PROGNOSIS OF INTENSIVE CARE UNIT ACQUIRED HYPERNATREMIA IN DIFFERENT AGE GROUPS AND GENDER

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ABSTRACT

Objective: To find out the frequency of intensive care unit acquired hypernatremia in critically ill patients and to find out the outcomes in terms of mortality/discharge with respect to age and gender.
Study Design: Cross sectional study.
Place and Duration of Study: Medical, trauma and surgical intensive care unit settings of Combined Military Hospital Kohat, from Jun 2018 to Jun 2019.
Methodology: A total of 100 patients were enrolled who were normonatremic at the time of intensive care unit admission. Patients were followed for 2 weeks of their stay for intensive care unit acquired complications and mortality. Serum sodium levels along with other investigations were carried out on daily basis from a single pathology laboratory. Data including the clinical diagnosis, APACHE II score and intensive care unit acquired complications was recorded on a proforma. Data was analyzed using SPSS version 22 and Microsoft Excel 365.
Results: The frequency of intensive care unit acquired hypernatremia was 46 (46%) further classified into mild 13 (13%), moderate 15 (15%) and severe 18 (18%) hypernatremia. The overall mortality was 30 (30%), 10 (18.5%) and 20 (43.5%) cases in normal and raised serum sodium group respectively. We reported a slightly higher frequency of Intensive care unit acquired hypernatremia in our study. The mortality was also significant in hyponatremic group.
Conclusion: Intensive care unit acquired hypernatremia was an invaluable marker for quality health care in critically ill patients and it's also an important risk factor for Intensive care unit associated mortality.

Keywords: Critically ill, Hypernatremia, Hypokalemia, Intensive Care Unit Acquired Hypernatremia.

INTRODUCTION

Fluid and Electrolyte imbalance is common in hospitalized patients, but it is one of the grave complications occurring in critical care patients. This imbalance may lead to severe morbidity and mortality and is an invaluable prognostic marker[1]. Sodium ion is the most predominant electrolyte in human body and our body maintains it at physiological levels of 135 mmol/L to 145 mmol/L despite fluctuating sodium and water intake through out the day. A variety of physiological defense mechanisms including thirst response, renin-angiotensin aldosterone axis, secretion of antidiuretic hormones, sympathetic nervous system and vasopressins are responsible for strict and tight regulation of sodium ion in the body[2]. Patients admitted to ICU are prone to electrolyte imbalance due to limited access to fluids and already existing debilitated state. Dysnatremia is known as disorder of sodium homeostasis in the body and is further classified as hyponatremia (<135mmol/L) and hypernatremia (>145mmol/L). Hyponatremia being the commonest has been studied extensively so far, however lesser research is done on hypernatremia[3]. Hypernatremia is an important electrolyte disturbance in institutionalized patients. A relative decrease in total body water concentration to the existing electrolytes is the cause. Increased serum sodium concentration is almost always associated with hyperosmolality. It leads to intracellular dehydration which has drastic effects on bodily systems especially on central nervous system (CNS)[4]. The critically ill patients of medical, surgical and trauma intensive care setups are known to suffer from an entity called ICU-Acquired hypernatremia. ICU-

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Acquired Hypernatremia (IAH) is characterized by a rise of greater than 145 mmol/L in serum sodium concentration after 48 hours of ICU admission[5]. Hypernatremia is classified further as mild (145-149mmol/L), moderate (150-154mmol/L) and severe (>155mmol/L) hypernatremia. It is associated with a few ICU acquired complications which are assessed within 2 weeks of ICU stay after the onset of ICU-acquired hypernatremia. Several studies have shown increased length of ICU stay and higher mortality of ICU patients who had acquired hypernatremia[6]. Several studies have shown the incidence of acquired hypernatremia from 4% to 42.5% with higher mortality associated with it as compared to hypernatremia at admission[5]. Since, acquired hypernatremia is a preventable complication by appropriate fluid and electrolyte management, it's an instrument to gauge quality of critical care as well[7]. Recently, there has been a paradigm shift of investigators and researchers towards hypernatremia yet there is a room for accelerated research for this particular condition. The rationale of our study was to find the incidence of acquired hypernatremia in patients admitted to intensive care units and to determine the outcomes in terms of complications and mortality with respect to age and gender.

METHODOLOGY

It was a cross-sectional study carried out at surgical, trauma and medical ICU of Combined Military Hospital Kohat, for a duration of one year from June 2018 to June 2019. We sought informed written consent from patient's attendants. Institutional review board and hospital ethics review committee approved this study. We calculated the sample size using 'WHO sample size calculator' [CI 95%, Anticipated population proportion (prevalence of hypernatremia)=2 and 4% [1-5], absolute precision required=5%] and a sample size range of 31 to 59 was calculated but we included all the patients fulfilling the inclusion criteria during the study period i.e. 100. Non-probability consecutive sampling technique was used. The inclusion criteria in our study was, all adult patients of age 18 to 65 years and of both genders admitted to Surgical, medical and trauma Intensive care unit for >48 hours, and normonatremic (Na levels 135-145 mmol/l on admission). Patients with head trauma, post-operative cases of neurosurgery, renal insufficiency, craniopharyngioma or pituitary adenoma and incomplete information were excluded. The patients were divided into those with and without hypernatremia; based on serum sodium level. Detailed clinical assessment was done for all patients in the study. Clinical diagnosis, APACHE II score, and presence/absence of chronic medical ailment were documented. ICU-acquired complications developed within 2 weeks were comprised of onset of fever (documented temperature >101°F), hypokalemia (<3.5 mmol/l serum potassium concentration recorded on >2 occasions consecutively), metabolic acidosis (Blood pH <7.35), acute kidney injury (>26 µmol/l rise in serum creatinine levels or oliguria within 48 hours)[8], hypoproteinemia (serum albumin levels <35 g/l and total protein levels <64 g/l), impaired liver function (ALT> 55 U/l, rise in total serum bilirubin >1.5 mg/dl and >0.4 mg/dl conjugated bilirubin), and any GCS <15. Outcome was recorded in terms of mortality of the patient within 2 weeks of ICU stayor discharged home. We collected blood samples (venous) from all the patients with the help of expert nursing assistant. Serum sodium levels were analyzed in the same laboratory and were assessed by the same experienced pathologist. We strictly followed the exclusion and inclusion criteria in this study. Data was entered in and analyzed by SPSS version 22 and Microsoft Excel 365. For the quantitative variables we calculated mean and standard deviation. We presented frequency and percentages for qualitative variables. ICU acquired complications and mortality was compared by applying chi square test between patients with and without hypernatremia. A *p*-value ≤0.05 was considered statistically significant.

RESULTS

The mean age of patients was 50.62 ± 8.96 (30 to 65) years. Out of total 100 patients, 72 (72%) were male and 28 (28%) were female cases. The mean serum Na level was 137.95 ± 16.19 (mmol/

L) with range of 53 (mmol/L). In 54 (54%) of the cases the serum Na level was normal while in 46 (46%) of the cases serum Na level was raised. There were 13 (13%) cases that had mild, 15 (15%) cases had moderate and 18 (18%) cases had severe serum Na level (fig-1). Among cases who had normal serum Na level there were 34 (63%) cases who developed fever and 20 (37%) did not have fever, while among those who had raised serum Na level there were 30 (65.2%) cases were those who had fever and 16 (34.8%) cases had no fever. In patients having normal and raised serum Na level there were 17 (31.5%) cases and 16 (34.8%) cases that had hypokalemia respectively with no significant association.

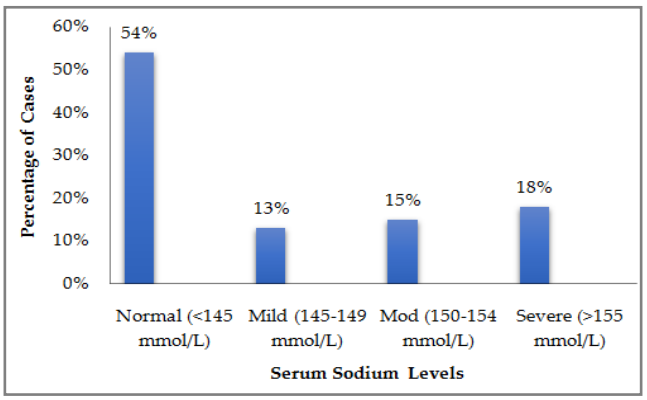

Figure-1: Frequency distribution of levels of serum Na (mmol/L).

Among patients having normal and raised serum Na level there were 48.1% cases and 56.5% cases had acute kidney injury respectively. On applying Chi-square test there was found a statistically insignificant association between serum Na level and acute kidney injury (table-I).

Metabolic acidosis was seen in 33 (61.1%) and 30 (65.2%) cases with normal and raised serum Na level respectively with no significant association. Impaired liver function was also seen in 17 (31.5%) and 18 (39.1%) of the cases in those who had normal and raised serum Na level respectively, result was statistically insignificant (*p*-value >0.05). There were 35 (64.8%) cases and 24 (52.2%) who had hypo-proteinemia and had normal and raised serum Na levels respectively (0.081). A total of 40 (74.1%) cases in normal serum Na group and 34 (73.9%) in raised serum Na level group had low GCS, again there was no significant association between the low GCS and serum Na level.

Table-I: Comparison of hypernatremia and acute kidney injury.

		Serum Na Level (mmol/L)		*p*-value
		Normal (<145)	Raised (≥145)	
Acute Kidney Injury	Yes	26 (48.1%)	26 (56.5%)	0.404
	No	28 (51.9%)	20 (43.5%)	

Table-II: Comparison of hypernatremia and mortality.

		Serum Na Level (mmol/L)		*p*-value
		Normal (<145)	Raised (≥145)	
Mortality	Yes	10 (18.5%)	20 (43.5%)	0.001
	No	44 (81.5%)	26 (56.5%)	

Table-III: Comparison of serum sodium levels and mortality with respect to age and gender.

		Mortality	Serum Na Level (mmol/L)		*p*-value
			Normal	Raised	
Age (Years)	30-45	Yes	6 (28.6%)	5 (38.5%)	0.549
		No	15 (71.4%)	8 (61.5%)	
	46-65	Yes	4 (12.1%)	15 (45.5%)	0.003
		No	29 (87.9%)	18 (54.5%)	
Gender	Male	Yes	7 (18.4%)	14 (41.2%)	0.034
		No	31 (81.6%)	20 (58.8%)	
	Female	Yes	3 (18.8%)	6 (50%)	0.040
		No	13 (81.2%)	6 (50%)	

A total of 30 cases died, as there were 10 (18.5%) cases and 20 (43.5%) cases in normal and

raised serum Na group who died. Result was statistically significant (0.001) (table-II).

When data was stratified for age and gender, we observed no association found between serum Na levels, gender and age, *p*-value >0.05. Association of sodium level and fever was seen in female cases only (*p*-value=0.02). Association of sodium level and hypo-proteinemia was seen in younger age group (*p*-value <0.05). Association of serum sodium level and mortality was seen in elder age groups of both genders (*p*-value <0.05) (table-III).

DISCUSSION

Sodium homeostasis is one of the most important requirements for appropriate functioning of body systems. Critically ill patients being debilitated and usually an elder population are vulnerable to fluctuations in serum sodium concentration. These fluctuations may lead to a cascade of catastrophic events and ultimately fatality[9].

Nicolini *et al*, has reported that ICU acquired hypernatremia as a single important risk factor for worst outcome in critically ill patients[10]. Critically ill are subjected to variety of treatments including intravenous blood and blood products, parenteral fluids they are often intubated, thus limiting their oral water intake. Often these treatments are the root cause for impending hypernatremia[11]. Hypernatremia effects the critically ill in a number of ways most important of which is the neurological complications rendering it more complicated and difficult to treat as sudden decrease in serum sodium level can also lead to cerebral edema[12]. In this single center prospective study carried out in surgical, medical and trauma ICU we came across a striking finding of higher incidence of ICU acquired hypernatremia (IAH). The incidence of IAH was 46% which is slightly higher than the previous studies on IAH in literature. Sakr *et al* reported >40% acquired hypernatremia at any stage in ICU admission[2]. Waite *et al*, in his study reported incidence of 4.3%. This huge variability may also occur because of difference in operational definitions as we labelled ICU acquired hypernatremia when serum sodium levels after 48 hours of ICU admission were greater than 145 mmol/L7. Laupland *et al*, reported that in 16 patients, fever was documented, and also identified the infection in all these cases. These 16 patients did not suffer a statistically significant higher mortality than those without fever (37% vs 27% *p*=0.38). In our study we have found that in normonatremic cases 54 (54%) there were 34 (63%) cases who developed fever and 20 (37%) did not have fever, while among those who had raised serum Na level there were 30 (65.2%) cases who had fever and 16 (34.8%) cases had no fever. These statistics are comparable to above study[13]. In a cohort study of 355 patients; all younger than 14 years of age Rao *et al* reported hypokalemia in 3.6%. One reason for this lower incidence could be the exclusion of patients who were dehydrated[14]. We, however, reported hypokalemia in higher number of cases, 17 (31.5%) cases with hypokalemia were having normal sodium level while 16 (34.8%) cases with hypokalemia were having raised serum sodium level without significant statistical association. A study reported frequency of acute kidney injury was in 50%[15]. Dubin *et al*, reported an incidence of acidemia in 14% cases[16] while Smith *et al*, reported ICU acquired acidemia in 42%[17]. However, majority of the patients in these studies had moderate acidemia (mean base excess of -3). In our study we have found that among patients having normal and raised serum Na level there were 26 (48.1%) cases and 26 (56.5%) cases had acute kidney injury, on applying Chi-square test there was significant association between serum Na level and acute kidney injury. Gunnerson *et al*, in a large study of 851 patients found out that the incidence of metabolic acidosis (mean base excess <-2 mmol/L) was 64%[18]. In another study, the incidence of metabolic acidosis was 6%[19]. In a study, the ICU acquired complications rate was noted as: fever (70.27%), hypokalemia (37.84%), metabolic acidosis (70.27%), impaired liver function (32.43%), hypo-proteinemia (52.70%), low GCS (71.62%)[15]. In current study found very different profile of complications like metabolic acidosis was seen in 33 (61.1%) and 30 (65.2%) cases with normal and raised serum Na level respectively with no

significant association. Impaired liver function was also seen in 17 (31.5%) and 18 (39.1%) of the cases in those who had normal and raised serum Na level respectively, and no statistically significant association was found between impaired liver function and hypernatremia (*p*-value >0.05). There were 35 (64.8%) cases and 24 (52.2%) who had hypoproteinemia and had normal and raised serum Na levels respectively, which is statistically insignificant. A total of 40 (74.1%) cases in normal serum Na group and 34 (73.9%) in raised serum Na level group had low GCS, again the association between the low GCS and serum Na level was not statistically significant.

Varun *et al*, reported that among hypernatremia patients, the mortality rate was 34.3%[20]. While Uchino *et al* and Mehta *et al*, added that incidences of Acute kidney injury in the intensive care unit (ICU) range from 1% to 25% with mortality rates ranging from 40% to 90% respectively[21,22]. Kumar *et al* reported that 9% of the patients with ICU Acquired Hypernatremia developed acute kidney injury (AKI) and odds of death in these patients was two fold[23]. Kinsuk Chauhan *et al* found no significant difference in terms of mortality amongst patients with pre admission hypernatremia versus ICU Acquired hypernatremia[24]. In current study a total of 30 cases died, as there were 10 (18.5%) cases and 20 (43.5%) cases in normal and raised serum Na group who died. Significant association was seen among ICU acquired hypernatremia and mortality. The mortality rate is almost similar as reported in above studies.

CONCLUSION

Our study showed a relatively greater frequency of ICU acquired hypernatremia in our population as compared to the recent studies in the literature. However, we could not find a statistically significant association between raised sodium concentration and ICU acquired complications, yet we found some association after we stratified sodium levels, gender, age and complications. We only found association in female gender and fever. Mortality, Serum sodium level and extremes of ages were also statistically associated. ICU acquired hypernatremia is a single important risk factor and is also an invaluable marker for quality health care provided to critically ill patients.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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