HYPONATREMIA IN SICK CHILDREN : A MARKER OF SERIOUS ILLNESS

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ABSTRACT

To study the association between hyponatremia (serum sodium < 130 mEq/L) and the final outcome of the illness, we correlated serum sodium concentration at the time of hospitalization with the length of hospital stay and mortality in a prospective study of 727 sick children aged upto 12 years, who sought emergency care. The mean ±SE duration of hospital stay (7.7 ± 0.4 days) among 217 children with serum sodium £ 130 mEq/L was about 30% longer than that of 510 children with serum sodium £ 131 mEq/L (5.9 ±0.3 days) (p<0.01). This remained unaffected by the sex and the age group, but was further prolonged in children with hypotonic - euvolemic type of hyponatremia as compared to those with hypovolemic hyponatremia. The mortality rate in 510 children with normal serum sodium concentration (≥ 131 mEq/L) was 5.3%. In contrast, it was 17% in 47 children with serum sodium <125 mEq/L (Relative Risk 3.2; 95% Confidence Interval 1.6-6.7) and 9.3% in 170 children with serum sodium between 126-130 mEq/L (Relative Risk - 1.8; 95% Confidence Interval 1.1-3.7) (p<0.01). Hyponatremia in acutely ill children at admission indicates a poor prognosis.

Key words: *Electrolyte disturbances, Hyponatremia, Hypokalemia, Sodium, Mortality*

Though hyponatremia has been reported to be the commonest electrolyte abnormality in hospitalized sick patients, yet the interpretation and significance of the condition is beset with controversy and confusion(l-5). Moreover, a precise information on pathophysiologic implications and outcome of hyponatremia in sick children is lacking(6-9). Some authors view it as having little clinical significance(5-10), whereas others believe that it is often associated with significant morbidity and mortality(ll-13). We studied the association between hyponatremia at the time of hospitalization and final outcome of the sick children who sought emergency care.

Material and Methods

Included in the study were 727 children upto 12 years of age. They attended the Pediatric Emergency service of Nehru Hospital, PGIMER, and were hospitalized during the summer months of May, June, July and August and winter months of November, December, January and February. On each day, the first 5 children who required hospitalization were included in the study irrespective of their primary diagnosis or severity of the illness. The study was approved by the Institute Ethics Committee. Demographic data (age and sex), primary diagnosis, length of hospital stay and final outcome (recovered or died) were recorded for each child.

Venous blood sample was obtained at

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the time of initial evaluation for estimation of serum sodium and potassium (by flame photometery), plasma osmolality (by freezing point depression), blood glucose (by Folin Wu method), blood urea (Monoxime method) and serum creatinine (Jaffe's method). In children with serum sodium <130 mEq/L, urinary osmolality and sodium concentration was also estimated.

Depending on the clinical assessment of-hydration and laboratory data at the time of hospitalization, hyponatremia was categorized as hypotonic-euvolemic (dilutional), hypovolemic, edematous, of renal failure and hyperglycemic type(2,6). Hyponatremic and normonatremic children were compared for the duration of hospital stay by t-test, and for mortality rate by χ^2-test. The comparisons were done within various diagnostic categories and for the total population. Relative risk (odds ratio) of mortality and its 95% confidence interval was calculated by appropriate method(14).

Results

A detailed distribution of the study population with respect to age, sex, season and serum sodium concentration has been presented elsewhere. In brief, the mean ± SD age of the study children was 3.14 ± 3.18 years. The serum sodium concentration was 125 mEq/L or below in 47 (6.4%) children, between 126-130 mEq/L in 170 (23.5%), 131-135 mEq/L in 154 (21%), and > 135 mEq/L in 356 (50%).

Hospital Stay: The mean ± SD duration of hospital stay was similar in S41 boys (6.1 ± 6.2 days) and 196 girls (6.1 ± 6.3) ($p>0.05$) and did not differ significantly between 341 children studied in summer (6.9 ± 6.9 days) and 386 studied in winter season (5.4 ± 5.4 days).

As shown in *Table I,* the mean duration of hospital stay in children with serum sodium <125 mEq/L was significantly longer than those with serum sodium between 126-

TABLE **I**-*Mean ± SE Length of Hospital Stay in Days, of Study Children with Respect to Serum Sodium Levels at the Tune of Admission in Different Age Groups*

Age group (years)	Serum sodium concentration mEq/L		
	125	126-130	131
All	8.3±1.1*	6.0±0.5	5.9 ± 0.3
≤1	7.6±2.1 (n=l1)	5.5±0.8 (n=45)	5.4 ± 0.4 (n=170)
1-2	6.4±1.4 (n=15)	4.8±0.8 (n=50)	5.9 ± 0.5 (n=131)
3-5	9.8±3.3* (n=12)	4.7±0.8 (n=33)	4.9 ± 0.5 (n=103)
6-12	10.3±2.3 (n=9)	8.0±1.4 (n=42)	7.7 ± 0.7 (n=106)

* $p < 0.025$, t-test, compared to each of the other two groups.

130 mEq/L and ≥131 mEq/L, while it was similar among children with serum sodium concentration above 125 mEq/L. The findings were similar when data was analysed according to the agt groups *(Table I),* or within some common diagnostic categories namely pneumonia, meningitis/ encephalitis, heart disease and acute liver disease *(Table II).* Hyponatremia associated with acute diarrheal illness was not associated with prolonged hospital stay *(Table II).*

Mortality: The overall mortality rate showed an increase with lowering of serum sodium concentration *(Fig 1).* When compared to the children with normal serum sodium (≤131 mEq/L) the relative risk of mortality in children with a serum sodium ≤125 mEq/L was 3.2 (95 % confidence interval 1.6-6.7), while in those with serum sodium between of 126-130 mEq/L it was 1.8 (95% confidence interval 1.1-3.7). The type of hyponatremia did not show any association with the mortality rate *(Table III).*

Hypokalemia was seen in 52 of 217 hyponatremie children and in 47 of 510 normonatremic children. The mortality rate in hypokalemic-hyponatremic children was 19% (10/52) while in hypokalernic-normonatremic children it was 8.5% (4/47) (p>0.1).

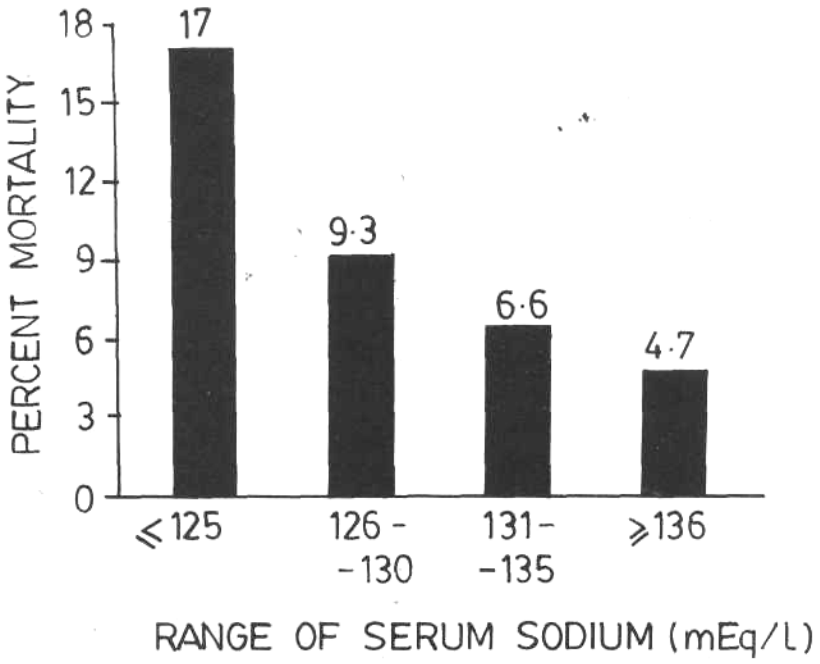

Fig 1. Mortality rate among 727 sick children with respect of serum sodium concentration at the time of hospitalization. The number of children with serum sodium ≤ 125 mEq/L was 47, between 126-130 mEq/L-170, 131-135 mEq/L-150, and with 136 mEq/L or above -356.

TABLE 11- *Mean* :t *SE Length of Hospital Stay in Days with Respect to Serum Sodium Concentration in Selected Diagnostic Categories*

Diagnostic category	Sodium Concentration mEq!L		
	S 125	126-130	131
Pneumonia	12.6 :t 3.2* (n=l1)	6.2 :t 1.3 (n=31)	5.8 :t 0.6 (n=119)
Acute diarrhea	2.7 :t 0.7 (n=6)	2.7 :f: 0.3 (n=39)	2.0 :t 0.3 (n=84)
Meningitis! -encephalitis	12.3 :t 3.1 (n=7)	9.0 :t 1.9 (n=18)	11.1 :t 1.1 (n=50)
Febrile illness! septicemia	5.2 :t 2.6 (n=4)	7.8 :t 1.2 (n = 13)	7.0 :t 0.9 (n=30)
Heart Disease	10.0 :t 4.5 (n=3)	6.0 :t 0.9 (n=l1)	6.0 :t 0.6 (n=42)
Acute liver disease	7.5 :t 2.3 (n=4)	5.0 :t 0.5 (n=5)	5.6 :t 1.2 (n=21)

* $p < 0.05$ compared to other two groups.

Discussion

We found that hyponatremia in acutely ill children attending our pediatric emergency service was associated with a higher mortality and prolonged hospitalization. Although, the study did not aim at defining various factors which could have contributed to the higher mortality, several factors including the underlying cause, the severity of the illness, and the severity and the rate of development of hyponatremia could have contributed. Possibly the severity of illness itself could have determined the severity of hyponatremia too, as shown in our subsequent studies on children hospitalized for meningitis (unpublished data) and pneumonia(15). Our finding together with the findings of other authors(2,3,13) suggest that hyponatremia is an indicator of severe un-

TABLE III - *Mortality Rate Among Hyponatremic Patients with Respect to Type of Hyponatremia*

Type of hyponatremia	Number	Number died (%)
Hypotonic-euvolemic (dilutional)	136	14(10%)*
Hypovolemic	60	6(10%)+
Hypervolemic (edematous)	11	1
Of renal failure	10	1

*4 deaths each with pyogenic meningitis and pneumonia, two with acute liver failure, one death each with encephalitis, tuberculous meningitis, disseminated staphylococcal infection, and septicemia

+4 deaths with acute diarrhea, one each with intestinal obstruction and diphtheria with dehydration.

derlying disease and a pointer to poor prognosis.

A significantly prolonged hospital stay was noted in children with severe hyponatremia (Serum sodium ≤125 mEq/L) in the diagnositc categories of pneumonia, heart disease and meningitis' encephalitis. All these children had euvolemic hyponatremia. In contrast to this, children with severe hypovolemic hyponatremia associated with diarrhea had a hospital stay similar to the normonatremic ones. This suggests that euvolemic type of hyponatremia prolonged the hospital stay on its own, or it was a marker of an underlying disease which required longer hospital stay.

Conflicting opinions have been expressed about mortality in adult patients with acute hyponatremia. Mortality rates ranging from 8% to 86% have been cited (5,17). Anderson *et al.(2)* in a study of 196 hospitalized patients found that the case fatality rate in the hyponatremia group was 11.2% as compared to 0.19% in the normonatraemic group. On the other hand, Stern(5) reported a mortality of 8% only in 64 adult patients who had a serum sodium < 110 mmol/L with sustained seizures and/or coma. In an accompanying review of 146 published cases of severely symptomatic hyponatremic patients, he found only 3 deaths. The review included 37 infants with water intoxication, none of whom died. However, this review overlooked single case reports to fatalities or small series devoted to adverse outcome(17).

Experimental studies also provide divergent data on the mortality from acute dilutional hyponatremia(17). Most studies have reported a high mortality varying from 30 % to 62% in rabbits, rats and dogs(18,19). In contrast, Sterns *et al.* reported that none of the 84 rats in whom serum sodium was lowered to 100 mmol/L within 6 hours died(20).

The reported mortality rate among hospitalized patients with hyponatremia evolving over the course of more than 48 hours has varied between 10% and 27%(17). This is similar to mortality of 17% in severe hyponatremia observed in the present study. Thus, our study has documented that sick children needing emergency care and hospitalization have as high a risk of mortality as observed in adult patients.

If hyponatremia is associated with an increased mortality, the question to be addressed is whether it should be treated? The subject has been discussed and reviewed recently(17,21). Untreated hyponatremia may lead to cerebral swelling and its consequences because of hypotonicity(22). Hyponatremic patients with ECF volume depletion should receive 0.9% saline while those with ECF volume expansion (hyponatremic or edematious hyponatremia) responds best of water restriction. Euvolemic (dilutional) hyponatremia are most difficult to treat. A standard therapy can not be applied in all such patients. In presence of symptom such as impaired sensorium or when the disturbance is acute, prompt correction with hypertonic (3 %) saline is required(17). A rate achieving a correction upto a maximum of 2.5 mEq/L/h or 20 mEq/L/day has been reported to be safe in adults(23). Hyponatremia that has developed over several days or has only mild symptoms requires a conservative approach correcting plasma sodium at 1.0 mEq/L/h(23); too rapid correction can lead to osmotic demyelination syndrome(19,24). Rossi advocate an approach which combines promotion of water excretion with help of furosemide, and replacement of urinary sodium and potassium losses with hyper-

tonic saline and potassium chloride solution respectively (25).

In conclusion, the study shows that in sick children seeking emergency care, severe hyponatremia is associated with a threefold increase in risk of death and prolonged hospitalization. Early detection and institution of rational therapy for hyponatremia should receive adequate attention regardless of underlying disease.

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