Study of Clinical Symptoms and Etiology of Hyponatremia in Elderly in Intensive Care Unit

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Introduction
Hyponatremia is a common electrolyte disturbances encountered in intensive care units especially in the elderly and contributes to substantial morbidity and mortality. It remains a common yet neglected area of clinical practice. Improved treatment of hyponatremia could lead to significant health and economic benefits. However, incorrect treatment can also add fuel to fire. Hyponatremia is defined as serum sodium concentration of less than 135mEq/L.¹ Hyponatremia can be classified on the basis of serum osmolality, volume status and urinary sodium into hypertonic, isotonic and hypotonic types. Hypotonic hyponatremia is further classified into hypervolemic, euvolemic and hypovolemic as follows²:

- Hypovolemic hyponatremia: Decreased total body sodium and decreased total body water. The sodium deficit exceeding water deficit
- Euvolemic hyponatremia: Normal body sodium with increase in total body water
- Hypervolemic hyponatremia: Increase in total body sodium with greater increase in total body water.

Patient may be asymptomatic or present with neurological symptoms attributable to cerebral edema. Studies suggest that hyponatremia may be present in 34.3% of patients in intensive care facilities³. This incidence is more in elderly due to impaired ability to maintain water and electrolyte homeostasis in response to dietary, environmental changes & physiological changes with age affecting the renal system.⁴ There are very limited studies available in our country with regard to hyponatremia in elderly. Thus, this study was undertaken to know the clinical features and etiology of hyponatremia in intensive care unit in the elderly and to correlate the outcome of this patients with different comorbidities.

Aims
1. To find the incidence of hyponatremia in elderly (above 60 years) ill patients in MICU
2. To explore the clinical profile of such patients
3. To evaluate the etiology and comorbidities associated with hyponatremia.
Materials And Methods
This observational study was conducted in MGM Medical College and Hospital between 1\textsuperscript{st} December 2015 to 31\textsuperscript{st} May 2016, of patients above the age of 60 years in the Medical Intensive Care Unit. A sample size of 100 people above the age of 60 years were included of which 60 people had serum sodium of $\leq 135\text{mmol/L}$ on admission. Relevant history including symptoms and signs at presentation, past medical history, drug history and clinical examinations were recorded in all patients at admission. History specially included compulsive water drinking and intake of diuretics. Volumetric status of the patient was assessed by examination. Routine investigations included complete blood count, renal function tests, serum electrolytes, liver function tests, serum osmolality, urine routine, urine osmolality. Chest radiograph and imaging studies were done to rule out other co-morbid conditions as indicated. Serum cortisol level and Serum T3, T4 and TSH were done when indicated in particular cases. All patients were treated for hyponatremia based on routine guidelines. Sodium concentrations were measured on the apparatus that uses ion-specific electrode technique ensuring measurement of true hyponatremia. The normal range of the laboratory for sodium is 135-145 mmol/L. Serum and urine osmolality was measured.

Inclusion Criteria
1. Patient with serum sodium level less than 135 mmol/L on admission.
2. Patient of 60 years and above.

Exclusion Criteria
Patients with dyslipidemia and hypoproteinemia.

Results
Out of 100 elderly patients admitted to MICU during 6 months 50\% were male & 50\% female, 60 patients were with hyponatremia ($<135\text{mmol/L}$). The mean age of our patients with hyponatremia was 69 years with a range of 60 to 87 years. 44\% of the total 100 were males with hyponatremia and 16\% of the total 100 were females with hyponatremia. (Fig 1) The mean sodium level on admission was 120.83 mMol/L and after correction was 129.54 mMol/L. Drowsiness(35\%), irrelevant talk (25\%), headache (17\%) and unresponsiveness(12\%) were the common presenting symptoms in our study. (Fig. 2) These patients also presented with other symptoms such as chest pain, abdomen pain, decreased appetite which could not be accounted for by hyponatremia. At admission, 80\% were euvoletic, 12\% were overloaded and 8\% dehydrated. There was no significant difference when the type of hyponatremia was analyzed with the outcome. The common co-morbid conditions were Ischemic Heart Disease (40\%), Hypertension (13.3\%), CVA (10\%), Carcinomas (10\%), CKD (6.66\%), CNS Infections(6.66\%), Diabetes Mellitus (3.33\%). Others including UTI, BA are 2\% each. (Fig.3) The common causes of hyponatremia were SIADH (30\%) followed by Drugs (24\%). Among the types of diuretics used hydrochlorothiazide was used by 83\%, frusemide by 10\% and chlorthalidone by 7\%. None of the subjects were on diuretics when SIADH was causing hyponatremia. Mannitol (6\%) and Cisplatin (5\%) were the other drugs found to be associated with drug induced hyponatremia. The number of days of MICU stay in people with hyponatremia is an average of 6 days as compared to 10 days of people without hyponatremia.(Fig.4) 10 patients succumbed to their primary illness with possible significant contribution secondary to hyponatremia. Female patients tolerated hyponatremia better with a mortality of 6.25\% as compared to males with a mortality of 20.45\%.

Fig. 1
Fig. 2

Symptoms Attributable to Hyponatremia on admission

- Headache: 27
- Unresponsiveness: 12
- Druny: 39
- Seizure: 8
- Confusion: 3
- Irrelevant Speech: 25

Sample Size: 60

Fig. 3

Common diseases with Hyponatremia

- CNS Infection: 4
- CVA: 6
- IHD: 24
- HTN: 8
- DM: 2
- CKD: 4
- Carcinoma: 6
- UTI: 2
- BA: 2
- Other: 2

Figure 4:

Number of Days of ICU Stay

- With hyponatremia: 6 Days
- Without hyponatremia: 10 Days

Number of Days of ICU Stay
Discussion

This study was undertaken keeping in view the challenges that the clinicians face of appropriate diagnosis due to the frequent occurrence of hyponatremia in the elderly sick patients who are at higher risk of development of electrolyte disturbance, as these people have age related physiological changes in the function of kidneys and other multiple co-morbid condition.

The prevalence was more in males compared to females in our study. Increased intracranial space due to naturally occurring age related brain atrophy is known to play an important role in brain adaptation to hyponatremia. This finding suggests that even in the presence of cerebral edema, if the brain is able to swell without generating a significant increase of intracranial pressure, the prospects for patient survival may be substantially improved. Only 5% of the total patients presented with seizures in the present study. Studies have shown that both aging and male gender confers protection against hyponatremia induced seizures, although the reasons are unclear.

Most of the patients in our study had multiple co-morbid conditions of which ischemic heart disease (40%), hypertension(13.3%) and CVA(10%) were the most common.

Like most other causes of hyponatremia, heart failure impairs the ability to excrete ingested water by increasing antidiuretic hormone levels. When cardiac output and systemic blood pressure are reduced, "hypovolemic" hormones - renin (with a subsequent increase in angiotensin II formation), antidiuretic hormone (ADH), and norepinephrine, respond. Although edematous patients with heart failure have increased plasma and extracellular fluid volumes, the body perceives volume depletion (reduced effective arterial blood volume) since the low cardiac output decreases the pressure perfusing the baroreceptors in the carotid sinus and the renal afferent arteriole.

The degree of neurohumoral activation is generally related to the severity of cardiac dysfunction, as assessed by left ventricular ejection fraction or functional class. The neurohumoral changes limit both sodium and water excretion in an attempt to return perfusion pressure to normal. ADH release directly enhances water reabsorption in the collecting tubules, whereas angiotensin II and norepinephrine limit distal water delivery (and thereby water excretion) by lowering the glomerular filtration rate (due to a marked reduction in renal perfusion) and by increasing proximal sodium and water reabsorption. In addition, both the low cardiac output and high angiotensin II levels are potent stimuli to thirst, leading to enhanced water intake.

Glucose being an osmotically active molecule, hyperglycemia can induce a fall in serum sodium levels by shifting water from intra-cellular to extra-cellular compartments. It has been calculated that serum sodium falls by 1.6 to 2.4 mmol/L for every 5 mmol/L rise in serum glucose levels.

Hyponatremic hypertensive syndrome is a well known entity, the most common association being in patients with essential hypertension receiving diuretics. Most of the hypertensive patients in our study group were on thiazide or potassium sparing diuretics which are known to interfere with metabolism of various electrolytes and predispose them to electrolyte imbalance. Along with their effect on sodium-chloride co-transporter channel, thiazide diuretics are known to cause non-osmotic release of vasopressin.

SIADH was the most common cause of hyponatremia in our study (30%). Nearly half the patients with severe hyponatremia had SIADH in the study done by Clayton et al. Laczi reported that SIADH was the most common cause of euvolemic hyponatremia in their study in Hungary.

Of all the etiologies, the worrisome cause is Drug induced hyponatremia of which a major chunk was diuretics. Many studies have reported that drugs especially thiazide diuretics are a major cause of hyponatremia in elderly. Though JNC VII recommends diuretics as the first line drug for treatment of hypertension, a word of caution
should be maintained while prescribing diuretics in the elderly and when required doses should be modified according to body weight and should begin with the lowest dose. Many studies in the past indicate a higher mortality in the elderly patients with severe hyponatremia, with mortality ranging from 33% to 86%.\textsuperscript{16} Hyponatremia did not appear to have any significant effect on the duration of ICU stay. Two studies (Chua et al 2007, Gill et al 2006)\textsuperscript{18,19} have independently shown that the drop in hyponatremia had a greater effect than the severity of hyponatremia on length of stay in hospital, mortality & institutionalization.

**Conclusion**

Hyponatremia can be more common in male than female, although reasons remain unclear. Hyponatremia with ischemic heart disease might hold more leverage in increasing morbidity and mortality than realized. If hyponatremia in elderly is due to diuretics, regular monitoring of electrolytes when diuretics are prescribed for co morbid illness will prevent morbidity and mortality in elderly.

**References**

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