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ORIGINAL ARTICLE

Clinical Profile Of Hyponatraemia In Adult Patients Admitted To Hamad General Hospital, Qatar: Experience With 53 Cases

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ABSTRACT

Background: There is limited information about the clinical profile of hyponatraemia in Qatar.
Objectives: The aim of this study was to describe the clinical presentation and aetiology of moderate and severe hyponatraemia in patients admitted to Hamad general hospital.
Patients And Methods: This descriptive observational hospital-based study was conducted at Hamad general hospital from June 2007 to July 2008; it involved all adult patients who were admitted to Hamad general hospital with moderate and severe hyponatraemia.
Results: During the 12-month study period, 53 consecutive patients with moderate and severe hyponatraemia were admitted to Hamad general hospital. 33 (62.3%) were males and 20 (37.7%) were females). The mean age of the patients was 56± 20 years (range of 17-93 years). Females had a significantly higher mean age than males (63.9±16.9 versus 51.6±21.2, p = 0.02). Hyponatraemia due to extra-renal sodium loss was the most frequent cause of hyponatraemia, it was found in 18 (33.9%) patients; whereas the aetiology of hyponatraemia remained unknown in four patients. Of all, 31 (58.4%) patients had moderate hyponatraemia, whereas 22 (41.6%) patients had severe hyponatraemia. Impairment of consciousness was found in 13 (24.5%), it ranged from confusion to coma in 13 patients with impairment of consciousness, 10 (76.9%) had severe hyponatraemia and 3 (9.6%) had moderate hyponatraemia.
Conclusions: Hyponatraemia due to extra-renal loss was the most frequent cause of hyponatraemia in our study; it was more prevalent among elderly patients than in younger patients. No significant gender related difference differences were found in the relative frequency rates. Moreover, no significant differences were found between moderate and severe hyponatraemia with respect to consciousness impairment.

Key Words: Hyponatraemia; Diuretics; SIADH; renal failure

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Introduction

Hyponatraemia is the most common disorder of electrolytes encountered in clinical practice, occurring in up to 15% to 30% of both acutely and chronically hospitalized patients [1]. Significant hyponatraemia also can be found in healthy individuals who participate in high-endurance exercises such as marathon and iron man triathlons [2].

Although most cases are mild and relatively asymptomatic, hyponatraemia is important clinically because: (1) acute severe hyponatraemia can cause substantial morbidity and mortality; (2) mortality is higher in patients with hyponatraemia who have a wide range of underlying diseases; and (3) overly rapid correction of chronic hyponatraemia can cause severe neurological deficit and death [3].

Despite the awareness on hyponatraemia since the mid-20th century, this common disorder remains incompletely understood in many basic areas because of its association with a plethora of underlying disease states, and its multiple aetiologies with differing pathophysiological mechanisms [4]. Data on the characteristics of patients with hyponatraemia among all patients admitted to the Hamad General Hospital (HGH) is lacking; the aim of this study was to describe the prevalence, clinical presentation, aetiological factors and outcome of hyponatraemia among the hospitalized patients at HGH, and to compare the results with previously reported studies.

Methodology

This prospective observational hospital-based study was conducted at Hamad General Hospital from June 2007 to July 2008.

Inclusion Criteria

1. patients aged ≥ 15 years
2. patients with true hyponatraemia (low plasma osmolality <260 mOsm/kg)
3. patients with moderate and severe hyponatraemia:

Definitions

a) Moderate hyponatraemia is defined as plasma [Na^+] of 115-124 meq/l, while severe hyponatraemia is defined as plasma [Na^+] of less than 115 meq/l
b) Syndrome of inappropriate ADH secretion (SIADH): Euvolaemic hyponatraemia with plasma osmolality of less than 280 mOsm./kg; urine osmolality of more than 100 mOsm./kg; urine sodium of more 20 meq/l; and exclusion of renal, adrenal, thyroid, and pituitary dysfunction.
c) Hyponatraemia due to renal loss is characterized by renal sodium excretion of >20 mmol/L, whereas hyponatraemia due to extra-renal loss is characterized by renal sodium excretion of <10 mmol/L.
d) The diagnosis of heart failure- induced hyponatraemia required the following criteria: evidence of heart failure (clinically as well as by echocardiography), urine sodium of less than 10 meq/l in the absence of liver cirrhosis, renal failure and other causes of hyponatraemia.
e) Liver cirrhosis hyponatraemia was defined as hyponatraemia that occurred in the setting of liver cirrhosis with ascites, with hypervolaemic status and shows urine sodium of less 10 meq/l.
f) Diuretics are considered to be a cause of hyponatraemia when urine sodium is more than 20 meq/l in hypovolaemic or apparently euvolaemic patients excluding other causes of hyponatraemia.
g) Extra-renal fluid loss including vomiting, diarrhoea, and diaphoresis is considered as a cause of hyponatraemia when urine sodium is less than 10 meq/l, in the presence of hypovolaemic status.

Data Collection

Data was collected by one of the authors into a special form which included demographic data, clinical data, treatment, and outcome.

Data Analysis

Statistical analysis was carried out using the software EpiInfo2000. Quantitative variables are expressed as mean ± standard deviation. Student t- test was used for continuous variables and the Mann-Whitney

U test was used if variables were not normally distributed. Fisher exact test or Chi Square test were used when appropriate, to compare the data in young vs. older patients. Results were considered significant if P-values were less than 0.05.

Research Committee Approval

The study was approved by the Research Committee and Medical Research Centre at the Hamad Medical Corporation (HMC). Informed consent was obtained from each participant before any interview or physical examination was conducted.

Results

During the 12-month study period, 53 consecutive patients with moderate and severe hyponatraemia were admitted to Hamad General Hospital. There were 33 (62.3%) males and 20 (37.7%) females) with no significant gender- related differences in the relative frequency rates. The mean age was 56± 20 years (range of 17-93 years). Females had a significantly higher mean age than males (63.9±16.9 versus 51.6±21.2, p = 0.02).

Twenty one (39.6%) patients were Qatari. Non-Qatari patients were 32 (60.4%) of whom 8 (15.1%) were Nepalese, 5 (9.4%) were Indians, 3 (5.7%) were Saudis, 3 (5.7%) were Pakistani, 3 (5.7%) were Sudanese, 2 (3.8%) were Palestinians and there was one (1.9%) each from Bangladeshi, British, Chinese, Jordanian, Philippino, Somali, South African and Turkish ethnicities.

Hyponatraemia due to extra-renal loss was the most frequent cause of hyponatraemia, which was found in 18 (33.9%) patients. Other most frequent causes were SIADH in 11 (20.8%), diuretics in 10 patients (18.9%), heart failure in 3 patients (5.7%) and renal failure in 3 patients (5.7%). In four patients, the aetiology of hyponatraemia remained unknown. Other causes of hyponatraemia are shown in [Table/Fig 1].

(Table/Fig 1) Clinical Characteristics Of Patients Admitted With Hyponatremia (Qatar 2007)

Variables	N (%) (mean ± SD)
M/F	33/20
Age	56±20
Age group	
15.24	5 (9.4)
25.34	3 (5.7)
35.44	8 (15.1)
45.54	8 (15.1)
55.64	10 (18.9)
≥ 65	19(35.8)
Nationality	
Qatari	21(39.6)
Non-Qatari	32 (60.4%)
Causes of hyponatremia	
Extra-renal fluid loss (Vomiting, diarrhea and diaphoresis)	18(20.8)
SIADH	11(20.8)
Diuretics	10(18.9)
CHF	3(5.7)
Renal failure	3(5.7)
Liver cirrhosis	2(3.8)
Endocrine causes	
Hypopituitrism	1(1.9)
Hypothyroidism	1(1.9)
Unknown	4(7.5)
Outcome	
Survived	47(88.7)
Died	6(11.3)

Of all, 31 (58.4%) patients had moderate hyponatraemia, whereas 22 (41.6%) patients had severe hyponatraemia. Impairment of consciousness (ranged from confusion to coma) was found in 13 (24.5%), 10 patients (76.9%) had severe hyponatraemia and 3 (9.6%) had moderate hyponatraemia. A comparison between young and older patients was made and no significant differences were found in relation to aetiology and outcome, except for the number of patients in each group; the number of older patients with hyponatraemia was greater than that in young patients (37 vs. 16; p=0.01). Moreover, CNS manifestations were more prevalent among older patients than in young patients [Table/Fig 2].

(Table/Fig 2) A Comparison Between Young And Older Patients With Hyponatremia (Qatar 2007)

Variables	Young 15-45 year N = 16	Older >45 year N= 37	*P* value
M/F	14/2	19/18	0.01
Causes of hyponatremia			
Extra-renal fluid loss	10 (31.25%)	8 (16.22%)	Ns
SIADH	5 (18.75%)	6 (19%)	Ns
Diuretics	2 (12.5%)	8 (21.6%)	Ns
CHF	0	3 (8.1%)	Ns
Renal failure	1 (6.25%)	2 (5.4%)	Ns
Liver cirrhosis	2 (12.5%)	0	Ns
Hypopituitrism	0	1 (2.7%)	Ns
Hypothyroidism	1 (6.25%)	0	Ns
Unknown	0	4 (11.4%)	Ns
CNS manifestations	1 (6.25%)	12 (32.44%)	0.03
Outcome			
Survived	15 (93.75%)	32 (86.5%)	Ns
Died	1 (6.25%)	5 (13.5%)	Ns

Total in hospital mortality was 11.3% (6 out of 53 patients); 3 patients (5.7%) presented with moderate hyponatraemia while the other three had severe hyponatraemia.

Discussion

We found that hyponatraemia accounted for approximately (0.8%) of admissions to the medical ward of Hamad General Hospital in Qatar during the period of the study, which is less than that found in many reports. [1],[4],[5] The reason for this is not clear; it could have resulted from the exclusion of mild hyponatraemia in this study, which represented the majority of admitted cases in other reports. We have studied moderate to severe hyponatraemia in our study because of the fact that this is the level usually associated with symptoms and requires a prompt but cautious approach towards treatment in order to avoid cerebral oedema on one side and iatrogenic central myelinolysis on the other side.

In similarity to other reports [6],[7],[8] hyponatraemia in this study was more prevalent among elderly patients than in younger patients (37 vs. 16; p=0.01).

Because there are many causes of hyponatraemia and the treatment differs according to the cause, a thorough understanding of the pathophysiological process of hyponatraemia and its associated risk factors is of great importance for prevention and prompt and effective intervention in this potentially life-threatening disturbance.

Hyponatraemia is ascribed to either water retention or (less often) loss of effective solute (sodium plus potassium) in excess of water. Because the capacity for water excretion normally is so great, the retention of water resulting in hyponatraemia takes place only in the presence of conditions that impair renal excretion of water. An exception to this rule is primary polydipsia, in which the excessive water intake can overwhelm even normal excretory capacity. Given that suppression of arginine vasopressin (antidiuretic hormone [ADH]) secretion is essential for the excretion of any water load, the presence of high serum ADH concentrations is the sine qua non for the development and maintenance of hyponatraemia.

Virtually, all causes of hyponatraemia (except renal failure and primary polydipsia) are characterized by an excess of ADH (despite the presence of hypotonicity), which is most frequently caused by the syndrome of inappropriate ADH secretion (SIADH) or effective circulating volume depletion (which is a normal stimulus to ADH secretion) [9],[10].

Distinguishing the cause(s) of hyponatraemia may be challenging in clinical practice. In a prospective study conducted in a general medical-surgical setting, [9] 66 patients (34%) had euvolaemic hyponatraemia, 38 (19%) had hypervolaemic hyponatraemia associated with oedematous disorders, and 33 (17%) had hypovolaemic conditions, chiefly related to G.I fluid loss or diuretic use. Extra-renal fluid loss including vomiting, diarrhoea, or diaphoresis was the most frequent cause of hyponatraemia in our study and it was found in 18/53 (33.9%) patients.

In spite of being the most usual aetiological factor for hyponatraemia in hospitalized elderly patients [11] as well as the most common cause of normovolaemic hyponatraemia, the syndrome of inappropriate ADH secretion (SIADH) is normally diagnosed by exclusion of other causes including diuretics and renal, liver, thyroid, adrenal, and pituitary diseases. [12] SIADH was considered to be the cause in 11/53 (20.7%) patients included in our study.

Diuretics (mainly thiazide) were found to be the cause of hyponatraemia in 10/53 (18.9%) of our patients; all of them were over the age of 45 years, in consistence with

several studies that showed thiazide to be the major diuretic causing hyponatraemia [13],[14],15],[16],[17],[18]. They also demonstrated that older patients, particularly women, were more vulnerable to thiazide-induced hyponatraemia because they generally have a decreased ability to excrete water load due to reduced intra-renal generation of prostaglandins [19],[20],[21].
The clinical presentations of severe hyponatraemia can range from mild non specific symptoms such as nausea, headache, and lethargy, to severe symptoms causing seizure and coma [22]. Thirteen of our patients (24.5%) presented with impaired level of consciousness that ranged from confusion to coma and most of them had serum sodium of less than 115meq/l. There was no significant age or gender difference, despite the evidence from animal studies that showed females to have greater sensitivity to vasopressin than males and less ability to extrude sodium from brain than males [23]. Furthermore, oestrogen has been shown to stimulate the release of vasopressin, which potentially increases water retention, while testosterone reduces ADH levels [24].

Not only is hyponatraemia associated with severe manifestations, but it also predicts mortality and this has been demonstrated in patients with heart failure in whom sodium levels less than 125 meq/l represents near end stage disease [25]. This is an adverse predictor of short term outcomes[26],[27] mainly in patients with liver cirrhosis and ascites in whom there is a correlation between severity of hyponatraemia and the degree of ascites, impaired renal function, degree of hepatic encephalopathy, spontaneous bacterial peritonitis, and hepatorenal syndrome [28]. Hyponatraemia has also been shown to be a strong predictor of death in cirrhosis [29],[30],[31].

In our study, two out of three patients with heart failure, and two patients with liver cirrhosis died during hospitalization, emphasizing the prognostic value of hyponatraemia.

The endocrine causes of hyponatraemia are not infrequently missed and as they can be easily treated with hormone replacement, they should be looked for; these include hypothyroidism, primary adrenal insufficiency, and hypopituitarism. Hypothyroidism was documented in one patient, and hypopituitarism in another patient in our study.

As noted, the total in hospital mortality was 11.3% (6 out of 53 patients); whereas no case of clinically evident central myelinosis was documented, following the treatment of hyponatraemia.

A limitation of this study was the small number of patients. Moreover, the study was hospital based rather than population based, which necessitates further prospective population based studies.

Conclusion

Hyponatraemia was found to be more prevalent among elderly patients than in younger patients. Extra-renal loss and SIADH were the most frequent causes of hyponatraemia in our study. No significant gender -related differences were found in the relative frequency rates; moreover, no significant differences were found between moderate and severe hyponatraemia with respect to consciousness impairment.

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