

ORIGINAL ARTICLE

Development of a hyponatremia screening tool (ABCDF-S score) for patients with hypertension using thiazide diuretic agents

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Abstract

What is known and objective: Hyponatremia is a common side effect of thiazide diuretics that can lead to increased mortality and hospitalization. A rapid and accurate screening tool is needed for rapid and appropriate management. In this study, we report on the development of a simple clinical screening tool for hyponatremia using thiazide diuretics.

Methods: This nested case-control study was performed by collecting data from 1 January 2015 to 30 June 2017. Univariable and multivariable logistic regressions were used to identify potential risk factors. The regression coefficients were converted into item scores by dividing each regression coefficient with the minimum coefficient in the model and rounding to the nearest integer. This value was then summed to the total score. The prediction power of the model was determined by the area under the receiver operating characteristic curve (AuROC).

Results and discussion: Six clinical risk factors, namely age ≥ 65 years, benzodiazepine use, history of a cerebrovascular accident, dose of hydrochlorothiazide ≥ 25 mg, female sex and statin use, were included in our ABCDF-S score. The model showed good power of prediction (AuROC 81.53%, 95% confidence interval [CI]: 78%–84%) and good calibration (Hosmer-Lemeshow $X^2 = 23.20$; $P = .39$). The positive likelihood

ratios of hyponatremia in patients with low risk (score ≤ 6) and high risk (score ≥ 8) were 0.26 (95% CI: 0.21–0.32) and 3.89 (95% CI: 3.11–4.86), respectively.

What is new and conclusion: The screening tool with six risk predictors provided a useful prediction index for thiazide-associated hyponatremia. However, further validation of the tool is warranted prior to its utilization in routine clinical practice.

KEYWORDS

hypertension, hyponatremia, screening tool, thiazide diuretics

1 | WHAT IS KNOWN AND OBJECTIVE

Hypertension is a crucial global health risk due to its high prevalence and sequelae, which includes cardiovascular and chronic kidney disease. Hypertension is the leading preventable risk factor for premature death and disability worldwide.¹ A previous study estimated that 26.4% of the global adult population, or 972 million people, had hypertension in the year 2000.² The major outcome trials, such as ALLHAT³ and SHEP,⁴ have demonstrated that thiazide diuretics can reduce cardiovascular complications. As a result, the Eighth Joint National Committee⁵ consider thiazide diuretics as an initial drug therapy for the treatment of hypertension.

Adverse effects of thiazide diuretics include hyponatremia, hypokalemia, hyperuricemia and hyperglycaemia.⁶ Hyponatremia is the most common electrolyte abnormality detected in patients and can increase mortality.^{7,8} The clinical presentation of hyponatremia can range from mild to severe. Severe hyponatremia, with a serum sodium concentration of 110–114 mEq/L, can be correlated with symptoms, including seizure, brainstem herniation, coma and death.^{9,10} A previous report found that the incidence of severe hyponatremia was 2.6%–6.2%.⁸ Typically, almost every case of severe diuretic-induced hyponatremia is linked to thiazide diuretics.^{10,11} A study to investigate the relation between plasma sodium and volume regulation is necessary in order to better understand the causes of hyponatremia. The primary negative feedback mechanism, glomerular tubular balance, is responsible for sodium and plasma volume regulation. A decrease in intravascular volume causes a decrease in the glomerular filtration rate (GFR). Sodium and chloride are reabsorbed in the loop of Henle, causing less sodium and chloride ions to reach the distal tubule. This decrease in sodium and chloride ions is detected by the juxtaglomerular complex, which consequently releases renin, leading to the release of aldosterone and antidiuretic hormone (ADH). This release increases sodium and water reabsorption in the distal tubule and collecting duct. In addition, stimulation of thirst and vasoconstriction of the efferent arteriole maintains GFR and filtration pressure at the glomerulus, resulting in a balanced intravascular volume. Thiazide diuretics inhibit the sodium/chloride co-transporters in the distal tubule. Reabsorption of these ions is inhibited, causing their excretion in the urine and thereby resulting in hyponatremia.¹² Thiazide-induced hyponatremia has been reported to occur rapidly and unpredictably.¹³ In most

cases, thiazide diuretics can induce hyponatremia within 2 weeks after use. Nonetheless, hyponatremia can be induced any time. Hyponatremia as a result of thiazide use depends on contributory factors, such as old age, decreased renal function or concomitant use of other medications.¹⁰

In a previously published report, thiazide-associated hyponatremia risk score was reported to display good discrimination. However, that study had some limitations, such as only patients hospitalized with hyponatremia, not hyponatremia outpatients, were included. Furthermore, that study did not clarify which group had stated risk. Another limitation was that the predictive model was difficult to apply in clinical practice, which may be due to its complex nature.¹⁴

Therefore, the present study aimed to develop a reliable, easy-to-use screening tool to predict severe hyponatremia in hypertensive patients taking thiazide diuretics. This screening tool may help clinicians in the primary care unit by preventing severe hyponatremia and facilitating appropriate management and monitoring.

2 | METHODS

2.1 | Study size and study population

We calculated the sample size by applying the two independent proportions of risk factors, similar to a prior study (59.4% vs 49.2%).¹⁴ A sample size of 409 participants per group would be required to have alpha error and beta error of 0.05 and 0.2, respectively.¹⁵

This research was performed at Phrae Hospital, a 500-bed secondary care medical centre situated in the northern part of Thailand. Qualified subjects were selected from a cohort of patients who used thiazide diuretics according to the standard treatment for hypertension⁵ in Phrae Hospital from January 2015 to June 2017. The medical physician diagnosed hyponatremia based on laboratory values and clinical manifestations, while the clinical pharmacist used Naranjo's algorithm (probable level and above) for confirmation. Hyponatremia diagnosis depended on consensus of the following conditions: (a) serum sodium lower than 135 mEq/L and (b) occurring after administration of thiazide diuretics. Patients who used thiazide diuretics for other indications (e.g. calcium nephrolithiasis, oedema) were excluded. In addition,

participants with missing data in the electronic database were excluded. Patients were stratified into two groups: hyponatremia (study group) and non-hyponatremia (control group). For the control group, patients were randomly selected from the electronic database using a computer programme.

2.2 | Study design and data collection

This nested case-control study aimed to develop a screening tool to predict hyponatremia in hypertension patients taking thiazide diuretics. The electronic database was used to obtain patients' characteristics. Comorbidities were identified from the International Classification of Disease, 10th revision (ICD-10) codes version 2016, including E78.5 (for hyperlipidemia); E11.0-E11.9 (for diabetes mellitus type II); I61.0-I61.9, I62.0-I62.9 and I63.0-I63.9 (for cerebrovascular accident); N18.3-N18.5 (for chronic kidney disease); I50.0-I50.9 (for chronic heart failure); M15.0-M15.9, M16.0-M16.9, M17.0-M17.9, M18.0-M18.9 and M19.0-M19.9 (for osteoarthritis); M06.9 (for rheumatoid arthritis); and M10.9 (for gout). Data relating to concurrent medications with thiazide diuretics at least 2 weeks were collected. Data were collected from 1 January 2015 to 30 June 2017.

2.3 | Statistical analyses

Descriptive statistics on research variables are exhibited as mean (SD), median (interquartile range) or frequency count (percentage), as appropriate. Every factor was screened for a relationship with hyponatremia by univariable analysis using chi-square or Fisher's exact test and summed with odds ratios (ORs) and 95% confidence intervals

(95% CIs); factors with P -value $\leq .1$ were transferred into multivariable analyses. Significant risk factors were then analysed by multivariate logistic regression. Any variable with P -value $< .05$ was retained in the model.

2.4 | Model development

The relevant variables were compared among subjects with and without hyponatremia using univariate comparative statistics and summed with ORs and 95% CIs. Clinically and statistically significant variables from the univariate analysis were chosen for the multivariate stepwise logistic regression. Coefficients of significant variables from the multivariable analysis were weighted and converted to item scores by dividing each regression coefficient with the smallest coefficient in the model and rounding to the nearest integer.^{16,17} To evaluate the discriminative power of the generated predictive score, a receiver operating characteristic (ROC) curve was plotted, and a Hosmer-Lemeshow goodness of fit test was performed.¹⁸ Cut-off scores were taken to classify subjects into three groups: low, moderate and high risk of hyponatremia. The specificity, sensitivity, accuracy, positive likelihood ratio (LR+) and negative likelihood ratio (LR-) were obtained.^{19,20} The multi-collinearity and effect modification were obtained by the variance inflation factor (VIF) and the stratified analysis, respectively.

2.5 | Ethics statement

The study was approved by the Ethical Committee for Clinical Research in Phrae Hospital (No. 29/2561).

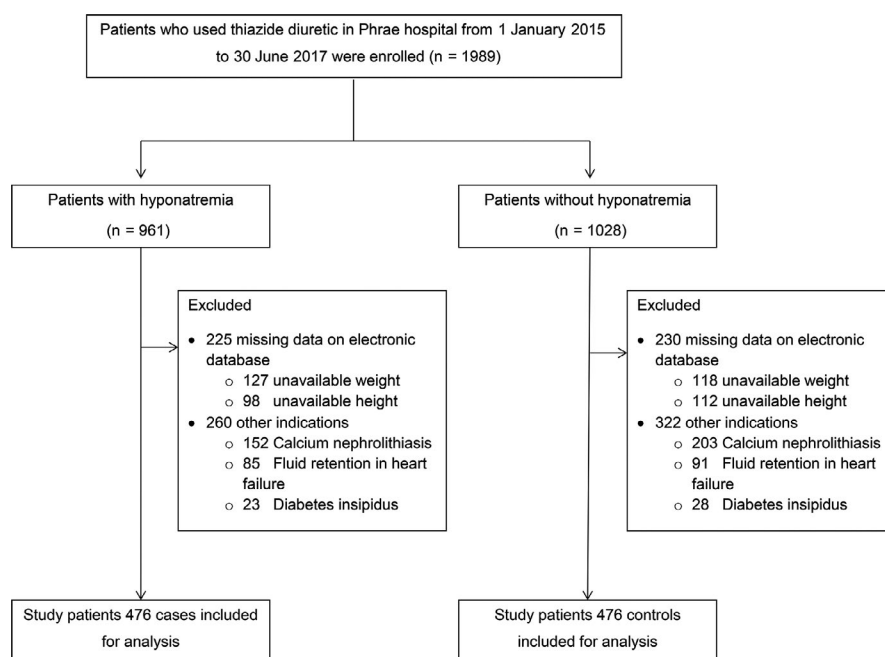


FIGURE 1 Selection of study patients

3 | RESULTS

3.1 | Patient characteristics

Of the 1989 patients who were taking thiazide diuretics, 952 patients were included in the study, among which 476 patients (50%) belonged to the hyponatremia group (Figure 1). Participants were between 26 and 92 years of age. The majority of patients were women (72.79%). Body mass index ranged from 13.33 to 39.67 kg/m². All participants were Asian and used hydrochlorothiazide, with 79.62% patients taking doses ≥ 25 mg per day. A higher percentage of benzodiazepine use was observed in the hyponatremia (study) group than in the control group ($P = .002$). A higher percentage of use of statins and angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor antagonists (ARBs) was noted in the control group than in the study group ($P < .001$, $P = .092$ respectively). No

significant difference was found between patients taking tricyclic antidepressants, non-steroidal anti-inflammatory drugs (NSAIDs) and selective serotonin reuptake inhibitors (SSRIs). The four most common comorbid conditions present in the study group were hyperlipidemia, cerebrovascular accident (referred to as ischaemic stroke or haemorrhagic stroke), chronic kidney disease and rheumatoid arthritis. Baseline characteristics of both groups are exhibited in Table 1.

3.2 | Predictors of hyponatremia in hypertension patients who used thiazide diuretics

The results from the univariate analysis of the risk factors associated with hyponatremia are shown in Table 2. There were 11 risk factors associated with hyponatremia, namely age ≥ 65 years (OR 3.38,

TABLE 1 Clinical and demographic characteristics of both groups

Characteristics	Total ^a (n = 952)	Hyponatremia ^b (n = 476)	Non-hyponatremia ^b (n = 476)	P-value
Age, mean ($\pm$ SD)	66.49 ($\pm$ 11.03)	69.99 ($\pm$ 9.76)	62.98 ($\pm$ 11.11)	<.001
Female sex, No. (%)	693 (72.79)	401 (84.24)	292 (61.34)	<.001
Body mass index, mean ($\pm$ SD)	23.35 ($\pm$ 4.11)	22.07 ($\pm$ 3.61)	24.63 ($\pm$ 4.19)	<.001
Ethnicity, No. (%)				
Asian	952 (100.00)	476 (100.00)	476 (100.00)	
Type of thiazide diuretics, No. (%)				
HCTZ	952 (100.00)	476 (100.00)	476 (100.00)	
Dose of thiazide diuretics, No. (%)				
≥ 25 mg per day of HCTZ	758 (79.62)	455 (95.59)	303 (63.66)	<.001
Concurrent medications, No. (%)				
ACEIs/ARBs	454 (47.69)	214 (44.96)	240 (50.42)	.092
Tricyclic antidepressants	30 (3.15)	13 (2.73)	17 (3.57)	.458
NSAIDs	429 (45.06)	211 (44.33)	218 (45.80)	.648
SSRIs	14 (1.47)	9 (1.89)	5 (1.05)	.420
BZDs	266 (27.94)	155 (32.56)	111 (23.32)	.002
Statins	372 (39.08)	131 (27.52)	241 (50.63)	<.001
Intercurrent conditions, No. (%)				
Hyperlipidemia	326 (34.24)	134 (28.15)	192 (40.34)	<.001
Type 2 diabetes mellitus	323 (33.93)	158 (33.19)	165 (34.66)	.681
Cerebrovascular accident	30 (3.15)	21 (4.41)	9 (1.89)	.040
Chronic kidney disease	120 (12.61)	47 (9.87)	73 (15.34)	.014
Chronic heart failure	23 (2.42)	8 (1.68)	15 (3.15)	.204
Osteoarthritis	15 (1.58)	11 (2.31)	4 (0.84)	.116
Rheumatoid arthritis	15 (1.58)	12 (2.52)	3 (0.63)	.034
Gout	29 (3.05)	10 (2.10)	19 (3.99)	.130

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor antagonists; BZDs, benzodiazepines; HCTZ, hydrochlorothiazide; NSAIDs, non-steroidal anti-inflammatory drugs; SSRIs, selective serotonin reuptake inhibitors.

^aData are presented as percentage of patients with a specific condition per total number of study patients.

^bData are presented as percentage of patients with a specific condition in case or control groups per number of the patients in that group (case/control).

**TABLE 2** Univariate analysis of risk factors associated with hyponatremia

Variable	Total (n = 952)		
	Odds ratio	95% CI of odds ratio	P-value
Age (≥ 65 y old)	3.38	2.55-4.47	<.001
Female	3.37	2.45-4.64	<.001
BMI (≤ 18.5 kg/m ²)	1.45	0.99-2.15	.060
Hyperlipidemia	0.57	0.44-0.77	<.001
Type 2 diabetes mellitus	0.94	0.71-1.24	.681
Cerebrovascular accident	2.39	1.04-6.00	.040
Chronic kidney disease	0.60	0.40-0.91	.014
Chronic heart failure	0.53	0.19-1.34	.204
Osteoarthritis	2.79	0.82-12.09	.116
Rheumatoid arthritis	4.08	1.09-22.63	.034
Gout	0.52	0.21-1.18	.130
Dose HCTZ ≥ 25 mg per day	12.37	7.61-20.92	<.001
ACEIs/ARBs	0.80	0.62-1.04	.092
Tricyclic antidepressants	0.76	0.33-1.68	.458
NSAIDs	0.94	0.72-1.23	.648
SSRIs	1.82	0.54-6.94	.420
BZDs	1.59	1.18-2.14	.002
Statins	0.37	0.28-0.49	<.001

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor antagonists; BMI, body mass index; BZDs, benzodiazepines; HCTZ, hydrochlorothiazide; NSAIDs, non-steroidal anti-inflammatory drugs; SSRIs, selective serotonin reuptake inhibitors.

95% CI: 2.55-4.47, $P < .001$), female sex (OR 3.37, 95% CI: 2.45-4.64, $P < .001$), body mass index ≤ 18.5 kg/m² (OR 1.45, 95% CI: 0.99-2.15, $P = .060$), hyperlipidemia (OR 0.57, 95% CI: 0.44-0.77, $P < .001$), cerebrovascular accident (OR 2.39, 95% CI: 1.04-6.00, $P = .040$), chronic kidney disease (OR 0.60, 95% CI: 0.40-0.91, $P = .014$), rheumatoid arthritis (OR 4.08, 95% CI: 1.09-22.63, $P = .034$), dose of hydrochlorothiazide ≥ 25 mg per day (OR 12.37, 95% CI: 7.61-20.92, $P < .001$), use of ACEIs/ARBs (OR 0.80, 95% CI: 0.62-1.04, $P = .092$), use of benzodiazepines (OR 1.59, 95% CI: 1.18-2.14, $P = .002$) and use of statins (OR 0.37, 95% CI: 0.28-0.49, $P < .001$).

3.3 | Model development

After univariable and multivariable analyses, six variables remained in the model using backward stepwise logistic regression and these variables were used to construct a screening scoring system. This system for screening hyponatremia in hypertension patients who

used thiazide diuretics includes the summation of each point based on the following factors: Age ≥ 65 years old (no = 0, yes = 2), use of Benzodiazepines (no = 0, yes = 1), history of Cerebrovascular accident (no = 0, yes = 3.5), Dose of hydrochlorothiazide ≥ 25 mg (no = 0, yes = 5), Female sex (no = 0, yes = 2) and use of Statins (no = 0, yes = -2). The point for each factor is obtained from a weighted coefficient and converted to its nearest integer as the assigned score (Table 3). We named this tool the 'ABCDF-S score', which is acquired from a letter from each factor to facilitate its use.

The screening scoring was generated by defining the cut-off value according to the separation plot and performance of diagnostic parameters to identify the patients at risk of hyponatremia. The cut-off scores of six and eight were chosen to classify subjects in three groups. Subjects with total scores ≥ 8 were placed in the high-risk group. The accuracy of the predictions for subjects in the group was 79.55% (284/357). Subjects with scores ≤ 6 were placed in the low-risk group. Meanwhile, absence of hyponatremia in the low-risk group was predicted in subjects without hyponatremia 79.38% (308/388). Revised prediction of the absence or presence of hyponatremia was based on the following calculation: $(308 + 284)/(388 + 357) = 79.4\%$. The inaccurate prediction rate was based on the following calculation: $(80 + 73)/(388 + 357) = 20.5\%$ (Table 4). Based on this scoring system and two cut-off points, the score obtained was differentiated between patients with and without hyponatremia and validated (AuROC 81.53%; Figure 2) and a well-calibrated predictive model was developed (Hosmer-Lemeshow $\chi^2 = 23.20$; $P = .39$).²¹

The probability of hyponatremia as a function of the screening score is presented in Figure 3. Subjects were classified in 3 groups using the cut-off score: low risk (score ≤ 6), moderate risk (score 6.5-7.5) and high risk (score ≥ 8). The distribution of patients between the three groups was statistically significant with $P < .001$.

4 | DISCUSSION

Our research demonstrated that the 'ABCDF-S score' can be applied as a screening tool to classify subjects at risk of hyponatremia. In this study, we developed a primary clinical score for the screening of hyponatremia in patients taking thiazide diuretics in Thailand.

In this research, we discovered six clinical risk factors that can predict hyponatremia in patients taking thiazide diuretics, namely advanced age, female sex, use of benzodiazepines, history of cerebrovascular accident, dose of hydrochlorothiazide and use of statins. These conclusions are similar to those of a prior publication on this topic, which showed that the risk of patients with thiazide-associated hyponatremia was characterized by female sex, advanced age and increased doses of thiazide diuretics. Thus, our study includes the same three risk factors as the previous study.^{22,23} The correlation of hyponatremia with female sex or advanced age is unclear; however, an animal study found that the female rodent has a greater quantity of sodium-chloride co-transporter. Hence, a high response was obtained during the administration of a thiazide diuretic. Additionally, another study found that a

Predictors	Coefficients	P-value	Transformed coefficients	Assigned score
Age				
<65 y	-	-	-	0
≥65 y	0.9422104	<.001	1.82	2
Use of Benzodiazepines				
No	-	-	-	0
Yes	0.5171928	.003	1	1
History of Cerebrovascular accident^a				
No	-	-	-	0
Yes	1.733214	0.001	3.35	3.5
Dose of Hydrochlorothiazide				
<25 mg	-	-	-	0
≥25 mg	2.526021	<.001	4.88	5
Female				
No	-	-	-	0
Yes	1.099314	<.001	2.13	2
Use of Statins				
No	-	-	-	0
Yes	-1.052673	<.001	-2.04	-2

^aCerebrovascular accident was referred to as an ischaemic stroke or haemorrhagic stroke.

TABLE 3 Multivariable analysis and significant predictors of hyponatremia (ABCDF-S score)

N = 952	Low risk (score ≤ 6)	Moderate risk (score 6.5-7.5)	High risk (score ≥ 8)	Total
Total	388	207	357	952
Non-hyponatremia	308	95	73	476
Hyponatremia	80	112	284	476
Diagnostic performance				
Sensitivity	64.71%	23.53%	59.66%	
Specificity	83.19%	80.04%	84.66%	
Accuracy	73.95 (95%CI: 71.04-76.71)	51.79 (95%CI: 48.56-55.00)	72.16 (95%CI: 69.20-74.99)	
Likelihood ratio (+)	0.26 (95%CI: 0.21-0.32)	1.18 (95%CI: 0.92-1.50)	3.89 (95%CI: 3.11-4.86)	
Likelihood ratio (-)	3.85 (95%CI: 3.12-4.75)	0.85 (95%CI: 0.66-1.08)	0.26 (95%CI: 0.20-0.32)	
Interpretation	Absence of hyponatremia (70.21% certainty)	Presence of hyponatremia (79.55% certainty)		

TABLE 4 Distribution of the risk of hyponatremia in patients with hypertension taking thiazide diuretics, as well as diagnostic performance and interpretation

population of elderly women had an increased risk of hyponatremia, caused by reduced body mass and total body water.²⁴⁻²⁶ In our study, we also found that patients with cerebrovascular accident had an increased risk of hyponatremia, which may be induced by the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) or cerebral salt wasting syndrome (CSWS).^{27,28} The use of benzodiazepines can also lead to an increased risk of hyponatremia. Whether this is a direct or indirect correlation is unclear, and we can only hypothesize about

the associated mechanism. This drug has been shown to interact with vasopressinergic neurons due to the effect of the neurotransmitter gamma-aminobutyric acid.²⁹ There is one documented case of lorazepam-induced hyponatremia, caused by induced SIADH.^{23,30,31} An alternative hypothesis is that sleep conditions, for which benzodiazepines are usually prescribed, are correlated with hyponatremia. Sleep deprivation can decrease cortisol levels, which increase vasopressin, thereby potentially causing hyponatremia.³² Some evidence shows



that patients who used thiazides in combination with benzodiazepines had a more severe degree of hyponatremia.³³ Meanwhile, this study found that those who used statins experienced a protective effect and a previous study showed that statins can decrease fractional excretion of sodium (FE_{Na}), and increase serum sodium.³⁴ Hyperlipidemia was removed from our model, because the relationship between hyperlipidemia and hyponatremia in this research is marked as pseudohyponatremia due to the increase in free water or absence of loss of sodium. Therefore, it did not have clinical significance. In addition, the laboratory centre at Phrae hospital uses indirect ion-selective electrode (ISE) methods for measuring serum sodium. Consequently, serum sodium may seem low when the specimen has hyperlipidemia due to the space-occupying effects of lipids in the blood.^{35,36}

In our research, the cut-off was dependent on the evaluation of specificity, sensitivity, accuracy, positive likelihood ratio and negative likelihood ratio. The ABCDF-S score is used to identify those patients for whom thiazide diuretic use may need to be discontinued. Patients

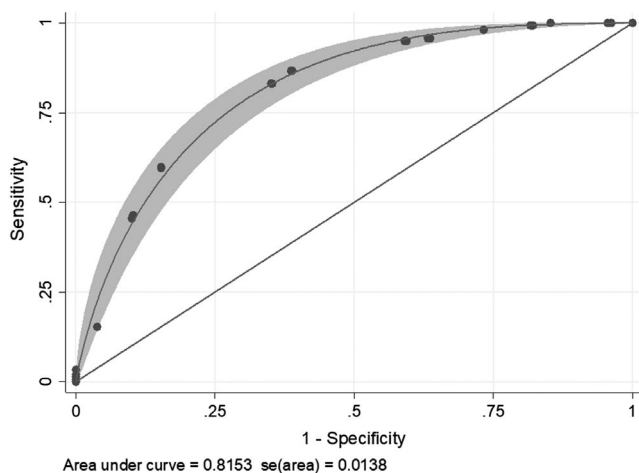


FIGURE 2 Receiver operator characteristic (ROC) curve of the scoring system in predicting hyponatremia in patients with hypertension taking thiazide diuretics

with a calculated score of ≤ 6 would be considered to have low risk and would only require monitoring of serum sodium every 3 months. Meanwhile, patients with a score of 6.5–7.5 would be considered to have moderate risk and would need to have their serum sodium monitored every month, in addition to a reduction in hydrochlorothiazide dose. Finally, patients with a calculated ABCDF-S score ≥ 8 would be considered to have high risk and would need to have their hydrochlorothiazide discontinued. The ABCDF-S score generated in our research is different from previous screening tools¹⁴ in a number of aspects. First, past models were generated in the mixed community and essentially with Caucasian individuals, while ours was generated in Asian people who were taking thiazide diuretics to treat hypertension. Second, past models were complex, requiring a calculator to perform the summation of the entire score. For example, for hospitalizations related to thiazide-associated hyponatremia (HTAH) risk score, the equation for calculation is: HTAH risk score = $2.4 + (0.06 \times \text{age}) - (0.01 \times \text{weight}) + (3.64 \times \text{hypokalemia}) + (1.05 \times \text{GERD}) + (0.84 \times \text{diabetes}) + (1.37 \times \text{UTI}) + (0.62 \times \text{ACEIs})$. Meanwhile, our model is easier to use.

Our study has several strengths. First, we used data from real-world practice and the data may be used in similar settings. Second, our research included all types of patient settings (outpatient and inpatient), while previous research for predicting hyponatremia included only the inpatient population.¹⁴ Third, a power analysis was performed, which reinforced that the study was sufficiently powered to detect a difference between the two groups. Fourth, the score contains only six clinical parameters, which are easy to remember ('ABCDF-S'), without the additional cost of laboratory testing.

The limitations of this research include the following: the data were collected from only one hospital; therefore, the findings may not be generalizable. However, in settings with a similar health system, this tool can be used. This study does not include information on the diet of the patients. Although diet is an important factor to consider in hyponatremia, the retrospective nature of the study, which collects data via electronic databases, was a limiting factor. Furthermore, accurate information about a patient's diet is difficult in precisely determining

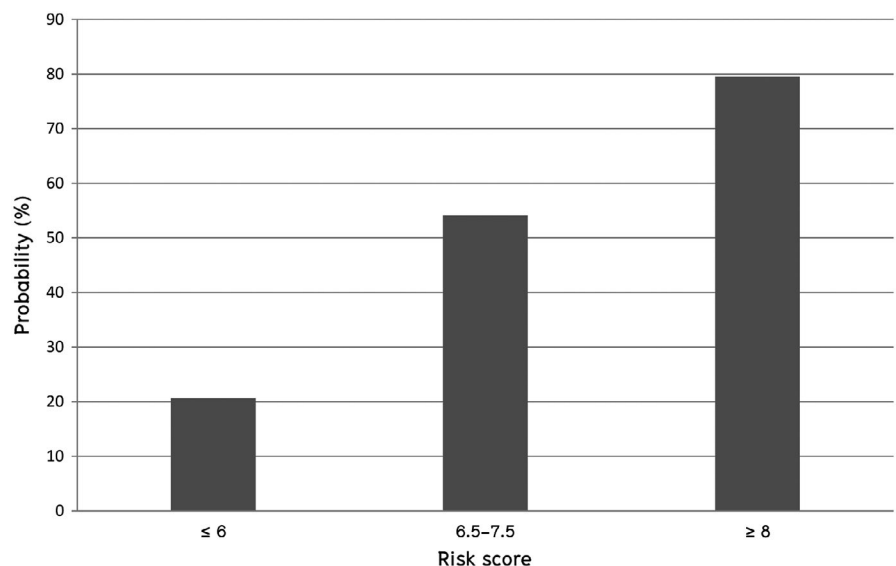


FIGURE 3 Probability of hyponatremia in hypertension patient taking thiazide diuretics stratified by the risk score

the amount of sodium present in one's own diet. Additionally, some patients were eliminated due to missing data in the electronic database (unavailable weight or height). Since this research is a retrospective study, these issues are the major concerns. Moreover, concurrent medications were collected with unspecified dose; thus, the association between the dose of medication and serum sodium remains unclear. Therefore, the results should be interpreted with caution.

Notwithstanding these limitations, this screening tool (ABCD-S score) including six risk factors for hyponatremia in patients diagnosed with hypertension taking thiazide diuretics in the primary care setting was generated and assessed. In addition, a medical provider in the primary care setting can use this screening score to assess the electrolytes of hypertension patients taking thiazide diuretics. If the result of the total score is ≤ 6 , the patient is considered to have low risk and should have serum sodium monitored every 3 months. Patients with a score of 6.5–7.5 are considered to have moderate risk. For these patients, we recommend decreasing the hydrochlorothiazide dose to lower than 25 mg per day and monitoring serum sodium every 1 month. Patients with score ≥ 8 are considered to have high risk. For this patient group, we recommend discontinuing thiazide diuretics and switching to other classes of drugs.

5 | WHAT IS NEW AND CONCLUSION

A simple screening tool was developed for predicting hyponatremia in patients taking thiazide diuretics. The scores are based on six clinical predictors. This simple screening tool can potentially be useful in clinical practice. This study may help clinicians determine the risk of hyponatremia in patients in order to guide clinical decision making. However, this screening score should be validated before use in the clinical setting.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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