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ORIGINAL ARTICLE

Outcomes in medical admissions with hyponatraemia in Ghana – a single-centre study

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ABSTRACT

Introduction: Hyponatraemia is the most common electrolyte abnormality in hospitalized patients and is associated with poor prognosis and high mortality. There is a paucity of data on hyponatraemia in Ghana. We set out to describe the prevalence of this condition, its associations and the outcomes in terms of in-hospital mortality and length of hospital stay.

Methods: We conducted a retrospective study of all admissions from October 2017 to April 2018 on the medical ward at the Komfo Anokye Teaching Hospital (KATH). Demographic information, medical diagnoses as well as clinical and laboratory data were documented. Means (± standard deviation) were recorded for normally distributed data, whereas non-normally distributed data were recorded as medians [interquartile range (IQR)]. Chi-squared and Fisher's exact tests were used to test categorical variables. ANOVA and Kruskal-Wallis tests were used for the analysis of hyponatraemia severity; a p value of < 0.05 was considered statistically significant.

Results: Within the study period, 406 patients with hyponatraemia were identified in 1477 medical admissions, a prevalence of 27.6%. Their mean age was 51.5 ± 19.0 years. There were 217 males (53.5%). The mean serum sodium was 128.7 ± 6.5 mmol/L. Two hundred and forty (59%) had mild hyponatraemia, 106 (26%) had moderate hyponatraemia and 60 (15%) had severe hyponatraemia. The most common associated medical conditions were infections (26%), chronic liver disease (17%), hyperglycaemia (17%), chronic kidney disease (16%) and chronic heart failure (8%). In-hospital mortality was 31.8% and varied with the severity of the hyponatremia. The median length of hospital stay was 7 days (IQR 4–10 days) and did not vary with the severity of hyponatraemia. Mortality was associated with serum sodium concentration ($p = 0.007$) and lower levels of consciousness (Glasgow Coma Scale, GCS, ≤ 13) at presentation ($p < 0.001$).

Conclusions: Hyponatraemia is common in medical admissions in Ghana, and is mostly associated with infections, and chronic liver, kidney and heart diseases. It is associated with high in-hospital mortality, especially when hyponatraemia is more severe or accompanied by relatively low GCS scores.

Keywords: hyponatraemia; mortality; Ghana.

INTRODUCTION

Hyponatraemia, defined by a serum sodium concentration of less than 135 mmol/L, is the most common electrolyte abnormality in hospitalized patients [1,2]. It is present in approximately 15% of hospital admissions [3], is associated with increased morbidity and mortality, and is often poorly recognised and managed. Normally, serum sodium concentration is tightly controlled by mechanisms including antidiuretic hormone (ADH) and the thirst response. Abnormalities in serum sodium concentration indicate a disruption in the body's control systems for water [2,4].

There are many causes that may contribute to hyponatraemia. They include medications, malignancies, infections, cardiac failure, liver failure and renal disease. These

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conditions are mostly described as causing the syndrome of inappropriate anti-diuretic hormone (SIADH) secretion, where ADH is acting when the serum sodium concentration and/or serum osmolality is low. Non-osmotic states such as pain, anxiety and nausea can also cause ADH secretion and hyponatraemia [5]. Acute hyponatraemia has also been described in long-distance runners due to water overload [6]. The condition may present with symptoms ranging from headache, nausea, vomiting and fatigue to seizures and coma.

In hospitalized patients, a serum sodium concentration of less than 125 mmol/L has been associated with poor prognosis. Mortality rates associated with hyponatraemia range from 0.9–29.6% of hospital admissions with the highest among patients in the intensive care units [7,8]. It is not certain whether hyponatraemia contributes to the higher mortality or is just a marker of the poor prognosis in chronic conditions [9].

In Ghana, there has been no study on the prevalence and outcomes of hyponatraemia in hospitalized patients. There have been case studies describing the condition in patients with hypothyroidism [10] and bronchial carcinoma [11]. In this study, we describe the prevalence of hyponatraemia in a tertiary institution in Ghana, and describe the causes and outcomes among patients in terms of in-hospital mortality and length of hospital stay.

METHODS

We conducted a retrospective study of adult (>18 years) medical admissions at the Komfo Anokye Teaching Hospital (KATH) with serum sodium concentration less than 135 mmol/L. The study period was from 1 October 2017 to 30 April 2018. KATH is a 1200-bed hospital in the Ashanti region, which receives referrals from about half of Ghana's 27 million population in the northern half of the country. The hospital has twelve clinical directorates including the Internal Medicine directorate with a bed capacity of 203.

Two patients among the medical admissions were not considered for inclusion as they did not have serum sodium measurements. Demographic data including age and sex were recorded. Presenting symptoms such as nausea, vomiting, oedema, seizures and pain were recorded if documented in the clinical notes. Level of consciousness graded using the Glasgow Coma Scale (GCS) was also recorded. Low level of consciousness was defined as GCS of ≤ 13. Serum sodium concentration was categorised as mild when between 130–134 mmol/L, moderate between 125–129 mmol/L and severe when less than 125 mmol/L. Critical hyponatraemia was defined as serum sodium concentration of less than 120 mmol/L. The medical diagnoses were also recorded and the most likely contributory causes of the hyponatraemia were identified. Outcome variables documented were the length of hospital stay and in-hospital mortality.

Means and standard deviation were used to describe normally distributed variables and medians and interquartile range for variables not normally distributed. Figures and tables were used to describe data where appropriate. The chi-squared and Fisher's exact tests were used for categorical variables. Student's t test and the Wilcoxon sign rank test were used for continuous variables. ANOVA and Kruskal-Wallis tests were used to test for differences related to the severity of hyponatremia. Multiple logistic regression was then used to identify predictors of mortality. A P value of < 0.05 was considered statistically significant.

Ethical approval was granted before the start of the study from the Committee on Human Research, Publications and Ethics, School of Medical Sciences, Kwame Nkrumah University of Science and Technology.

RESULTS

The study identified 406 patients with hyponatraemia in 1479 medical admissions within the study period, yielding a prevalence of 27.6%. The mean age was 51.5 ± 19.0 years. There were 217 males (53.5%). The mean serum sodium concentration was 128.7 ± 6.5 mmol/L (Table 1).

The most common medical conditions associated with hyponatraemia were infections (105 patients, 26%), chronic liver disease (69, 17%), diabetes mellitus (68, 17%) and chronic kidney disease (66, 16%) (Figure 1). When hyponatraemia was classified by volume status, 17% were hypovolaemic, 41% were euvolaemic and 43% were hypervolaemic.

In-hospital mortality was 32%. Of the patients who died, mortality varied significantly with the diagnosis ($p = 0.012$), with the highest rate among patients with malignancies (46%), cranial pathologies (44%), chronic liver disease (41%), chronic kidney disease (38%) and infections (35%) (Figure 1).

In-hospital mortality also varied with the severity of hyponatraemia. Mild hyponatraemia had an associated mortality rate of 21%, moderate hyponatraemia 45% and severe hyponatraemia 52% ($p < 0.001$). Mortality did not vary with volume status.

Table 1. Demographics and clinical data of patients with hyponatraemia.

Variable	Total n = 406	Mild n = 240	Moderate n = 106	Severe n = 60	P value
Male n (%)	217 (53.5)	123 (51.3)	59 (55.7)	35 (58.3)	0.535
Age (years)	51.5 ±19.0	52.6 ±19.7	47.9 ±18.3	53.5±16.0	0.068
Pain n (%)	264 (65.0)	161 (67.1)	72 (67.9)	31(51.7)	0.062
Nausea n (%)	112 (27.6)	51 (21.3)	38 (35.9)	23 (38.3)	0.002
Oedema n (%)	142 (35.0)	36 (31.3)	16 (28.6)	12 (41.4)	0.283
Seizures n (%)	38 (9.4)	20 (8.3)	9 (8.4)	9 (15.0)	0.267
GCS ≤ 13 n (%)	76 (18.7)	36 (15.0)	19 (17.9)	21 (35.0)	0.002
Systolic BP (mmHg)	134.5 ± 36.8	132.6 ±3 4.6	132.0 ± 36.6	146.4 ± 43.7	0.024
Diastolic BP (mmHg)	82.3 ± 22.3	81.6 ± 21.1	81.1 ± 24.3	87.3 ± 23.3	0.170
Serum sodium (mmol/L)	128.7 ± 6.5	132.3 ± 1.4	127.3 ± 1.6	116.4 ± 7.9	< 0.001
Random blood glucose (mmol/L)	8.7 (6.9–11.3)	8.8 (7.1–11.6)	8.2 (6.8–11.0)	9.1 (7.2–10.8)	0.528
Haemoglobin (g/dL)	10.2 ± 3.1	10.5 ± 3.1	9.5 ± 2.8	9.9 ± 3.4	0.013
Serum albumin (g/L)	31.6 ± 16.5	31.4 ± 9.1	28.6 ± 7.8	29.4 ± 12.0	0.026
Serum urea (mmol/L)	6.9 (3.9–15.6)	5.5 (3.4–11.1)	7.7 (4.9–24.5)	11.5 (5.5–29.0)	0.0001
Serum creatinine (µmol/L)	59 (61–232.5)	86 (60–153)	96 (61–349)	148 (75.5–486.5)	0.002
In-hospital mortality n (%)	129 (31.8)	50 (20.8)	48 (45.3)	31 (51.7)	< 0.001
Length of hospital stay (days)	7 (4–10)	7 (4–10.5)	6.5 (3–10)	6.5 (3–11)	0.639

Continuous variables reported as mean ± standard deviation or median (interquartile range); GCS, Glasgow Coma Scale.

The median duration of hospital stay was 7 days (IQR 4–10 days) and did not vary significantly with the severity of hyponatraemia.

Among patients with GCS ≤13, 67% died ($p < 0.001$). The mean serum sodium for those who died was lower, 126.0 ± 8.5 mmol/L versus 129.9 ± 4.8 mmol/L ($p < 0.001$). The in-hospital mortality of those with critical hyponatraemia was 70%.

Multiple logistic regression revealed that serum sodium concentration ($p = 0.007$) and GCS ≤ 13 ($p < 0.001$) were predictors of mortality (Table 3).

DISCUSSION

This is the first study of hyponatremia in Ghana describing the prevalence, causes and outcomes of the condition. We report a hyponatraemia prevalence of 27.6% in our hospitalized medical cases, similar to prevalences in other studies of 15–36% [3,12]. Hyponatraemia was seen mostly in patients with infections and chronic oedematous conditions such as liver, heart and kidney disease, and had a high in-hospital mortality. Mortality was associated with the severity of hyponatraemia and decreased level of consciousness.

There were more males with hyponatraemia, which contrasts with other reports in which females were at higher risk as a result of their lower body weight and total body water [13]. Higher proportions of males have also been reported in hospitalized patients, especially among those with chronic heart failure, chronic liver disease and malignancies [14]. Our higher proportion of males may be due to the frequency of chronic liver disease, alcoholism and CKD in our study.

Infections were the most common cause of hyponatremia in our cohort. Infections such as pneumonia have been reported as a cause of hyponatraemia in 28% of cases in another study [15]. Hyponatraemia in the setting of infections may be due to renal hypoperfusion, leading to

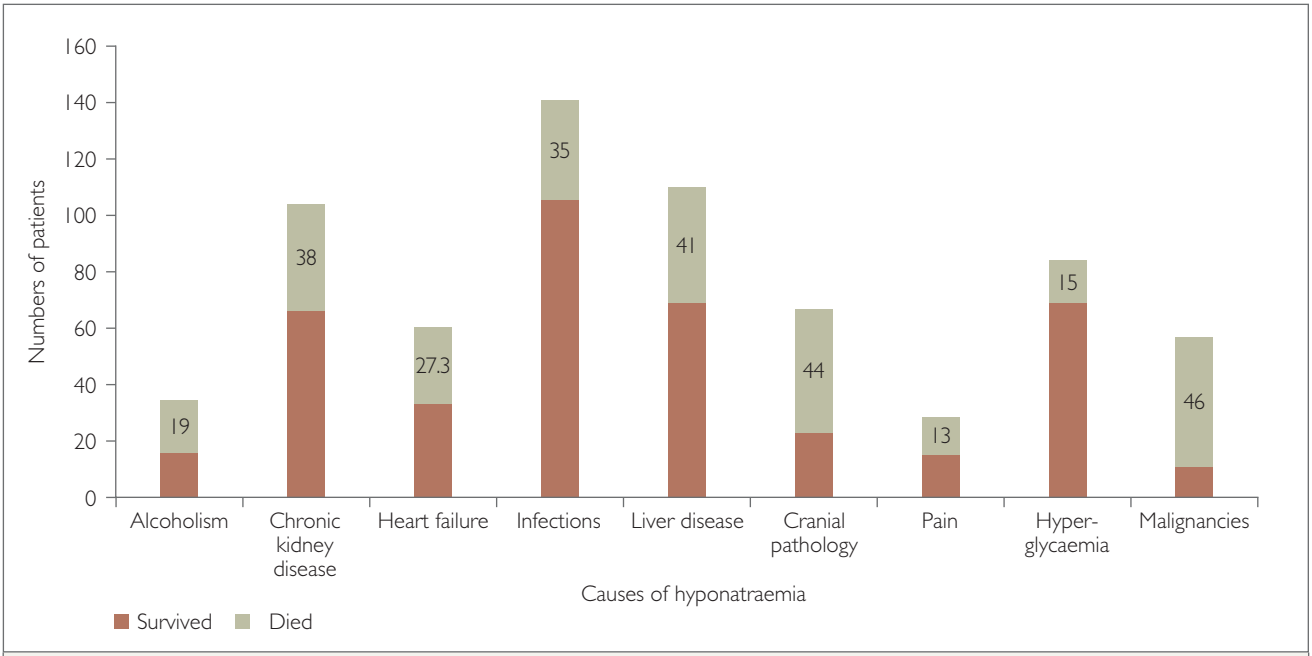

Figure 1. Causes of hyponatraemia and associated mortality in medical admissions.

Table 2. Determinants of mortality among patients with hyponatraemia.

	Died (n = 129)	Survived (n = 277)	P value
Male n (%)	71 (33)	146 (67)	0.661
Age (years)	51.2 ± 19.7	51.7 ± 18.7	0.807
Pain n (%)	75 (28.4)	189 (71.6)	0.047
Nausea n (%)	43 (38.4)	69 (61.6)	0.077
Dehydration n (%)	28 (29.8)	66 (70.2)	0.637
Oedema n (%)	38 (26.8)	104 (73.2)	0.112
Seizures n (%)	17 (44.7)	21 (55.3)	0.071
GCS ≤ 13	51 (67.1)	25 (32.9)	< 0.001
Systolic BP (mmHg	134.8 ± 36.1	134.3 ± 37.2	0.890
Diastolic BP (mmHg)	82.3 ± 22.3	82.4 ± 22.6	0.890
Serum sodium (mmol/L)	126.0 ± 8.5	129.9 ± 4.8	< 0.001
Critical hyponatraemia n (%)	19 (70.4)	8 (29.6)	< 0.001
Random blood glucose	8.6 (7.1–11.1)	8.7 (6.8–11.5)	0.981
Haemoglobin (g/dL)	9.7 ± 3.1	10.4 ± 3.1	0.027
Serum albumin (g/L)	28.4 ± 10.2	31.3 ± 8.7	0.006
Serum urea (mmol/L)	8.3 (4.8–20.7)	6.2 (3.5–12.7)	0.005
Serum creatinine (µmol/L)	103 (71–342)	89 (59–176)	0.026
Length of hospital stay (days)	4 (2–9)	7 (4–11)	< 0.001

Continuous variables reported as mean ± standard deviation or median (interquartile range); GCS, Glasgow Coma Scale.

Table 3. Logistic regression for variables associated with mortality in patients with hyponatraemia.

	Odds ratio (95% confidence interval)	P value
Serum albumin concentration	0.97 (0.95–1.00)	0.124
Haemoglobin	0.93 (0.85–1.02)	0.114
Critical hyponatraemia	1.13 (0.25–5.16)	0.867
Serum sodium concentration	0.91 (0.87–0.98)	0.009
GCS ≤ 13	7.7 (4.09–14.50)	< 0.001
Pain	0.94 (0.55–1.61)	0.829

Critical hyponatraemia refers to serum sodium less than 120 mmol/L; GCS, Glasgow Coma Scale.

ADH release and water retention [2,4]. Infections identified in our cohort included pneumonia, encephalitis, urinary tract infection, sepsis, and HIV with its related infections. Hyponatremia occurs in around 30% of HIV-infected patients [16]. Infections are more common in low- and lower-middle-income countries and this may account for the prominence of infections as a cause of hyponatraemia in our cohort.

Hypervolaemic conditions, such as chronic liver disease (CLD), were identified as a significant cause of hyponatraemia in our cohort. CLD causes hyponatraemia in 30% of cases. The pathophysiology includes renal hypoperfusion, secondary hyperaldosteronism, ADH release and hypoalbuminemia [17]. Hyponatraemia is associated

with a poor prognosis in patients with CLD [18] or other oedematous conditions such as heart failure [19].

Heart failure accounted for 8.1% of patients with hyponatraemia in our cohort, which is less than reported in many other studies [20]. The mechanism is multifactorial but mainly due to arterial under-filling, which leads to neurohormonal stimulation. Medications for heart failure, such as thiazide diuretics, are also known causes of hyponatraemia [20]. Mild hyponatraemia, even without severe cardiac dysfunction, is associated with increased morbidity and mortality [21].

Diabetes mellitus was associated with 17% of the cases in our cohort. Hyperglycaemia-induced hyponatraemia is well described in the literature [22]. The high serum tonicity leads to movement of water from the intracellular to extracellular fluid compartments and hence results in a decrease in serum sodium concentration [23]. Osmotic diuresis also leads to hypovolaemia, which increases ADH secretion. Moreover, polydipsia contributes to dilutional hyponatraemia [24].

CKD is another cause of hypervolaemic hyponatraemia, with a prevalence of 6% in non-dialysis CKD patients [25]. CKD accounted for 6% of our cases. Chronic kidney disease is common in hospital admissions in Ghana and patients often present late, with advanced disease [26]. Hyponatraemia in CKD patients is associated with increased mortality [27].

Mortality occurred in over a third of cases of hyponatraemia in our study. This was higher than in most studies, which report prevalences of 15–27% [7]. Mortality was highest among patients with malignancies, similar to other studies [28]. Mortality increased significantly with severity of hyponatraemia; this has also been reported in other studies [14,29]. Serum sodium predicts mortality as shown in most studies [7,14,27]. Mortality was significantly higher among those with impaired consciousness. This may be due to their underlying conditions and not necessarily the hyponatraemia [9,23]. Many medical conditions have hyponatraemia as a poor prognostic factor for the underlying condition [10,14,20].

In our study, those who died with hyponatraemia had significantly higher median serum urea and creatinine values. Renal impairment worsens the prognosis of most medical conditions [30].

CONCLUSIONS

Hyponatraemia is common in medical admissions in Ghana, and is mostly associated with infections, chronic liver disease, chronic kidney disease and chronic heart failure. There is high in-hospital mortality and this is associated with serum sodium concentration and an impaired level of consciousness.

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