Chronic versus New-Onset Hyponatremia in Geriatric Patients Undergoing Orthopedic Surgery

Abstract

Background: Hyponatremia is a common electrolyte disorder encountered in geriatric population undergoing an orthopedic surgery and is associated with adverse clinical outcomes. There is a paucity in literature comparing the effects of chronic- and new-onset hyponatremia on patient outcomes. **Materials and Methods:** A prospective study on 220 patients of age ≥60 years with an orthopedic injury was carried out over 1 year. The aim of this study was to determine the prevalence of chronic hyponatremia during hospitalization and the incidence of new-onset hyponatremia developing perioperatively and compare between the two groups with regard to the severity of hyponatremia, perioperative morbidities, serum sodium level trend in the early postoperative period, and mortality. **Results:** The prevalence of chronic hyponatremia was 14.1%, with an incidence of new-onset hyponatremia of 22.7%. Patients who developed new-onset hyponatremia were mostly of mild grade (130–134 mmol/L) and were significantly different from those with chronic hyponatremia who were more likely to be of profound grade (<125 mmol/L). When aggressively managed with adequate sodium corrections and strict monitoring, new-onset hyponatremia corrected within 48 h, whereas chronic hyponatremia had a gradual rise in serum sodium levels and did not achieve full correction within 48 h ($P < 0.05$). Those with chronic hyponatremia had a longer duration of hospital stay ($P < 0.0001$). No significant differences were obtained in mortality between the two groups. **Conclusions:** Patients developing new-onset hyponatremia are of milder grade and recover faster. Patients with chronic hyponatremia require a more cautious approach as they are more likely to be of profound grade and take longer time to correct.

Keywords: *Chronic hyponatremia, geriatric, new-onset hyponatremia, orthopedic surgery*

Sumant Chacko Verghese, Anupam Mahajan[1], Bharti Uppal[2]

Departments of Orthopaedics, [1]Orthopaedics and [2]Biochemistry, Christian Medical College and Hospital, Ludhiana, Punjab, India

Introduction

Electrolytes play a vital role in maintaining homeostasis within the body. Abnormalities in serum sodium and potassium levels are among the most serious electrolyte disturbances.[1] Other electrolyte imbalances are less common which usually occur in conjunction with major electrolyte changes.

Hyponatremia is low sodium concentration in blood. Normal serum sodium levels range between 135 and 145 mmol/L (mEq/L).[2] Published research suggests using a threshold of 48 h to distinguish “chronic” from “acute” hyponatremia, but in clinical practice the distinction between chronic and acute hyponatremia is often unclear, particularly for patients presenting to the emergency room.[2] As per literature, hyponatremia is noted in approximately 15%–30% of all hospital emergency admissions.[1] It has been increasingly noticed that mild hyponatremia with minor derangements is associated with an increased risk to falls, leading to fractures in the elderly.[3-5] Moreover, mild hyponatremia has been associated with increased in-hospital, 1-year, and 5-year mortality, with a risk of mortality increasing with worsening severity of hyponatremia.[6] For every 1 mmol/L drop in serum sodium below 135 mmol/L, there is a 23% increase in mortality.[6]

Patients undergoing an orthopedic surgery have the strongest association between hyponatremia and mortality. There is a 2.1-fold increased risk of death with mild grade (130–134 mmol/L) and a 4.6-fold increased risk of death with severe grade (<125 mmol/L) of hyponatremia.[1] Hyponatremia also increases the risk for perioperative morbidities including major coronary events, wound infection, and pneumonia, as well as prolonged hospitalization.[7] Whether hyponatremia is

How to cite this article: Verghese SC, Mahajan A, Uppal B. Chronic versus new-onset hyponatremia in geriatric patients undergoing orthopedic surgery. Int J App Basic Med Res 2019;9:37-43.

Received: 22 November, 2018.
Accepted: 08 January, 2019.

Address for correspondence:
Dr. Anupam Mahajan, Department of Orthopaedics, Christian Medical College and Hospital, Ludhiana, Punjab, India.
E-mail: dranupammahajan@gmail.com

Access this article online

Website: www.ijabmr.org

DOI: 10.4103/ijabmr.IJABMR_374_18

Quick Response Code:

an independent predictor of patient outcomes or a marker of the severity of the disease is controversial. Nevertheless, it is very treatable, so its association with multiple poor clinical outcomes is important.[8]

Most existing studies have focused on patients admitted to medical services, and very few studies have been carried out exclusively in the elderly with an orthopedic problem. We have, therefore, designed this study to determine the prevalence of chronic hyponatremia in elderly patients with an orthopedic problem and the incidence of new-onset hyponatremia postoperatively along with differences if any on clinical, biochemical, and outcomes such as perioperative morbidities and mortality. To the best of our knowledge, there is no other study which compares chronic with new-onset hyponatremia in the perioperative period.

Materials and Methods

This study was conducted in the Department of Orthopedics at a tertiary hospital. Prior Ethics Committee Approval was obtained vide Ref. CMC/2855. It was a 12-month prospective study from June 1, 2016, to May 31, 2017. The study design is depicted in Figure 1. A total of 301 patients of age >60 years admitted to orthopedic department for a single elective or emergency orthopedic procedure were included in the study. Eighty-one cases were excluded as per the exclusion criteria including six cases which discontinued treatment at our hospital.

Exclusion criteria

1. Patients managed nonoperatively (24 patients)
2. Patients with diseases known to cause hyponatremia such as cirrhosis, renal failure, or congestive heart failure or those suffering from AIDS

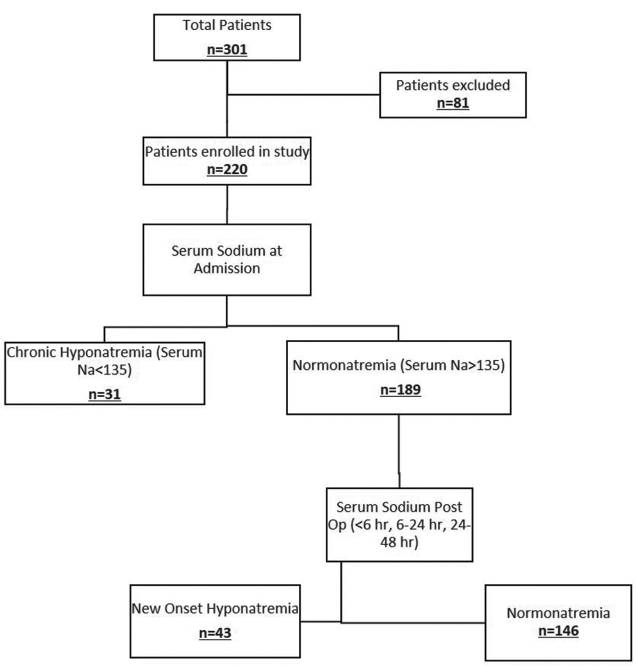

Figure 1: Study design

3. Patients with conditions known to cause syndrome of inappropriate anti-diuretic hormone secretion (pulmonary conditions such as aspergillosis, lung abscess, pneumonia, positive-pressure breathing, and tuberculosis and neurological disorders such as acute intermittent porphyria, acute psychosis, brain abscess, encephalitis, Guillain–Barre syndrome, head trauma, meningitis, stroke, subarachnoid, or subdural hemorrhage)
4. Patients suffering from an infection (e.g., diabetic foot and septic arthritis) who are more likely to be hyponatremic during the perioperative period
5. Patients who were on drugs during the perioperative period (tramadol and morphine) which are known to cause symptoms which could mimic those of hyponatremia
6. Patients with open wounds which would require multiple surgeries and subsequent prolonged duration of hospital stay.

Serum sodium levels were determined in 220 patients requiring surgery on admission from which the prevalence of chronic hyponatremia was calculated (serum sodium <135 mmol/L). Thirty-one patients were found to be hyponatremic on admission and were taken to be having chronic hyponatremia. The remaining 189 patients were then observed for the development of new-onset hyponatremia postoperatively by evaluating serum sodium levels on postoperative day (POD) 0 (within 6 h), POD 1 (within 24 h), and POD 2 (24–48 h) from which the incidence of new-onset hyponatremia was calculated. The patients were then grouped into three categories as follows:

1. Normonatremia: Patients who had serum sodium levels ≥135 mmol/L at all times during their hospital stay, preoperatively, and postoperatively
2. Chronic hyponatremia: Patients who had serum sodium levels <135 mmol/L on admission prior to surgery
3. New-onset hyponatremia: Patients who had serum sodium levels ≥135 mmol/L prior to surgery, but were found to have serum sodium levels <135 mmol/L within 48 h postsurgery.

Statistical analysis

Categorical variables were presented in number and percentage, and continuous variables were presented as mean ± standard deviation and median. Normality of data was tested by the Kolmogorov–Smirnov test. If the normality was rejected, then nonparametric test was used.

Statistical tests were applied as follows:

1. Quantitative variables were compared using independent *t*-test/Mann–Whitney test (when the data sets were not normally distributed) between the two groups
2. Qualitative variables were correlated using the Chi-square test/Fisher's exact test
3. Diagnostic tests were used to find sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

$P < 0.05$ was considered statistically significant. The data were entered into MS Excel spreadsheet, and analysis was done using the Statistical Package for the Social Sciences software version 21, IBM, Armonk, NY, United States of America.

Results

Among the 220 patients who underwent surgery, 189 patients were normonatremic prior to the surgery and 31 patients presented with hyponatremia (chronic hyponatremia). The prevalence of chronic hyponatremia was found to be 14.1%. Forty-three patients developed hyponatremia within 48 h of surgery. The incidence of new-onset hyponatremia was 22.7%. Nearly 33% ($n = 74/220$) of the patients were hyponatremic at some point of time during their hospital stay, either preoperatively or postoperatively.

Comparative Group A: Hyponatremia versus normonatremia

Comparative data of normonatremic and hyponatremic patients is given in Table 1. The mean age of the study patients was 68.27 ± 8.1 years. Patients with hyponatremia were found to be older than those without hyponatremia (69 vs. 67 years), but no significant relationship was noted with increasing age. We observed a significant relationship with a male predominance to developing perioperative hyponatremia ($P = 0.017$).

A statistically significant relationship was observed between diabetes mellitus and perioperative hyponatremia ($P = 0.019$). No similar relationship was found with other comorbidities. Patients during hospitalization were screened for prior intake of medications known to cause hyponatremia, namely, diuretics, proton pump inhibitors, antiepileptic medications, and selective serotonin reuptake inhibitors. However, no statistically significant relationship was noted.

Postoperative hyponatremia-related symptoms

Only thirty (13.63%) patients had symptoms related to hyponatremia such as nausea, headache, vomiting, confusion, and disorientation in the early postoperative period. Patients with hyponatremia were more likely to experience nausea ($P < 0.0001$) and vomiting ($P = 0.0004$) after surgery.

The PPV of nausea was found to be 79.1% with a NPV of 71.9%. Similarly, the PPV and NPV for vomiting were determined to be 83.3% and 69.2%, respectively [Table 2].

Patients with hyponatremia had a longer duration of hospital stay (10.2 vs. 8.5 days) with a statistically significant relationship ($P = 0.014$).

No significant relationship was observed between in-patient mortality till the time of discharge and perioperative hyponatremia.

Table 1: Comparative data of normonatremic and hyponatremic patients

	Overall (*n*=220)	Normonatremia (*n*=146)	Hyponatremia (*n*=74)	Statistical test	*P*
Demographics					
Age (years)	68.27±8.06	67.83±7.78	69.14±8.57	*t*-test=1.136	0.257
Male	127	76	51	χ^2=5.723	0.017 (S)
Female	93	70	23		
Comorbidities (some conditions overlapped) (%)					
Diabetes mellitus	75 (34.09)	42 (28.77)	33 (44.59)	χ^2=5.475	0.019 (S)
Coronary artery disease	39 (17.73)	24 (16.44)	15 (20.27)	χ^2=0.494	0.482
Systemic hypertension	83 (37.73)	50 (34.25)	33 (44.59)	χ^2=2.238	0.135
Hypothyroidism	7 (3.18)	5 (3.42)	2 (2.7)	Fischer exact test	1.000
Medications (some drugs overlapped) (%)					
Diuretics	36 (16.36)	21 (14.38)	15 (20.27)	χ^2=1.243	0.265
Proton pump inhibitors	69 (31.36)	45 (30.82)	24 (32.43)	χ^2=0.059	0.808
Antiepileptics	1 (0.45)	0	1 (1.35)	Fischer exact test	0.336
SSRIs	6 (2.73)	4 (2.74)	2 (2.7)	Fischer exact test	1.000
Average duration of hospital stay (days)		8.58±4.81	10.26±4.61	*t*-test 2.476	0.014 (S)

SSRIs: Selective serotonin reuptake inhibitor, S: Significant

Table 2: Sensitivity, specificity, positive predictive value, and negative predictive value of nausea and vomiting in postoperative period

	Sensitivity	Specificity	PPV	NPV
Nausea (95% CI)	25.68 (16.22-37.16)	96.58 (92.19-98.88)	79.17 (57.85-92.87)	71.94 (65.09-78.11)
Vomiting (95% CI)	13.51 (6.68-23.45)	98.63 (95.14-99.83)	83.33 (51.59-97.91)	69.23 (62.48-75.43)

PPV: Positive predictive value; NPV: Negative predictive value; CI: Confidence interval

Comparative Group B: Chronic- versus new-onset hyponatremia

Comparative data between Chronic and New-Onset hyponatremia is given in Table 3.

Demographic distribution

Among the 74 patients with hyponatremia, those with chronic hyponatremia were older (69 vs. 68 years). However, there was no statistically significant relationship with increasing age. Even though there was a male predominance to perioperative hyponatremia, no significant relationship to gender was noted between chronic- and new-onset hyponatremia.

There was an equitable distribution among the occurrence of hyponatremia with various surgeries as well as anesthesia given to the patient ($P > 0.05$).

Timing and grading of hyponatremia

Among the 43 patients with new-onset hyponatremia, 41 patients (95.34%) developed hyponatremia within the first 24 h of surgery. Only two patients (4.66%) developed hyponatremia in the subsequent 24 hours.

Forty (93.02%) patients with new-onset hyponatremia were of mild grade, whereas there was an almost equal distribution in those with chronic hyponatremia between mild (15 [48.39%]) and moderate grades (13 [41.94%]). Three (9.68%) patients with chronic hyponatremia were of profound grade. Patients with chronic hyponatremia were more likely to be of profound grade, and these findings were statistically significant ($P < 0.05$).

Serum sodium level trend during hospital stay

Serum sodium levels of patients who developed new-onset hyponatremia corrected within 48 h of surgery, whereas patients with chronic hyponatremia had a more gradual rise in serum sodium levels and did not achieve full correction, and this was found to be statistically significant ($P < 0.05$) [Figure 2].

Duration of hospital stay

Patients with chronic hyponatremia when compared to those who developed new-onset hyponatremia had a longer duration of total days of hospital stay (12.9 vs. 8.3 days). A statistically significant relationship of $P < 0.0001$ between chronic hyponatremia and longer hospital days stay was determined.

Table 3: Comparison between chronic- and new-onset hyponatremia

	Presented with hyponatremia (chronic) (*n*=31)	Developed postoperative hyponatremia (new onset) (*n*=43)	Statistical test	*P*
Demographics				
Age (years)	69.97±8.67	68.54±8.55	*t*-test=0.707	
Gender				
Male	22	29	Chi-square test=0.105	0.746
Female	9	14		
Rural background	11	23	Chi-square test=2.351	0.125
Grading of hyponatremia (%)				
Mild (130-134 mmol/L)	15 (48.39)	40 (93.02)	χ^2=19.172	<0.0001 (S)
Moderate (125-129 mmol/L)	13 (41.94)	3 (6.98)		
Severe (120-124 mmol/L)	3 (9.68)	0		
Serum sodium level trend				
On admission	128.94±3.79	136.6±1.65	Independent *t*-test=−10.56	<0.0001 (S)
POD 0 (within 6 h)*	131.81±7.18	132.51±1.74	Mann-Whitney test=−1.63	0.103
POD 1 (within 24 h)	132.9±4.5	134.98±2.26	Mann-Whitney test=−2.36	0.049 (S)
POD 2 (next 24 h)	133.74±3.65	136.14±3.02	Mann-Whitney test=−2.90	0.004 (S)
Type of surgery (%)				
Hip	18 (58.1)	15 (34.8)	Chi-square test=3.036	0.081
Knee	4 (12.9)	8 (18.6)	Fisher exact test	0.750
Foot and ankle	5 (16.1)	3 (6.9)	Fisher exact test	0.267
Upper limb	2 (6.4)	9 (20.9)	Fisher exact test	0.106
Type of anesthesia (%)				
General	2 (6.4)	9 (20.9)	Fisher exact test	0.106
Regional	29 (93.6)	34 (79.1)		
Duration of hospital stay (days)	12.94±3.92	8.33±4.1	*t*-test=4.86	<0.0001 (S)
Mortality (%)				
No	29 (93.55)	43 (100)	Fischer exact test	0.172
Yes	2 (6.45)	0		

POD: Post-Operative days, *S: Significant

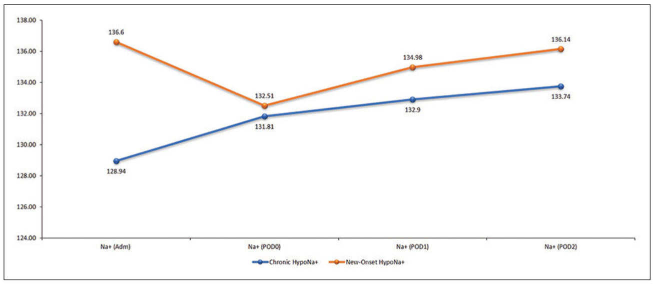

Figure 2: Trend of serum sodium concentration in chronic- and new-onset hyponatremia with correction

Mortality

In our study sample of 220 patients, three cases of mortality were noted out of which two patients were chronically hyponatremic prior to surgery and one patient remained normonatremic throughout the hospital stay. No significant relationship was present between mortality and perioperative hyponatremia. Even when compared between chronic- and new-onset hyponatremia, no significant relationship was noted.

Discussion

Epidemiology of hyponatremia

In the present study, 39 patients presented to the hospital with hyponatremia, and the prevalence of hyponatremia during hospitalization was found to be 14.1%. Studies by Waikar *et al*.[6] and Cumming *et al*.[9] observed similar findings with prevalence of hyponatremia to be 14.5% and 13.4%, respectively. Mohan *et al*.[10] and Hennrikus *et al*.[11] observed lower prevalence (1.72% and 7%) of hyponatremia, probably because these studies included patients of younger age (≥18 years) with a mean age of 45 years and 62.5 years, respectively. Our study included patients aged ≥60 years with a mean age of 68.2 ± 8.1 years, which was higher than those of Mohan *et al*.[10] and Hennrikus *et al*.[11] However, Grant *et al*.[12] noticed a higher prevalence of hyponatremia of 21%, probably because the study included patients of older age than the present study (mean age = 82 years).

Among the 189 patients who were normonatremic prior to surgery, 43 patients developed acute new-onset hyponatremia postoperatively with an incidence of 22.7%. This finding was in keeping with studies by Grant *et al*.[12] and Rudge and Kim.[13] The incidence noted by McPherson and Dunsmuir[14] and Tambe *et al*.[15] was much lower than our present study, which was probably because these studies used serum sodium level <130 mmol/L as the definition for hyponatremia.

Timing of acute new-onset hyponatremia development

Majority of the patients (95.34%) developed new-onset hyponatremia within the first 24 hours of surgery. This result was similar to the study by Hennrikus *et al*.[11] (93%). Findings of studies by McPherson and Dunsmuir[14] and Tambe *et al*.[15] were not comparable with those of the present study as both studies defined hyponatremia as serum sodium <130 mmol/L.

Demographic distribution

The mean age of the patients with hyponatremia was found to be more than that of the patients who were normonatremic (69.1 vs. 67.8 years). However, no significant relationship was noted.

A significant relationship to gender with a male predominance to hyponatremia was observed ($P = 0.017$). These findings were similar to the study by Leung *et al*.;[7] however, Mohan *et al*.[10] and Grant *et al*.[12] observed that the incidence of postoperative hyponatremia was more likely in females. Studies by Hagino *et al*.,[16] Rudge and Kim,[13] Cumming *et al*.,[9] and Hennrikus *et al*.[11] did not find any significant relationship between gender and hyponatremia. No statistically significant relationship was observed between perioperative hyponatremia and residential area, cause for admission, or ambulatory status prior to injury/admission.

Relationship to comorbidities and medications' intake prior to admission

It was also observed that patients with coronary artery disease on diuretics were more likely to present with hyponatremia on admission ($P = 0.029$), whereas patients with diabetes mellitus were more likely to develop hyponatremia at some point during their hospital stay, either preoperatively or postoperatively ($P = 0.019$).

Trend of serum sodium level in perioperative period

Patients with new-onset hyponatremia had a drop in serum sodium levels within 6–24 hours after surgery which was corrected within 48 hours of surgery with adequate management of hyponatremia. However, those with chronic hyponatremia had a more gradual rise in serum sodium levels in spite of appropriate management and did not achieve full correction within 48 hours of postoperative period.

Most cases of new-onset hyponatremia develop within the first 24 hours of surgery. Treatment is simple and should be prompt; the risk of not treating acute cerebral edema far exceeds the small risk of osmotic demyelination from treatment.[17,18] Fluid infusions should be restricted to normal or hypertonic saline, and sodium concentrations should be monitored every 2 hours. The aim is to raise serum sodium by 1–2 mmol/L/h (depending on the severity of neurological symptoms) until symptoms resolve. A loop diuretic such as furosemide may be used to enhance free water excretion and hasten the restoration of normal sodium concentrations.[17,18]

To the best of our knowledge, no other study has observed the trend of serum sodium levels in the perioperative period.

Grading of hyponatremia in postoperative period

Patients with chronic hyponatremia were found to continue to be hyponatremic after surgery, with an equal distribution between mild (48.3%) and moderate (41.9%) grades of hyponatremia. However, 93.1% of patients with new-onset hyponatremia were of mild grade, with the remaining 6.9% of moderate grade. None of the patients with new-onset hyponatremia were of profound grade, whereas 9.6% of those with chronic hyponatremia were of profound grade postoperatively. McPherson and Dunsmuir[14] noticed that 66.6% of patients were of moderate grade, whereas the remaining were of severe grade. These results vary from our study as McPherson and Dunsmuir defined hyponatremia as <130 mmol/L and severe hyponatremia as <125 mmol/L. The study by Rudge and Kim[13] had less cases of mild grade and more cases of moderate grade, probably because the study included patients of older age group with a higher mean age when compared to the present study (82 vs. 68 years).

Postoperative hyponatremia-related symptoms

Patients with hyponatremia were more likely to experience nausea ($P < 0.0001$) and vomiting ($P = 0.0004$) in the early postoperative period (within 48 h) when compared to those patients who remained normonatremic during their hospital stay.

The PPV for nausea and vomiting was 79.17% and 83.33%, respectively. This means that, among the patients who had nausea, 79.17% of them were hyponatremic either preoperatively or postoperatively, and among the patients who had vomiting, 83.33% of them were hyponatremic either preoperatively or postoperatively. To the best of our knowledge, no other study has determined the PPV for hyponatremia-related postoperative symptoms.

Duration of hospital stay

A longer duration of stay for patients with hyponatremia (10.2 ± 4.6 vs. 8.5 ± 4.8 days) was noted with a statistically significant relationship ($P = 0.014$). This finding was comparable to the results by various other studies by Hennrikus *et al*.,[11] Cumming *et al*.,[9] Hagino *et al*.,[16] and Rudge and Kim.[13]

Among the patients with hyponatremia, it was observed that patients with chronic hyponatremia had a longer duration of stay (12.9 ± 3.9 vs. 8.3 ± 4.1 days). This result was statistically significant ($P < 0.0001$) and was probably because serum sodium levels of most patients with new-onset hyponatremia were corrected within 48-h postsurgery (mean serum sodium level on POD 2, 136.14 mmol/L). To the best of our knowledge, no other study compared the relationship of total hospital days between chronic- and new-onset hyponatremia.

Relationship to mortality

No statistically significant relationship was found between perioperative hyponatremia and mortality. We observed mortality in 2.7% of the patients who were hyponatremic.

The main limitation of our study was that it was from a single center, and we suggest that a better representation of the population may be obtained by a multicentric trial. It is also suggested that these patients may also be followed up for a longer period of time to study morbidity and mortality.

Conclusions

The prevalence and incidence of chronic- and new-onset hyponatremia were 14.1% and 22.7%, respectively. It is evident from the study that chronic hyponatremia and new-onset hyponatremia have different manifestations and effects during the course of hospital stay.

Patients who presented with chronic hyponatremia were of more severe grade and had a gradual rise in serum sodium levels even with appropriate management protocols, without achieving full correction in the early postoperative period. These cases would require a more cautious and guarded approach. They also had longer duration of hospital stay.

Most cases of new-onset hyponatremia develop within the first 24 hours of surgery. They are of lesser grade and respond quickly to correction. We should be on the lookout for new-onset acute hyponatremia and its complications as the risk of not treating acute cerebral edema far exceeds the small risk of osmotic demyelination from treatment.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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