 60 subjects who received different doses of lithium.

### Statistical Analysis

The differences between various methods were evaluated by one-way analysis of variance (ANOVA) at the 0.05 level of significance. The predictive performance of all methods for clearance and daily dosage requirements was determined by calculating the percent error (41) as:

$$\% \text{ Error} = 100 \left( \frac{\hat{Y} - Y}{Y} \right)$$

where $\hat{Y}$ is the predicted value and $Y$ is the observed value. The bias of prediction was determined by the mean prediction error (MPE):

$$\text{MPE} = \frac{\sum_{i=1}^{n} (\hat{Y}_i - Y_i)}{n}$$

and precision of prediction was measured by mean absolute error (MAE) and root mean square error (RMSE):

$$\text{MAE} = \frac{\sum_{i=1}^{n} |\hat{Y}_i - Y_i|}{n}$$

$$\text{RMSE} = \left( \frac{\sum_{i=1}^{n} (\hat{Y}_i - Y_i)^2}{n} \right)^{1/2}$$

The statistical significance of bias and precision was tested using ANOVA. The data were analyzed using the Statistical Package for Social Sciences (SPSS), version 13.0 for Windows (SPSS Inc., Chicago, IL, USA).

### Results and Discussion

The data from 60 psychiatric patients were utilized to develop new equations for the prediction of lithium clearance and daily dosage requirements by performing stepwise linear regression. Lithium clearance was correlated with creatinine clearance. In addition to sex-dependent variability in lithium clearance, we have reason to believe that lithium clearance may also vary between inpatients and outpatients. Many factors may contribute to this difference, including non-compliance, activity, non-restricted diet and disease severity. Poor compliance may prove to be a detrimental factor in causing lithium clearance changes. The fluctuation in serum levels is quite common, particularly with erratic treatment compliance (4, 42, 43). Furthermore, Hopkins and Gelenberg (11) suggested that lithium clearance might increase during manic depressive episodes and consequently lithium levels would decrease. Also, the changes in salt intake, diet and caffeine intake may alter serum lithium levels. Caffeine can increase the excretion of lithium, thereby decreasing lithium concentrations. Furthermore, Schaub et al. (44) found that many of the psychiatric patients, especially older patients who had been receiving lithium for years, did not have sufficient knowledge about lithium therapy. Therefore, disregarding these influences on lithium clearance might produce a biased estimate of lithium daily dosage requirements.

The correlation between creatinine clearance (L/h, independent variable) versus lithium clearance (L/h, dependent variable) was evaluated by multiple linear regression. The regression equations which gave the best correlation coefficient ($r$) were the following:

- For inpatients:
  $$CL_{Li}(\text{males}) = 1.415 + 0.124CL_{Cr}$$
  $$CL_{Li}(\text{females}) = 0.534 + 0.228CL_{Cr}$$

- For outpatients:
  $$CL_{Li}(\text{males}) = 1.055 + 0.137CL_{Cr}$$
  $$CL_{Li}(\text{females}) = 0.979 + 0.148CL_{Cr}$$

Since the calculation of creatinine clearance by Cockcroft and Gault’s (40) method accounts for gender differences, these equations were further simplified to produce a lithium clearance value combined for both males and females as follows:

$$CL_{Li}(\text{inpatients}) = 0.932 + 0.185CL_{Cr}$$
$$CL_{Li}(\text{outpatients}) = 1.021 + 0.141CL_{Cr}$$

Figure 1 shows the relationship between lithium clearance and creatinine clearance in 60 adult psychiatric inpatients.

The variables chosen by the stepwise linear regression analysis for the prediction of lithium daily dosage requirements (mg) were lithium
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concentration (mmol/L), age (years), weight (kg), tricyclic antidepressants (TCA) (yes = 1, no = 0), CLCr (L/h), BUN (mmol/L) and sex (male = 1, female = 0). The determination coefficients ($r^2$) with this combination of variables were 0.59 ($p = 0.00458$, ANOVA) and 0.746 ($p = 0.00017$, ANOVA) for inpatients and outpatients, respectively. The resulting regression equations for the prediction of daily dosage requirements of lithium carbonate (mg) in these patients were as follows:

- **For inpatients:**
  \[
  \text{Daily dose} = 350.15 + 289.92(\text{desired lithium level}) + 0.84(\text{weight}) - 1.76(\text{age}) + 34.43(\text{TCA}) + 62.1(\text{CLCr}) + 13.1(\text{BUN}) + 40.9(\text{sex})
  \]

- **For outpatients:**
  \[
  \text{Daily dose} = 784.92 + 530.22(\text{desired lithium level}) + 8.61(\text{weight}) - 12.09(\text{age}) - 11.14(\text{TCA}) - 7.63(\text{CLCr}) - 42.62(\text{BUN}) - 23.43(\text{sex})
  \]

If the patients are not concomitantly administering tricyclic antidepressants, a simplified version of both equations could be used for the preliminary estimation of daily dosage requirements of lithium for both sexes:

\[
\text{Daily dose} = 382.54 + 348.29(\text{desired lithium level}) + 67.19(\text{CLCr})
\]

Comparison to other methods

When the developed equations were applied to another set of data for 60 other psychiatric patients, the predicted total body clearance of lithium was found to be $2.09 \pm 0.045$ and $1.88 \pm 0.051$ L/h for inpatients and outpatients, respectively, compared to the observed values of $2.09 \pm 0.112$ and $1.98 \pm 0.086$ L/h for inpatients and outpatients, respectively. The lithium clearance calculated by the method of Pepin et al. (21) averaged 1.46 and 1.44 L/h for inpatients and outpatients, respectively. On the other hand, the empirical method and the method of Jermain et al. (31) produced estimates of 1.56 and 1.026 L/h for inpatients, and 1.53 and 1.0 L/h for outpatients, respectively. Table 1 shows the lithium clearance values predicted by various methods. All methods, with the exception of our method, tended to underestimate lithium clearance for both inpatients and outpatients. The method of Jermain et al. (31) proved to be the least accurate among all methods for the prediction of lithium clearance and the empirical method produced better estimates of clearance than the method of Pepin et al. (21) (Table 2).

The predicted daily dosage requirements in the 60 psychiatric patients by the method of Pepin et al. (21) averaged $1140.3 \pm 87.0$ mg (range 90.7–4008.1 mg) compared to $1014.5 \pm 19.9$ mg (range 650.8–1498.4 mg) predicted by our method for inpatients. On the other hand, predictions of daily dosage requirements by the methods of Zetin et al. (25) and Terao et al. (32) averaged $1088.7 \pm 26.1$ mg (range 611.8–1571.3 mg) and $743.8 \pm 26.1$ mg (range 228.6–1196.0 mg), respectively. One-way ANOVA for the MPE, MAE and RMSE showed statistically significant differences

### Table 1. Lithium clearance predicted by various methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Inpatients</th>
<th>Outpatients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical</td>
<td>1.56 ± 0.064 (0.73–3.02)</td>
<td>1.53 ± 0.08 (0.61–2.92)</td>
</tr>
<tr>
<td>Jermain et al. (31)</td>
<td>1.026 ± 0.031 (0.53–1.58)</td>
<td>1.00 ± 0.036 (0.53–1.52)</td>
</tr>
<tr>
<td>Pepin et al. (21)</td>
<td>1.46 ± 0.06 (0.69–2.84)</td>
<td>1.44 ± 0.076 (0.58–2.74)</td>
</tr>
<tr>
<td>Abou-Auda et al. (present study)</td>
<td>2.088 ± 0.051 (1.22–3.29)</td>
<td>1.88 ± 0.045 (1.37–2.67)</td>
</tr>
</tbody>
</table>

The observed lithium clearance in 60 patients was $2.09 \pm 0.112$ L/h (range 0.58–3.29 L/h) for inpatients and $1.88 \pm 0.045$ L/h (range 0.57–5.07 L/h) for outpatients.
as the prediction of daily dose. Figure 2 shows a plot of predicted dose by the current method as a function of the administered dose for 60 inpatients. The method of Terao et al. (32) extremely underpredicted the daily dosage requirements for these patients by almost 25%, whereas the methods of Pepin et al. (21) and Zetin et al. (25) overpredicted the dosage by approximately 13%. The deviation in our method was less than 4%.

Similar analysis performed for outpatients revealed that the empirical method, and the methods of Jermain et al. (31) and Pepin et al. (21), also significantly underpredicted lithium clearance for outpatients (Table 1). The deviation in our method was < 7%, whereas the deviation in the method of Jermain et al. (31) exceeded 44% (Table 3). The method of Pepin et al. (21) predicted the lithium daily dosage requirements to be 1212.4 ± 99.9 mg (range 440.3–3408.0 mg), compared to 1003.7 ± 26.3 mg (range 651.1–1463.4 mg) predicted by our method, with a deviation of less than 3% from the observed dose actually prescribed for these patients, whereas the deviation in the method of Pepin et al. (21) was more than 18%. Again, the method of Terao et al. (32) significantly underpredicted the dose. Conversely, dosage prediction by method of Jermain et al. (31) was reasonably unbiased for these patients compared to other

![Fig. 2. A plot of predicted dose by the current method described in this study versus administered dose for 60 inpatients.](image)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Method</th>
<th>Percent error</th>
<th>MPE</th>
<th>MAE</th>
<th>RMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clearance</td>
<td>Empirical</td>
<td>−19.53 ± 3.72</td>
<td>−0.53 ± 0.104</td>
<td>0.63 ± 0.09</td>
<td>0.89 ± 0.51</td>
</tr>
<tr>
<td></td>
<td>Jermain et al. (31)</td>
<td>−46.37 ± 2.69</td>
<td>−1.066 ± 0.107</td>
<td>1.07 ± 0.105</td>
<td>1.29 ± 0.67</td>
</tr>
<tr>
<td></td>
<td>Pepin et al. (21)</td>
<td>−24.36 ± 3.50</td>
<td>−0.618 ± 0.103</td>
<td>0.68 ± 0.10</td>
<td>0.95 ± 0.54</td>
</tr>
<tr>
<td></td>
<td>Abou-Auda et al. (present study)</td>
<td>10.31 ± 5.77</td>
<td>0.002 ± 0.10</td>
<td>0.49 ± 0.07</td>
<td>0.69 ± 0.45</td>
</tr>
<tr>
<td>Daily dose</td>
<td>Pepin et al. (21)</td>
<td>13.39 ± 6.39</td>
<td>143.13 ± 74.39</td>
<td>257.97 ± 57.37</td>
<td>534.92 ± 355.38</td>
</tr>
<tr>
<td></td>
<td>Zetin et al. (25)</td>
<td>12.45 ± 4.66</td>
<td>68.36 ± 32.64</td>
<td>181.13 ± 20.98</td>
<td>229.36 ± 110.72</td>
</tr>
<tr>
<td></td>
<td>Terao et al. (32)</td>
<td>−23.13 ± 3.39</td>
<td>−265.72 ± 33.51</td>
<td>292.64 ± 30.49</td>
<td>352.85 ± 161.56</td>
</tr>
<tr>
<td></td>
<td>Abou-Auda et al. (present study)</td>
<td>3.96 ± 3.32</td>
<td>0.68 ± 26.6</td>
<td>142.9 ± 16.86</td>
<td>184.57 ± 95.99</td>
</tr>
</tbody>
</table>

MPE = mean prediction error; MAE = mean absolute error; RMSE = root mean square error.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Method</th>
<th>Percent error</th>
<th>MPE</th>
<th>MAE</th>
<th>RMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clearance</td>
<td>Empirical</td>
<td>−16.37 ± 3.56</td>
<td>0.34 ± 0.073</td>
<td>0.47 ± 0.05</td>
<td>0.58 ± 0.24</td>
</tr>
<tr>
<td></td>
<td>Jermain et al. (31)</td>
<td>−44.34 ± 2.75</td>
<td>−0.902 ± 0.068</td>
<td>0.91 ± 0.07</td>
<td>0.99 ± 0.35</td>
</tr>
<tr>
<td></td>
<td>Pepin et al. (21)</td>
<td>21.39 ± 3.34</td>
<td>−0.437 ± 0.071</td>
<td>0.52 ± 0.055</td>
<td>0.624 ± 0.255</td>
</tr>
<tr>
<td></td>
<td>Abou-Auda et al. (present study)</td>
<td>6.62 ± 4.80</td>
<td>0.004 ± 0.063</td>
<td>0.334 ± 0.035</td>
<td>0.40 ± 0.165</td>
</tr>
<tr>
<td>Daily dose</td>
<td>Pepin et al. (21)</td>
<td>18.47 ± 7.20</td>
<td>208.74 ± 82.93</td>
<td>374.48 ± 66.79</td>
<td>546.5 ± 110.06</td>
</tr>
<tr>
<td></td>
<td>Zetin et al. (25)</td>
<td>8.76 ± 3.92</td>
<td>47.79 ± 26.68</td>
<td>147.24 ± 17.55</td>
<td>190.95 ± 94.92</td>
</tr>
<tr>
<td></td>
<td>Terao et al. (32)</td>
<td>−18.83 ± 3.34</td>
<td>−218.43 ± 27.74</td>
<td>248.08 ± 20.59</td>
<td>280.17 ± 108.30</td>
</tr>
<tr>
<td></td>
<td>Abou-Auda et al. (present study)</td>
<td>2.95 ± 3.12</td>
<td>0.026 ± 23.47</td>
<td>111.5 ± 15.5</td>
<td>148.46 ± 72.16</td>
</tr>
</tbody>
</table>

MPE = mean prediction error; MAE = mean absolute error; RMSE = root mean square error.
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References