Scholars Academic Journal of Biosciences
Abbreviated Key Title: Sch Acad J Biosci
ISSN 2347-9515 (Print) | ISSN 2321-6883 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Biology

Hyponatremia in an Intensive Care Unit: Biological, Epidemiological, and Prognostic Patterns

Taha Hounain[1*], Mina Elkhayari[1], Abdelhamid Hachimi[1]

[1]Medical Intensive Care Unit, Mohammed VI University Hospital, Marrakech, Morocco

DOI: 10.36347/sajb.2023.v11i04.002 | **Received:** 02.03.2023 | **Accepted:** 08.04.2023 | **Published:** 18.04.2023

***Corresponding author:** Taha Hounain
Medical Intensive Care Unit, Mohammed VI University Hospital, Marrakech, Morocco

Abstract **Original Research Article**

Hyponatremia is an electrolyte balance disorder frequently encountered in the intensive care setting. Its prevalence is high but not well known. Its clinical expression varies and its management depends on the mechanisms related to its installation. The prognosis of hyponatremia may be severe, and this severity may be due to underlying conditions, treatment related complications and time lapse before treatment is initiated. This is a prospective, descriptive, analytic, prognostic study. Patients admitted to the ICU with hyponatremia lower than 135mmol / l were included over a period of thirteen months. Several parameters were identified (demographic, anamnestic, clinical, biological, therapeutic, progression and severity scores) and compared between patients with or without hyponatremia. During the study period, 84 patients (32.60%) had hyponatremia out of the 258 who were included in our study. Hyponatremia was hypervolemic in 27.72%, normovolemic in 19.28%, hypovolemic in 51% of patients. The median duration of onset of hyponatremia acquired in the intensive care unit is 5.79 days. The mortality rate was 56% and the predicted mortality was 44% according to the APACHE II score. Some variables were significantly associated with hyponatremia: age ($p < 0.005$), comorbidities ($p = 0.02$), tumor history ($p = 0.001$), metabolic history ($p = 0.003$), diabetes ($p = 0.008$), recent surgical history ($p = 0.002$), previous hepato-gastroenterological history ($p = 0.017$). Four variables were significantly associated with ICU-acquired hyponatremia: shock ($p = 0.008$), consciousness disorders ($p = 0.008$), APACHE II ($p < 0.001$). In conclusion, hyponatremia is quite common in intensive care patients. Management must be rapid and include symptomatic as well as etiological treatment. Mortality is largely related to other factors and not to hyponatremia itself.
Keywords: Hyponatremia, Mortality, Prognosis.

INTRODUCTION

Hyponatremia is a hydroelectrolytic disorder frequently encountered in intensive care. The incidence and prevalence of hyponatremia are high but not well known and vary according to the severity threshold, the population studied (age, sex), and the mode of onset (hyponatremia on admission or acquired during hospitalization). In intensive care units, the prevalence of hyponatremia defined as less than 135 mmol/l varies from 15 to 30% [1, 2].

The clinical expression of hyponatremia is not very specific and varies according to its severity and speed of onset. The difficulties in the management of hyponatremia are related to the plurality of mechanisms and etiologies. Hyponatremia can be severe because of its severity, underlying pathologies, and complications related to treatment and time to management. Its prognosis can be severe, although study data are inconsistent and debated. Few studies are devoted to hyponatremia encountered in the intensive care unit. Hospital mortality associated with hyponatremia is increased [3]. However, it is difficult to consider hyponatremia as an independent factor of mortality. The main objective of this study is to determine the epidemiological, clinical and prognostic characteristics of hyponatremia in a medical intensive care unit.

EXPERIMENTAL SECTION/MATERIAL AND METHODS

Department Overview:

The medical ICU is a 10-bed unit with 2 teaching professors, 2 physicians and 5 interns. At the paramedical level, 13 nurses provide care to patients.

All patients admitted during the study period were eligible for the study. Our population included 258 patients. This population is divided into two groups P1 and P2. P1: all patients with hyponatremia during our study period P2: all patients without hyponatremia during our study period.

Incomplete records were excluded from this study.

The different parameters were collected for each patient, divided as follows: Demographic data; anamnestic data; the clinical and biological profile of hyponatremia; severity scores; management; and the outcome.

Statistical study:

The results and numbers obtained were expressed as a percentage. Prevalence was measured as the ratio of the number of patients with hyponatremia to the number of patients admitted during the study period. Incidence was measured as the number of new cases of hyponatremia that occurred on the ward after admission. The mean and median were calculated, using an SPSS file. Statistical analysis of the data was performed at the clinical research department of CHU Mohamed VI by SPSS version 16 software.

- Quantitative data are expressed as mean ± standard deviation and Gaussian distribution and medians and quartiles when the distribution was not uniform.
- Qualitative data are compared by Fischer's exact test.
- To test the qualitative hypotheses, we had used the Chi2 test, a probability $p < 0.05$ was retained as statistically significant.

Comparison of the mean of the parameters in the groups was performed by Student's t-test.

RESULTS AND DISCUSSION

I. Descriptive study

1) The prevalence of hyponatremia

Several studies, mostly involving small groups of patients, have described the prevalence of hyponatremia in at-risk populations [4]. Hyponatremia is common in critically ill patients [5]. In our setting, the prevalence of hyponatremia in ICU patients is approximately 32%.

DeVita *et al.*, [6] retrospectively reviewed 98 ICU patients over a 3-month period and observed hyponatremia (at least a serum sodium level of 134 mEq/L) in approximately 25% of patients. A retrospective analysis of more than 2000 French patients showed that the incidence of hyponatremia (serum sodium level of 130 mEq/L) on admission to the ICU was 14% [7].

However, our statistics do not exceed the percentages of hyponatremia recorded in hospitalized patients in the literature. Previous studies have shown varying levels of up to 40% in hospitalized patients [8, 9].

In geriatric hospitals, the prevalence of hyponatremia ranges from 10 to 25% [10-12]. In emergency departments, 4 to 5% of patients present with hyponatremia [13], but this frequency can rise to 30% in cirrhotic patients [14].

2) Age and sex

The incidence of hyponatremia is variable, [15] but may be six times higher in elderly patients [10]. And the incidence of hyponatremia was equal between the two sexes according to several authors [16-18].

Shapiro found a higher prevalence of hyponatremia ≤ 125 mEq/l in hospitalized elderly women (8.1% vs 4.0%; $p < 0.001$) [19].

3) Past history

In the literature, in general, cardiovascular pathologies, notably hypertension and heart failure, appear in the foreground, but with neoplasia, and liver failure in the context of cirrhosis [20-22]. The underlying pathologies play an influential role in the occurrence of hyponatremia and in the pathophysiological mechanisms at the origin of these hyponatremias. Decompensation of an underlying disease can lead to hyponatremia. It should also be noted that the patient's condition is often poly-pathological. In our series, comorbidities were mainly represented by metabolic history (38%), including diabetes (27%), followed by cardiovascular diseases (35%) and neurological and respiratory diseases (13% each).

4) Reasons for admission

Neuropsychological symptoms represent one of the important causes of admission for our patients in our study, topping the list were neurological symptoms, representing 45% of the reasons for hospitalization.

This is the same case in Angers, in a polyvalent medicine department, and in Grenoble in internal medicine. Neurological or neuropsychological disorders were at the top of the list with 58% and 27.8% of the reasons for hospitalization in Angers and Grenoble respectively [20, 21].

These differences are due to the variability of the study sites. In medical or intensive care units, neurological symptoms remain the primary reason for hospitalization. This is not the case for surgical intensive care units: falls, alteration of the general state and postoperative effects are the main reasons for hospitalization.

5) Mortality

Mortality ranges from 5 to 50% depending on the severity and mode of onset [22-24]. The mortality rate of 56% observed in our series of patients is much higher than that cited in a similar study [25], which recorded a mortality rate of 34%, for patients with serum sodium concentrations of 134 mmol/L or less.

This figure may overestimate the number of deaths due to hyponatremia or its treatment. Most deaths occurred in patients who were so ill that their low serum sodium level may have been an incidental finding. The same observation has been made in other series of patients with moderate hyponatremia [26].

II. Analytical Study

1. Epidemiological factors of hyponatremia in the ICU

The incidence of hyponatremia differed by age according to several authors [27-29].

This is the case in our study where the prevalence of hyponatremia varied according to the age of the patients. From the age of 40 onwards, the prevalence of patients increases from range to range. Our findings corroborate perfectly with those of Mohan *et al.,* who present the same observations [30].

In a New York City-based study, subjects with hyponatremia were significantly older (52.8 vs. 45 years, p<0.001) and the prevalence of hyponatremia increased with age in both sexes, but more so in women (1.6% to 4.1%). The risk of hyponatremia also increased significantly with age and in women compared to men [30]. Their analysis demonstrates an increase in the prevalence of hyponatremia with age and a higher prevalence of hyponatremia in women in the general population, a suspected finding given similar trends previously reported in acute and long-term care patient cohorts [31, 32].

2. Association between hyponatremia and comorbidities

We note in our series that there is an association between hyponatremia and patients' prior health status. Those with hyponatremia had more comorbidities. This finding in our series is similar to other series [33] in which a relationship between havingvcomorbidities and the presence of hyponatremia has been observed. This is the case in Marco's study from Spain, where there are significant differences in prior health status between patients with and without hyponatremia [34]. The comorbidities for which there was a significant difference between hyponatremic and normonatremic patients were cancer, metabolic history, diabetes, hepato-gastroenterological history, recent surgery. In a prospective study conducted at Boston University Center in Massachusetts between 2000 and 2003, notable differences in the clinical characteristics of hyponatremics versus normonatremics included a higher frequency of congestive heart failure, sepsis, pneumonia, metastatic disease, and hypovolemia. Compared with those with normonatremia, patients admitted with hyponatremia had more comorbidities [35]. Findings from the Mohan *et al.,* study reveal that subjects with one or more comorbidities had a significantly higher prevalence of hyponatremia than the overall cohort at 2.26% (P ¼ .0001). Specifically, the prevalence of hyponatremia was significantly higher in subjects with hypertension, diabetes, coronary artery disease, cancer, stroke, chronic obstructive pulmonary disease, and psychiatric disorders. Of note, the prevalence of hyponatremia was not significantly higher in patients with congestive heart failure, thyroid disease, liver disease, or renal disease. In contrast, the prevalence of hyponatremia was significantly lower in subjects with no identifiable comorbidities [30].

Recent analyses of small cohorts of hospitalized patients with hyponatremia have suggested that hyponatremia is merely a surrogate for the underlying pathology rather than an independently detrimental factor [36, 37].

3. Other factors associated with hyponatremia

Few factors were significantly associated with hyponatremia in our study. This could be explained by the small sample size of our series. The length of stay in our study was not associated with hyponatremia. For a duration of less than 5 days, the prevalence of hyponatremia was: 31.5%, for a duration between 5 and 10 days: 30%, for a duration greater than 10 days: 39% in bi-variate analysis. However, in the literature, the average length of stay for patients in intensive care units was higher in patients with hyponatremia [38]. The findings of the study by Mohan *et al.,* revealed that hyponatremic subjects had more hospital stays in the past year [30]. Our study is the first to investigate the association between shock and hyponatremia. In bi-variate analysis shock was significantly associated with hyponatremia. Patients who had been in shock were more likely to have hyponatremia compared to those who were not in shock (82% vs. 28%, p=0.000). It was not studied in the different studies found in the literature. The Glasgow score in bi-variate analysis was not significantly associated with hyponatremia in our study. In contrast, patients who had hyponatremia, compared to those who never had hyponatremia, had lower admission GCS 12 (10-14) compared to 14 (13-14); (p = 0.01) and similar APACHE II scores 10, respectively (9-12) compared to 10 (10-11) (p = 0.69) at admission in Theresa Human's work in the USA [39].

In our series, we found a significant association between the Charlson score and the patient's natraemia. The higher the Charlson score, the higher the number of patients with hyponatremia increases. This finding is similar to that of other series [40] in which a relationship between higher comorbidity determined by the Charlson index and the presence of hyponatremia was observed. For example, there were significant differences in the Charlson index between patients with and without hyponatremia in Marco's study from Spain [41]. More than half of our hyponatremic patients were symptomatic, consistent with previous studies [42-44].

In the study by Krummel *et al.,* the incidence of severe neurologic symptoms was not associated with the mode of onset of hyponatremia, i.e., acute or chronic, although the mode of onset could not be determined in more than half of the patients because of the absence of previous plasma sodium values. Hyponatremia has not been associated with the presence of symptoms [45]. Although neurological, infectious and respiratory symptoms were associated with hyponatremia in our study.

4. Factors associated with acquired hyponatremia in the ICU

To our knowledge, very few studies have investigated the risk factors of acquired hyponatremia. Indeed, length of stay in the ICU was associated with acquired hyponatremia both in intensive care units and in post-cardiac surgery intensive care [46, 47]. This relationship probably also reflects the multiple risk factors that add up during the stay, including worsening of the severity of the pathology in patients with long hospital stays and long-term exposure to adverse clinical events [48]. In our study, in bi-variate analysis, patients with acquired hyponatremia had significantly longer length of stay compared to patients with hyponatremia at admission (p= 0.005).

Also, a high APACHE II score was associated with acquired hyponatremia [46, 47]. All these observations raise the question: are acquired hyponatremias disturbances that independently increase the risk of death, markers of severity of the pathologies or both. This is especially true since natraemia has been incorporated into the calculation of the APACHE II score [49]. However, Stelfox *et al.,* in 2008 and after adjustment for renal function, mechanical ventilation and APACHE II score, demonstrated that acquired sodium disturbances are independently associated with mortality [46]. In addition to these parameters, Stelfox *et al.,* in 2010 reported that hyperglycemia and changes in kalemia (hyperkalemia or hypokalemia) were independent predictors of acquired sodium disturbances [47]. The nature of our study did not allow evaluation of this association due to the fact that data regarding other ionic disturbances in patients with normal natraemia were not identified.

5. Prognosis of hyponatremia

5.1. Association between mortality and hyponatremia

Concerning the prognosis of hyponatremia on patients, we could not objectify in our series that hyponatremia is associated with mortality. The mortality rate remains high for patients with and without hyponatremia (56% versus 48%). Similar results were noted in the study of Abidi in Morocco.

A strong association between hyponatremia and increased in-hospital mortality was demonstrated in the study by Jinling Hao *et al.,* where overall in-hospital mortality was 6.15% in hyponatremic patients compared to 0.48% in non- hyponatremic patients [50] and in several other studies [51-55]. Hyponatremia was also found to be an independent predictor of in-hospital mortality in Vandergheynst's single-center series of emergency department patients [56].

In addition, it was shown that the risk of mortality was 5 times higher in hyponatremic subjects and no concomitant disease was identified compared with similar subjects with normal natraemia in Mohan's work. After adjustment for age, sex, comorbidities, and other factors that may affect mortality, hyponatremia remains associated with a significantly increased risk of mortality in all subjects, suggesting an inherent negative impact associated with a chronically hypotonic state beyond the underlying disease [30]. Recent small studies have shown similar associations between hyponatremia and all-cause mortality, but these have been limited to elderly patients in community settings [57, 58]. However, whether hyponatremia contributes to mortality or simply represents a surrogate marker of the severity of underlying disease remains a controversial issue. Some authors have suggested that hyponatremia simply reflects other comorbidities, i.e., an epiphenomenon of disease [59].

5.2. Prognostic factors for hyponatremia

a. Demographic and anamnestic factors associated with mortality

The contribution of hyponatremia to death in affected patients remains debatable, however. Indeed, the most recent studies suggest that patients are more likely to die from their comorbidities than from hyponatremia per se [60, 61]. In our study, we found that toxicological history was negatively associated with mortality in patients with hyponatremia. This has been little discussed in the literature. In the study by Eugenia *et al.,* cigarette smoking was found to be negatively associated with hyponatremia in uni-variate analyses, but not in multivariate analyses or with mortality [62]. Cigarette smoking has never been reported to protect against hyponatremia; instead, smoking was previously positively related to hyponatremia in psychiatric patients [63, 64]. Nicotine is known to stimulate vasopressin release [65]. It is possible that the result is spurious because of information bias.

The patient history in our study was not associated with mortality. Among patients with hyponatremia, 61.5% of patients with no history had died compared with 55% in patients with at least one previous history. In 2013, a meta-analysis including more than 80 studies reported that hyponatremia was independently associated with an excess risk of mortality regardless of comorbidities, even for very moderate hyponatremia [66]. Recent analyses of small cohorts of hospitalized patients with hyponatremia have suggested that hyponatremia is merely a surrogate for the underlying pathology rather than an independently detrimental factor [61, 67]. Chawla *et al.*, show that hyponatremic patients <120 mmol/l who died all had acute decompensation of an underlying pathology [61]. Waikar *et al.*, objectified an increased association between hyponatremia and in-hospital mortality in metastatic cancer, cardiac disease, and patients admitted for orthopedic surgery [35]. The prognostic value of low serum sodium concentrations for mortality has previously been described for acute myocardial infarction [68, 69], congestive heart failure [70, 71], and cancer [72].

b. Biological factors associated with mortality

The relationship between the rapid onset, mortality, and morbidity of hyponatremia is widely established [73-76]. Erasmus *et al.*, [77]; Lee *et al.*, [78] showed that the severity of hyponatremia significantly influenced mortality.

Several studies have sought to show a severity relationship between the severity of hyponatremia and mortality, with inconsistent results [79]. Some studies show that mortality is higher in hyponatremic subjects than in normonatremic subjects, both in terms of hospital mortality and long-term mortality up to 5 years after hospitalization [80, 81]. However, studies show that below a certain threshold of natraemia, mortality is no longer related to hyponatremia: in the study by Waikar *et al.*, found that hyponatremic patients of any severity had higher mortality during hospitalization, at 1 year, and at 5 years. The differences in mortality persisted after adjustment for all categories of hyponatremia (classified by severity), except for hyponatremia below 120 mmol/l, for which the 5-year mortality was no longer significantly higher [35]. For Chawla *et al.*, the hospital mortality rate increases with the severity of hyponatremia up to the threshold of 120 mEq/l, at which point the trend is reversed: the mortality rate falls with decreasing serum sodium levels [61]. Some authors have not demonstrated a link between the level of natraemia and the death of patients [82, 83]. Our results are in line with these studies where no difference was objectified for mortality according to the variation of sodium levels. For a natraemic level between 135 and 130, a mortality of 45%, a level between 129 and 125, a mortality of 49%, a level between 124 and 120, a mortality of 77% and a level below 120, a mortality of 71%. In addition, a recent study found that a decrease in serum sodium below a threshold of 132 mmol/L did not contribute to an additional increase in overall mortality risk [84]. These findings may challenge the assumption that there is a causal link between hyponatremia and mortality. Hyponatremia may be a marker of the severity of an underlying disease. Similar to the findings of Chawla *et al.*, As soon as the serum sodium concentration fell below 120 mmol/L, mortality did not appear to increase with increasing severity of hyponatremia [61].

A possible mechanism for the increase in mortality associated with hyponatremia independent of the underlying disease and the overall lack of further increase in mortality risk when serum sodium decreases below 132 mmol/L could be hyponatremia-induced oxidative stress [85]. It is possible that even small decreases in serum sodium below 139 mmol/l are sufficient to induce accumulation of free oxygen radicals and thus damage proteins, lipids and DNA. There is increasing evidence that inflammatory mediators, such as interleukins 1 and 6, can induce hyponatremia by excessive release of vasopressin [86, 87]. This could explain the low potential mortality observed in patients with serum sodium levels below 120 mmol/l, among whom a large proportion would have hyponatremia induced by drug treatment rather than severe underlying disease, and consequently a lower level of inflammation [88]. Krummel *et al.*, report in their study that mortality was closely related to hypo-albuminemia, suggesting that decreased serum albumin and hyponatremia may act synergistically to increase the risk of death in these patients [45].

c. Clinical symptoms associated with mortality

Other studies have sought to show a severity relationship between the underlying etiology of hyponatremia and mortality. For Clayton *et al.*, mortality was higher in hyponatremic patients with congestive heart failure or decompensated liver disease, and lower for drug etiologies with thiazide diuretics. Patients with multiple etiologies had a higher mortality rate. For the authors, the prognosis of severe hyponatremia depended on the etiology, not the serum sodium level [89].

In our series, shock was significantly related to mortality in bi-variate analysis ($p = 0.008$). Similar results were found in the series of Bennani ($p=0.02$ and $RR=1.80$). It was not studied in the different studies found in the literature.

A cohort study conducted in a Danish population-based medical registry objective that the risk of mortality was increased due to the severity of hyponatremia in patients with a primary diagnosis of cancer, liver disease, respiratory disease, and sepsis [84]. In a meta-analysis published in 2013, they were able to conclude that the risk of mortality was independent of factors such as age, gender, and diabetes mellitus as an associated morbidity. They found an increased risk of mortality in hyponatremic patients with myocardial infarction (total number of patients 6096, of which 18.3% had hyponatremia), cirrhosis (total number of patients 906, of which 42.6% were hyponatremic), or pulmonary infections (total number of patients 10047, of which 12% were hyponatremic). Some studies (n = 26) reported data for other diseases or mixed subpopulations (e.g., elderly), which could not be grouped. The most represented diseases among these patients (37864 in total, including 15.1% hyponatremic) were AIDS, malaria, and malnutrition. Finally, some studies (n = 14, total number of patients 615410, of which 16.7% were hyponatremic) were considered separately, because the effect of hyponatremia on mortality was studied retrospectively and diagnoses were not specified. The meta-analysis of these studies also revealed an increased risk of overall mortality. In fact, only diabetes mellitus could have been used as a possible confounder in the meta-analysis. Therefore, it should be recognized that unmeasured potential confounders, such as other chronic diseases, in addition to diabetes mellitus, may have caused residual confounding, but measured factors correlated with these confounders would have mitigated the bias. To date, few studies have attempted to address the problem of a direct effect of hyponatremia on mortality or other adverse outcomes [90].

d. Association between mortality and severity scores
In the literature, the percentage of death correlated with comorbidities based on the Charlson score is:

- Score = 0 corresponds to 8%.
- Score between 1 and 2 corresponds to 25%.
- Score between 3 and 4 corresponds to 48%.
- Score greater than or equal to 5 corresponds to 59% [91].

The mortality rates observed in our department according to the score are largely above the expectations. Furthermore, there is no significant difference between the different mortality rates objectified for each score category in our series. We concluded that there was no association between Charlson score and mortality in patients with hyponatremia.

However, the work of Jinling Hao *et al.,* reveals that examination of deceased patients with severe hyponatremia showed that death was primarily due to conditions other than hyponatremia. Analysis of the results showed that the Charlson comorbidity index and age were the only significant predictive risk factors for mortality in severe hyponatremia [51]. The Charlson Comorbidity Index is a well-known prognostic score validated in a multitude of diseases, including severe hyponatremia [92, 93]. Altered consciousness is also for many authors a poor prognostic factor [93-96]. Our results are in disagreement with these data; in fact, the disorders of consciousness evaluated on the Glasgow scale were not a factor of bad prognosis in bi-variate analysis. The severity of the disease at inclusion is one of the major factors determining the prognosis of patients in the intensive care unit. In general, the risk of in-hospital mortality correlates with the severity of illness, as measured by physiological severity scores. Bennani's study used the severity score, IGS II which was significantly higher among decedents ($p < 0.001$).

e. Association of mortality and management, outcome and length of stay.

Patients transferred to the ICU had cardiovascular, respiratory or neurological failures. In the study by Béatrice de Guilbert [20], hyponatremia was not considered the cause of death. The causes of transfer to the intensive care unit and the causes of death were, in order of frequency: neoplastic, infectious, neurological, cardiological, hepato-gastro- enterological. Also in his study [20], hyponatremia developed during hospitalization seems to be associated with a high risk of unfavorable evolution. The rate of transfer to the intensive care unit and mortality were significantly higher than in the group of patients with hyponatremia at hospital admission. Hyponatremia per se was not the reason for resuscitation transfer or death in the patients; the outcome was frequently the result of vital organ failure, of which hyponatremia only one reflection of the severity of the clinical situation was underlying condition. Although iatrogeny was attributed in 4 cases to the occurrence of hyponatremia during hospitalization (hemodilution due to filling for 2 patients, transfusion for 1 patient, and SIADH after introduction of an antidepressant treatment with a serotonin reuptake inhibitor for 1 patient), the reason for transfer to the intensive care unit or the cause of death was never hyponatremia of iatrogenic cause. The medical intensive care unit in Marrakech is a service that takes care of patients with severe conditions. The length of stay can vary depending on the patient. For those with hyponatremia, the length of stay was not associated with mortality. In Sturdik's study, lack of correction was a predictive factor for increased mortality strongly associated with hyponatremia [18]. This agrees with the results of our study where an association was objectified between correction of hyponatremia and mortality. In the presence of correction of hyponatremia, the mortality rate decreased. Krummel *et al.,* in their multivariate analysis, found that patients with normalized plasma sodium had significantly better survival (HR 0.35 [0.20-0.62]), independent of underlying comorbidities (Charlson Comorbidity Index and serum albumin). In addition, patients with successful plasma sodium normalization had a similar Charlson index to those without. The lack of a relationship between plasma sodium normalization and in-hospital mortality suggests that the lack of normalization is not due to premature in-hospital mortality before plasma sodium normalization, but rather that subsequent mortality may be due to the lack of plasma sodium normalization. However, nearly 60% of patients who died during hospitalization had normalized plasma sodium levels [45]. Krummel's results are identical to ours in that patients with correction of hyponatremia had a better survival 78% compared to those with uncorrected natraemia 25% ($p<0.001$).

CONCLUSION

Hyponatremia in the ICU can have a varying prevalence in different studies. Hyponatremia was found to be often encountered in elderly patients with comorbidities, admitted for pathologies with neurological, infectious or respiratory manifestations. Their management includes symptomatic and etiological treatment.

The prognosis of hyponatremia in the ICU is poor as demonstrated by the high mortality rate recorded in our study, 56%. It is associated with other ionic disturbances and can see its prognosis worsened in the presence of hypo-albuminemia, coma, and shock. Cautious correction is necessary as well as rapid management before admission to the intensive care unit if detected earlier in order to reduce the mortality rate.

Our study has allowed us to discuss some clinical, etiological and therapeutic aspects that influence its prevalence, prognosis and occurrence, which should be confirmed by studies on a larger scale.

REFERENCES

1. Schrier RW, Bansal S. Diagnosis and management of hyponatremia in acute illness. Curr Opin Crit Care 2008; 14:627-34. [Medline]
2. Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia. Am J Med 2006; 119(7 Suppl. 1):S30-S5.
3. Aurélie Vuagniaux, Peter Vollenweider. Approche diagnostique de l'hyponatrémie ; Rev Med Suisse 2010; 6- 2074-9:1.
4. Léon A, Lepousé C, El Hijri A Les hyponatrémies. Conférences d'actualisation 2000, p .551-569 Eds scientifiques et médicales Elsevier SAS, et SFAR
5. Upadhyay, Ashish, Jaber, Bertrand L., & Madias, Nicolaos E. Epidemiology of hyponatremia. Seminars in nephrology. WB Saunders, 2009. p. 227-238.
6. DeVita MV, Gardenswartz MH, Konecky A, Zabetakis PM. Incidence and etiology of hyponatremia in an intensive care unit.Clin Nephrol. 1990; 34:163-6.
7. Bennani, S. L., Abouqal, R., Zeggwagh, A. A., Madani, N., Abidi, K., Zekraoui, A., & Kerkeb, O. (2003). Incidence, causes and prognostic factors of hyponatremia in intensive care. *La Revue de Medecine Interne*, *24*(4), 224-229.
8. Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia. Am J Med 2006; 119:S30-5.
9. Hawkins RC. Age and gender as risk factors for hyponatremia and hypernatremia. Clin Chim Acta 2003; 337:169-72.
10. Miller M, Morley JE, Rubenstein LZ. Hyponatremia in a nursing home population. J Am Geriatr Soc, 1995; 43: 1410-3.
11. Anpalahan M. Chronic idiopathic hyponatremia in older people due to syndrome of inappropriate antidiuretic hormone secretion (SIADH) possibly related to aging. J Am Geriatr Soc 2001; 49: 788-92.
12. Lim JK, Yap KB. Hyponatraemia in hospitalised elderly patients. Med J Malaysia 2001; 56: 232-5.
13. Lee CT, Guo HR, Chen JB. Hyponatremia in the emergency department. Am J Emerg Med 2000; 18: 264-8.
14. Borroni, G., Maggi, A., Sangiovanni, A., Cazzaniga, M., & Salerno, F. (2000). Clinical relevance of hyponatraemia for the hospital outcome of cirrhotic patients. *Digestive and Liver Disease*, *32*(7), 605-610.
15. Wilkinson, T. J., Begg, E. J., Winter, A. C., & Sainsbury, R. (1999). Incidence and risk factors for hyponatraemia following treatment with fluoxetine or paroxetine in elderly people. *British journal of clinical pharmacology*, *47*(2), 211-217.
16. Ashish Upadhyay, Bertrand L. Jaber, and Nicolaos E. Madias Incidence and Prevalence of Hyponatremia The American Journal of Medicine (2006) Vol 119 (7A), S30–S35
17. D. S. Shapiro, M. Sonnenblick, I. Galperin, L. Melkonyan, & G. Munter, Severe hyponatraemia in elderly hospitalized patients: prevalence, aetiology and outcome Intern Med J, vol. 40, no 8, p. 574-580, août 2010.
18. Sturdik, I., Adamcova, M., Kollerova, J., Koller, T., Zelinkova, Z., & Payer, J. (2014). Hyponatraemia is an independent predictor of in-hospital mortality. *European journal of internal medicine*, *25*(4), 379-382.
19. Douglas I. Hyponatremia: Why it matters, how it presents, how we can manage it. Cleaveland Clinic Journal of Medicine 2006; 73(suppl 3): p. S4-S12
20. De Guibert B. Caractéristiques des patients présentant une hyponatrémie sévère en service de médecine. Thèse d'exercice : Médecine : Grenoble. [En ligne]. 2012. Disponible à partir de : http://dumas.ccsd.cnrs.fr/docs/00/76/97/83/PDF/2012GRE15143_guibert_beatrice_de_1_D_.pdf [Page consultée le 10/01/2019].
21. Creusot, Marie-Laure & CLOS Prophette, Fabienne. Etude rétrospective des hyponatrémies hospitalisées dans un service de médecine polyvalente sur 13 mois. 2014.
22. J. Kengni Tameze, S. Etia Mbongo, N. Daoudi, B. Kennes, O. Vanachter, V. Verhaeghe. Prévalence de l'hyponatrémie chez le patient âgé admis pour chute : étude rétrospective d'une série de 108 patients. La revue de médecine interne ; Volume 30, n° S2 page 130 (juin 2009).
23. Ashish Upadhyay, Bertrand L. Jaber, and Nicolaos E. Madias Incidence and Prevalence of Hyponatremia The American Journal of Medicine (2006) Vol 119 (7A), S30–S35
24. Sandy Craig. Hyponatremia.e-medicine, January 4, 2006, www.emedicine.com
25. Eric E Simon. Hyponatremia. e-medicine, july 2006, www.emedicine.com
26. Anderson RJ. Hospital-associated hyponatremia. Kidney Int. 1986; 29:1237-47.
27. Ashish Upadhyay, Bertrand L. Jaber, and Nicolaos E. Madias Incidence and Prevalence of Hyponatremia The American Journal of Medicine (2006) Vol 119 (7A), S30–S35
28. Sandy Craig. Hyponatremia.e-medicine, January 4, 2006, www.emedicine.com
29. Eric E Simon. Hyponatremia.e-medicine, july 2006, www.emedicine.com

30. Mohan, S., Gu, S., Parikh, A., & Radhakrishnan, J. (2013). Prevalence of hyponatremia and association with mortality: results from NHANES. *The American journal of medicine*, *126*(12), 1127-1137.
31. Mannesse, C. K., Vondeling, A. M., van Marum, R. J., van Solinge, W. W., Egberts, T. C., & Jansen, P. A. (2013). Prevalence of hyponatremia on geriatric wards compared to other settings over four decades: a systematic review. *Ageing research reviews*, *12*(1), 165-173.
32. Hawkins RC. Age and gender as risk factors for hyponatremia and hypernatremia. Clin Chim Acta. 2003; 337:169-172
33. Callahan, M. A., Do, H. T., Caplan, D. W., & Yoon-Flannery, K. (2009). Economic impact of hyponatremia in hospitalized patients: a retrospective cohort study. *Postgraduate medicine*, *121*(2), 186-191.
34. Marco, J., Barba, R., Matía, P., Plaza, S., Méndez, M., Canora, J., & Zapatero, A. (2013). Low prevalence of hyponatremia codification in departments of internal medicine and its prognostic implications. *Current medical research and opinion*, *29*(12), 1757-1762.
35. S. S. Waikar, D. B. Mount, & G. C. Curhan, « Mortality after hospitalization with mild, moderate, and severe hyponatremia », Am. J. Med., vol. 122, no 9, p. 857-865, sept. 2009.
36. Chawla A, Sterns RH, Nigwekar SU, Cappuccio JD. Mortality and serum sodium: do patients die from or with hyponatremia? Clin J Am Soc Nephrol. 2011; 6:960-965.
37. Kang, S. H., Kim, H. W., Lee, S. Y., Sun, I. O., Hwang, H. S., Choi, S. R., ... & Choi, B. S. (2012). Is the sodium level per se related to mortality in hospitalized patients with severe hyponatremia?. *Clinical nephrology*, *77*(3), 182-187.
38. Deitelzweig, S., Amin, A., Christian, R., Friend, K., Lin, J., & Lowe, T. J. (2013). Health care utilization, costs, and readmission rates associated with hyponatremia. *Hospital practice*, *41*(1), 89-95.
39. Human, T., Cook, A. M., Anger, B., Bledsoe, K., Castle, A., Deen, D., ... & Brophy, G. (2017). Treatment of hyponatremia in patients with acute neurological injury. *Neurocritical Care*, *27*, 242-248.
40. Callahan, M. A., Do, H. T., Caplan, D. W., & Yoon-Flannery, K. (2009). Economic impact of hyponatremia in hospitalized patients: a retrospective cohort study. *Postgraduate medicine*, *121*(2), 186-191.
41. Marco, J., Barba, R., Matía, P., Plaza, S., Méndez, M., Canora, J., & Zapatero, A. (2013). Low prevalence of hyponatremia codification in departments of internal medicine and its prognostic implications. *Current medical research and opinion*, *29*(12), 1757-1762.
42. Clayton JA, Le Jeune IR, Hall IP. Severe hyponatraemia in medical inpatients: aetiology, assessment and outcome. QJM. 2006; 99:505–11.
43. Nzerue CM, Baffoe-Bonnie H, You W, Falana B, Dai S. Predictors of outcome in hospitalized patients with severe hyponatremia. J Natl Med Assoc. 2003; 95:335–43.
44. Hoorn EJ, Lindemans J, Zietse R. Development of severe hyponatraemia in hospitalized patients: treatment-related risk factors and inadequate management. Nephrol Dial Transplant. 2006; 21:70–6. 167. Krummel, T., Prinz, E., Metten, M. A., Borni-Duval, C., Bazin-Kara, D., Charlin, E., ... & Hannedouche, T. (2016). Prognosis of patients with severe hyponatraemia is related not only to hyponatraemia but also to comorbidities and to medical management: results of an observational retrospective study. *BMC nephrology*, *17*(1), 1-12.
45. Stelfox, H. T., Ahmed, S. B., Khandwala, F., Zygun, D., Shahpori, R., & Laupland, K. (2008). The epidemiology of intensive care unit-acquired hyponatraemia and hypernatraemia in medical-surgical intensive care units. *Critical care*, *12*, 1-8.
46. Stelfox H, Ahmed S, Zygun D, Khandwala F, Laupland K. Characterization of intensive care unit acquired hyponatremia and hypernatremia following cardiac surgery. Can J Anesth 2010; 57(7): 650-658.
47. Stelfox H, Bates D, Redelmeier D. Safety of patients isolated for infection control. JAMA 2003; 1899-1905.
48. Bigatello, L. M., Stelfox, H. T., Berra, L., Schmidt, U., & Gettings, E. M. (2007). Outcome of patients undergoing prolonged mechanical ventilation after critical illness. *Critical care medicine*, *35*(11), 2491-2497.
49. Charlson M, Pompei P, Ales K, CR M. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic dis 1987; 40: 373-83.
50. Hao, J., Li, Y., Zhang, X., Pang, C., Wang, Y., Nigwekar, S. U., ... & Chen, L. (2017). The prevalence and mortality of hyponatremia is seriously underestimated in Chinese general medical patients: an observational retrospective study. *BMC nephrology*, *18*, 1-8.
51. Holland-Bill, L., Christiansen, C. F., Heide-Jørgensen, U., Ulrichsen, S. P., Ring, T., Jørgensen, J. O. L., & Sørensen, H. T. (2015). Hyponatremia and mortality risk: a Danish cohort study of 279 508 acutely hospitalized patients. *European journal of endocrinology*, *173*(1), 71-81. doi: 10.1530/EJE-15-0111.
52. Wald R, Jaber BL, Price LL, Upadhyay A, Madias NE. Impact of hospital associated hyponatremia on selected outcomes. Arch Intern Med. 2010; 170:294–302. doi:10.1001/archinternmed.2009.513.

53. Gill, G., Huda, B., Boyd, A., Skagen, K., Wile, D., Watson, I., & Van Heyningen, C. (2006). Characteristics and mortality of severe hyponatraemia–a hospital-based study. *Clinical endocrinology*, *65*(2), 246-249.
54. Whelan, B., Bennett, K., O'riordan, D., & Silke, B. (2009). Serum sodium as a risk factor for in-hospital mortality in acute unselected general medical patients. *QJM: An International Journal of Medicine*, *102*(3), 175-182.
55. Sturdik, I., Adamcova, M., Kollerova, J., Koller, T., Zelinkova, Z., & Payer, J. (2014). Hyponatraemia is an independent predictor of in-hospital mortality. *European journal of internal medicine*, *25*(4), 379-382.
56. Vandergheynst, F. Contribution à la description phénotypique du syndrôme d'antidiurese inappropriée nephrogénique et à l'étude de la morbidité: Mortalité de l'hyponatrémie (Unpublished doctoral dissertation) Université libre de Bruxelles, Faculté de Médecine – Médecine, Bruxelles (2016).
57. Hoorn, E. J., Rivadeneira, F., van Meurs, J. B., Ziere, G., Stricker, B. H., Hofman, A., ... & Zillikens, M. C. (2011). Mild hyponatremia as a risk factor for fractures: the Rotterdam Study. *Journal of Bone and Mineral Research*, *26*(8), 1822-1828.
58. Sajadieh, A., Binici, Z., Mouridsen, M. R., Nielsen, O. W., Hansen, J. F., & Haugaard, S. B. (2009). Mild hyponatremia carries a poor prognosis in community subjects. *The American journal of medicine*, *122*(7), 679-686.
59. Clayton, J. A., LE JEUNE, I. R., & HALL, I. P. Severe hyponatraemia in medical in-patients: aetiology, assessment and outcome. Journal of the Association of Physicians, 2006, vol. 99, no 8, p. 505-511.
60. Kang, S. H., Kim, H. W., Lee, S. Y., Sun, I. O., Hwang, H. S., Choi, S. R., ... & Choi, B. S. (2012). Is the sodium level per se related to mortality in hospitalized patients with severe hyponatremia?. *Clinical nephrology*, *77*(3), 182-7.
61. A. Chawla, R. H. Sterns, S. U. Nigwekar, & J. D. Cappuccio, « Mortality and serum sodium: do patients die from or with hyponatremia? », Clin J Am Soc Nephrol, vol. 6, no 5, p. 960-965, mai 2011.
62. Siegler, E. L., Tamres, D., Berlin, J. A., Allen-Taylor, L., & Strom, B. L. (1995). Risk factors for the development of hyponatremia in psychiatric inpatients. *Archives of internal medicine*, *155*(9), 953-957.
63. Ellinas PA, Rosner F, Jaumee JC. Symptomatic hyponatremia associated with psychosis, medications and smoking. J Natl Med Assoc. 1993; 85:135-141.
64. Allon M, Allen HM, Deck LV, Clark ML. Role of cigarette use in hyponatremia in schizophrenic patients. Am J Psychol. 1990;147:1075-1077
65. Sklar AH, Schrier RW. Central nervous system mediators of vasopressin release. Physiol Rev. 1983;63:1243-1280.
66. Corona, G., Giuliani, C., Parenti, G., Norello, D., Verbalis, J. G., Forti, G., ... & Peri, A. (2013). Moderate hyponatremia is associated with increased risk of mortality: evidence from a meta-analysis. *PloS one*, *8*(12), e80451.
67. Kang, S. H., Kim, H. W., Lee, S. Y., Sun, I. O., Hwang, H. S., Choi, S. R., ... & Choi, B. S. (2012). Is the sodium level per se related to mortality in hospitalized patients with severe hyponatremia?. Clinical nephrology, 77(3), 182-7.
68. Goldberg, A., Hammerman, H., Petcherski, S., Nassar, M., Zdorovyak, A., Yalonetsky, S., ... & Aronson, D. (2006). Hyponatremia and long-term mortality in survivors of acute ST-elevation myocardial infarction. *Archives of internal medicine*, *166*(7), 781-786.
69. Singla, I., Zahid, M., Good, C. B., Macioce, A., & Sonel, A. F. (2007). Effect of hyponatremia (< 135 mEq/L) on outcome in patients with non–ST-elevation acute coronary syndrome. *The American journal of cardiology*, *100*(3), 406-408.
70. Milo-Cotter, O., Cotter, G., Weatherley, B. D., Adams, K. F., Kaluski, E., Uriel, N., ... & Felker, G. M. (2008). Hyponatraemia in acute heart failure is a marker of increased mortality but not when associated with hyperglycaemia. *European journal of heart failure*, *10*(2), 196-200.
71. Tribouilloy, C., Rusinaru, D., Mahjoub, H., Souliere, V., Levy, F., Peltier, M., ... & Massy, Z. (2008). Prognosis of heart failure with preserved ejection fraction: a 5 year prospective population-based study. *European heart journal*, *29*(3), 339-347.
72. Berghmans T, Paesmans M, Body JJ. A prospective study on hyponatraemia in medical cancer patients: epidemiology, aetiology and differential diagnosis. Support Care Cancer. 2000;8:192-197.
73. Lestavel P, Boumbar Y, Crouzet S. Conduite à tenir devant une hyponatremie. Actualités en Reanimation et urgences 2001, 19eme congres, p : 264279. Editions scientifiques et Medicales Elsevier SAS.
74. Adrogué HJ, Madias NE. Hyponatremia. N engl J Med 2000 ; 342 : 1581-1589
75. Kumar S, Brel T. Sodium. Lancet 1998; 352: 220-228
76. Agha A, Thornton E, O'Kelly P, Tormey W, Phillips J, Thompson CJ. Posterior pituitary dysfunction after traumatic brain injury. J Clin Endocrinol Metab 2004; 89:5987–92.
77. Er Erasmus RT, Matsha TE. The frequency, aetiology and outcome of severe hyponatraemia in adult hospitalised patients. Cent Afr J Med 1998;44:154–8
78. Lee CT, Guo HR, Chen JB. Hyponatremia in the emergency department. Am J Emerg Med 2000; 18:264–8.

79. K. Asadollahi, N. Beeching, & G. Gill Hyponatraemia as a risk factor for hospital mortality QJM, vol. 99, no 12, p. 877-880, janv. 2006.
80. J. A. Clayton, I. R. Le Jeune, & I. P. Hall Severe hyponatraemia in medical inpatients: aetiology, assessment and outcome QJM, vol. 99, no 8, p. 505-511, août 2006
81. W. M. Tierney, D. K. Martin, M. C. Greenlee, R. L. Zerbe, & C. J. McDonald The prognosis of hyponatremia at hospital admission J Gen Intern Med, vol. 1, no 6, p. 380-385, déc. 1986.
82. Brunsvig PF, Os I, Frederichsen P. Hyponatremia. Tidsskr nor Loegeforen 1990; 110:2367–9.
83. Ayus JC, Arieff AI. Chronic hyponatremic encephalopathy in postmenopausal women: association of therapies with morbidity and mortality. JAMA 1999; 281:2299–304.
84. Holland-Bill, L., Christiansen, C. F., Heide-Jørgensen, U., Ulrichsen, S. P., Ring, T., Jørgensen, J. O. L., & Sørensen, H. T. (2015). Hyponatremia and mortality risk: a Danish cohort study of 279 508 acutely hospitalized patients. *European journal of endocrinology*, *173*(1), 71-81.
85. Barsony J, Sugimura Y & Verbalis JG. Osteoclast response to low extracellular sodium and the mechanism of hyponatremia-induced bone loss. Journal of Biological Chemistry 2011 286 10864–10875. (doi:10.1074/jbc.M110.155002)
86. Mastorakos G, Weber JS, Magiakou MA, Gunn H & Chrousos GP. Hypothalamic–pituitary–adrenal axis activation and stimulation of systemic vasopressin secretion by recombinant interleukin-6 in humans: potential implications for the syndrome of inappropriate vasopressin secretion. Journal of Clinical Endocrinology and Metabolism 1994 79 934–939. (doi:10.1210/jcem.79.4.7962300)
87. Park SJ& Shin JI. Inflammation and hyponatremia: an underrecognized condition? Korean Journal of Pediatrics 2013 56 519–522. (doi:10.3345/kjp.2013.56.12.519)
88. Chawla A, Sterns RH, Nigwekar SU & Cappuccio JD. Mortality and serum sodium: do patients die from or with hyponatremia? Clinical Journal of the American Society of Nephrology 2011 6 960–965. (doi:10.2215/CJN.10101110)
89. J. A. Clayton, I. R. Le Jeune, & I. P. Hall Severe hyponatraemia in medical inpatients: aetiology, assessment and outcome QJM, vol. 99, no 8, p. 505-511, août 2006.
90. Corona, G., Giuliani, C., Parenti, G., Norello, D., Verbalis, J. G., Forti, G., ... & Peri, A. (2013). Moderate hyponatremia is associated with increased risk of mortality: evidence from a meta-analysis. *PloS one*, *8*(12), e80451.
91. Odile Beyne-Rauzy. Les comorbidités & la fragilité : comment les utiliser en pratique? Disponible sur : (http://www.oncomip.org/docs/site/espace-professionnel/cr-reunions/5-reunion/6_cr_oncomip_path_ myeloides_2008_comorbidites.pdf) Consulté le 25/02/2019. Page 10
92. Kang, S. H., Kim, H. W., Lee, S. Y., Sun, I. O., Hwang, H. S., Choi, S. R., ... & Choi, B. S. (2012). Is the sodium level per se related to mortality in hospitalized patients with severe hyponatremia?. *Clinical nephrology*, *77*(3), 182-7.
93. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40:373–83.
94. Erasmus RT, Matsha TE. The frequency, aetiology and outcome of severe hyponatraemia in adult hospitalised patients. Cent Afr J Med 1998; 44:154–8.
95. Brunsvig PF, Os I, Frederichsen P. Hyponatremia. Tidsskr nor Loegeforen 1990; 110:2367–9.
96. Ellis SJ. Severe hyponatremia: complications and treatment. QJM 1995; 88:905–9.