ORIGINAL ARTICLE

FREQUENCY, RISK FACTORS AND THE OUTCOMES OF PATIENTS ADMITTED WITH HYPONATREMIA IN A TERTIARY CARE SETUP

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ABSTRACT

Objective: To determine the clinical profile and risk factors associated with hyponatremia in subjects presented to a private tertiary care hospital.

Material & Methods: The prospective observational study was performed from July, 2017 to December 2018 at the Northwest General Hospital and Research Centre Peshawar. Convenient sampling was used and a structured format was used for data collection. The study comprised data of all patients who had sodium level less than 135 mmol/L.

Results: Out of 500 patients recruited for the study, 296(59.2%) were male and 204(40.8%) were female with a mean age of 52.5years. Mostly patients had euvolemia (65.6%). Altered mental status (76.6%), lethargy (21%), dizziness (18.4%) and headache (14.4%) were the most common symptoms. Hypertension (42.4%) and diabetes (50.8%) were most common risk factors. In all, 225 of patients had sodium level of 130-134 (45%), 156 had level of 120-129 (31.2%), 85 had 110-119 (17%) and 34 patients had sodium level less than 109 mg/dl (6.8%). Of the total 26 patients expired while 474 were discharged with improved sodium levels.

Conclusion: Hyponatremia increases in-hospital mortality risk. Physicians should be aware of the risk factors associated with hyponatremia for early diagnosis and prompt treatment.

Key Words: Electrolytes, Hyponatremia, Osmolality, Sodium.

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INTRODUCTION

Hyponatremia occurs primarily due to water imbalance, inability of the kidneys to excrete water and disturbance in antidiuretic hormone (ADH).[1,2] Electrolyte imbalance including hyponatremia, and fluid abnormalities are commonly found in hospitalized patients and known to be the most common causes of morbidity and mortality in hospitalized subjects.[3,4] Approach to hyponatremia is based on the medical history, physical examination and laboratory measurements. The specific causes of hyponatremia are divided on the basis of serum osmolality.[5] Based on the osmolality and volume status, etiology can be specified.[6]

Patients may be asymptomatic or complain of nausea and malaise. As the level of sodium falls, the symptoms progress to include headache and altered mental status. Severe neurological symptoms such as seizures and coma usually do not usually occur unless the sodium level is below 120 mmol/L or decreases rapidly, below normal.[7] Congestive heart failure, cirrhosis, nephrotic syndrome, and other underlying illnesses can be detected with a thorough history and physical examination. In practice, determining volume status can be difficult, however it should be estimated by looking at skin turgor, pulse rate, postural blood pressure difference, and jugular venous pressure, as well as looking at fluid balance charts.[8] A good

number of patients with hyponatremia are admitted daily in an acute care settings with a high morbidity and mortality.[5] Therefore current study was proposed to determine the frequency, risk factors and the outcomes of patients admitted with hyponatremia in a tertiary care setup.

MATERIAL AND METHODS

This prospective observational study was conducted at the Northwest General Hospital and Research Centre Peshawar. The hospital is a highly reputed tertiary care hospital situated in Peshawar to the residents of Khyber Pakhtunkhwa and Afghanistan. Data collection was done after taking approval from the department of general medicine and ethical committee of the Hospital. Non-probability convenient sampling technique was used. Duration of the study was from July, 2017 to December 2018.

The sample size was calculated using the formula $N=z^2p\ (1-p)\ /\ d2$. Different proportions of hyponatremia in hospital settings have been reported by different studies. According to a study by Nauman Tari,f 6.7% of hospitalized patients had moderate to severe hyponatremia.[14] Keeping in mind the study design, 500 patients were enrolled in the study due to the use of nonprobability sampling for a period of 18 months. Patients who had sodium level less than 135 performed as part of their evaluation were included. All patients with pseudohyponatremia secondary to hyperglycemia, hyperlipidemia and paraproteinemia were excluded. A structured format was designed and used for data collection which included demographic data including age, gender, clinical parameters, risk factors, drug used, and comorbidities. Patients volume status was determined by clinical examination by assessing the jugular venous pressure, presence and absence of peripheral edema, blood pressure, postural hypotension, skin turgor, dry mucous membranes and chest auscultation. This examination divided the cohort into three classes: hypovolemic, euvolemic and hypervolemic.

Serum osmolality was calculated using the serum osmolality formula, checking serum sodium, urea and glucose on arrival. Following formula was used for the calculation of serum osmolality: [9,10] Calculated Serum osmolality = (2 x serum [Na, in mmol/L]) + [glucose, in mg/dL]/18 + [blood urea nitrogen, in mg/dL]/2.8.The multiplier 2 accounts for the osmotic contributions of the anions accompanying sodium and potassium. The value of potassium is not used in the formula as the number is too small to be considered. Hyponatremia was defined as a serum sodium level of 135 mmol/L, as detected by laboratory tests.

The questionnaires were filled after an informed consent and patients were assured that all information was kept confidential. Daily review of the patients was done with a strict intake/output record, drugs monitoring, fluid management (resuscitation, restriction or diuretics) throughout the hospital stay. The risk factors including hypertension, diabetes, renal failure, malignancy, liver cirrhosis, cardiac failure, syndrome of inappropriate antidiuretic hormone secretion, hypothyroidism, drugs, remote vomiting, diarrhea, extra renal loss and recent surgeries were studied. A careful drug history was taken for the other possible cause of hyponatremia. Clinical outcome of the patients including discharge or expiry was also noted. A daily serum electrolyte was performed to assess the trend of hyponatremia. A value of serum sodium was also done at discharge to assess the final status. Renal profile including sodium, potassium, chloride, bicarbonate, urea, creatinine, also blood glucose, liver function tests, albumin, thyroid function tests, serum cortisol and lipid profile were noted wherever needed. Descriptive statistics were used. Frequency and percentages /mean and standard deviation were calculated. Data is presented in the form of tables and analysis was carried out through SPSS.

RESULTS

Out of 500 patients, 296 were males (59.2%) and 204 females (40.8%) with a mean age of 52.5 years. Out of 500, 225 of patients had sodium level of 130-134 (45%), 156 had levels of 120-129 (31.2%), 85 had 110-119 (17%) and 34 patients had sodium level less than 109mg/dl

(6.8%). In all, 447 patients had calculated serum osmolality of less than 280 mOsm/kg (89%), 25 patients had osmolality of 280 to 295 mOsm/kg (5%) and 28 patients had serum osmolality of more than 295 mOsm/kg (5.6%).

Most of the patients had euvolemia (65.6%) followed by hypervolemia 18.8%) and the least common being hypovolemia (15.6%). Majority of the 435 patients were symptomatic (87%). Out of those, most of the patients presented with altered mental status (AMS) (76.6%) and lethargy (21%), followed by dizziness (18.4%) and headache (14.4%). Only 3 patients presented with fits (0.6%). Out of the total patients studied, hypertension (42.4%) and diabetes (50.8%) were most common in the patients with hyponatremia followed by coronary artery disease (33.4%) and chronic kidney disease (20.8%). Drugs that caused hyponatremia were diuretics (45.2%), NSAIDs (38.6%) and ACE inhibitors (38.8%) (Table 1). The management of patients was dependent upon clinical presentation, severity of symptoms and volume status. Free water restriction was done in 381 patients. Patients with hypovolemic and euvolemic status were treated with intravenous normal saline and/or as per clinical condition. In cases of severe hyponatremia with neurological symptoms, Nasogastric tube was passed in 122 patients and oral 3% saline was administered till symptoms resolution. Drugs including ACE-inhibitors, antipsychotics were put on hold till sodium level improved. NSAIDs use strictly avoided.

Of the total 500, 26 patients expired due to critical conditions while 474 were discharged. Out of the 474 patients, 385 of the patients had sodium level normalized above 135 mmol/L, 55 of the discharged patients had sodium level from 130-134 mmol/L and 34 patients had sodium level 125-129 mmol/L.

Table 1: Clinical features on presentation, drug use history and underlying major diseases

Clinical presentation	**Frequency (n)**
Altered Mental Status	383
Headache	72
Dizziness	92
Nausea/ Vomiting	83
Fits	3
Lethargy	105
Asymptomatic	65
Associated Co morbidities	
Hypertension	212
Diabetes Mellitus	254
Chronic Kidney Disease	104
Malignancy	26
Coronary Artery Disease	167
Asthma/Chronic Obstructive Pulmonary Disease	99
Known history of Psychiatric Disorder	9
Thyroid Dysfunction	41
Benign Prostate Hyperplasia	61
Drugs	226
Diuretics	61
Antipsychotics	194
ACE inhibitors	52
Sulfonylureas	2
Opioids	7
Barbiturates	17
Chlorpropamide	1
Vincristine	193

DISCUSSION

Hyponatremia is the most frequent electrolyte imbalance seen in clinical practice, and it is associated with considerable mortality as well as morbidity.[5] It occurs in about 20% of the patient being admitted to a hospital.[11] Systematic approach including history, physical examination, and laboratory evaluation are required to determine the underlying cause of hyponatremia.
Despite being a frequent electrolyte imbalance, hyponatremia is a poorly known condition. It is associated with various underlying diseases states, as well as its various etiologies and pathophysiological mechanisms, make diagnosis difficult. [5,12,13] This study was performed to assess the clinical profile, risk factors and outcomes of hyponatremia in hospitalized patients.

Among the total patients 296 were males (59.2%) and 204 females (40.8%) with a mean age of 52.5 years (range 23-82), males being predominant. As compared to a study performed by Nauman et al. and Mohan et al., their study had even distribution of male and female gender. Whereas the severity of hyponatremia increased with increasing age and is similar in both the studies.[14,15] Most of our patients were euvolemic 65.6%, 18.8% were hypervolemic and 15.6% were hypovolemic. The findings are in line with a study by Amit K. Jai, 48% subjects were euvolemic, 28% hypovolemic and 24% were hypervolemic and another by Bhattacharjee et al.[16,17] When compared to the other groups, patients with euvolemic status had more severe hyponatremia symptoms.. Another study conducted in Pakistan by Tarif et al. had most of their patients presenting with hypervolemia (51.6%).[14] Yawar et al reported that euvolemic hyponatremia as the most common presentation consistent with our study.[18]

Hyponatremia symptoms varied across the study participants, with 13% of them being asymptomatic. Majority of the 435 patients were symptomatic (87%). Altered mental status (76.6%) was the most frequent symptom. The majority of patients with blood sodium levels below 125 mmol/L experienced neurological symptoms such as sleepiness; however, those with serum sodium levels below 110 mmol/L experienced severe neurological symptoms such as unconsciousness and 3 of them had seizures. As compared to a study by Rao et al. conducted in elderly population, their result had 33% of the subjects presented with altered mental status and 29% with lethargy.[19] Similarly another study by Prakash et al. had 61% patients presenting with neurological symptoms including altered mental status (48%).[3]

Most of the patients in our study had pre-existing illness with the majority having hypertension (42.4%), diabetes (50.8%) and coronary artery disease (33.4%). As compared to a study by Prakash et al. Patients with a history of hypertension were found in 49% of cases, whereas those with diabetes mellitus were found in 29%. [3] Another study by Saeed et al. found that 37% of patients had hyponatremia together with other illnesses (renal disorders 21% and CHF 9%).[20] Drug intake is one of the common etiologies of hyponatremia. 45.2% of the patients in our study were taking diuretics and 38.8% were on ACE-inhibitors. As compared to a study done in Pakistan, Nauman et al. reported ACE inhibitors and selective serotonin reuptake inhibitors as a reason of hyponatremia.[14] Saeed et al. reported that 33.3% while Huda et al. reported that 63.6% cases of hyponatremia were due to diuretic use.[20,21]

According to studies, there has been a substantial increase in mortality of hyponatremia in hospitalized subjects.[22-24] The overall mortality of particpants in our study was 5.2% which is less as compared to a study by Prakash et. al[3] with 6% mortality and another study by Chike et al. with a high mortality rate (20.2%).[24] Our study had some limitations. We relied on the calculated osmolality rather than estimated since it was adding more cost to the diagnostic value and it was not readily available to help with immediate diagnosis and management of the patient. Second limitation was some of the diagnosis, such as syndromes of inappropriate antidiuretic hormone was not studied since urinary sodium was not measured.

CONCLUSION

Hyponatremia is a common occurrence in hospitalized patients, and it is associated with increased morbidity and mortality. Thus appropriate investigations and treatment are required. It has a wide range of clinical manifestations, from minimal symptoms to life-threatening neurological consequences.. Hyponatremia has a variety of etiologies and risk factors, and identifying the underlying causes allows for more effective treatment.

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