

Outcome predictors in profound hyponatremia



*Nica Frech, *Bettina Winzeler, *Nicole Nigro, Isabelle Suter-Widmer, Philipp Schuetz, Birsan Arici, Martina Bally, Claudine Blum, Andreas Bock, Andreas Huber, Beat Müller, Mirjam Christ-Crain
*Equally contributing authors

Background and Aim

• Hyponatremia is the most common electrolyte abnormality in clinical practice and given its impact on mortality and morbidity a very relevant medical condition.
• Little is known about factors influencing long-term outcome in profound hyponatremia and controversial data regarding hyponatremia severity and mortality exists.

Aim of study

To prospectively explore the predictive value of clinical and laboratory parameters in patients with profound hyponatremia.

Methods

• Prospective observational study with 12-month-follow-up of patients with s-sodium level ≤ 125 mmol/L.
• Patients recruited from medical emergency department of two tertiary care centers in Switzerland between 2011-2013.
• Follow-up was done by structured phone interview and review of medical records.
• The association of different clinical and laboratory parameters with the following three outcomes was analysed: mortality, rehospitalisation, recurrent profound hyponatremia.

Results

From primarily 298 included patients complete follow-up data was available in 281.

Table 1: Baseline characteristics n=281	
age (years)	72 [61-80]
sex (female)	66.5 (187)
Charlson Comorbidity Index	2 [1-5]
Aetiology of hyponatremia	
Malignant SIAD	7.1 (20)
Non malignant SIAD	54.1 (152)
SIAD drugs/diuretics	40.2 (113)
SIAD idiopathic	4.6 (13)
SIAD lung	3.2 (9)
SIAD CNS	6 (17)
Hypervolemic hyponatremia	11.4 (32)
Heart failure	5.3 (15)
Liver failure	4.3 (12)
Kidney failure	1.8 (5)
Hypovolemic hyponatremia	19.9 (56)
Primary Polydipsia	7.5 (21)
Laboratory findings	
S-sodium at admission (mmol/L)	120 [116-123]
S-sodium at discharge (mmol/L)	134 [130-137]
S-sodium ≥ 135 mmol/L at discharge	49.1 (138)
Plasma glucose (mmol/L)	6.6 [5.7-8.1]
Therapeutic findings	
S-sodium correction first 24h (mmol/L)	5 [2-8]
ICU admission	36.7 (103)
3% NaCl Infusion	8.5 (24)
Data in % (n) and median [IQR=interquartile range, 25th-75th]	

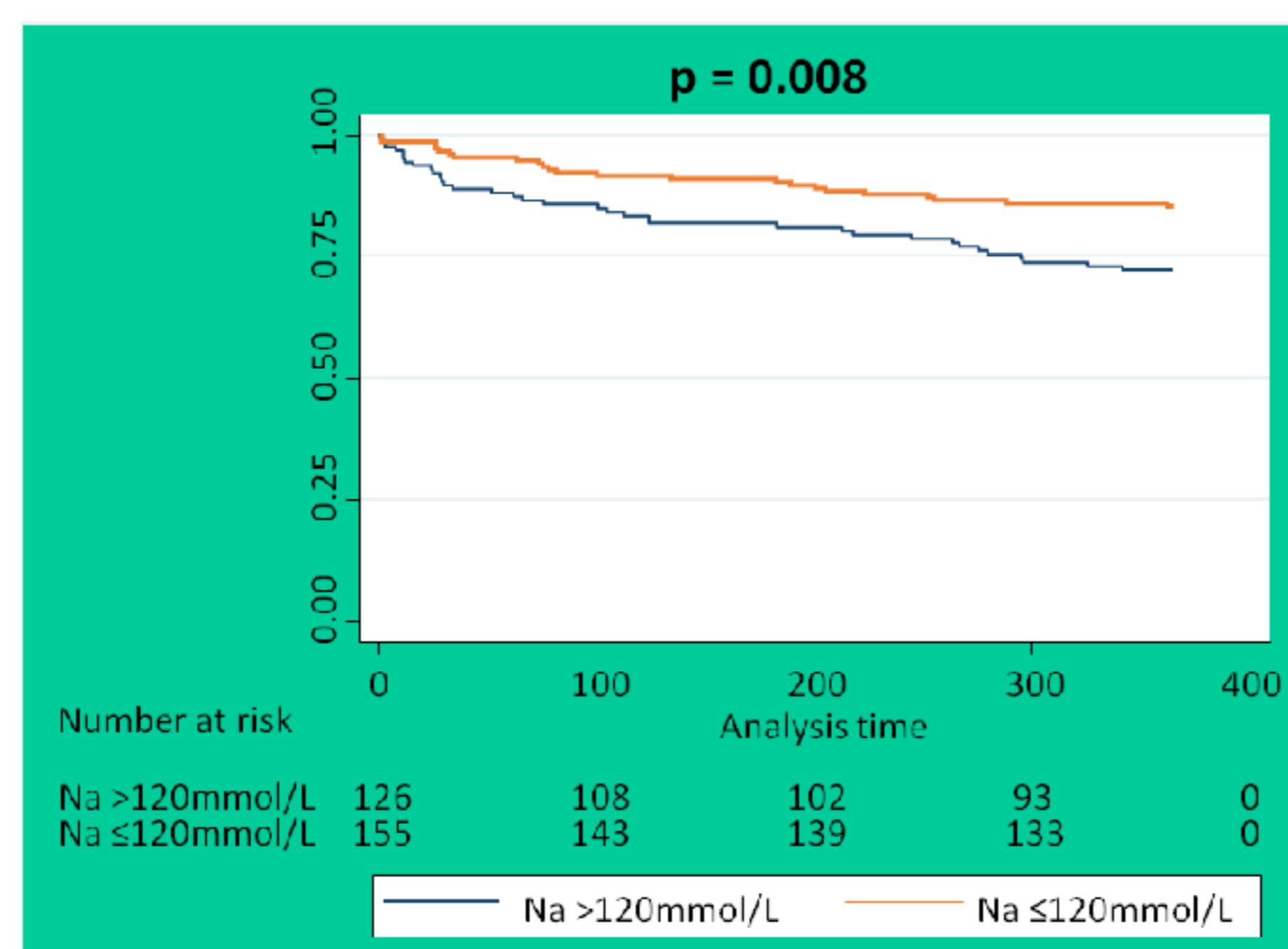
Table 2: Outcome parameters	
Overall mortality	20.6 (58)
Rehospitalisation	56.2 (158)
Time to rehospitalisation (days)	75 [21-206]
Re-Hyponatremia	42.7 (120)
Recurrent profound hyponatremia	16 (45)
Data in % (n) and median [IQR=interquartile range, 25th-75th]	

The following parameters revealed significant association with our outcomes, also after multivariate analysis: «charlson comorbidity index (=CCI)», «initial s-sodium level» and «correction of hyponatremia».

Table 3: Univariate and multivariate analysis						
	Univariate analysis		Model 1		Model 2	
	OR (95%CI)	p-value	OR (95%CI)	p-value	OR (95%CI)	p-value
Outcome 1: Mortality						
CCI	1.5 (1.3-1.7)	<0.001	1.5 (1.3-1.7)	<0.001	1.4 (1.3-1.7)	<0.001
S-sodium at admission	1.2 (1.1-1.3)	0.005	1.2 (1.0-1.3)	0.04	1.2 (0.1-1.3)	0.05
Correction of hyponatremia	0.5 (0.3-0.8)	0.01	0.5 (0.2-1.0)	0.04	0.5 (0.2-0.9)	0.03
Outcome 2: Rehospitalisation						
CCI	1.1 (0.9-1.2)	0.16	1.1 (0.9-1.2)	0.15	1.1 (0.9-1.1)	0.39
S-sodium at admission	1.0 (0.9-1.1)	0.69	0.9 (0.9-1.0)	0.22	1.0 (0.9-1.0)	0.37
Correction of hyponatremia	0.6 (0.4-0.9)	0.03	0.6 (0.3-0.9)	0.02	0.6 (0.4-1.0)	0.03
Outcome 3: Recurrent profound hyponatremia						
CCI	1.1 (1.0-1.2)	0.09	1.1 (0.9-1.2)	0.10	1.1 (0.9-1.2)	0.36
S-sodium at admission	0.8 (0.7-1.0)	0.005	0.7 (0.6-0.9)	<0.001	0.8 (0.6-0.9)	0.001
Correction of hyponatremia	0.4 (0.2-0.8)	0.009	0.4 (0.2-0.8)	0.01	0.4 (0.2-0.8)	0.01
OR=Odds Ratio, CI=Confidence Intervall						
Model 1: adjusted for age, CCI, s-sodium at hospital admission, s-sodium ≥ 135 mmol/L at discharge, Delta s-sodium 24h, ICU admission.						
Model 2: adjusted for age, CCI, s-sodium at hospital admission, s-sodium ≥ 135 mmol/L at discharge, Delta Na 24h, ICU admission, hypervolemic hyponatremia, malignant SIAD.						

Concerning hyponatremia aetiology, hypervolemic hyponatremia and malignant SIAD were associated with mortality, while non malignant SIAD was not.

Mortality was higher in patients with higher s-sodium at admission (>120 mmol/L vs. ≤ 120), see Kaplan Meier Curve:



Aetiology of hyponatremia and therapeutic findings differed in patients with s-sodium level \leq vs. $>$ 120mmol/L.

Table 4: Characteristics of patients with s-sodium \leq and $>$ 120mmol/L			
Parameters	S-sodium ≤ 120 mmol/L (n=155)	S-sodium > 120 mmol/L (n=126)	p-value
age (years)	73 [62-81]	70 [58-79]	0.08
sex (female)	65.8 (102)	67.5 (85)	0.77
Charlson Comorbidity Index	2 [1-4]	2 [1-5]	0.04
Aetiology of hyponatremia			
Malignant SIAD	7.7 (12)	6.3 (8)	0.65
Non malignant SIAD	62.6 (97)	43.7 (55)	0.002
SIAD drugs/diuretics	49 (76)	29.4 (37)	0.001
SIAD idiopathic	5.2 (8)	4 (5)	0.64
SIAD lung	3.2 (5)	3.2 (4)	0.98
SIAD CNS	5.2 (8)	7.1 (9)	0.49
Hypervolemic hyponatremia	7.7 (12)	15.9 (20)	0.03
Heart failure	3.9 (6)	7.1 (9)	0.23
Liver failure	1.9 (3)	7.1 (9)	0.03
Kidney failure	1.9 (3)	1.6 (2)	0.83
Hypovolemic hyponatremia	15.5 (24)	25.4 (32)	0.04
Primary Polydipsia	6.5 (10)	8.7 (11)	0.47
Laboratory findings			
S-sodium at admission (mmol/L)	117 [113-120]	123 [122-124]	<0.0001
S-sodium ≥ 135 mmol/L at discharge	52.3 (81)	45.2 (57)	0.24
Therapeutic findings			
S-sodium correction first 24h (mmol/L)	5 [2-9]	4.5 [1-6]	0.02
ICU admission	48.4 (75)	22.2 (28)	<0.0001
3% NaCl Infusion	12.3 (19)	4 (5)	0.01
Outcome parameters			
Overall mortality	14.8 (23)	27.8 (35)	0.008
Rehospitalisation	56.1 (87)	56.3 (71)	0.97
Time to rehospitalisation (days)	72 [25-197]	81 [15-220]	0.70
Recurrent profound hyponatremia	21.3 (33)	9.5 (12)	0.008
Data in % (n) and median [IQR=interquartile range, 25th-75th]			

Conclusion

• Hyponatremia goes along with a high 1-year-mortality, recurrence, and rehospitalisation rate.
• The positive correlation of s-sodium level and mortality emphasizes the importance of the underlying disease, which determines outcome beside hyponatremia itself.

References

Greenberg et al., Current treatment practice and outcomes. Report of the hyponatremia register, Kidney Int., 2015; Holland-Bill et al., Hyponatremia and mortality risk: a Danish cohort study of 279 508 acutely hospitalized patients, Eur J Endocrinol, 2015; Chawla et al., Mortality and serum sodium: do patients die from or with hyponatremia?, Clin J Soc Nephrol, 2011; Waikar et al., Mortality after hospitalization with mild, moderate, and severe hyponatremia, Am J Med, 2009.

