DOI: 10.7860/JCDR/2022/59795.17058

Postoperative Hyponatraemia following Major Orthopaedic Surgeries: Incidence and Risk Factor Assessment

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ABSTRACT

Introduction: Postoperative Hyponatraemia (POH) commonly goes unrecognised and untreated. Previous studies have shown that POH is fairly common following orthopaedic surgeries. However, there are very limited prospective studies to estimate the incidence of POH, especially in the Indian scenario.

Aim: To evaluate the serum sodium level change postoperatively in patients undergoing major orthopaedic surgeries and to evaluate its risk factors for the same.

Materials and Methods: A prospective longitudinal study was conducted for a period of six months (September 2019 to February 2020) at a tertiary hospital in Sikkim, India. A total of 98 adult patients undergoing major orthopaedic surgical procedures of the lower limb and spine (fixation of long bones, joint replacement surgeries, spine fixation surgeries), were observed for development of early (day 1) and delayed (day 5) POH. Various risk factors (such as age, gender, preoperative sodium level, type of surgery, duration of surgery, co-morbidities, and perioperative fluid used) were analysed for the development of POH were evaluated.

Results: The study found that 17 (17.3%) out of the total 98 patients, developed POH within 24 hours of surgery and no delayed POH was observed. Those who developed early POH started with low serum Na levels preoperatively and the mean change in Na level was significantly higher among them (5.42±1.4 mmol/L, p-0.001) as compared to postoperative normonatraemia patients (4.3±1.2 mmol/L). Increasing age, diabetes mellitus, preoperative sodium (Na) level, duration of surgery, and use of dextrose fluid intraoperatively were found to be significantly associated with developing early POH. After adjusting for the factors which showed a significance of p<0.1 in the univariate analysis, low preoperative Na (mmol/L) (AOR=0.48; 95% CI=0.32- 0.72; p<0.001) and duration of surgery (in hours) (AOR=1.8; 95% CI=1.04-3.2; p-0.035) were found to be the most statistically significant risk factors for POH. All of 17 patients with POH had normal sodium levels by postoperative day five, showing the transient nature of the drop in Na level.

Conclusion: Although POH is fairly common after orthopaedic surgeries (17.3%), it is early and transient in nature and easily correctable. Preoperative sodium level, duration of surgery are the major risk factors for POH.

Keywords: Fluid balance, Orthopaedic surgery, Postoperative complication, Sodium

INTRODUCTION

Sodium is the principal cation present in the extracellular fluid and sodium levels are controlled by intricate homeostatic mechanisms. Hyponatraemia (<135 mmol/L) is a common electrolyte imbalance among all branches of medicine, including patients undergoing orthopaedic surgery, occurring postoperatively in about 30% of orthopaedic surgeries [1]. The greatest association between hyponatraemia and mortality is seen in patients with cardiovascular disease, metastatic cancer and those undergoing orthopaedic surgery, with orthopaedic surgery exhibiting the highest risk [2]. Both hyponatraemia and hypernatraemia are associated with an increased 30 day mortality risk [3]. This could result in an increased length of hospital stay as compared to normonatraemic patients, thereby incurring greater healthcare costs which increase the patient burden [3,4]. The POH presents with vague symptoms and is commonly misdiagnosed as postoperative sequelae [5,6]. Thus, hyponatraemia commonly goes unrecognised and untreated.

Studies have identified multiple risk factors for the changes in serum sodium levels perioperatively. Hypovolemia and Syndrome of Inappropriate Anti-Diuretic Hormone secretion (SIADH) have been found to be the most common causes of POH [1]. Medications such as thiazide diuretics, non steroidal anti-inflammatory drugs, and selective serotonin reuptake inhibitors have been shown to affect serum sodium levels in hospitalised patients [2,4,7]. Hypotonic fluids have been shown to cause POH [6]. Greater number of hyponatraemia cases are reported in patients receiving hypotonic fluids when compared to those receiving isotonic fluids [8,9]. Among the isotonic fluids administered, the commonest choices being Normal Saline (NS) solution (0.9%) and Ringers Lactate (RL) solution, POH depends on the amount of isotonic fluid being administered [2].

Although previous studies have recorded hyponatraemia to be common following orthopaedic surgeries [2-6], a majority of them were retrospective studies. To the best of our knowledge, no prospective studies have been done to estimate the incidence of the POH have been done in the Indian scenario. Owing to the differences in both anaesthetic and surgical practices in different countries, regionalised studies are needed to estimate the disease burden and to take suitable measures in preventing and treating POH. Thus, the present study was conducted to evaluate the serum sodium level change postoperatively, to estimate the incidence of POH in patients undergoing major orthopaedic surgeries, and evaluate risk factors for the same.

MATERIALS AND METHODS

A prospective longitudinal study was conducted in the Department of Orthopaedics, at a tertiary care centre in Sikkim, India. The study was conducted for the duration of six months i.e. from September 2019 to February 2020. Ethical clearance was obtained from the Institutional Ethics Committee (IEC) (SMIMS IEC Registration No: IEC/522/19-55). Informed consent was obtained from the participants.

Inclusion criteria: Adult patients undergoing major orthopaedic surgical procedures of the lower limb and spine (fixation of long bones, joint replacement surgeries, spine fixation surgeries) from September 2019 to February 2020, were included in the study.

Exclusion criteria: Patients with head injury, polytrauma, and co-morbidities that can affect sodium levels such as congestive cardiac failure, chronic kidney disease, liver cirrhosis, hyperglycaemia, and pregnant women were excluded from the study. Patients on medications that can affect sodium levels such as thiazide diuretics and warfarin were also excluded.

A total of 100 patients who underwent internal fixation for fracture of long bones of lower limb and spine, primary hip or knee arthroplasty were enrolled for the study following the inclusion and exclusion criteria mentioned above. Of these, complete data were missing in two patients, hence 98 patients were included in the study.

Morning venous samples on the day of surgery were used to measure preoperative serum sodium (Na) levels. Sodium levels were corrected for hyperglycaemia using the formula: measured Na level + 2.4X(glucose level [mg/dL] - 100)/100 [10]. Hyponatraemia was defined as a Na level of <135 mmol/L [11]. Development of hyponatraemia on postoperative day one was considered as 'early POH', and on day five was considered as 'delayed POH'. Patient demographic details(age, gender, Body Mass Index (BMI)), co-morbidities, type of surgery, and preoperative sodium level were recorded preoperatively. The anaesthesia records were evaluated for intraoperative variables such as duration of surgery, intraoperative intravenous fluids, drugs administered, and blood transfusion. Similarly, postoperatively serum sodium levels on postoperative day one and five were measured to determine early and delayed hyponatraemia respectively. Postoperatively development of symptoms such as nausea, vomiting, weakness, and any neurological symptoms were recorded. Patients were monitored for the development of postoperative complications.

STATISTICAL ANALYSES

Data collected were analysed using Statistical Package for Social Sciences (SPSS) version 20.0 for Windows10 (IBM®). Data were reported as frequency and percentage for categorical variables and mean and standard deviation (SD) for normally distributed continuous variables. Categorical variables were analysed using the Chi-square test. Continuous variables, between the groups who developed POH and those who did not, were compared using an 'independent sample t-test. Logistic regression analysis was used to determine factors associated with hyponatraemia. The 'adjusted Odds Ratio'(AOR) was calculated by entering variables with a p-value of <0.1 in the bivariate analysis into a multivariable binary logistic regression analysis to identify the independent risk factors for POH. AOR with a corresponding 95% Confidence Interval (CI) was used to investigate the strength of the association. Statistical significance was considered at a 95% level of confidence and p-value <0.05.

RESULTS

The study group consisted of 57 (58%) males and 41 (42%) females. The mean age of the participants was 47±17 years. No patient had more than one surgery [Table/Fig-1]. POH was seen in 17 (17.3%) out of the total 98 patients, all of which developed within 24 hours of surgery (early POH). Increasing age, diabetes mellitus, preoperative Na level, duration of surgery, and use of DNS intra-operatively were found to be significantly associated with developing early POH [Table/Fig-1]. After adjusting for the factors which showed a significance of p<0.1 in the univariate analysis, age, preoperative Na (mmol/L), and duration of surgery (in hours) were found to be the most statistically significant predictors [Table/Fig-2]. Although increasing age was significantly associated with POH, it was seen that age did not increase the risk of POH (AOR=1.04; 95% CI=1-1.08, p-0.022). Both preoperative Na and duration of surgery were treated as continuous variables. Present study found a reduced risk of POH (AOR=0.48; 95% CI=0.32- 0.72; p<0.001) for every 1 mmol/L increase in preoperative Na and an increased risk of POH (AOR=1.8; 95% CI=1.04-3.2; p-0.035) for every one hour increase in duration of surgery [Table/Fig-2].

Variables	Total group	Hyponatraemia		p-value
		Yes	No	
Gender (n,%)				
Male	57 (58)	9 (16)	48 (84)	0.631
Female	41 (42)	8 (19)	33 (81)	
Age (mean±SD)	47±17	56±13	45±17	0.012*†
BMI (mean±SD)	25.4±3	26±3	25±4	0.652†
Co-morbidities (n,%)				**0.004#****
None	71 (71)	9 (13)	62 (87)	0.11
Diabetes	11 (11)	5 (45)	6 (55)	0.01**
Hypertension	14 (14)	3 (21)	11 (79)	0.08
Hypothyroidism	2 (2)	0	2 (100)	0.99
Preoperative Na (mean±SD)	144±2.4	141±3	144±±2	0.001†**
Type of surgery (n,%)				**0.556#**
Fracture fixation	59 (60)	9 (15)	50 (85)	0.77
Joint replacement	30 (30)	7 ((23)	23 (77)	0.88
Spine fixation	9 (10)	1 (11)	8 (89)	0.80
Duration of surgery (mean±SD)	3.2±1	4±0.9	3±±1	0.001†**
Anaesthesia (n,%)				**0.449#**
Spinal	85 (87)	16 (19)	69 (81)	0.9
GA	13 (13)	1 (8)	12 (92)	0.8
Intraoperative IVF (mean±SD)				
NS	113±273	176±430	100±±229	0.297†
RL	1751±698	1676±±635	1766±714	0.631†
DNS	15±86	58±166	6±55	0.022†*
Perioperative PRBC transfusion (mean±SD)	71±158	61±137	73±163	0.78
Intraoperative antibiotic (n,%)				
Ceftriaxone + Amikacin	62 (63)	10 (16)	52 (84)	0.612
Tazobactam+ Piperacillin	36 (37)	7 (19)	29 (81)	
Change in sodium from preoperative and postoperative day1 (mean±SD)	5.6±2.3	7.34±2.9	5.3±2	0.001†**
Mean change in sodium from postoperative day 1 and postoperative day5 (mean±SD)	4.5±1.3	5.42±1.4	4.31±1.2	0.001†**
Length of stay (mean±SD)	17±4	21±5	17±4	0.003†**

[Table/Fig-1]: Comparison of variables of patients with and without postoperative hyponatraemia.
BMI: Body mass index; GA: General anaesthesia; IVF: Intra venous fluid; NS: Normal saline; RL: Ringer's lactate; DNS: Dextrose normal saline; PRBC: Packed red blood cells
†Independent t-test was used to compare continuous variables;
#Binary logistic regression was used to compare variables within the independent variable.
*p-value <0.05.

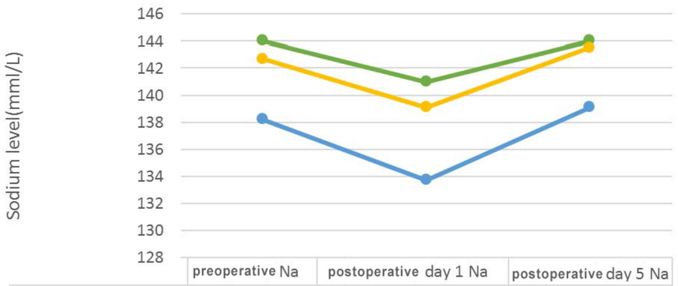
Variable	Adjusted odds ratio	95% Class interval		p-value
		lower	higher	
Age	1.04	1.00	1.08	0.022*
Preoperative sodium	0.48	0.32	0.72	0.001**
Duration of surgery	1.8	1.04	3.2	0.035*
Intraoperative DNS	1	0.99	1.00	0.763
Diabetes	1.1	0.7	11	0.936
HTN	1.4	0.1	20	0.783

[Table/Fig-2]: Risk assessment for postoperative hyponatraemia.
AOR-Adjusted Odds Ratio, calculated by the multivariable logistic regression model * p-value <0.05. ** p-value <0.01. DNS- dextrose normal saline, HTN-hypertension.

Those who developed early POH started with low serum Na levels preoperatively and the mean change in Na level was significantly higher among them (5.42±1.4 mmol/L, p-0.001) as compared to postoperative normonatremia patients (4.3±1.2 mmol/L).

POH was associated with nausea in five patients. No other complications were experienced among those who developed hyponatraemia. All 17 patients with postoperative day one Na

<135 mmol/L, had normal sodium levels by postoperative day five, showing the transient nature of the drop in Na level [Table/Fig-3] shows the mean Na at preoperative day one and day five. shows the mean Na at preoperative, day one, and day five.



	preoperative Na	postoperative day 1 Na	postoperative day 5 Na
total	144	141	144
hyponatraemia	138.2	133.7	139.1
no hypontraemia	142.7	139.1	143.5

Time

[Table/Fig-3]: Comparison of mean sodium levels between groups.

DISCUSSION

Hyponatraemia is a common occurrence in both medical and surgical units and is considered to be the most common electrolyte imbalance. Apart from medical causes, surgery is considered one of the major risk factors for developing hyponatraemia. Postoperative hyponatraemia can occur after all surgical procedures in general, [12] particularly it is more common after organ transplantation, cardiovascular, [13] gastro-enterology, and trauma surgery [14]. Orthopaedic patients are particularly at risk of developing POH because of the fragility, the fracture, the co-morbidities, the multiple pharmacological therapies, the perioperative fluid restrictions, and surgery [6,14,15]. Hence, the various previously published reports on hyponatraemia after orthopaedic surgeries have reported the incidence to be 4-40% [2,10,16-18]. The majority of them have been retrospective studies and include different kinds of orthopaedic surgical procedures. The present study found the incidence of POH to be 17.3%, which was less than few of the recently published studies (30%, [2] 27%, [17] 22% [18]). The difference in fluid management, and basic patient parameters, nature of the injury, surgical procedures could all be the causes for discrepancies in the incidence rate of POH. In the present study, all POH cases developed within 24 hours of surgery and were normonatraemic within five days with adequate fluid management, similar to the studies by Hennrikus E et al., [2] and Sinno E et al., [17] giving an impression that POH is early and transient.

Commonly mild hyponatraemia presents with vague symptoms such as nausea, vomiting, and weakness which often go unrecognised and untreated as these vague symptoms are sometimes attributed to the postoperative status of the patient. Confusion, weakness, etc. due to hyponatraemia in a geriatric patient with skeletal trauma can potentially increase the risk of falls when mobilisation is attempted or delay this process [6]. Hence having a watchful eye and regular monitoring of serum electrolytes during the postoperative period is necessary. The exact aetiopathogenesis of POH still is uncertain. However, most accepted theories are the ones related to stress-induced responses during surgery. A stress-induced increase increase in antidiuretic hormone secretion, is recognised as a possible mechanism of this electrolyte disorder [19]. Another stress-induced response is the increased cellular membrane permeability, which could be considered in the redistribution of solutes during surgery [20]. Although the cause is not clear, several risk factors have been identified for the drop in sodium levels following surgical procedures. Age, gender, ongoing medications, preoperative serum sodium and glucose level, type of surgery, duration of surgery, and perioperative fluid management have all been identified as risk factors for POH [2-6,16-18].

Among the patient characters, age, female sex, low body weight, and diabetes mellitus have been found to be predominant risk factors [2-6,16-18] Probable risk of hyponatraemia with an increase in age has been attributed to increased incidence of idiopathic SIADH, and 'frailty' [21,22]. Frailty is defined as a clinical syndrome, characterised by progressive sarcopenia or loss of skeletal muscle mass [23]. Similarly in the present study, it was found that increasing age is associated with POH, however, on multivariate analysis the adjusted risk was almost equal to 1. The relatively young age group (mean age 47±17 years) of present study population could explain this statistically significant yet relatively reduced risk (AOR=1.04; 95% CI=1-1.08; p-0.022). Serum glucose and sodium act co-dependently. It is well established that hyperglycaemia reduces serum sodium levels. Diabetes mellitus has been associated with an increased incidence of hyponatraemia in community studies and with increased ADH levels [24,25]. The presence of diabetes was shown to be significantly high among those who developed POH as compared to normothermic, however, on multivariate analysis it was not found to be an independent risk factor suggesting that there may be other contributory mechanisms as stated by Cunningham E et al., [18]. The most consistent risk factor in studies related to POH, including ours, is the preoperative level of sodium. Mean change in sodium level is an important factor to consider. The average drop in sodium level in previous studies has been found to be 3 to 4 mmol/L, which is an important fact to be considered [17,18]. The mean change of the total study group (4.5±1.3 mmol/L) as well as in those who developed POH (5.42±1.4 mmol/L) in present study was found to be higher than in these studies. The mean difference in sodium level was found to be a significant factor (p-0.001). However, the starting point of sodium level in present study group was higher to begin with, which might explain the lower incidence of POH as compared to these studies.

Intraoperative factors such as intraoperative fluid, in particular, RL and dextrose-containing fluids, type of surgery, and duration of surgery have been associated with an increased risk of POH. Administration of hypotonic fluids was also established as a cause of hyponatraemia [1,4]. In their study of defining the cause of POH in the orthopaedic patient, Hennerikus E et al. observed that the two major causes were hypovolemia and SIADH, in both the cases, hypotonic fluids will decrease plasma Na and should be avoided [1]. Carandang F et al., [8] established the greater risk of developing hospital-acquired hyponatraemia with hypotonic fluids as compared to isotonic in children. Neville KA et al., concluded that the risk of hyponatraemia was decreased by isotonic saline solution and not fluid restriction in postoperative children [9]. In the present study, although dextrose was found to be a significant association with POH, but not a significant risk factor (AOR=1.1; 95% CI=0.9-1; p-0.763). Considerably less amount of DNS use (mean=15±86 mL) might affect the interpretation of this result. Hennrikus E et al., [2] showed that spine surgery (AOR-2.76; 95% CI=1.63 - 4.70; p<0.001) and hip joint replacement (AOR-1.76; 95% CI=1.25 - 2.48; p<0.001) had a higher risk for POH as compared to knee replacement surgery. The present study identified only the duration of surgery to be a significant risk factor and not the type of surgery. Both surgeon and anaesthetist-related factors as well as intraoperative patient conditions play a role in this. Variables in surgical techniques among surgeons and intraoperative fluid management methods differ between institutions limiting the generalisation of this finding. However, prolonged surgical time, especially in orthopaedics implores a higher fluid balance challenge which might explain the increased risk. Patients who developed hyponatraemia had a longer hospital stay thus also increasing the cost incurred. Such longer hospital stays were also observed by various previous studies [2-4]. Although POH has been related to increased duration of hospital stay in these studies, including the present study POH being the sole cause for this prolonged stay is questionable as study have found that there are varied causes for it [18].

Being a prospective study, unlike many previous studies, authors were able to get most of the data accurately and also treat the newly diagnosed POH cases, hence were able to show the transient nature of the POH in orthopaedic patients. As the pre-existing medical co-morbidities, which would affect sodium levels were excluded, it is believed that the study represents a near accurate measure of POH. Patients presenting with hyponatraemia were excluded from the study. Sodium level was measured on the day of the surgery rather than at the time of admission, hence negating the effect of dehydration, fluid infusion, or other medications which might affect the sodium level.

Limitation(s)

The study did not attempt to classify hyponatraemia as euvolemic, hyper, or hypovolemic hyponatraemia, which prevents us from predicting the aetiology of the condition. The study did not measure intraoperative blood loss, postoperative intensive care admission, amount of analgesics used, which might have an effect on postoperative sodium level. Patient profile, surgical techniques, and anaesthesia protocols differ among institutions, which might limit the generalisation of the study.

CONCLUSION(S)

Although POH is fairly common after orthopaedic surgeries (17.3%), it is early and transient in nature and easily correctable. Preoperative sodium level and duration of surgery are the major risk factors for POH. Sodium level change is predictable and hence, maintaining normal sodium levels preoperatively and developing protocols for the management of geriatric patients, and reducing operating time could help in preventing POH.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Sep 03, 2022
- Manual Googling: Sep 27, 2022
- iThenticate Software: Sep 30, 2022 (15%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 22, 2022**
Date of Peer Review: **Sep 14, 2022**
Date of Acceptance: **Oct 01, 2022**
Date of Publishing: **Nov 01, 2022**