SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Intensive Care Unit

Epidemiological and Prognostic Profile of Hyponatremia in the Intensive Care Unit

Siham Elarras[1*], Sara Maaroufi[1], Ikarm Berramou[1], Amina Elkhayari[1]

[1]Intensive Care Unit, Marrakech, Morocco

DOI: 10.36347/sasjm.2023.v09i05.023 | **Received:** 13.04.2023 | **Accepted:** 17.05.2023 | **Published:** 21.05.2023

***Corresponding author:** Siham Elarras
Intensive Care Unit, Marrakech, Morocco

Abstract **Original Research Article**

The prevalence of hyponatremia in the intensive care unit varies according to the studies. We conducted a retrospective study of 258 cases, including patients hospitalized in the intensive care unit of the ARRAZI hospital of MARRAKECH. Hyponatremia is frequent in our department and 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 unfortunate given the high mortality rate recorded in our department. Cautious correction is necessary as well as rapid management before admission to the intensive care unit if it is detected earlier in order to lower the mortality rate.

Keywords: Reanimation – Hyponatremia -Disorders - Mortality – Prognosis.

INTRODUCTION

Hyponatremia is a hydro-electrolyte disorder frequently encountered in intensive care. The incidence and prevalence of hyponatremia are high but poorly known and vary according to the severity threshold used, the population studied (age, sex), 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 its speed of installation. Difficulties in the management of hyponatremia are linked to the plurality of mechanisms and etiologies. Hyponatremia can be serious in terms of its severity, the underlying pathologies and the complications related to the treatment and the time taken to take care of it. Its prognosis can be severe although the data of the studies are not very homogeneous and discussed. Few studies have been devoted to hyponatremia encountered in the intensive care unit. Hospital mortality associated with hyponatremia is increased [3].

The main objective of this study is to determine the epidemiological, clinical and prognostic characteristics of hyponatremia in a medical intensive care unit.

MATERIALS AND METHODS:

I. Presentation of the study

This is a descriptive and analytical retrospective study, carried out in the medical intensive care unit of the University Hospital Center in Marrakech, over a period of thirteen months, from June 1, 2016 to June 31, 2017.

II. Service Overview

The medical resuscitation service is a 10-bed unit with 2 teaching professors, 2 doctors and 2 interns. At the paramedical level, 13 nurses.

III. Target population

All patients admitted during this period were eligible for the study. Our population contained 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.

IV. Inclusion/exclusion criteria

Inclusion criteria:

This study included all patients admitted to medical intensive care for the management of a medical pathology or intensive monitoring aged 15 or over.

Exclusion criteria: Incomplete files are excluded from this study.

V. Data collection

The different parameters were collected for each patient essentially in the first 24 hours of his admission to intensive care from the exploitation of patient files.

For each patient, an operating sheet was drawn up, broken down as follows:

- Demographic data;
- Anamnestic data
- Clinical and biological data of hyponatremia
- Severity scores;
- The management of;
- And evolution.

Our operating sheet which was drawn up included the following data:

1. Age

The ages were collected by age group of 10 years except for the first category comprising an age group of 5 years. The age groups 15 to 20, 21 to 30, 31 to 40, 41 to 50, 51 to 60, 61 to 70, 71 to 80, 81 to 90, 91 and over.

2. Sex

3. Comorbidities

A plethora of comorbidities may be related to the occurrence of hyponatremia. Those that are most often implicated in the occurrence of hyponatremia have been studied: Neurological comorbidities including ischemic and hemorrhagic cerebrovascular accidents (CVA), head trauma, epilepsy and other pathologies neurological by domage to the central and peripheral nervous system; cardiovascular comorbidities such as arterial hypertension, heart disease; neoplastic pathologies, toxic history, psychiatric history, pulmonary history, entero-hepato-gastrological comorbidities, immunosuppression such as HIV infection, recent surgery (with a delay of less than 6 months) and the others which include drug poisoning.

4. Reason for admission

The reasons for admission are grouped into 11 categories. Patients admitted for neurological, cardiovascular, digestive, respiratory symptoms, kidney disease, shock, burns, severe infectious syndrome, and other reasons (drug intoxication, etc.)

5. Natremia depth

Hyponatremia was retained below 135mmol/L. It is classified into four levels according to its depth,

- Very severe hyponatraemia: Na+ < 120 mmol/L;
- Severe hyponatraemia: 120 mmol/L ≤ Na+≤ 124 mmol/L;
- Moderate hyponatremia : 125 mmol/L ≤ Na+ ≤ 129 mmol/L ;
- Mild hyponatremia : 130 mmol/L ≤ Na+ < 135 mmol/L.

6. Installation speed

Two installation methods have been selected with respect to a deadline of 48 hours. Acute onset hyponatremia was defined for an onset time of less than 48 hours. A slow onset of hyponatremia was retained when the onset lasted longer than 48 hours [4].

7. State of hydration

The clinico-biological assessment of the extracellular hydration state, [after having eliminated false hyponatremia such as hypertonic and isotonic hyponatremia] makes it possible to characterize the following three hydration states: hypovolemia, hypervolemia and euvolemia depending on the state of extracellular hydration.

8. Discovery mode

Hyponatremia can be discovered incidentally, be the reason for admission or acquired hyponatremia which is hyponatremia occurring during hospitalization in a patient who had not had hyponatremia before.

9. Associated hydro-electrolyte disorders

Potassium, glycemic, uremic and albumin disorders were selected for study.

- Normal serum potassium: We retained values ranging from 3.5 to 5 mmol/l [5]
- Blood sugar: The low blood sugar threshold used to support the diagnosis of hypoglycaemia is between 0.5 and 0.6 g/l (2.8—3.3 mmol/l) [6]. And hyperglycaemia for a value greater than 2g/l.
- Uremia: urea values were interpreted according to the age and sex of each patient.
- Albuminemia: the values were interpreted according to the age of each patient.

10. Associated symptoms

This is to identify the clinical manifestations often associated with hyponatremia. Neuropsychic signs (consciousness disorders, headaches, convulsions), digestive signs (nausea, vomiting) were noted.

11. Severity scores and comorbidity indices

Three severity scores and a comorbidity index were studied here: the Glasgow score, the Mac Cabe score, the Apache II and the Charlson index.

12. Treatments and speed of correction.

Treatments:

The treatments highlighted here are the administration of: saline, glucose serum, antagonists of the renin angiotensin system (angiotensin-converting enzyme inhibitors, angiotensin receptor ARA II antagonists), diuretics (loop, thiazides and potassium-

sparing agents) and the rest of the therapies to treat the basic pathology of the patient.

Correction speed:

- Greater than 2 mmol/L/H
- Between 1.5 and 1.9 mmoml/L/H
- Between 1 and 1.4 mmoml/L/H
- And less than 1mmoml/L/H

13. Length of stay

Three levels of stay have been defined. A short duration equivalent to a duration of hospitalization of less than 5 days, a long duration which is greater than 10 days of hospitalization. And an average duration of between 5 and 10 days.

14. Complications

All complications occurring during hospitalization in subjects in intensive care were classified into four groups: infectious complications, complications such as acute respiratory distress syndrome (ARDS), states of shock and others.

- State of shock: This is defined by the persistence of systolic blood pressure below 90 mmHg for more than 1 hour after volume expansion [22].
- Sepsis: It is defined by the presence of a documented source of infection associated with at least 2 of these signs: heart rate > 90/min, respiratory rate > 20 cycles/min, temperature > 38°C or < 36°C and rate white blood cells < 4,000 or > 12,000 elements/mm3 [23].
- Acute respiratory distress syndrome (ARDS) in adults is a permeable pulmonary edema occurring as a result of direct or indirect aggression of the alveolar-capillary membrane, associated with intense pulmonary inflammation and severe hypoxemia.

15. Evolution

At the end of hospitalization, three outcomes were possible: deceased patients, patients who are transferred to a medical service and patients who go home regardless of the correction of the sodium level.

RESULTS

I. Descriptive study

1. Demographic and anamnestic data

1.1. Prevalence of hyponatremia in the department

In our study,

- Out of 258 patients, 84 patients presented with hyponatremia, i.e. a prevalence of 32.6%.
- The prevalence of hyponatremia occurring during hospitalization in the department is estimated at 23%.

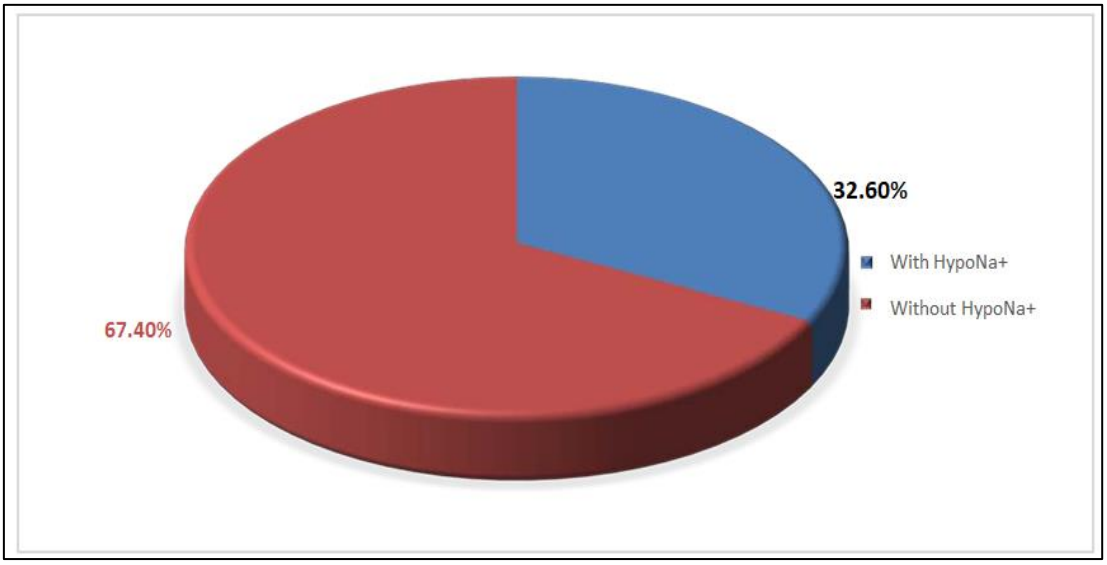

Figure 1: Prevalence of hyponatremia in the CHU Arrazi medical intensive care unit

1.2. Age

The average age of patients with hyponatremia is 47 +/- 22 years.

We recorded a high rate of patients with hyponatremia below 135 mmol/L in young patients between 31 and 40 years old, which represents 18% of patients with hyponatremia, seconded by the category of elderly patients between 61 and 70 years, or 17%.

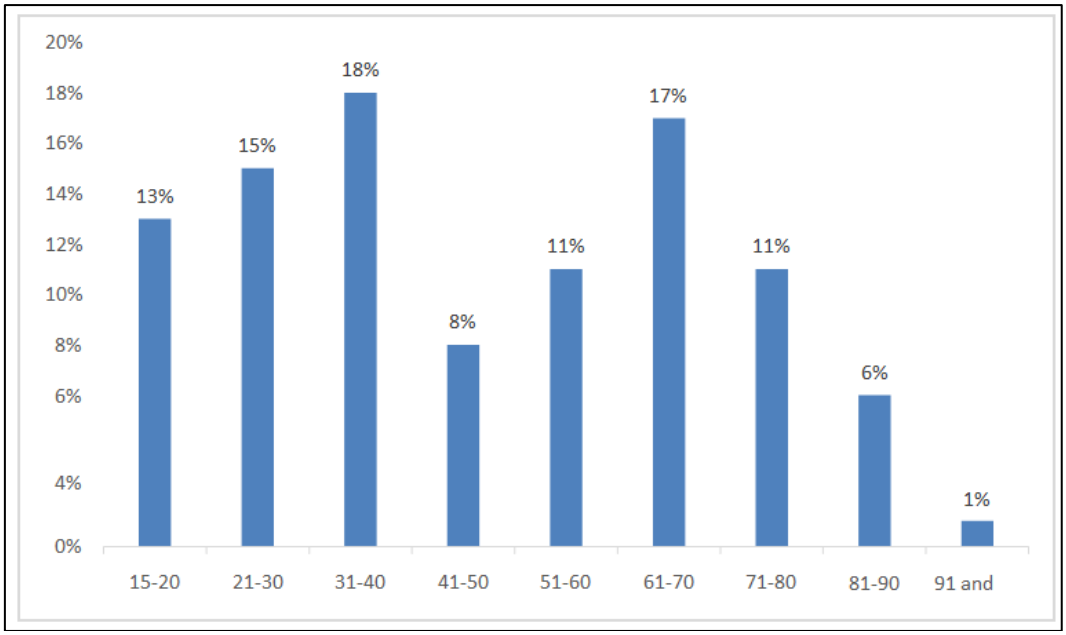

Figure 2: Distribution by age group of patients with hyponatremia

1.3. The gender:

- The sex ratio (M/F) is 0.95
- 43 patients (51.2%) were female

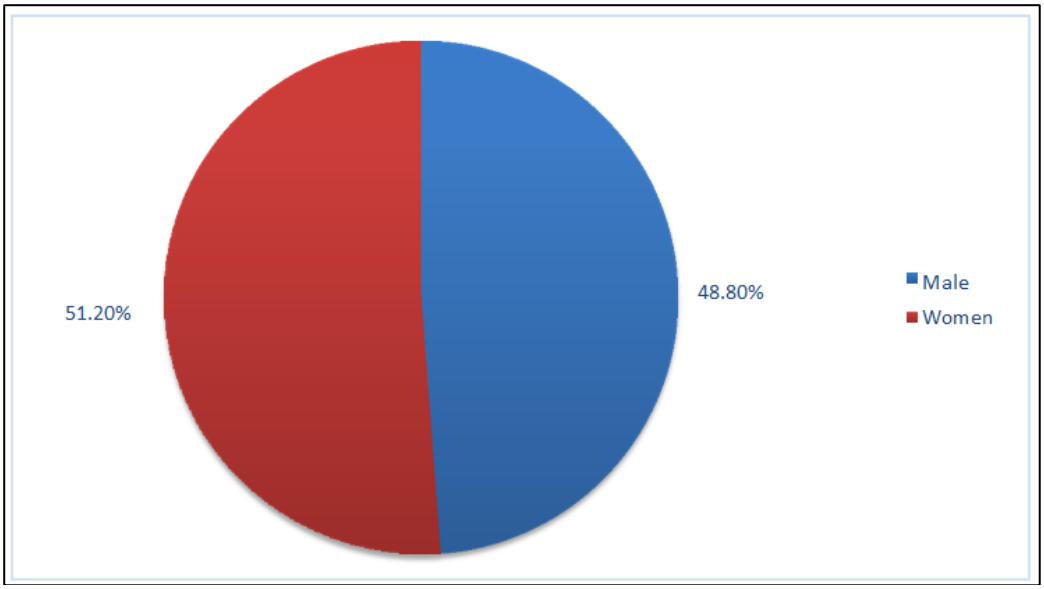

Figure 3: Gender distribution of patients with hyponatremia

1.4. Reason for hospitalisation

During our study, neurological conditions were the main reason for hospitalization in medical intensive care in patients with hyponatremia (45%), followed by respiratory conditions (37%). They are followed by far by digestive pathologies which represent 15% of the reasons for hospitalization.

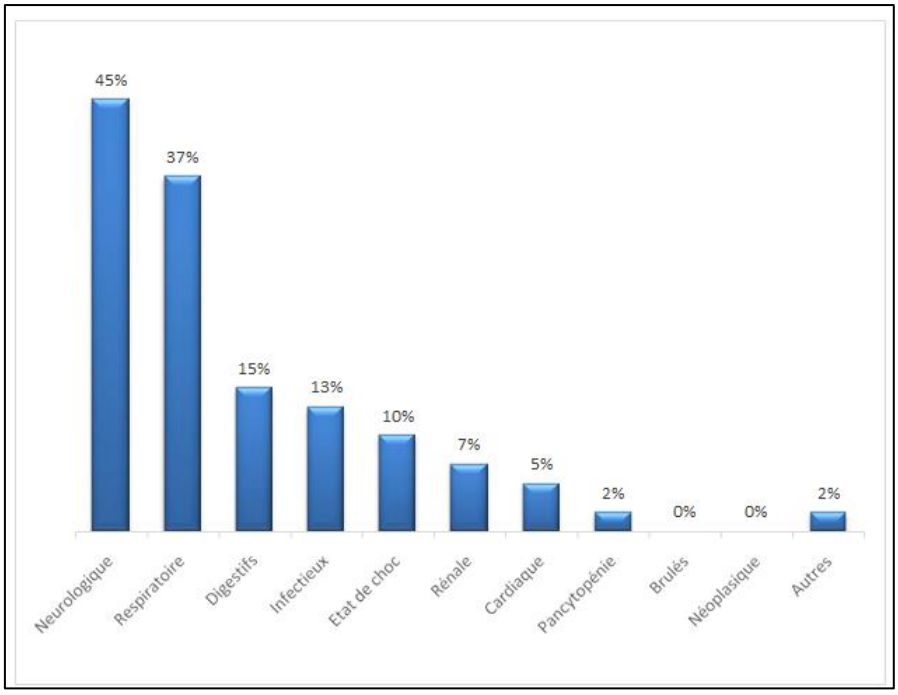

Figure 4: Distribution of patients with hyponatremia by reason for hospitalization

1.5. Background:

Eighty-five percent (85%) of patients with hyponatremia had at least one pathological history.

At the top of the pathological antecedents were the metabolic pathologies including diabetes which represents 27%, closely followed by the cardiovascular antecedents (35%), then the neurological and pulmonary antecedents which each represent 13% of the antecedents. The hepato-gastro-enterological antecedents represent only 12% as well as the toxicological antecedents.

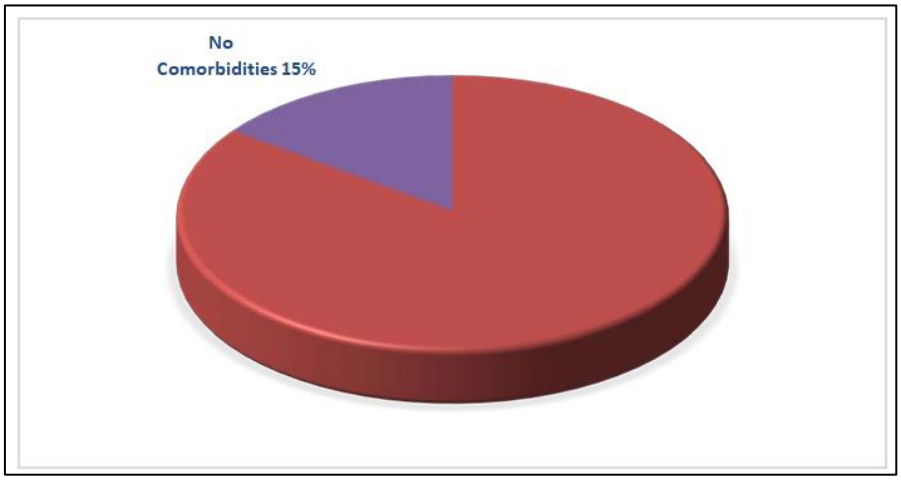

Figure 5: Frequency of comorbidities in patients with hyponatremia

Table I: Prevalence of history in the intensive care unit

		Number	Percentage
Metabolic ATCDs		32	38%
metabolic	Diabetes	23	27%
	IRC	12	14%
	Hypothyroidism	2	2%
Cardiovascular ATCDs		29	35%
Neurological ATCDs		11	13%
Neurological	Epilepsy	5	6%
	PNS pathologies	3	4%
	stroke	2	2%

Others	1	1%
Respiratory ATCDs	11	13%
Hepato-gastroenterological ATCD	10	12%
Toxicological ATCDs	10	12%
ATCD of cancer, tumor or leukemia	8	10%
Immunosuppression ATCD (HIV)	7	8%
Recent surgical ATCDs	6	7%
Psychiatric ATCDs	4	5%
Other ATCDs	7	8%

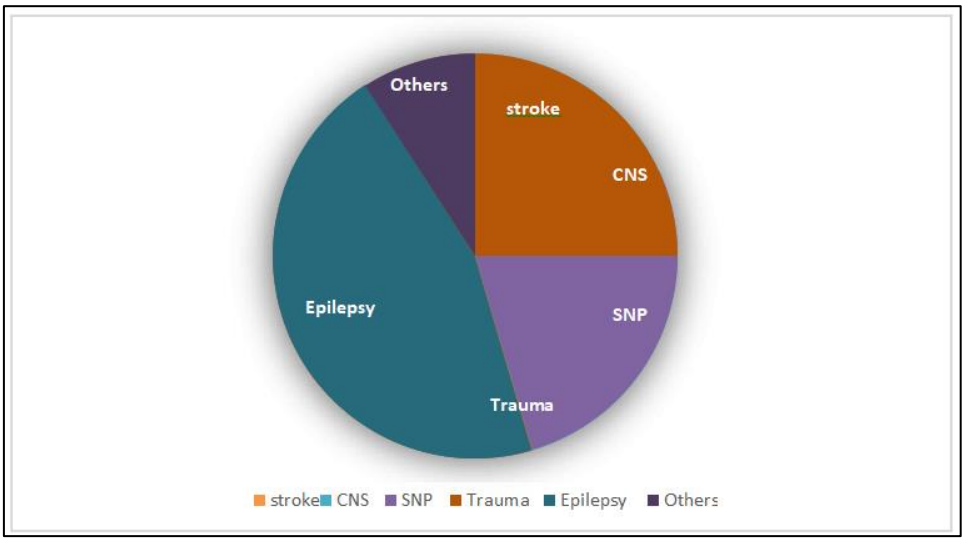

Figure 6: Frequency of neurological ATCDs in patients with hyponatremia

The metabolic history is dominated by diabetes 71.88% followed closely by chronic renal failure 37.50%.

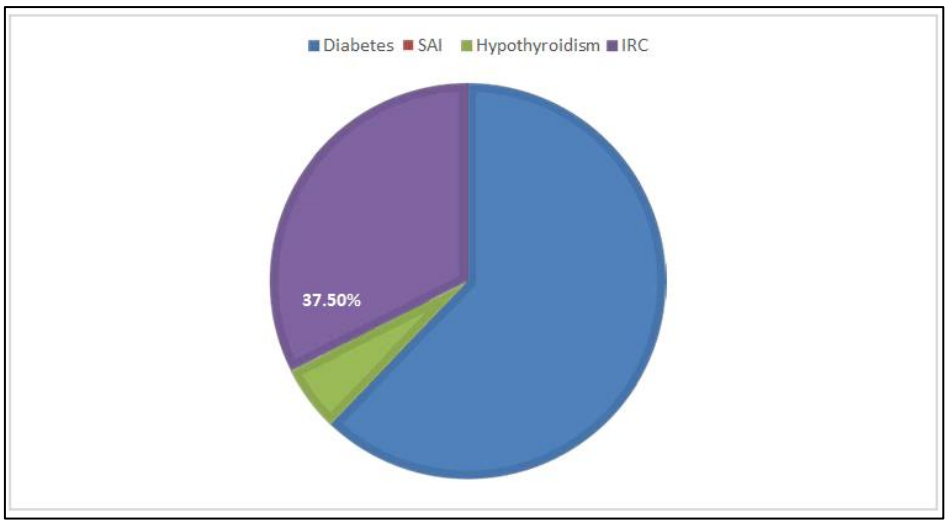

Figure 7: Frequency of metabolic ATCDs in patients with hyponatremia

1.6. Mode of discovery of hyponatremia:

Hyponatremia was incidentally discovered in 59 patients, ie 70% of patients with hyponatremia.

In very few cases, ie in 6 patients (7%), hyponatremia was one of the reasons for hospitalization in medical intensive care.

During our study period, 23% of patients developed hyponatremia in the department after hospitalization.

1.7. Duration of onset of hyponatremia in medical intensive care:

The average duration of onset of hyponatremia during hospitalization is 5.79 days after hospitalization

with a standard deviation of 4.9 days. The median is 4 days.

The minimum duration of onset of hyponatremia = 1 day after hospitalization.
The maximum duration= 20 days after hospitalization.

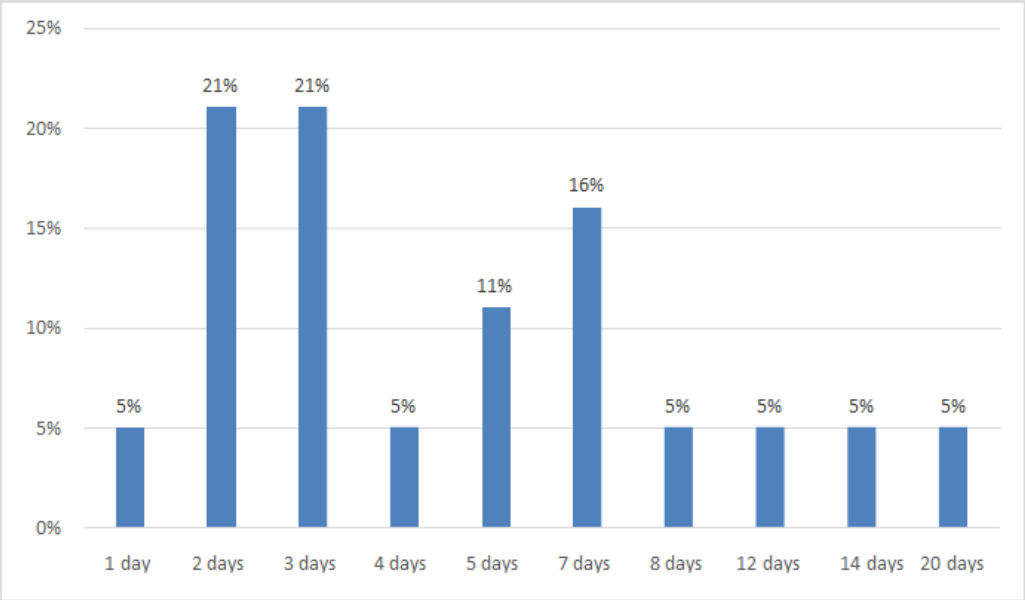

Figure 8: Duration of onset of hyponatremia in patients during hospitalization

2. Biological characteristics of hyponatremia

2.1. Depth of hyponatremia

Severe hyponatremia (120-124 mmol/L) is predominant in our study.

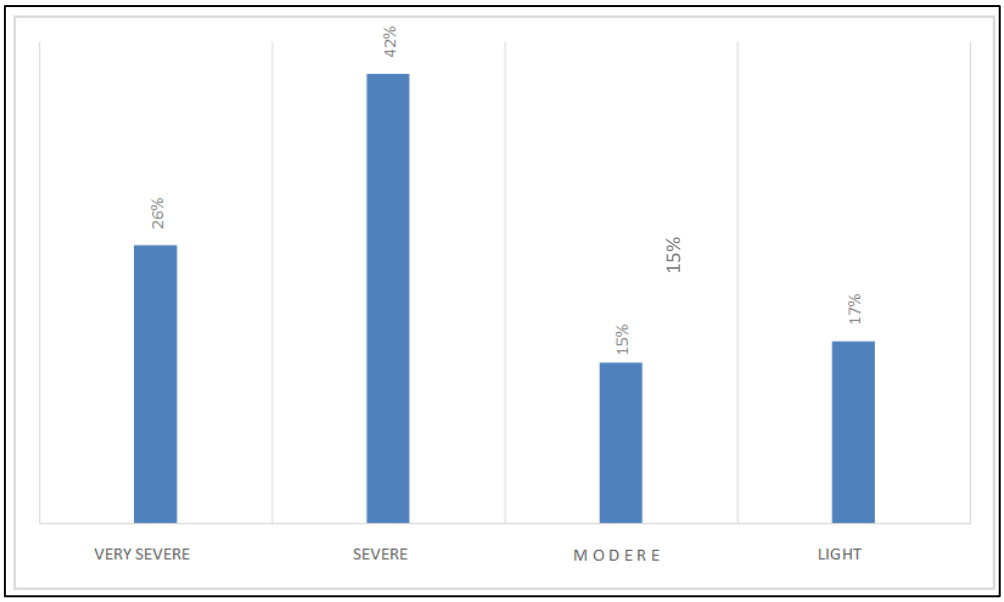

Figure 9: Prevalence of hyponatremia according to its depth

2.2. Mode of onset of hyponatremia

The hyponatremia was:

- Acute onset in 43 patients (51.20%) and
- Slow installation at 48.80%.

3. Clinical features of hyponatremia

3.1. Hyponatraemia: associated clinical signs:

- Hyponatremia was clinically evident in 80% of patients.
- Consciousness disorders (Glasgow score < 13) were frequently observed (58% of patients with hyponatremia). They are followed by digestive disorders (41%).

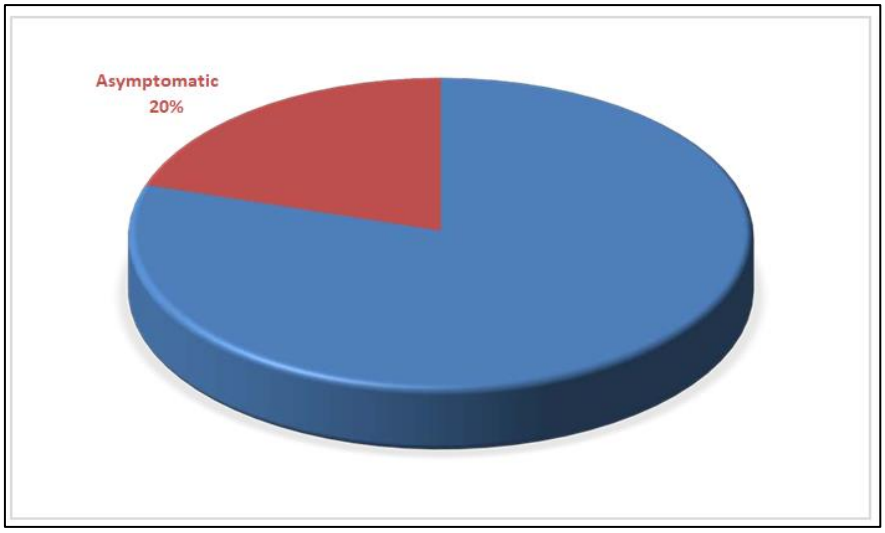

Figure 14: Prevalence of overt hyponatremia on admission

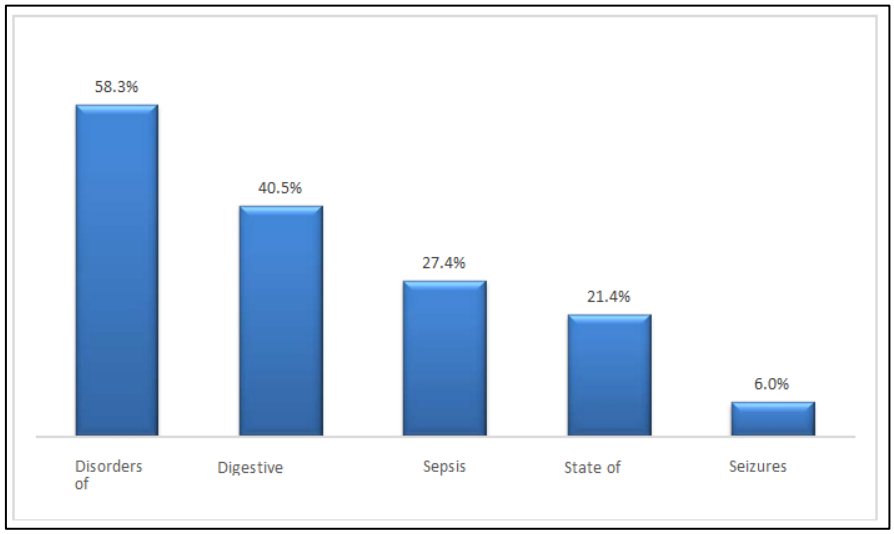

Figure 15: Prevalence of symptoms related to hyponatremia

3.2. State of hydration and their etiologies

We distinguish:

- Hypervolemic hyponatremia : 27.72%
- Hypovolemic hyponatremia : 51%
- Normovolemic hyponatremia : 19.28%

Their etiologies are summarized in the following table:

Table II: Frequency of the various mechanisms of onset of hyponatremia with their etiologies

State of hydration	Causes		Number	Percentage
Hyper-volemian=23 27.72%	Heart failure		14	17%
	Nephrotic syndrome		8	9.5%
	Hepatic cirrhosis		1	1%
Hypovolemia n= 44 51%	Digestive losses		32	37%
	Kidney losses		12	14%
Normo-volaemian=16 19.28%	SIADHP	Pneumonia	7	8%
		Meningitis purulent	1	1%
		Meningitis tuberculosis	1	1%
		Tuberculosis pulmonary	1	1%
		Other causes	2	2%
	No SIADHP		5	5%
Total			82	100%

4. Treatment given to patients with hyponatremia

4.1. Treatment before admission to intensive care

A (rapid) treatment had been initiated in 38% of patients before their admission to our intensive care unit aimed at correcting hyponatremia.

4.2. Symptomatic treatments

Saline intake was undertaken in 81% of patients. Diuretics were used in 39% of patients.

Fluid restriction was a therapeutic option in 4% of patients.

Among the diuretics, figure the diuretics of the loop which were administered in majority in 33% of the patients.

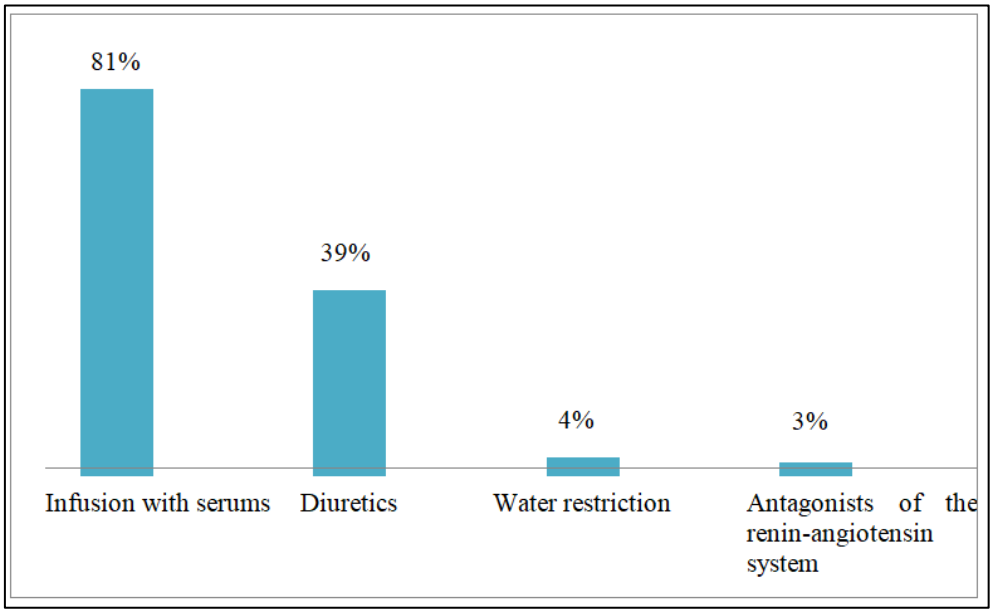

Figure 17: Percentage of symptomatic treatments administered

4.3. Other treatments administered

PPIs were used in 86% of patients, antibiotic therapy in 71% of patients and insulin therapy in 31% of patients.

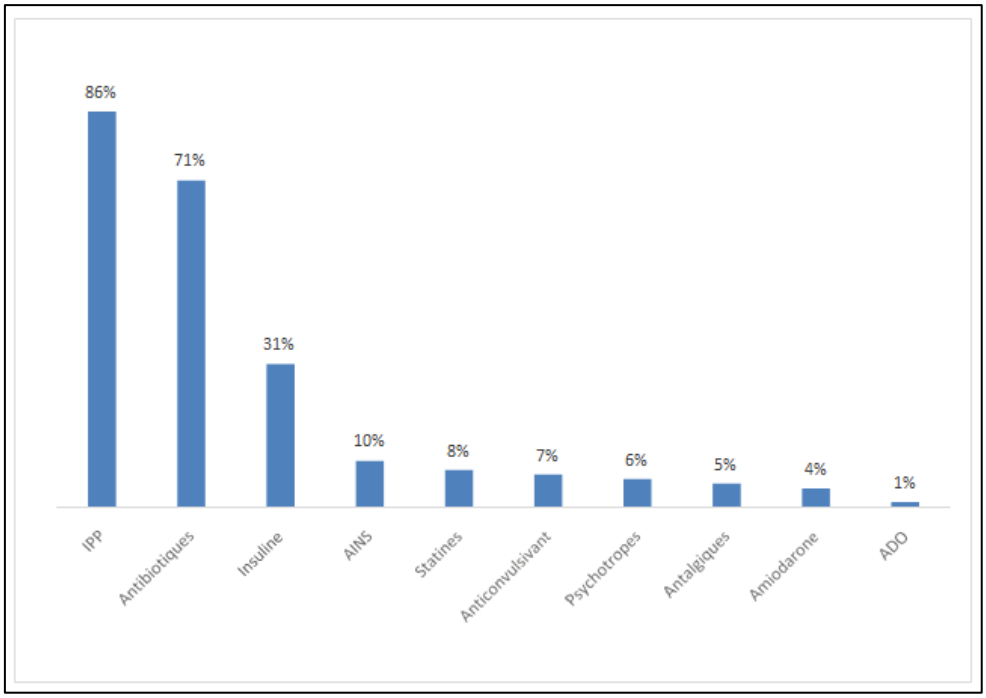

Figure 18: Percentage of other treatments administered in patients with hyponatremia

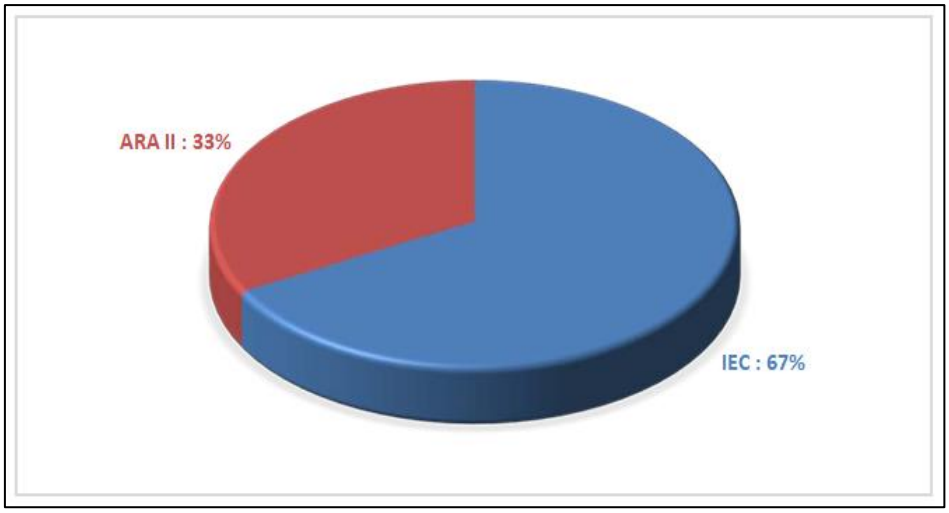

Figure 19: The different renin-angiotensin system antagonists used in patients with hyponatremia

4.4. Speed Correction

Correction of hyponatremia was very slow (less than 1 mmol/L) in almost all of them, ie in 91.7% of patients.

Table III: Speed of correction of hyponatremia

	1.5-1.9mmol/l/H	1-1.4 mmol/L/H	< 1 mmol/L/H	Total
Number	2	5	77	84
Percentage	2.4%	5.9%	91.7%	100%

5. Prognosis

5.1. Glasgow score

Referring to the Glasgow scale,

- The majority of patients, 57.1%, had impaired consciousness (GCS < 13).
- 35 patients or 42.9% had a GCS > 13.

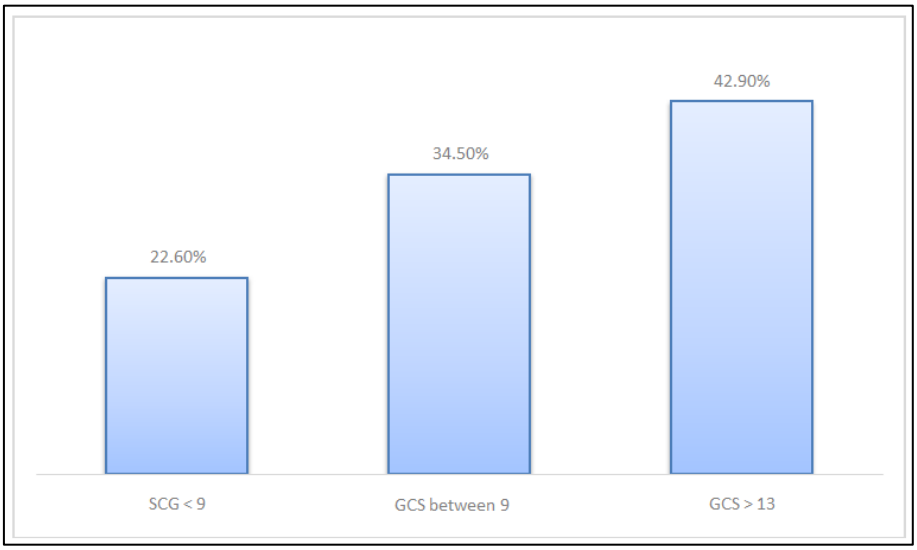

Figure 20: Glasgow score in patients with hyponatremia

5.2. McCabe score

- Without chronic disease, 31% of patients were classified as stage 0 on the Mac Cabe score.
- Having a chronic disease whose survival is at least five years, 44% of patients with hyponatremia were classified as stage 1.
- Having a chronic disease whose life expectancy does not exceed one year, 25% of patients with hyponatremia were classified stage 2 of the Mac Cabe score.

5.3. APACHE II

The average predicted mortality (MP) according to the APACHE II score is 44% and the average corrected predicted mortality is 43%.

5.4. Charlesson Score

- Patients with a Charlson score equal to 0 were 19 (23%).
- For a score between 1 and 2, we found 34 of the patients or 40%.
- For a score between 3 and 4, we found 16 patients, or 19%
- For a score greater than or equal to 5, we found 15 patients, or 18%.

6. Evolution

6.1. Complications

Among the patients who had hyponatremia, 31 (37%) patients were able to benefit from a correction of the natremia to its normal value before leaving the medical intensive care unit.

Only 17% of patients with hyponatremia presented complications such as:

- A state of shock in 11% of patients with hyponatremia,
- Sepsis in 4% of patients and
- An acute respiratory distress syndrome in 2 patients or 3%

6.2. Mortality rate

The observed mortality (OM) is 56% in patients with hyponatremia. The ratio of observed mortality (OM) to predicted mortality (MP) is 1.27.

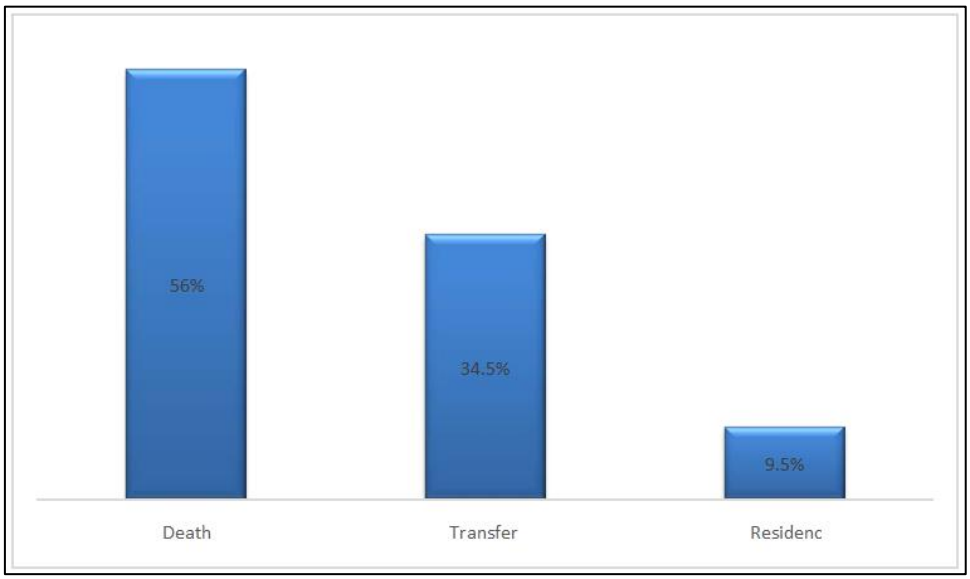

Figure 21: Evolution of patients with hyponatremia in intensive care

II. ANALYTICAL STUDY

1. Demographic and anamnestic factors associated with hyponatremia

This analytical study will allow us to identify the factors that are associated with the presence or occurrence of hyponatremia in the patients covered by our study.

1.1. Association hyponatremia - Age

We objectified a significant association between age and hyponatremia ($p<0.005$).

According to the results of our study, there is a gradual increase in the prevalence of hyponatremia from the age group of 41 to 50 years up to 91 years and older.

Table IV: Frequency of hyponatremia according to age

Age	P1	P2	p
15-20	36%	65%	0.005
21-30	34%	66%	
31-40	45%	55%	
41-50	13%	87%	
51-60	25%	75%	
61-70	33%	67%	
71-80	56%	44%	
81-90	63%	38%	
91 and over	100%	0%	

P1: patients with hyponatremia
P2: patients without hyponatremia

1.2. Association hyponatremia - Sex

The prevalence of hyponatremia is the same regardless of patient gender. There is no association between hyponatremia and patient gender (p>0.05).

Table V: Frequency of hyponatremia according to sex

Sex	P1	P2	P
Male	33%	67%	
Women	32%	68%	0.779

P1: patients with hyponatremia
P2: patients without hyponatremia

1.3. Association hyponatremia - Comorbidities

There is a significant association (p=0.02) between hyponatremia and comorbidities. In patients with at least one history, we note that the percentage of hyponatremia was higher compared to patients without hyponatremia (36% versus 21%).

Among the comorbidities, the association with hyponatraemia was significant for: a tumor history, a metabolic history, diabetes, a hepato-gastroenterological history or a recent surgical history (operation having taken place within the last 6 months).

For other comorbidities, the association with hyponatremia was not significant in our study.

Table VI: Percentage of hyponatremia according to the history.

Background			P1	P2	P	P<0.05*
Presence of history		Yes	36%	64%	0.02	*
		No	21%	79%		
Cardiovascular		Yes	40%	60%	0.1	
		No	30%	70%		
Neurological		Yes	33%	67%	0.919	
		No	33%	68%		
Neoplasia, cancer or tumor		Yes	80%	20%	0.001	*
		No	31%	69%		
metabolic		Yes	47%	53%	0.003	*
		No	27%	73%		
Metabolic	Diabetes	Yes	49%	51%	0.008	*
		No	29%	71%		
	Hypothyroidism	Yes	67%	33%	0.205	
		No	32%	68%		
	Renal failure	Yes	48%	52%	0.077	
		No	31%	69%		
Toxic		Yes	48%	52%	0.124	
		No	31%	69%		
Psychiatric		Yes	44%	56%	0.439	
		No	32%	68%		
Pulmonary		Yes	30%	70%	0.692	
		No	33%	67%		
Hepato-gastroenterological		Yes	59%	41%	0.017	*
		No	31%	69%		
Immunocompromised		Yes	50%	50%	0.152	
		No	32%	68%		
Recent surgery		Yes	86%	14%	0.002	*
		No	31%	69%		

2. Prognostic factors for hyponatremia

This analytical study will allow us to identify these factors that can impact the prognosis of patients with hyponatremia in the intensive care unit.

2.1. Association mortality – hyponatremia

The death rate in patients with hyponatremia is 56%. While the death rate in patients without hyponatremia is 48%.

Our study did not show a significant association between hyponatremia and death (p=0.214).

2.2. Prognostic factors for hyponatremia

The mortality rate of patients with hyponatremia has been identified according to the presence and absence of certain factor.

a) Biological factors associated with mortality:

The association of mortality in patients with hyponatremia was significant with serum albumin. The mortality rate is inversely proportional to the value of albuminemia.

Table X: Mortality rate according to biological factors

		Death	survivors	P	* P<0.05
Depth	Less than 120	71%	29%	0.14	
	120-124	77%	23%		
	125-129	49%	51%		
	130-134	45%	55%		
State of hydration	Hypovolemia	56%	44%	0.65	
	Eu-volemia	44%	56%		
	Hyper-volemia	64%	36%		
Installation mode	acute	66%	34%	0.07	
	Slow	46.5%	53.5%		
Kalemia	Hyperkalemia	58%	42%	0.08	
	Normo-kalaemia	45%	55%		
	Hypokalemia	79%	31%		
Blood sugar	Hyperglycemia	51%	49%	0.76	
	Eu-glycaemia	56%	44%		
	Hypoglycemia	67%	33%		
Uremia	Hyperuremia	58%	42%	0.36	
	Normo-uremia	61%	39%		
	Hypo-uraemia	36%	64%		
Albuminemia	Hyperalbuminemia	0%	100%	<0.05	*
	Normalbumineme	32%	68%		
	Hypoalbuminemia	70%	30%		

b) Clinical symptoms associated with mortality

Clinically, we have objectified, in patients with hyponatremia, a significant association between mortality and: symptomatic hyponatremia, state of shock, impaired consciousness (a Glasgow score of less than 13).

- The mortality rate of patients with impaired consciousness is higher than that of patients without impaired consciousness: 65% versus 43%.
- The mortality rate of patients with a state of shock is higher than that of patients without a state of shock: 83% against 43.5%.

c) Severity scores associated with mortality

Among the different scores used in our bivariate analysis, only the Apache II is associated with mortality in patients with hyponatremia.

- The average predicted mortality among the deceased is higher than among the survivors: 44.46% against 27.44%.
- The average corrected predicted mortality is also higher among the deceased than among the survivors: 42.69% against 26.70%.

Table XII: Mortality rate according to severity scores

		Death	**survivors**	**P**	*** P<0.05**
Glasgow score	Less than 9	68%	32%	0.07	
	9 -13	66%	34%		
	Greater than 13	42%	58%		
McCabe score	Stage 0	50%	50%	0.25	
	Stage 1	51%	49%		
	Stage 2	71%	29%		
Charlesson Score	0	58%	42%	0.68	
	1-2	62%	38%		
	3-4	44%	56%		
	< 5	53%	47%		
Apache II	Average total score	22.1	16.30	0.001	*
	Predicted mortality mean	44.46%	27.44%	0.001	*
	rage corrected mortality	42.69%	26.70%	0.000	*

d. Association of mortality and care, progression and length of stay

- In patients with hyponatremia, mortality was significantly associated with:
- Treatment undertaken before admission to intensive care (speed of management). Indeed, the mortality rate of patients who benefited from therapeutic measures before their entry into intensive care is lower than the mortality rate of patients who did not benefit from treatment before their admission: 34% against 69%.
- The presence of a complication,
- Correction of hyponatremia. Indeed, the mortality observed in patients whose sodium levels had returned to normal values before leaving the intensive care unit was much lower than the mortality observed in those whose hyponatremia was not corrected before leaving the unit: 22% versus 75%.

Table XII: Mortality rate according to treatment, length of stay and evolution

		Death	survivors	P	* P<0.05
Treatment before admission	Yes	34%	66%	0.002	*
	No	69%	31%		
Duration of stay	Less than 5 days	61%	39%	0.60	
	5-10 days	50%	50%		
	More than 10 days	50%	50%		
Complication	ARDS	100%	0%	0.01	*
	Infectious	67%	33%		
	State of shock	49%	51%		
	No complications	100%	0%		
Fixed hyponatremia	Yes	22%	78%	0.00	*
	No	75%	25%		
Speed of correction (mmol/lh)	< 1	54.5%	45.5%	0.53	
	1 – 1.5	80%	20%		
	1.5 – 1.9	50%	50%		

DISCUSSION

I. Etiopathogenesis of hyponatremia

Hyponatremia is defined as a serum sodium lower than 135 mEq/l.

1. Classification of hyponatremia

Hyponatremia corresponds to a decrease in plasma sodium concentration.

There are three types of hyponatremia whose distinction is based on the assessment of plasma tonicity. Thus, we distinguish:

a. False hyponatremia or hyperosmolar hyponatremia

Hypertonicity is linked to the accumulation of active osmoles, this is responsible for intracellular dehydration resulting from the passage of water from the intracellular environment to the extracellular environment. The most common cause of this type of hyponatremia is hyperglycemia; mannitol is more rarely responsible [40, 41, 29, 30].

b. Pseudo-hyponatremia or iso-osmolar hyponatremia

They are due to the presence in the plasma of abnormally high quantities of macromolecules, this is the case of hyper-protidemia or hyperlipidemia [42, 27, 30, 29, 40].

In these situations, the plasma water is reduced, the natremia is low, the plasma osmolarity as well as the cellular hydration are normal [30, 40, 41].

There is also a rare situation of iso-osmolar hyponatremia, this is a situation encountered after endoscopic surgery using large quantities of isotonic irrigating solutions (sorbitol). Patients may develop profound hyponatremia associated with neurological signs while plasma osmolarity is normal [30].

c. True hyponatremia or hypo-osmolar hyponatremia

True hyponatremias have been classified according to the pathophysiological mechanism responsible, into 3 large groups. This classification is based on the evaluation of the extra cellular volume which is based on clinical criteria (AP, weight, presence or absence of oedemas, etc.) and biological criteria (protidemia, hematocrits, etc.) [43, 44, 27-36].

- Hypovolaemic or depletion hyponatremia:

It is retained in the presence of clinical or biological signs of extracellular dehydration (dehydration fold, arterial hypotension, haemoconcentration, etc.) [45, 46, 47, 25-28].

- Normovolemic hyponatremia or by dilution

It is retained in front of a normal volemia.

- Hyponatremia hypervolaemic or by water-soda inflation

Observed in the presence of clinical and biological signs of extracellular hyperhydration (edema, haemodilution) [45, 25, 46, 28, 47].

2. Etiologies of hyponatremia

For each type of hyponatremia, there are a number of etiologies that are responsible for it.

a. Hypovolemic hyponatremia

Hyponatremia with decreased VEC reflects greater loss of NaCl than loss of water.

- Salt losses can be extrarenal. A natriuresis of less than 20 mmol/L indicates hypovolemia due to extrarenal losses [48].
- Digestive losses: Digestive losses can be observed during secretory diarrhoea, digestive fistulas and vomiting. Rarely, in patients with vomiting and metabolic alkalosis, bicarbonaturia may occur.
- Constitution of a third sector: peritonitis, pancreatitis, ileus;
- Cutaneous loss: extensive burns, bullous dermatosis, sweating of the marathon runner compensated by hypotonic contributions.
- Taking thiazides
- Hyponatraemia attributable to thiazide diuretics is frequent; they are sometimes very acute occurring in the days following the introduction of the treatment but they can also be seen after a prolonged treatment. It seems that advanced age, female sex and a low body mass index are more frequently associated with the occurrence of hyponatremia under thiazides [49, 50, 48].
- Renal salt losses
- A natriuresis greater than 20 mmol/L indicates a renal loss of salt. The causes are frequent.
- Overdose of diuretics
- Overdoses other than thiazides are much rarer.
- Acute adrenal insufficiency
- Tubulointer stitial nephropathy
- Brain salt wasting syndrome Cerebral salt wasting syndrome is described in neurosurgery departments [50]. Occurring in patients with cerebral lesions (trauma, infection, tumour, haemorrhage), the biological picture is that of SIADH but the extracellular sector is reduced.

b. Normovolemic hyponatremia

It is a hyponatremia reflecting an excess of water responsible for an almost pure intracellular hyperhydration by persistence of an "anti-diuresis"

- Hyponatremia of endocrine origin
- Inadequate antidiuretic hormone secretion (SIADH) or syndrome of inappropriate antidiuresis: The diagnosis of SIADH is a diagnosis of exclusion but is very frequent. The diagnostic criteria for SIADH are summarized in Table XIV [53 54]. Measurement of serum HAD concentration is not routinely recommended. Urinary osmolality greater than 150 mOsm/L, unsuited to plasma osmolality, indicates inappropriate anti-diuresis".
- Water poisoning: Excessive water intake is seldom sufficient, if the kidney is normal, to cause
- hyponatremia. The dilution capacities of the kidney must be reduced or the daily intake of osmoles must be low. Urinary osmolality is adapted to low plasma osmolality, less than 150 mOsm/L.

Table XIV: Diagnostic criteria for inadequate antidiuretic hormone secretion (SIADH)

Major criteria	Decreased plasma osmolarity < 280 mOsm/L
	Inadequate urinary osmolarity > 150 mOsm/L
	Normal extracellular volume: no orthostatic hypotension, tachycardia, edema or ascites
	Natriuresis > 30 mmol/L in a normalized diet
	Normal thyroid and adrenal functions
Minor criteria	No recent diuretic intake
	Absence of serum sodium correction after infusion of 0.9% saline
	Correction of serum sodium after water restriction

Table XV: Causes of syndrome of inappropriate antidiuretic hormone secretion

Tumor pathologies	Carcinomas: small cell lung, mesothelioma, oropharynx, stomach, duodenum, pancreas, ureter, bladder, prostate, endometrium
	Lymphomas, sarcomas
Lung conditions	Bacterial, viral infections, tuberculosis, aspergillosis
	Asthma
	cystic fibrosis
Central nervous system disorders	Infections: encephalitis, meningitis, brain abscess, infection with HIV Brain tumors
	Head trauma, hydrocephalus, cavernous sinus thrombosis Multiple sclerosis, Guillain-Barré syndrome, withdrawal syndrome,
	acute intermittent porphyria
Drugs increasing the production of ADH by the hypothalamus	tricyclics, serotonin reuptake inhibitor, MAOI
	Anti-psychotics: phenotiazine, haloperidol

Antidepressants	Anti-epileptics: carbamazepine, valproic acid
	Anti-cancer: alacaloids, platinum salts, alkylating agents, methotrexate, interferon, monoclonal antibodies
	Opiate analgesics: tramadol, morphine
	Miscellaneous: proton pump inhibitors, nicotine, "ecstasy" (MDMA), clofibrate
Drugs potentiating the effect of HAD	Antiepileptics: carbamazepine, lamotrigine
	Antidiabetics: chlorpropamide, tolbutamide
	Anti-cancer: intravenous cyclophosphamide
	Nonsteroidal anti-inflammatory drugs
Medicines with a HAD activity	Desmopressin, oxytocin, vasopressin
Others	Genetics: Idiopathic HAD receptor activating mutation
	Transient : endurance exercise, stress, nausea, pain, anesthesia

c. Hypervolemic hyponatremia

This is hyponatremia with a relative excess of water greater than the excess of salt (Figure 25). Normally, the increase in pressure in the left atrium decreases the secretion of ADH and increases that of the atrial natriuretic peptide, which leads to an increase in the secretion of water and sodium. In chronic heart failure, these reflexes are abolished. Stimulation of the RAA system and the sympathetic system increases the proximal tubular reabsorption of water and NaCl explaining the edematous syndrome and low natriuresis. Hyponatremia is the witness of the production of ADH, stimulated by effective hypovolemia and angiotensin

It is seen in congestive heart failure, decompensated cirrhosis and nephrotic syndrome. It is a poor prognostic marker in cirrhosis and heart failure, found in more than 20% of patients with advanced disease [58, 59].

II. Descriptive study

Several studies have targeted a general hospital population and that of the elderly, but very few have focused on intensive care patients.

1. Prevalence of hyponatremia

Several studies, most often involving small groups of patients, have described the prevalence of hyponatremia in at-risk populations [27]. Hyponatremia is common in critically ill patients [60]. In our context, the prevalence of hyponatremia in patients hospitalized in intensive care is about 32%.

DeVita *et al*., [61] retrospectively examined 98 intensive care 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 2,000 French patients showed that the incidence of hyponatremia (serum sodium level of 130 mEq/L) on admission to intensive care was 14% [62].

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 [63, 64].

In geriatric hospitals, the prevalence of hyponatremia varies from 10 to 25%. [65-67]. In emergency departments, 4 to 5% of patients present with hyponatremia, [68] but this frequency can rise to 30% in cirrhotic patients [69].

A "given day" type multicentre descriptive study was carried out in internal medicine departments in western France [70]. The overall prevalence of hyponatremia was 12.1%.

A British study [71], carried out in a neurology intensive care unit and published in January 2006, reported a higher frequency of hyponatremia in neurology and neurosurgery patients, particularly in cases of head trauma and basilar meningitis, reaching up to 15% of patients with mortality ranging from 7 to 60%.

The current prevalence of hyponatremia in hospitalized patients depends on the population studied and the rate of hyponatremia studied [72 73 74 75 76], thus, it is estimated at 20% for a plasma sodium level below 136 mmol/ l and from 1 to 4% for a sodium level below 130 mmol/l in the USA.

The table compares the prevalence of hyponatremia in our study to those found in the literature.

Table XVI: Prevalence of hyponatremia according to several studies

Study	Country	Service	Prevalence %
Aegerter *et al*., [27]	France paris)	Intensive care versatile	7 – 12%
From Vita *et al*., [61]	USA (New York)	Intensive care versatile	30%
Bennani *et al*., [43]	Morocco (Rabat)	Medical reanimation	13.7%
Tisdal *et al*., [73]	Britain	Intensive care of neurology	1 – 15%

Ryo *et al*., [42]	Korea (Seoul)	Cardiology	16.4%
Felker et al. [43]	Israel	Cardiology	22%
Maggioni *et al*., [77]	Italy (Florence)	Cardiology	27.4%
Potter *et al*., [78]	France (West)	Internal Medicine	12.1%
Hawkins [56]	Singapore	Emergency room	22.1%
Caird *et al*., [79]	Scotland (Glasgow)	Geriatrics	7%
Beck *et al*., [70]	USA (Florida)	Internal Medicine	15 – 18%
Miller *et al*., [65]	USA (New York)	Rest house, Medicine, surgery	50%
Anderson *et al*., [60]	USA (Colorado)	Gynecology and psychiatry	1 – 2.5%
Chung *et al*., [60]	USA (Colorado)	Post-operative follow-up	4.4%
Lee *et al*., [68]	taiwan	Internal Medicine	4%
Wassima IDHAMOU [80]	Morocco (Casablanca)	Resuscitation of emergency room	26.1%
Abidi [81]	Morocco (rabat)	Medical reanimation	21%
Our study	Morocco (Marrakesh)	Medical reanimation	32%

2. Age and Sex

The frequency of hyponatremia is variable [82] but can be six times higher in elderly patients [65]. And the incidence of hyponatremia was equal between the two sexes according to several authors [83-85].

In a Moroccan study [86], carried out at the University Hospital of Rabat, between January 1996 and February 2001, three hundred patients with hyponatremia on admission were included among 2188 patients admitted, ie an incidence of 13.7%. The age was 42.1 ± 1.1 years with a sex ratio of 1.1 (153 men and 147 women).

Shapiro found a higher prevalence of hyponatremia ≤ 125 mEq/l in hospitalized elderly women (8.1% vs 4.0%; p < 0.001) [87].

Table XVII: Comparison of age and sex in patients with hyponatremia according to different studies

	Natremia (mmol/l)	Middle age	Sex ratio
J Hao, in China [88]	<135	48.8±15.9	0.94
Béatrice, internal medicine, at Grenoble [92]	<120	71.6	1
Bennani, resuscitation, Rabat [62]	<130	42.1 ± 1.1	1.1
Das, medical resuscitation, France [89]	<120	59.1±16.8	0.98
Shapiro [87]	<125	82.1±8.7	0.49
Abidi, medical resuscitation [83]		50 ±19	1.2
Our study	<135	47±21.8	0.95

A study carried out in Singapore [56] between 2001 and 2002 compared the prevalence of hyponatremia between groups of patients according to the level of hyponatremia, age group and gender:

Table XVIII: Prevalence of hyponatremia in the different groups of patients

	Care emergency hospital	Ambulatory hospital care	Care in city medicine	Age > 60 (%)	Age > 70 years (%)
Na < 136 mmol/l	28.2	21	7.2	23.6	27.3
Na < 135 mmol/l	22.1	14.7	4.3	18.2	21.7
Na < 126 mmol/l	2.6	0.96	0.14	2.2	2.9
Na < 116 mmol/l	0.49	0.17	0.03	0.44	0.6

3. Background

In the literature, in general, cardiovascular pathologies, in particular hypertension and heart failure, appear in the foreground, but with neoplasia, and liver failure in the context of cirrhosis [90-92, 85]. The underlying pathologies play an influential role in the occurrence of hyponatremia and on the physiopathological mechanisms at the origin of these hyponatremias. Decompensation of underlying pathology can lead to hyponatremia. It should also be noted that the terrain is often poly-pathological.

In our series, comorbidities were mainly represented by metabolic antecedents (38%) including diabetes (27%) followed by cardiological pathologies (35%) and neurological and respiratory pathologies (13% each).

It should be noted that diabetes is the most frequent antecedent but cardiovascular antecedents remain the first comorbidities of patients with hyponatremia as demonstrated in a similar study [92] where cardiovascular antecedents represent 69.4% of comorbidities with hypertension arterial in mind, or 61.1% [30]. Similar in the study of Abidi, in Morocco [81], diabetes in mind also represents 24% of comorbidities, arterial hypertension 21% and heart failure 20%.

4. Reasons for hospitalization

The neuropsychic symptoms represent one of the causes of important admission in our patients in our study, at the top of the list appeared the neurological symptoms, that is to say 45% of the reasons for hospitalization.

On the other hand, in another study on hyponatremia in a surgical intensive care unit in Casablanca, patients were mainly admitted for postoperative course in 46% of cases [80].

It is the same case in Angers, in a general medicine service and in Grenoble in internal medicine. Neurological or neuropsychic disorders are in the lead with 58% and 27.8% of the reasons for hospitalization respectively in Angers and Grenoble [93, 94].

Even moderate hyponatremia can promote falls in elderly patients, which represent an important cause of admission [94]. This is not the case in our study, since it is only focused on patients in medical intensive care which receives patients with medical pathologies excluding surgical cases such as patients requiring surgery.

These differences lie in the variability of the places of study. In medical or medical resuscitation services, neurological symptoms remain the main reasons why patients are hospitalized. This is not the case for surgical resuscitation services: falls, deterioration in general condition and post-operative consequences are the main reasons for hospitalization.

Table XIX: Comparison of reasons for admission to different departments in patients having hyponatremia

Reason for admission	General medicine, Angers [93]	Surgical emergency resuscitation, Casablanca [80]	Medical resuscitation [81]	Our study
Neurological	58%	(stroke) 9%	29%	45%
Disorders psychiatric	26.3%	-	-	-
Disorders Digestive	13.1%	(Pancreatitis) 9%	-	15%
Severe sepsis or septic shock	-	13%	18%	13%
Cardiological	-	-	7%	5%
Fall	15.8%	-	-	-
Respiratory	-	-	26%	37%
Sequels operating	-	46%	-	-
Trauma	-	28%	-	-

5. Mode of discovery and mode of onset of hyponatremia during hospitalization

Hyponatremia can be symptomatic and is very often discovered incidentally. This is the case in our series where 70.24% of hyponatremia were incidentally discovered.

Data on the incidence of hyponatremia on admission compared to that of acquired hyponatremia are scarce [60]. Thus, the study carried out by Vandergheynet et al, in 2013 had shown that the incidence of hyponatremia on admission was almost similar to that of hyponatremia acquired in intensive care (12.3% vs 13.1% respectively). Also, the study by Sa et al. had not demonstrated a difference (hyponatremia on admission 11% vs acquired hyponatremia 13%) [95]. These data do not corroborate not only with the result obtained in the study carried out at the CHU de casa and in Marrakech where the incidence of acquired hyponatremia was lower than that of hyponatremia on admission: in 2008 in Casa, the incidence of hyponatremia on admission and acquired hyponatremia was 14.8% and 6.1%, respectively [81]. In 2019 in Marrakech, in a military intensive care unit, 93% of patients presented with hyponatremia on admission and only 7% developed hyponatremia during their hospitalization [96].

The incidence of hyponatremia in the series carried out in the military neuro-resuscitation service in Rabat (30.25%) is close to that of our study [97]. Its frequency depends largely on the clinical circumstances, but it is estimated to occur in approximately 15–30% of short- or long-term hospitalized patients [98].

These hyponatremias acquired during hospitalization in intensive care units deserve special attention because of their non-negligible frequency. This could be related to a lack of sodium intake and/or a dilution of filling solutions.

6. Biological characteristics of hyponatremia

6.1. Depth of hyponatremia

Of the 258 patients admitted during the period from June 2017 to June 2018 of our study, 5.5% of patients had hyponatremia below 130 mmol/L, 5% had hyponatremia between 125 and 129 mmol/L, 13.6 % hyponatremia between 120 and 124 mmol/L and 8.5% had hyponatremia below 120 mmol/L. In the Cub-Rea database [99 100], among the 96,193 patients hospitalized from 1997 to 2001, 1332 (1 to 1.5% of patients/year) had a hyponatremia below 120 mmol/l during their stay in intensive care. On admission to the medical intensive care unit of the Saint-Antoine hospital in Paris, among the 865 patients admitted in 2001, 14.8% had hyponatremia below 130 mmol/l and 2.1% hyponatremia below 120 mmol/l. In 2001, among the 47,018 patients who consulted at the emergency department of this same hospital, 1.5% had hyponatremia below 130 mmol/1 and 0.2% hyponatremia below 120 mmol/1. The rate of profound hyponatremia (less than 120) recorded is higher than those found in the literature.

Table XX: Comparison of serum sodium according to studies carried out in Morocco

	Natremia mmol/l			
	< 120	120-124	125-129	130-134
Bennani [86]	12%	28.7%	59.3%	-
Abidi [81]	45.6%			54.4%
Our study	26%	42%	15%	17%

6.2. Ionic disorders

To our knowledge, there is almost no study that shows the association among other ionic disorders with hyponatremia.

In our study, patients with hyponatremia most often have normal kalemia, normal venous glycemia, hyperuremia, hypoalbuminemia.

Indeed, urea is a marker of blood volume and increases more rapidly in the face of hypovolemia than creatinine. Its measurement can help confirm hypovolaemia, while not forgetting to interpret it according to renal function [101]. The hyperuremia observed in 60% of patients can be explained by this significant proportion of hypovolemic hyponatremia observed in our study, 51%. In the literature, hypoalbuminemia is the 3rd fairly common cause of hyponatremia, and most often due to malnutrition. Incidentally the hypo albuminemia is due to cirrhosis and massive protein losses in the urine [102]. Malnutrition is a frequent situation in intensive care (40 to 60%) [103]. This could therefore explain this increased frequency of hypoalbuminemia in half of our patients.

Bennani's study found the following values: an average patient serum potassium of 4 mmol/L ±1, an average uremia of 15.7 mmol/L ± 0.2, an average blood sugar level of 6.3 mmol/L ±0.6 [86].

1.3 Installation mode

The severity of hyponatremia depends on the adaptive capacities of the cerebral volume, essentially conditioned by the rapid onset of the disorder [104, 105]. In most series, including ours, it is difficult to distinguish between acute hyponatremia and chronic hyponatremia.

Most authors use this threshold value of 48 h to define the acute nature of hyponatremia [106-108]. It is therefore reasonable to consider as acute hyponatremia: compulsive ingestion of water, post-marathon hyponatremia, hyponatremia acquired in hospital (postoperative, bladder irrigation accidents with glycocollated solutions, etc.) and hyponatremia related to the recent prescription of thiazides [109]. Acute hyponatremia is much rarer than chronic hyponatremia.

However, we found an acute installation mode in 49% of patients. This is in contradiction with data from the literature. It is difficult to compare our data with those in the literature.

7. Clinical features of hyponatremia

7.1. Prevalence of symptomatic hyponatremia

Most patients with hyponatraemia greater than 125 mmol/l are asymptomatic. Between 125 and 130 mmol/l, the symptoms are essentially gastrointestinal (nausea and vomiting). Neuro-psychiatric symptoms (lethargy, confusional state, convulsions and coma) appear for values below 120 mmol/l and dominate the clinical picture.

They are the consequence of cerebral edema, the onset of which depends on the severity and rapidity of onset of hyponatremia (less than 48 hours) [110].

In our medical intensive care unit, hyponatremia was symptomatic in 80% of patients and manifested by disorders of consciousness in 58.3% of patients, digestive disorders in 40.5% of patients, a state of shock in 21 .4% of patients and seizures in 6%.

In a medical intensive care unit, at the Rabat-Salé university hospital center, 39.7% of patients presented with disorders of consciousness, the Glasgow score was between 13 and 9 in 105 patients (35%) and less than 9 in 14 patients (4.7%). A state of shock in 11.3% of cases and convulsions were found in 25 patients (8.3%) [86].

In a retrospective study of 64 episodes of hyponatremia less than < 110 mmol. l– 1 on admission, coma and convulsions were more frequent in case of acute hyponatremia than in case of chronic hyponatremia (respectively 70 and 30% versus 17 and 7%) [111]. Analysis of the Cub-Réa database also reveals a greater frequency of neurological symptoms in hyponatremic patients: coma 23.8% versus 18.1% ($p < 0.001$); confusion: 8.8% versus 2.4% ($p < 0.001$); seizures 9.5% versus 2.3% ($p < 0.001$) [99]. The frequency of clinical symptoms during chronic hyponatremia is certainly rarer than during acute hyponatremia: a series published in 1999 reports 53 cases over 10 years [112].

This high frequency in our study compared to a lower frequency of symptomatic hyponatremia in the other studies is explained by the difficulty of knowing whether the digestive disorders frequently encountered appeared before or after the hyponatremia in the case where they were chronic, the same is true for the disturbances of consciousness that appear in patients in the context of chronic hyponatremia. There is a difficulty in link all disturbances of consciousness to hyponatremia, since the underlying pathology could lead to these disturbances in some cases.

7.2. State of hydration

True hyponatremias have been classified according to the pathophysiological mechanism responsible, into 3 large groups. This classification is based on the evaluation of the extra cellular volume which is based on clinical criteria (BP, weight, presence or absence of oedemas, etc.) and biological criteria (protidemia, hematocrits, etc.) [113, 114].

- Hypovolaemic or depletion hyponatremia: This is retained in the presence of clinical or biological signs of extracellular dehydration (dehydration fold, arterial hypotension, haemoconcentration, etc.) [113, 114].
- Normovolemic hyponatremia or by dilution: It is retained in front of a normal volume.
- Hypervolemic hyponatremia or hyponatremia due to sodium and water inflation: Observed in the presence of clinical and biological signs of extracellular hyperhydration (oedema, haemodilution) [113, 114].

Although some authors believe that it is not very efficient, the classification of hyponatremia according to the hydration status of the patients, determined clinically and biologically, is recommended in the majority of studies [115 116 117]. Overall, it can be seen that normovolemic hyponatremia is the most common in all series, accounting for approximately 50%.

This is not the case in our series. Normovolemic hyponatremia affected only 19.28% of patients, hypervolemic hyponatremia affected 27.72% of patients and hypovolemic hyponatremia affected 51% of patients.

Practically similar results were noted in a study carried out in the military medical intensive care unit in Marrakech. Normovolemic hyponatremia was found in 6 patients (13%), hypovolaemic hyponatremia was found in 10 patients (21%). Hypervolemic hyponatremia was found in 11 patients (23%) [98].

In an intensive care unit in Rabat, hypervolemic hyponatremia concerned 23.7% of cases (n = 71): hepatic cirrhosis in 52 patients (17.3%), congestive heart failure in 18 patients (6%) and nephrotic syndrome in one patient (0.3%). Normovolemic hyponatremia was found in 50.6% of cases (n = 152). SIADHP accounted for 49.7% of observations [86].

It is difficult to compare our results with those of other series. The major divergences observed are related

- In the first place with the mode of recruitment of the various services: our recruitment was largely dependent on secondary transfers from all the other medical formations of the CHU and sometimes, even from regional centers. Moreover, the current high prevalence of certain pathologies such as kidney failure and diabetes, in the general population of our country, as well as that of our study, explains the great preponderance of hypovolemic hyponatremia.
- Digestive disorders such as vomiting and diarrhea which are frequent in our study (at 33%).

8. Duration of stay

Few data are available for the length of stay of patients with hyponatremia in intensive care because

- Few studies have been done on hyponatremia in intensive care
- The studies that have looked at hyponatremia have also looked at other disorders in parallel and the duration has been calculated for several disorders.

The length of stay was less than 5 days for more than half of the patients in our medical intensive care unit in Marrakech. In the military intensive care unit Avicenna from Marrakech the duration is 5 days on average [96]. However, in the medical intensive care unit in Rabat [86] and the surgical intensive care unit in Casablanca [80], the lengths of stay are respectively 9.5 ± 0.7 days and 17 ± 18 days on average.

9. Supported

9.1. Treatment

The therapeutic modalities for the management of hypotonic hyponatremia, and particularly its speed of

correction, have been the subject of controversy [118-121].

The treatment of hypotonic hyponatremia must take into account the mechanism of hyponatremia and whether or not it is symptomatic. Prompt correction is only performed for symptomatic acute hyponatremia. Prompt correction of asymptomatic acute hyponatremia is not recommended [122].

Various therapeutic modalities are considered depending on the origin of the hyponatremia.

- Treatment of acute hyponatremia

These are vital emergencies and hospitalization in intensive care should be considered. A rapid correction must be undertaken until the symptoms of cerebral suffering disappear. The treatment is based on the administration of 3% hypertonic saline combined if necessary, with furosemide. This treatment is discontinued as soon as the symptoms disappear. In 2005, a consensus conference proposed, in water poisoning among marathon runners, to take 100 ml of 3% saline solution to increase serum sodium by 2 mmol/L [123]. The Adrogué and Madias formula [124] is used to calculate the volume to be infused with a solute according to the change in serum sodium required: Na for one liter of solute = ([Na]mmol/L infused – [Na]mmol /L of the patient) / (total water + 1), total water being estimated by weight × 0.6 in men, × 0.5 in women.

For example, for 1 liter of 3% sodium, in a 70 kg patient with a serum sodium of 110 mmol/L, the (expected Na is (30 × 17) – 110/(70 × 0.5 + 1) = 11 mmol/L.

Another formula can estimate the volume of 3% NaCl infused per hour by multiplying the patient's weight by the desired "increase" in serum sodium in mmol/L per hour [27]. For example, for a patient weighing 70 kg, if one wishes to increase his serum sodium by 1 mmol/L per hour, one must infuse (1 × 70) = 70 mL of 3% saline in one hour. If one wishes to increase the sodium level by 0.5 mmol/L per hour, it will be necessary to infuse (0.5 × 70) = 35 ml. This treatment should be discontinued as soon as the symptoms have subsided, if the sodium concentration is greater than 120 mmol/L or if the correction is greater than 18 mmol/L every 48 hours. Natremia should be monitored very closely.

- Treatment of chronic hyponatremia:

There is no urgency to undertake treatment and the diagnostic approach is an essential prerequisite except in the case of neurological symptoms. To reduce the risk of osmotic demyelination, an increase in serum sodium of 12 mmol/L in the first 24 hours and 18 mmol/L in the first 48 hours should not be exceeded [125, 126]. Patients with hyponatremia associated with low blood volume or linked to the intake of desmopressin or a thiazide are particularly at risk of Centro pontine myelinolysis because once the cause has been corrected, the secretion of HAD stops suddenly; an aqueous diuresis can then occur with the risk of a too rapid correction of the natremia. It is then necessary to provide hypotonic solutes.

In our series, 81% of patients benefited from a 0.9% saline or 5% glucose serum intake and 39% were put on diuretics. The quasi-permanent recourse to rehydration and an average use of diuretics were observed. These results are consistent with those noted in other studies. Patients received 0.9% isotonic saline in 64.28% of cases. A similar percentage of treatment with saline is observed in the study conducted by Sofia FAIZ at the AVICENNE MARRAKECH military hospital. Patients received saline isotonic in 72% of cases [98]. In New York, hypertonic saline was given in 43% of cases at Rochester General Hospital, but only in 14% of cases at Strong Memorial Hospital [127].

In the military medical intensive care unit, therapeutic measures have been associated. They all benefited from the administration of hypotonic water and in 5 of them (9%), a sodium restriction was also recommended. Recourse to artificial ventilation was necessary in 27 patients (58%). Isotonic saline intake in 90% of patients, use of diuretics in 23% of patients, 2 patients (4%) did not receive treatment for their hyponatremia [98].

9.2. Correction speed

It depends on the mode of installation, its depth and the presence or absence of clinical symptoms. Correction of serum sodium must be gradual at a rate of 1.5 to 2 mmol/l/h without exceeding 15 mmol/day to avoid centropontal myelinolysis [128].

The speed of correction in our study was lower than the usual recommended speeds. It was less than 1 mmol/l/h in 92% of patients but never exceeded 1.9 mmol/l/h. In all cases the correction was slow and careful, under strict supervision.

Some studies have, as in our case, used slower speeds:

- Pizotti *et al*., [129] conducted the treatment of their patients at an average correction rate of 0.16 mmol/l/h.
- Bennani [88] used an average correction rate of 0.25 ± 0.02 mmol l–1h–1.
- Ellis *et al*., [130] used an average rate of 0.35mmol/l/h. Other studies have advocated higher correction speeds:
- Hojer *et al*., [131] used a rate of 2.6 mmol/l/h.
- In the study by Ichai *et al*., [124], the speed of correction can reach 4 to 5 mmol/l/h in the presence of serious neurological signs, then it is 2 mmol/l/h until the signs disappear. without exceeding 15mmol/l the first 24 hours.

1O. Prognosis

The severity of the disease on inclusion is one of the major factors determining the prognosis of patients in intensive care units. In general, the risk of hospital mortality is correlated with the severity of the disease, measured by physiological severity scores. The severity scores used in our study are: the Glasgow score, the Mac Cabe score, the Charlson score, and the APACHE II. The APACHE II is one of the most frequently used scores. They have been proposed as decision-making tools for the medical management of patients [132-134].

In our work, we found a Glasgow score greater than 14 in 42.9% of patients, a GCS between 13 and 9 in 34.5% of patients and a GCS less than 9 in 22.6% of patients. The GCS was less than 13 in more than 55% of patients.

On the other hand, in Bennani's work, the GCS was less than 13 in 39.7% of patients. The Glasgow score was greater than 14 in 181 patients (60.3%), between 13 and 9 in 105 patients (35%) and less than 9 in 14 patients (4.7%).

According to Mac Cabe's classification, class 0 was found in 73.3% of cases, class 1 in 22% and class 2 in 4.7%. The GSI II was 25.9 ± 0.8.

Patients who presented with hyponatremia had an admission GCS of 12 (10-14); and an APACHE II score of 10 (9–12) at admission in the work of Theresa Human in the United States [135].

II. Mortality

Mortality is 5 to 50% depending on the severity and the mode of installation [136 137 138]. The mortality rate of 56% observed in our series of patients is much higher than that cited in a similar study [96] which recorded a mortality rate of 34%, for patients whose serum sodium concentration was 134 mmol/L or less.

This figure may overestimate the number of deaths due to hyponatremia or its treatment. Most of the deaths occurred in patients so ill that their low serum sodium level may have been an epiphenomenon. The same observation was made in other series of patients with moderate hyponatremia [139, 60].

Due to the retrospective nature, we only report hospital mortality, i.e. short-term mortality, and not long-term mortality which would imply longer follow-up and a prospective study in this objective. In the literature, the hospital mortality rate in patients with hyponatremia below 120 mmol/l varies from 6.1 to 51% [140,141,142].

For Chawla *et al*., the hospital mortality rate increases with the severity of the hyponatremia up to the threshold of 120 mEq/l, threshold from which the trend is reversed: the mortality rate falls with the reduction in the rate of serum sodium. Hyponatremic patients <120 mmol/l who died all had acute decompensation of an underlying pathology [143].

Comparing our mortality figures with other studies is difficult, as there is no agreed definition of hyponatremia.

For example, Baron and Hutchinson defined hyponatremia <128 mmol/l and observed a mortality rate of 27%. Saeed and colleagues found 50% mortality in a group with Na <120 mmol/L [144]. Hockman *et al*., reported a 30% mortality in a group with a Na level <132 mmol/l [145]. One more study carried out in Hong Kong [146] described a mortality of 42% in 202 hospitalized patients with a Na level <125 mmol/l.

For Bennani, the mortality rate in the medical intensive care unit is 37.3% [88].

In a very large meta-analysis [147] including 81 studies comparing 850222 patients, hyponatremia has been associated with increased in-hospital mortality [148] [147], but no comprehensive meta-analysis analyzing the mortality rate in subjects with or without hyponatremia had been performed. nowadays. Recently, the Meta-Analysis of Chronic Heart Failure Global Group (MAGGIC) published a meta-analysis including 14,766 patients from 22 studies recruiting patients with heart failure and reporting death from any cause [149]. Patients with hyponatremia (n = 1618) had an increased risk of death (21%) compared to patients with normal serum sodium (16%) and the risk of death appeared to increase linearly with serum sodium below 140 mmol/L. Hyponatremia was an independent predictor of death, either when patients were considered as a whole or when they were grouped according to the presence of a reduced (n = 1199) or preserved (n = 419) ejection fraction. The MAGGIC meta-analysis was limited to patients with heart failure and was considered a study published in late 2008.

III. Analytical study

1. Epidemiological factors of hyponatremia in intensive care

1.1. Association hyponatremia – Age and sex

The incidence of hyponatremia differed according to age according to several authors [150, 151,152].

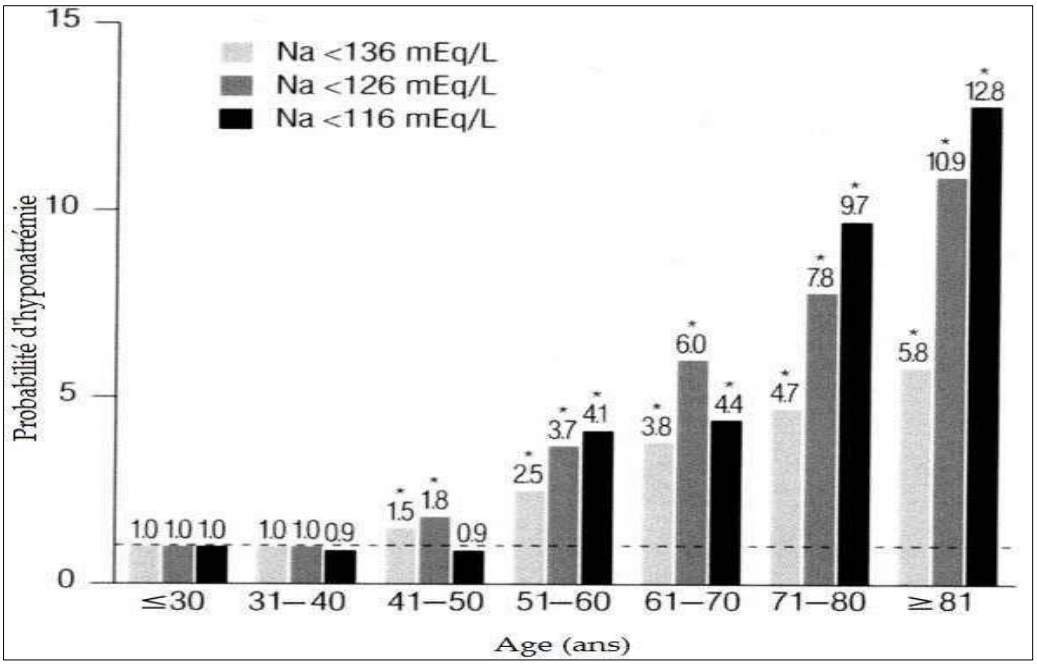

Figure 29: Relationship between age and the risk of developing hyponatremia acquired at hospital, study done in an inpatient emergency department, *P < 0.05, control group was under 30 years old. The analysis was adjusted for gender. (According to Clin Chim Acta)

This is the case in our study where the prevalence of hyponatremia varied according to the age of the patients. From the age of forty, the prevalence of patients increases from slice to slice. Our conclusions corroborate perfectly with those of Mohan and Al who present the same remarks [153].

Regarding sex, its prevalence is the same regardless of the sex of the patient in our study. The results of Bennani and Al at the medical intensive care unit, Ibn- Sina, Center Hospitalier Universitaire Rabat-Salé are in agreement with our results which also find that there is no association between mortality linked to hyponatremia and sex [86].

In a New York 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 risks of hyponatremia also increased significantly with age and in women compared to men [153]. Their analysis demonstrates an increase in the prevalence of hyponatremia with age and a higher prevalence of hyponatremia in females in the general population, a suspected finding given similar trends previously reported in institutional patient cohorts. short-term and long-term care [154, 155].

A study carried out in Singapore [56] between 2001 and 2002 compared the prevalence of hyponatremia between groups of patients according to the level of hyponatremia, age group and gender:

Table XXII: Age and sex as risk factors for hyponatremia

	Na < 136 mmol/l	Na < 126 mmol/l	Na < 116 mmol/l
Male	1.23* (1.19-1.27)	1.05 (0.95-1.18)	0.83 (0.66-1.05)
31 – 40 years old	1.08* (1.01-1.14)	0.90 (0.67-1.22)	0.60 (0.24-1.46)
41 – 50 years old	1.04* (0.99-1.10)	1.33*(1.01-1.69)	1.21 (0.66-2.24)
51 – 60 years old	0.88* (0.84-0.93)	1.48*(1.19-1.84)	1.98*(1.18-3.33)
61 – 70 years old	1.06* (1.01-1.12)	2.49*(2.05-3.03)	2.76*(1.71-4.48)
71 – 80 years old	1.39* (1.32-1.47)	4.31*(3.57-5.21)	6.65* (4.24-10.44)
> 80 years	1.89* (1.78-2.01)	7.66*(6.33-9.27)	8.70* (5.44-13.90)

* p < 0.05

1.2. Association hyponatremia – comorbidities

We note in our series that there is an association between hyponatremia and the patients' previous health status. Those with hyponatremia had more comorbidities. This finding in our series is similar to that of other series [156] in which a relationship between higher comorbidities and the presence of hyponatremia was observed.

This is the case in Marco's study conducted in Spain, where there are significant differences with regard to previous health status between patients with and without hyponatremia [157]. The comorbidities for which a significant difference was found between hyponatremic and normonatremic patients were cancers, metabolic history, diabetes, hepato-gastroenterological history, recent surgery.

In a prospective study performed at the Boston University Center in Massachusetts between 2000 and 2003, notable differences in the clinical characteristics of hyponatremics compared with normonatremia included a higher frequency of congestive heart failure, sepsis, pneumonia, metastatic disease and hypovolemia. Compared to those with normonatremia, patients admitted with hyponatremia had more comorbidities [141].

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% (P¼.0001). 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 kidney disease. In contrast, the prevalence of recent analyzes of small cohorts of hospitalized patients with hyponatremia have suggested that hyponatremia is only a surrogate for the underlying pathology rather than an independently detrimental factor [158, 159].

2. Prognosis of hyponatremia

Hyponatremia, on its own or added to certain factors, can be a source of increased mortality rates in patients in the intensive care unit or vice versa.

2.1. Association mortality and hyponatremia

Concerning the prognosis of hyponatremia on patients, we could not show 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, on dysnatremia, they did not objectivize an association between mortality and fluctuations in natremia (hyponatremia and hypernatremia) both on admission and during the stay in a medical intensive care unit [81]. These results do not corroborate with the vast majority of results from the literature where significant differences were found. And yet a very recent study conducted on mortality in our medical intensive care unit in Marrakech in 2019 objectified that profound hyponatremia was an independent factor of mortality [173].

Comparison of our results is difficult. These observed differences can be explained by:

- The fact that mainly the threshold set for the definition of hyponatremia varies enormously from one study to another.
- To our knowledge, in the literature, mortality has been studied for deep or severe hyponatremia in most cases.
- We considered all sodium levels below 135mmol/l as hyponatremia in our study.

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 [174] as well as in several other studies [175,176,177,178,179,141,143].

Hyponatremia was also found to be an independent predictor of in-hospital mortality in Vandergheynst's single-center series of emergency department patients [180].

Table XXIII: Comparison of intra-hospital mortality rates between patients with and without hyponatremia

Study	Service	Hyponatremia Definition (mmol/l)	With hyponatremia	Without hyponatremia	p
Bennani [86]	Intensive care medical	<120	37.3%	-	0.05
Rusinaru [181]	Meta- analysis		21%	16%	Factor independent
Germaine at Marrakesh [173]	Intensive care medical	<120	78.9%	45.3%	P<0.004
Our study, Marrakesh	Intensive care medical	<135	56%	48%	0.214

In addition, the risk of mortality was shown to be 5 times higher in hyponatremic subjects and no concomitant disease was identified compared to similar subjects with normal natremia in Mohan's work. After adjusting 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 condition chronic hypotonia beyond the underlying disease [153]. Small recent studies have shown similar associations between hyponatremia and all-cause mortality, but these have been limited to elderly patients in community settings [182,183].

However, whether hyponatremia contributes to mortality or simply represents a surrogate marker for the severity of underlying diseases remains a controversial issue. Some authors have suggested that hyponatremia simply reflects other comorbidities, i.e., an epiphenomenon of disease [143].

Mohan's study in New York [153] claims to be the first to demonstrate the clinical significance of hyponatremia in a nationally representative outpatient population of all adults over the age of 18 and demonstrates the associated increased risk of mortality. To hyponatremia, even in subjects between the ages of 18 and 50. They demonstrate a U-shaped association of serum sodium with the Hazard Ratio for mortality with no discernible threshold effect, suggesting that even slight variations in serum sodium in the general population are clinically significant. Their findings support growing evidence that mild hyponatremia is not benign and underscore the need to better understand the link between.

2.2. Prognostic factors for hyponatremia

a. Demographic and anamnestic factors associated with mortality

The contribution of hyponatremia to the death of affected patients nevertheless remains to be debated. Indeed, the most recent studies suggest that patients are more likely to die from their comorbidities than from hyponatremia per se.

We have objectified in our study that the toxicological history was negatively associated with mortality in patients with hyponatremia. This has been discussed very little in the literature. In the study by Eugenia et al., cigarette smoking was found to be negatively associated with hyponatremia in univariate analyzes but not in multivariate analyzes or with mortality. Smoking has never been reported to protect against hyponatremia; instead, smoking has previously been positively related to hyponatremia in psychiatric patients [187,188]. Nicotine is known to stimulate the release of vasopressin. It is possible that the result is misleading due to information bias.

History in our study is not associated with mortality. Among patients with hyponatremia, 61.5% of patients with no history had died compared to 55% in patients with at least one history. In 2013, a meta-analysis including more than 80 studies reported that hyponatremia is independently associated with an increased risk of mortality regardless of the comorbidities, even for very moderate hyponatremia.

Recent analyzes of small cohorts of hospitalized patients with hyponatremia have suggested that hyponatremia is only a surrogate for the underlying pathology rather than an independently detrimental factor.

Chawla *et al*., show that hyponatremic patients < 120 mmol/l who died all had acute decompensation of an underlying pathology [143].

Waikar *et al*., found an increased association between hyponatremia and in-hospital mortality in metastatic cancer, heart disease, and patients admitted for orthopedic surgery [141]. The prognostic value of low serum sodium concentrations for mortality has already been described for acute myocardial infarction, congestive heart failure and cancer.

b. Biological factors associated with mortality

The relationship between rapid onset, mortality and morbidity of hyponatremia is widely established. Erasmus *et al*., Lee *et al*., showed that the severity of hyponatremia significantly influenced mortality.

Several studies have sought to show a relationship of severity between the severity of hyponatremia and mortality, with inconsistent results. Some studies show that mortality is higher in hyponatremic subjects compared to normonatremic subjects, whether in hospital mortality or long-term mortality up to 5 years after hospitalization. But studies show that below a certain natremia threshold, mortality is no longer linked to hyponatremia: in the study by Waikar *et al*., hyponatremic patients regardless of severity had a higher mortality rate 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 [141]. For Chawla *et al*., the hospital mortality rate increases with the severity of the hyponatremia up to the threshold of 120 mEq/l, threshold from which the trend is reversed: the mortality rate falls with the reduction in the rate of serum sodium.

Some authors have not shown any link between the level of sodium and the death of patients. Our results go in the same direction as these studies where no difference was objectified for mortality according to the variation of sodium levels. For a serum sodium level between 135 and 130, a mortality of 45%, a rate between 129 and 125, a mortality of 49%, a rate between 124 and 120, a mortality of 77% and a rate below 120, a mortality by 71%. In addition, a recent study found that a decrease in serum sodium below a threshold of 132 mmol/L did not contribute to a further increase in overall mortality risk.

These results may call into question the hypothesis that there is a causal link between hyponatremia and mortality. Hyponatremia can be a marker of the severity of an underlying disease. Similar to the results of Chawla *et al*., once the serum sodium concentration fell below 120 mmol/L, the mortality rate did not appear to increase with increasing severity of hyponatremia.

A possible mechanism for the increased mortality associated with hyponatremia independent of underlying disease and the general lack of further increase in mortality risk when serum sodium decreases below 132 mmol/L could be oxidative stress induced by hyponatremia. 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 growing evidence that inflammatory mediators, such as interleukins 1 and 6, can induce hyponatremia by excessive release of vasopressin. 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 serious underlying disease, and therefore a lower level of inflammation.

Krummel *et al*., report in their study that mortality was closely related to hypoalbuminemia, suggesting that decreased serum albumin and hyponatremia may act synergistically to increase the risk of death in these patients.

Serum albumin can be considered as an additional marker of severity, independent of the Charlson index, which does not take into account nutritional status or inflammation.

However, despite numerous demonstrations showing a correlation between hypo-albuminemia and mortality in renal and non-renal diseases, such a prognostic link has not yet been described in hyponatremic patients.

c. Clinical symptoms associated with mortality

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

In our series, the state of shock was significantly linked to mortality in bivariate analysis (p = 0.008). Similar results were found in Bennani's series (p=0.02 and RR=1.80). It has not been studied in the various studies found in the literature.

A cohort study in a Danish population-based medical registry found 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.

In a meta-analysis published in 2013, they were able to conclude that the mortality risk was independent of factors such as age, sex 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, including 18.3% with hyponatremia), cirrhosis (total number of patients 906, including 42.6% hyponatremic), or pulmonary infections (total number of patients 10047, of whom 12% were hyponatremic). Some studies (n = 26) reported data for other diseases or mixed subpopulations (eg, older people), which could not be pooled. The diseases most represented among these patients (37,864 in total, including 15, 1% hyponatremic) were AIDS, malaria and malnutrition. Finally, some studies (n = 14, total number of patients 615,410, of which 16.7% were hyponatremic) were considered separately, because the effect of hyponatremia on mortality was studied retrospectively and the diagnoses did not been specified. 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 potential unmeasured 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 reduced the bias.

More recently, a significant strong positive relationship between an increase in serum sodium and a decrease in mortality was observed in 322 patients hospitalized for acute heart failure and followed for 1 to 3 years. On the other hand, an analysis study of 2888 patients hospitalized for acute heart failure in Korea confirmed that hyponatremia at admission was associated with a worse prognosis compared to normonatremia, but this relationship persisted whether or not hyponatremia improved during hospitalization. However, this report was a retrospective analysis from a registry, not a prospective randomized trial, and assessment of change in serum sodium level was performed only once, before or at discharge. 'hospital. Thus, whether hyponatremia is merely a marker or also a mediator of adverse patient outcomes is still uncertain with respect to heart failure and has not been studied in other diseases.

d. Association mortality and severity scores

In the literature, the percentage of deaths correlated with comorbidities according to 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%.

The mortality rates observed in our service according to the score are well above the forecasts. In addition, 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 and Al reveals that examination of deceased patients with severe hyponatremia showed that death was mainly 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.

The Charlson Comorbidity Index is a well-known prognostic score, validated in a multitude of diseases, including severe hyponatremia.

The alteration of the state of consciousness is also for many authors, a factor of poor prognosis. Our results disagree with these data; in fact, the disorders of consciousness evaluated on the Glasgow Coma scale did not constitute a factor of poor prognosis in bivariate analysis.

The severity of the disease on inclusion is one of the major factors determining the prognosis of patients in intensive care units. In general, the risk of hospital mortality is correlated with the severity of the disease, measured by physiological severity scores. Bennani's study used the severity score, the IGS II, which was significantly higher among the deceased ($p < 0.001$).

e. Association mortality and care, evolution and length of stay

Patients transferred to intensive care had cardiovascular, respiratory or neurological failures. In Béatrice de Guilbert's study, hyponatremia was not considered the cause of death. The causes of transfer to intensive care and the causes of death were, in order of frequency: neoplastic, infectious, neurological, cardiological, hepato-gastroenterological. Also, in his study, hyponatremia developed during hospitalization seems to be associated with a high risk of unfavorable outcome. The rate of transfer to intensive care unit and mortality were significantly higher than in the group of patients who presented with hyponatremia on admission to hospital. Hyponatremia as such does not was not the reason for transfer to intensive care or death in patients; the evolution frequently resulted from a failure of a vital organ of which hyponatremia was only one of the reflections of the seriousness of the clinical situation underlying. Although iatrogenicity was imputed in 4 cases in the occurrence of hyponatremia during hospitalization (hemodilution on filling for 2 patients, on transfusion for 1 patient, and SIADH after introduction of an antidepressant treatment with an inhibitor of serotonin reuptake for 1 patient), the reason for transfer to intensive care or the cause of death was never iatrogenic hyponatremia.

The medical resuscitation of Marrakech is a service taking care of patients with serious pathologies. Lengths of stay may vary from patient to patient. For those with hyponatremia, length of stay was not associated with mortality

In Sturdik's study, the absence of correction is a predictor of increased mortality strongly associated with hyponatremia. This is consistent with the results of our study where an association was objectified between the correction of hyponatremia and mortality. In the presence of correction of hyponatremia, the mortality rate decreased.

Krummel *et al*., in their multivariate analysis objective that: patients in whom plasma sodium has been normalized have a significantly better survival (HR 0.35 [0.20–0.62]), regardless of underlying comorbidities (index Charlson's comorbidity and serum albumin). In addition, patients with successful normalization of their plasma sodium had a Charlson index similar to that of patients who did not. The lack of relationship between plasma sodium normalization and in-hospital mortality suggests that the lack of normalization is not due to premature in-hospital mortality prior to plasma sodium normalization, but rather that the subsequent mortality may be due to lack of normalization of plasma sodium. However, nearly 60% of patients who died during hospitalization had normalized their plasma sodium levels. Krummel's results are identical to ours insofar as patients with a hyponatremia correction had a 78% better survival compared to those whose natremia had not been corrected 25% ($p<0.001$).

CONCLUSION

Hyponatremia in intensive care can have a variable prevalence depending on the studies. We carried out a retrospective study about 258 cases, including patients hospitalized in the intensive care unit of the ARRAZI hospital center in MARRAKECH.

Hyponatremia is frequent in our service and 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 generated by hyponatremia in intensive care is unfortunate given the high mortality rate recorded in our department, 56%. Careful correction is necessary as well as rapid management before admission to intensive care if detected earlier in order to lower the mortality rate.

Our study allowed us to discuss certain clinical, etiological and therapeutic aspects which act on its prevalence, its prognosis and its occurrence, which should be confirmed by prospective studies on a larger scale.

BIBLIOGRAPHY

1. Schrier RW, Bansal S. Diagnosis and management of hyponatremia in acute illness. Curr Opin CritCare 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. Diagnostic approach to hyponatremia; Rev Med Switzerland 2010;6-2074-9:1.
4. Edward. Hyponatremia for dummies or how to shine in front of a nephrologist. Legazier 2015
5. Ichai, C. Dyskalaemias. Resuscitation and emergencies, 2010, p. 171-177.
6. Cryer PE, Davis SN, Shamoon H. Hypoglycemia in diabetes. Diabetes Care 2003; 26:1902—12.
7. Teasdale G., Jennett B. Assessment of coma and impaired consciousness: a practical scale. Lancet 1974, 81-4
8. French Language Resuscitation Society: Guide to Evaluation Tools in Resuscitation, Arnette ed., Paris, 1995, 1 vol.
9. Knaus WA, Zimmerman JE, Wagner DP. APACHE — Acute physiology and chronic health evaluation: A physiologically based classification system. Crit Care Med 1981 ; 9:591-7.
10. Knaus WA: Prognostic value of disturbances of the internal environment. Réan Intensive Care Med urg 1985; 1:43-5.
11. Knaus WA, Draper EA, Wagner DP. Evaluating outcome from intensive care: a preliminary multihospital comparison. Crit Care Med 1982; 10: 491-6.
12. Le Gall JR, Loirat Ph, Alperovitch A. A simplified acute physiology score for ICU patients. Crit Care Med 1984; 12:975-7.
13. Knaus W, Draper E, Wagner D, Zimmerman J: Apache II: A severity of disease classification system. Crit Care Med 1985; 13:818-29.
14. Knaus WA, Draper EA, Wagner DP. An evaluation of outcome from intensive care in major medical centers. Ann InternMed 1986; 104: 410-8.
15. Lemeshow S, Teres D, Avrunin JS. A comparison of methods to predict mortality of intensive care unit patients. Crit Care Med 1987; 15:715-22.
16. Lemeshow S, Teres D, Pastides H. A method for predicting survival and mortality of UCI patients using objectively derived weights. Crit Care Med 1985; 13:519-25.
17. Cowen J, Kelley M: Errors and biases in using predictive scoring systems. Crit Care Clin 1994; 10:53-72.
18. Teres D, Lemeshow S: Using severity measures to describe high performance intensive care units. Crit Care Clin 1993; 9:543-54.
19. Teres D, Lemeshow S: Why severity models should be used with caution. Crit Care Clin 1994; 10:93-110.
20. Sabrina Figueiredo, BSc. Charlson Comorbidity Index (CCI). Stroke Info, 2009. Available (consulted on 21.01.2019).
21. Odile BEYNE-RAUZY. Comorbidities & frailty: how to use them in practice? Available on : (hyoutp://www.oncomip.org/docs/site/espace-professionnel/cr-meetings/5reunion/6_cr_oncomip_path_myeloides_2008_comorbidites.pdf) (Consulted on02/25/2019). page 10
22. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AH, KnausWA, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest 1992;101:1644–55.
23. Kanfer A. Kowlsky O. Hydration disorders: water and sodium. In: Nephrology and hydroelectrolytic disorders. Eds Masson, paris, 1997; 283-310
24. Raphael JC. Hydro-electrolyte disorders. In: goulon M. Summaries of medical resuscitation. Eds Masson 1995: 2nd eds: 29-49
25. Page Bernard. Renal control of hydro-electrolyte balance. In: Nephrology, Eds Marketing SA 1995; 31-35
26. Léon A, Lepouse C, El Hijri A Hyponatremia. Update Lectures 2000, p.551-569 Scientific and Medical Eds Elsevier SAS, and SFAR
27. Richet G. Fluid and electrolyte disorder Nephrology Eds Ellipses, 1988; 44-5
28. Ichai C, Theissen A and Glunti C. Hyponatremia in intensive care. Encycl Med Chir (Scientific and medical editions EL sevier SAS, Paris), anesthesia-reanimation, 36-360-A-05, 2002, 10p
29. Lestavel P, Boumbar Y, Crouzet S. What to do in the face of hyponatremia. News in Resuscitation and emergencies 2001, 19th congress, p: 264279 Scientific and Medical Editions Elsevier SAS.
30. Petitclerc T. Hydrosodic balance disorders. Encycl Med Chir, Nephrology-urology, 18-034-A-10 Emergencies, 24-130-C-10, 2001,10p
31. Kian Peng Goh. Management of hyponatremia. Am Fam physician 2004;69:2387-94
32. Paillard M, Froissart M, blanchard A, houillier P. Water balance and extracellular osmolality. Technical editions. Encycl. Med. Chir (paris-France), endocrinology-nutrition, 10-352-A-10,

1995,6P.
33. Fraser CF, Arieff AI. Epidemiology, Physiopathology, and management of hyponatremic encephalopathy. Am J Med, 1997, 102: 67-77.
34. Hiller TA, Abbott RD, Barret EJ. Hyponatremia: evaluating the correcting factor for hyperglycemia. AMJ Med, 1999;106:399-403.
35. Zerbe R, Robertson GL. Osmotic and non-Osmotic regulation OF thirst and vasopressin secretion. Narins RD ed. Clinical disorders of fluid and electrolyte metabolism. New York: Mc GRaw-HILL 1994:81-100
36. Adrogué HJ, Madias NE. Hyponatremia. Neng J Med 2000; 342: 1581-1589
37. Kumar S, Brel T. Sodium. Lancet 1998; 352: 220-228
38. Seguy B. Water reabsorption In: physiologie, EDs MALOINE, 3rd Eds 1996;265.
39. Thomas Vogel et al. Hyponatremia in the elderly. Review of the practitioner, General Medicine, Volume 15, n523
40. Muhand S El-twal, MD. Hyponatremia. E medicine specialties 2004
41. Fumes Z. Hyponatremia: diagnostic and therapeutic approach on an outpatient basis. Rev Medical Swiss 2003; volume-1. 22968. Available on (https://www.revmed.ch/RMS/2003/RMS-2435/22968).
42. Bennani S. Incidence, causes and prognostic factors of hyponatremia in intensive care.
43. Thesis in medicine, N 251, Year 2001
44. Karen Eyates, Michael singer and ross Morton. Salt and water: a simple approach to hyponatremia CMAJ. February 3, 2004; 170 (3): 365.
45. Crook MA, Velauthar U, Moran L, Griffiths W. Review of investigation and management of severe hyponatremia in a hospital population. Ann clink biochem, 1999; 36 (pt2): 158-62
46. Brunsvig PF, OS I, Frederichsen P. Hyponatremia. Tidsskr NOR loegeforen, 1990;110:2367-9
47. Pizzotti NJE, Madi JC, Lamanaca AI, Seguro AC, Rocha AS. Hyponatremia: study of its epidemiology and mortality.Rev Hosp CLin Fac Med Sao Paulo, 1989; 44: 307-11
48. Sanghvi SR, Kellerman PS, Nanovic L. Beer potomania: An unusual cause of hyponatremia at high risk of complications from rapid correction. Am J Kidney Dis 2007;50:673–80.
49. Noakes T. Fluid replacement during marathon running. Clin J Sport Med 2003;13:309–18.
50. Palmer BF. Hyponatraemia in neurosurgical patient: syndrome of inappropriate antidiuretic hormone secretion versus cerebral salt wasting. Nephrol Dial Transplant 2000;15:262–8.
51. Pizzotti, NJ, JC Madi, AI Iamanaca, AC Seguro, and AS Rocha Hyponatremia: study of its epidemiology and mortality. Revista do Hospital das Clinicas 44, no. 6 (1989): 307-311.
52. Diederich S, Franzen NF, Bahr V, Oelkers W. Severe hyponatremia due to hypopituitarism with adrenal insufficiency: report on 28 cases. Eur J Endocrinol 2003;148:609–17.
53. Ellison DH, Berl T. The syndrome of inappropriate antidiuresis. N Engl J Med 2007;356:2064–72.
54. Bartter FC, Schwartz WB. The syndrome of inappropriate secretion of antidiuretic hormone. Am J Med 1967;42:790–806.
55. Feldman BJ, Rosenthal SM, Vargas GA, Fenwick RG, Huang EA, Matsuda-Abedini M, et al. Nephrogenic syndrome of inappropriate antidiuresis. N Engl J Med 2005;352:1884–90.
56. Dundas B, Harris M, Narasimhan M. Psychogenic polydipsia review: etiology, differential, and treatment. Curr Psychiatr Rep 2007;9:236–41.
57. Stuart CA, Neelon FA, Lebovitz HE. Disordered control of thirst in hypothalamic-pituitary sarcoidosis. N Engl J Med 1980;303:1078–82.
58. Chin MH, Goldman L. Correlates of major complications or death in patients admitted to the hospital with congestive heart failure. Arch Intern Med 1996;156:1814–20.
59. Angeli P, Wong F, Watson H, Gines P. CAPPS Investigators. Hyponatremia in cirrhosis: results of a patient population survey. Hepatology 2006;44:1535–42.
60. Upadhyay, Ashish, Jaber, Bertrand L., and Madias, Nicolaos E. Epidemiology of hyponatremia. Seminars in nephrology. WB Saunders, 2009. p. 227-238.
61. DeVita MV, Gardenswartz MH, Konecky A, Zabetakis PM. Incidence and etiology of hyponatremia in an intensive care unit.Clin Nephrol. 1990;34:1636.
62. Bennani SL, Abouqal R, Zeggwagh AA, Madani N, Abidi K, Zekraoui A, et al. Incidence, causes and prognostic factors of hyponatremia in intensive care. Internal Rev Med. 2003; 24:224-9.
63. Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia. Am J Med 2006;119:S30-5.
64. Hawkins RC. Age and gender as risk factors for hyponatremia and hypernatremia. Clin Chim Acta 2003;337:169-72.
65. Miller M, Morley JE, Rubenstein LZ. Hyponatremia in a nursing home population.J Am Geriatr Soc 1995; 43:1410-3.
66. 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.
67. Lim JK, Yap KB. Hyponatraemia in hospitalized elderly patients. Med J Malaysia 2001; 56:232-5.
68. Lee CT, Guo HR, Chen JB. Hyponatremia in the emergency department. Am J Emerg Med 2000; 18:264-8.
69. Borroni G, Maggi A, Sangiovanni A, et al. Clinical relevance of hyponatraemia for the hospital

outcome of cirrhotic patients. Dig Liver Dis 2000; 32: 605-10.
70. Petitclerc, T. Hydro-sodium balance disorders. Medico-Surgical Encyclopedia Nephrology-Urology. Paris: Scientific Editions andMedical Elsevier SAS, 2000; 18-034-A-10, 10p, 2000.
71. Martin Tisdall, Matthew Crocker, Jonathan Watkiss, and Martin Smith. Disturbances of sodium in critically ill adult neurologic patients: a clinical review.J Neurosurg Anesthesiol. 2006 January 18(1): 57–63.
72. Leonardo De Luca, Liviu Klein, James E. Udelson et al, Hyponatremia in Patients with Heart Failure. American Journal of Cardiology 2005; 96[extra]:19L– 23L
73. Flear CT, Gill GV, Burn J. Hyponatremia: mechanisms and management. Lancet 1981; 320: 26–31.
74. Abramow M, Beauwens R, Cogan E. Cellular events in vasopressin action. Kidney Int 1987; (suppl 21):56–66.
75. Fall PJ. Hyponatremia and hypernatremia: a systematic approach to causes and their correction. Postgraduate Med 2000; 107:75 - 82.
76. Anderson RJ. Hospital-associated hyponatremia. Kidney International 1986; 29: 1237–1247.
77. AP Maggionl, G. Ansalone, G. Cacciatore, E Oliva, M. Porcu, D. Lucci, L. Gonzinl, L. Tavazzi. Prevalence and prognostic role of hyponatremia in 2807 patients admitted for acute heart failure in year 2004. European Journal of Heart Failure Supplements 5 (2006): 2-3.
78. Pottier, P., Agard, C., Trewick, D., et al. Prevalence and description of hyponatremia in internal medicine departments in western France. A “given day” type multicentre descriptive survey. The Journal of Internal Medicine, 2007, vol. 28, No. 4, pages 207-208.
79. Caird FI, Andrews GR, Kennedy RD. Effect of posture on blood pressure in the elderly. Br Heart J 1973;35:527-30.
80. Wassima Idahmou, et al. Hydro-electrolyte disorders in intensive care. Exercise thesis, Medicine, Casablanca 2007. Page 48-49.
81. Abidi, Mohammad. Dysnatremia on admission and acquired in a medical intensive care unit: incidence, prognosis, and influence of fluctuations in natremia on mortality. 2018. Doctoral thesis. page 18
82. Wilkinson TJ, Begg EJ, Winter AC, et al. Incidence and risk factors for hyponatraemia following treatment with fluoxetine or paroxetine in elderly people. Br J Clin Pharmacol 1999; 47:211-7.
83. Ashish Upadhyay, Bertrand L. Jaber, and Nicolaos E. Madias Incidence and Prevalence of Hyponatremia. The AmericanJournal of Medicine (2006) Flight 119 (7A), S30–S35
84. Sandy Craig. Hyponatremia. e-medicine, January 4, 2006,www.emedicine.com
85. Eric E-Simon. Hyponatremia. e-medicine, July 2006,www.emedicine.com
86. SL Bennani, R. Abouqal, A.-A. Zeggwagh, N. Madani, K. Abidi, A. Zekraoui, O. Kerkeb. Incidence, etiologies and prognostic factors of hyponatremia in intensive careDoctoral thesis in medicine
87. DS Shapiro, M. Sonnenblick, I. Galperin, L. Melkonyan, and G. Munter, Severe hyponatraemia in elderly hospitalized patients: prevalence, aetiology and outcome
88. Intern Med J, vol. 40, no. 8, p. 574-580, August 2010.
89. HAO, Jinling, LI, Yang, ZHANG, Xuehan, et al. The prevalence and mortality of hyponatremia is seriously underestimated in Chinese general medical patients: an observational retrospective study. BMC nephrology, 2017, vol. 18, No. 1, p. 328.
90. DAS, V. and Offenstadt, G. Hyponatremia in intensive care: news. Resuscitation, 2003, vol. 12, no. 4, p. 288-296.
91. Sturdik I, Adamcova M, Kollerova J, et al. Hyponatremia is an independent predictor of inhospital mortality. European Journal of Internal Medicine 2014; 25(4): p. 379-82.
92. 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
93. By Guibert B. Characteristics of patients with severe hyponatremia in the medical department. Exercise thesis: Medicine: Grenoble. [On line]. 2012. Available from:http://dumas.ccsd.cnrs.fr/docs/00/76/97/83/PDF/2012GRE15143_guibert_beatrice_de_1_D_.pdf [Page consulted on 10/01/2019].
94. Creusot, Marie-Laure and CLOS Prophette, Fabienne. Retrospective study of hospitalized hyponatremia in a general medicine department over 13 months. 2014.
95. J. Kengni Tameze a, S. Etia Mbongo b, N. Daoudi c, B. Kennes a, O. Vanachter a, V. Verhaeghe a. Prevalence of hyponatremia in elderly patients admitted for falls: retrospective study of a series of 108 patients. The Journal of Internal Medicine; Volume 30, No. S2 page 130 (June 2009).
96. Fall PJ. Hyponatremia and hypernatremia: a systematic approach to causes and their correction. Postgraduate Med 2000 ; 107:75 - 82.
97. Sofia Faiz. Hyponatremia in intensive care, retrospective study about 30 cases. 2019. Doctoral thesis.
98. Walid Atmani. Osmolarity disorders in neuroresuscitation (about 119 cases) at the Mohamed V military training hospital – rabat. 2017. Consulted THE 01/31/2019. Available on (http://ao.um5.ac.ma/xmlui/handle/123456789/15800)
99. Upadhyay, Ashish, Jaber, Bertrand L., and Madias, Nicolaos E. Incidence and prevalence of

hyponatremia. The American journal of medicine, 2006, vol. 119, No. 7, p. S30-S35.
100. Aegerter P, Auvert B, Buonamico G, Sznajder M, Beauchet B, Guidet B, et al. CUB-REA: Implementation and evaluation of a common database for intensive care units in Ile de France. Rev Epidemiol Health Publ 1998 ;46 :226–37.
101. Das, G. Offenstadt. Hyponatremia in intensive care: news. Resuscitation 12 (2003) 288–296
102. Freda BJ, Davidson MB, Hall PM. Evaluation of hyponatremia: A little physiology goes a long way. Cleve Clin J Med 2004 ;71 :639-50.
103. Etienne Robin. Who's afraid of the big bad hyponatremia. Dijon Printemps medical de Bourgogne, March 21, 2015. Accessed on 03/23/2019. Available on (http://www.printemps-medical-bourgogne.fr/upload/media/files/abstracts/PMB15%20Hyponatremie%20allegee%20ROBIN.pdf)
104. Giner M, Laviano A, Meguid MM, Gleason JR. In 1995 a correlation between malnutrition and poor outcome in critically ill patients still exists. Nutrition 1996;12:23—9.
105. Ichai C, Theissen A and Glunti C. Hyponatremia in intensive care. Encycl Med Chir (Scientific and medical editions EL sevier SAS, Paris), anesthesia – resuscitation, 36-360-A-05, 2002, 10p
106. Lestavel P, Boumbar Y, Crouzet S. What to do in the face of hyponatremia. News in Resuscitation and emergencies 2001, 19th congress, p: 264279. Scientific and Medical Editions Elsevier SAS.
107. Soupart A, Decaux G. Therapeutic recommendations for management of severe hyponatremia: current concepts on pathogenesis and prevention of neurologic complications. Clin Nephrol 1996; 46:149–69.
108. Ayus JC, Arieff AI. Chronic hyponatremic encephalopathy in postmenopausal women: association of therapies with morbidity and mortality. Jama 1999;281:2299–304.
109. Gross P. Treatment of severe hyponatremia. Kidney Int 2001;60: 2417–27.
110. Stems RH, Cappuccio JD, Silver SM, Cohen EP. Neurologic sequelae after treatment of severe hyponatremia: a multicenter perspective. J Am Soc Nephrol 1994;4:1522–30.
111. Strange K. Regulation of solute and water balance and cell volume in the central nervous system. J Am Soc Nephrol 1992; 3:12-27.
112. HR stems. Severe symptomatic hyponatremia: treatment and outcome, A study of 64 cases. Ann Intem Med 1987;107:656–64.
113. Ayus JC, Arieff AI. Chronic hyponatremic encephalopathy in postmenopausal women: association of therapies with morbidity and mortality. Jama 1999; 281:2299–304.
114. Bagshaw S, Townsend D, McDermid R. Disorders of sodium and water balance in hospitalized patients. Can J Anaesth 2009; 56: 151-167.
115. Flear CT, Gill GV, Burn J. Hyponatremia: mechanisms and management. Lancet 1981; 320: 26–31.
116. Pizzotti NJE, Madi JC, Iamanaca AI, Seguro AC, Rocha AS. Hyponatremia: Study of its epidemiology and mortality.Rev Hosp Clin Fac Med Sao Paulo 1989;44:307–11.
117. Brunsvig PF, Os I, Frederichsen P. Hyponatremia. Tidsskr Nor Loegeforen 1990;110:2367–9.
118. Hochman I, Cabili S, Peer G. Hyponatremia in internal medicine ward patients: causes, treatment and prognosis. Isr J Med Sci 1989;25:73–6.
119. Berl T. Treating hyponatremia: damned if we do and damned if we don't. Kidney int. 1990, 37, 1006-1018
120. Cluitmans FHM, Meinders AE. Management of severe hyponatremia: rapid or slow correction? American journal of medicine 1990, 88, 161-166
121. HR Sterns. The treatment of hyponatremia: first, do not harm. Am. J. Med. 1990, 88, 557-560
122. G. Offenstadt, MG Brunette. Acid-base and water-electrolyte disorders Edition Arnette Blackwell, under the direction of the French-language resuscitation society.
123. C. Ichai, A. Theissen, T. Giunti Hyponatremia in intensive care edico-surgical Encyclopedia (Scientific and Medical Editions EL Sevier SAS, Paris), anesthesia – resuscitation, 36-360-A-05, 2002, 10p
124. Noakes T. Fluid replacement during marathon running. Clin J Sport Med 2003;13:309–18.
125. Adrogue HJ, Madias NE, Hyponatremia. N Engl J Med 2000;342:1581–9.
126. Verbalis JG, Goldsmith SR, Greenberg A, Schrier RW, Sterne RH. Hyponatremia treatment guidelines 2007: Experts panel recommendations.Am J Med 2007;120:S1–21.
127. Sterns RH, Cappucio JD, Silver SM, Cohen EP. Neurologic sequelea after treatment of severe hyponatremia: a multicenter perspective. J Am Soc Nephrol 1994;4:1522–30.
128. HR Sterns. Severe symptomatic hyponatremia: treatment and out-come. A study of 64 cases. Ann Intern Med 1987;107:656–64.
129. Chemchik, H., El Hadj, B., Naija, W. Hyponatremia in intensive care. Journal of anesthesia-resuscitation and emergency medicine, 2011, vol. 3, no. 1, p. 1-7.
130. Pizzotti NJE, Madi JC, Lamanaca AI, Seguro AC, Rocha AS. yponatremia: study of its epidemiology and mortality.Rev Hosp Clin Fac Med Sao Paulo, 1989; 44: 307-11
131. Ellis SJ. Severe hyponatremia: complications and treatment. QJM, 1995; 88:905-9.
132. Hojer J. Prognosis and treatment of symptomatic hyponatremia: a study of 28 intensive care cases. Lakartidningen. 1992 sep9:89(37):2933-4. 2939-40
133. Cowen J, Kelley M: Errors and biases in using predictive scoring systems. Crit Care Clin 1994; 10:53-72.
134. Teres D, Lemeshow S: Using severity measures to

describe high performance intensive care units. Crit Care Clin 1993; 9:543-54.
135. Teres D, Lemeshow S: Why severity models should be used with caution. Crit Care Clin 1994; 10:93-110.
136. Human, Theresa, Cook, Aaron M., Anger, Brian. Treatment of Hyponatremia in Patients with Acute Neurological Injury. Neurocritical care, 2017, vol. 27, No. 2, p. 242-248.
137. 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
138. Sandy Craig. Hyponatremia. e-medicine, January 4, 2006,www.emedicine.com
139. Eric E-Simon. Hyponatremia. e-medicine, July 2006,www.emedicine.com
140. Anderson RJ. Hospital-associated hyponatremia. Kidney Int. 1986;29:1237-47.
141. RT Erasmus and TE Matsha, "The frequency, aetiology and outcome of severe hyponatraemia in adult hospitalized patients", Hundred Afr J Med, vol. 44, no. 6, p. 154-158, June 1998.
142. SS Waikar, DB Mount, and GC Curhan, "Mortality after hospitalization with mild, moderate, and severe hyponatremia", Am. J. Med., vol. 122, No. 9, p. 857-865, Sept. 2009.
143. MA Crook, U. Velauthar, L. Moran, and W. Griffiths, "Review of investigation and management of severe hyponatraemia in a hospital population", Ann. Clin. Biochem., vol. 36 (Pt 2), p. 158-162, March 1999.
144. Chawla, RH Sterns, SU Nigwekar, and JD Cappuccio, "Mortality and serum sodium: do patients die from or with hyponatremia? », Clin J Am Soc Nephrol, vol. 6, no. 5, p. 960-965, May 2011.
145. Saeed, BO, Beaumont, D., Handley, GH & Weaver, JU (2002). Severe hyponatraemia: investigation and management in a district general hospital. Journal of Clinical Pathology, 55, 893–896.
146. Hochman, I., Cabili, S. & Peer, G. (1989). Hyponatraemia in internal medicine ward patients: causes, treatment and prognosis. Israel Journal of Medical Sciences, 25, 73–76.
147. Natkunam, A., Shek, CC & Swaminathan R. (1991) Hyponatraemia in a hospital population. Journal of Medicine, 22, 83–96