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Original article

Role of Hyponatremia in Prediction of Outcome in Children with Severe Lower Respiratory Tract Infections

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Abstract

Background: Lower respiratory infection (LRTI) is one of the serious illnesses, especially in less than 5 years of age group requiring hospitalization and contributes to 30% of deaths yearly worldwide mainly due to pneumonia as the leading cause. **Aim** This study aimed to find the association of hyponatremia (serum sodium less than 135 mEq/L) with severe LRTI. **Methods:** This cross-sectional study was conducted on 100 children admitted to PICU with severe LRTI including bronchopneumonia (BPN), lobar pneumonia, bronchiolitis, and empyema, all children were subjected to full history taking, complete clinical examination and investigations as complete blood count, arterial blood gases, C-reactive protein, potassium and sodium levels and radiological investigations as chest X-ray and chest CT . The conditions were assessed by PRESS score. **Results:** Most cases had normal sodium (63%), 3% had severe hyponatremia, 10% had moderate hyponatremia, 19% had mild hyponatremia, and 5% had hypernatremia**.** Children with hyponatremia had statistically higher frequencies of MV, mortality and statistically longer duration of oxygen support and hospital stay**.** At sodium level <130.5 mmol/L, sodium could predict need of MV, with a sensitivity 73.7% and specificity 89.8%. At sodium level <128.5 mmol/L, sodium could predict mortality with a sensitivity of 90 % and specificity 94.5%.

Conclusion: hyponatremia is a frequent finding in children with LRTI and seems to be associated with disease severity, time for hospitalization and mortality. Further studies on the effects of sodium levels on clinical course of LRTI and on the pathophysiological pathway of LRTI-related hyponatremia are required.

Keywords: Hyponatremia; Outcome; Severe; Lower Respiratory Tract Infections

Introduction

Lower respiratory tract infection (LRTI) is an inflammation of the airways (pulmonary tissue), due to viral or bacterial infection, below the level of the larynx. LRTI includes various diseases such as: bronchiolitis, bronchopneumonia (BPN), Lobar pneumonia and Empyema. LRTI is one of the serious illnesses requiring hospitalization especially in children under 5 years of age. It accounts for 30% of deaths annually worldwide mostly due to pneumonia as a leading cause (1).

LRTIs contributed 6.8% of deaths in neonates, 20% of deaths in children aged 1–12 months, and 12% of deaths in children aged 1–4 years (2).

Pneumonia and bronchiolitis/bronchitis are the most common LRTIs in children with symptoms including coughs and an increased respiratory rate. Pneumonia causes the alveoli in the lung to fill with fluid or pus. Pneumonia contributed the largest share in the mortality in the children aged < 5 years globally. Bronchitis is the swelling or inflammation of the bronchial tubes. Seasonal influenza affects both the upper and lower respiratory tracts (3).

Hyponatremia associated with pediatric pneumonia is most commonly due to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) (4). This syndrome is characterized by hyponatremia and hypoosmolality and results from the inappropriate and continued secretion and/or action of antidiuretic hormone despite normal or increased plasma volume (5).

Recent studies have demonstrated that inflammatory cytokines (such as IL-1β and IL-6) may result in hyponatremia that is associated with various inflammatory conditions such as pneumonia, meningitis, and malaria. Moreover, increasing evidence suggest that these cytokines may increase the secretion of ADH. These findings suggest that increased inflammatory cytokine levels result in nonosmotic secretion of ADH, and thus, the development of hyponatremia. On basis of these data, we may reveal that serum sodium levels can be used as a marker of disease severity in LRTI (6).

This study aimed to find the association of hyponatremia (serum sodium less than 135 mEq/L) with severe lower respiratory infection (LRTI).

Patients and methods

This cross-sectional study was conducted at Benha university hospital, during the period from October 2023 to May 2024, and included 100 children admitted to PICU of Benha university hospital with severe lower respiratory tract infection.

Inclusion criteria:

- Age between 2 months and 16 years old admitted to the PICU with severe lower respiratory tract infection
- Both sexes were included
- Pediatric Respiratory Severity Score (PRESS) 4-5

Exclusion criteria:

- Patients < 2 months and > 16 years of age.
- Children with associated gastroenteritis, renal disorders , CNS infection, congestive heart failure and adrenocortical disorders.
- Children on drugs which can cause electrolyte imbalance such as diuretics, anticonvulsants.
- Refusal to participate.

Ethical considerations

The whole study design was approved by the local ethics committee, Faculty of Medicine, Benha University **(Code MS 19-4-2023).** After explaining the value of the study and the procedures that would be commenced, an informed written consent was obtained from the guardian of every participant before being included in the study

Complete history, physical examination, laboratory investigations included serum electrolyte level (Na+), and radiological investigations included chest X-ray and chest CT were examined to confirm the diagnosis. Pneumonia was diagnosed in patients presenting with fever, tachypnoea, grunting, and chest retraction. BPN and lobar pneumonia were further differentiated based on chest X-ray (patchy opacity in BPN and lobar involvement in lobar pneumonia). Bronchiolitis was confirmed based on tachypnoea, rhinorrhoea, wheezes, subcostal and intercostal retraction, nasal flaring. Empyema was characterized by systemic toxicity, breathing difficulty, decreased movement of the chest, decreased air entry, dull percussion, and obliteration of the costophrenic angle with varying degrees of opacification in chest X-ray.

After obtaining consent from the parent Blood samples and cultures were collected from peripheral veins. About 3 ml blood sample was taken from each subject One ml blood was put on EDTA and used for CBC. One ml was left to clot to separate serum for C-reactive protein, sodium and potassium. One ml blood by a heparinized needle was used to assess ABGs. The investigations were done as follows: Complete blood count was analyzed by flow cytometry (Beckman LH 780; Beckman Coulter, Brea, CA, USA). The following parameters were compared between groups: Hemoglobin (gm/dl)**,** Total leucocytes count ($10^3/mm^3$), Neutrophil (%)**,** Lymphocyte (%)**,** Platelets ($10^3/mm^3$)**,** C-Reactive Protein was measured by scattering immunoturbidimetry (Beckman Coulter AU5800)and Arterial blood gases (ABGs**)** a heparinized needle was used, and at least 0.2 ml of capillary blood samples for blood gas analysis. Blood gas analysis was performed using ABL 80 FLEX analyzer within 5 min of sample collection. The following acid base and blood gas values were recorded and analyzed: pH, partial pressure of carbon dioxide (pCO_2), base excess and bicarbonate.

Sodium and potassium level were measured by Ion selective electrodes analyzer. (AVL 9181, Roche diagnostics GmbH, Germany). Normal Serum Sodium were taken as 135-145mEq/L. Serum Sodium concentration of <135mEq/L were considered hyponatremia. Serum Sodium concentration of 131-134mEq/L were taken as mild hyponatremia,126-130mEq/L were taken as moderate hyponatremia and ≤125mEq/L were taken as severe hyponatremia.

Ethical considerations

The whole study design was approved by the local ethics committee, Faculty of Medicine, Benha University. After explaining the value of the study and the procedures that would be commenced, an informed written consent was obtained from the guardian of every participant before being included in the study.

Statistical Analysis

The collected data was revised, coded, tabulated using Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Shapiro test was done to test the normality of data distribution. Mean, Standard deviation (± SD) for parametric numerical data, while Median and range for non-parametric numerical data. Frequency and percentage of non-numerical data. Analytical statistics: Student T Test was used to assess the statistical significance of the difference between two study group means. Chi-Square test was used to examine the relationship between two qualitative variables. Correlation analysis: To assess the strength of association between two quantitative variables. The correlation coefficient defines the strength and direction of the linear relationship between two variables. The ROC Curve (receiver operating characteristic) provides a useful way to evaluate the sensitivity and specificity for quantitative diagnostic measures that categorize cases into one of two groups.

Results

This study included 100 children (56 males and 44 females) with severe lower respiratory tract infection (LRTI). The mean age in the studied group was 3.5±2.7 years, about 22% of the patients were 2-12 months, 56% of them were 1-6 years and 22% were above 6 years old. The prevalence of hyponatremia was highest in the age group (1-6) years 50% and lowest in the age group 1-12 months (21.9%). The prevalence of hyponatremia was higher in males (59.5%) than females (40.5%) However we cannot make any conclusion on this basis.

Forty percent of children had history of NICU admission and 16% had history of previous PICU admission.

Out of all the cases of severe LRTI, there was the highest number of cases for lobar pneumonia (51%), followed by bronchopneumonia (18%)**,** bronchiolitis (21%) and the lowest number of cases was empyema (10%). **(Figure 1).**

Children with hyponatremia had statistically lower lymphocytes, and statistically higher TLC ,neutrophils and CRP compared to children with normal sodium. While there was no statistical difference between both groups as regards to hemoglobin or platelets. Children with hyponatremia had statistically lower ph and HCO3 compared to children with normal sodium **Table 1.**

Most cases had normal sodium (63%), 3% had severe hyponatremia, 10% had moderate hyponatremia, 19% had mild hyponatremia, and 5% had hypernatremia. **Table 2.**

Sodium had significant positive correlations with (SPO2, PH, HCO3) and had significant negative correlations with (CRP, CO2, PRESS score). **Table 3.**

Most patients with hyponatremia (68.8%) were underweight, while most patients in the normal sodium group were of normal range weight (86.8%).

Children with hyponatremia had statistically higher grades of respiratory distress , PRESS score compared to children with normal sodium. While there was no statistical difference between both groups as regards to other clinical data**.** children with hyponatremia had statistically higher frequencies of MV, mortality and statistically longer duration of oxygen support and hospital stay compared to children with normal sodium. **Table 4.**

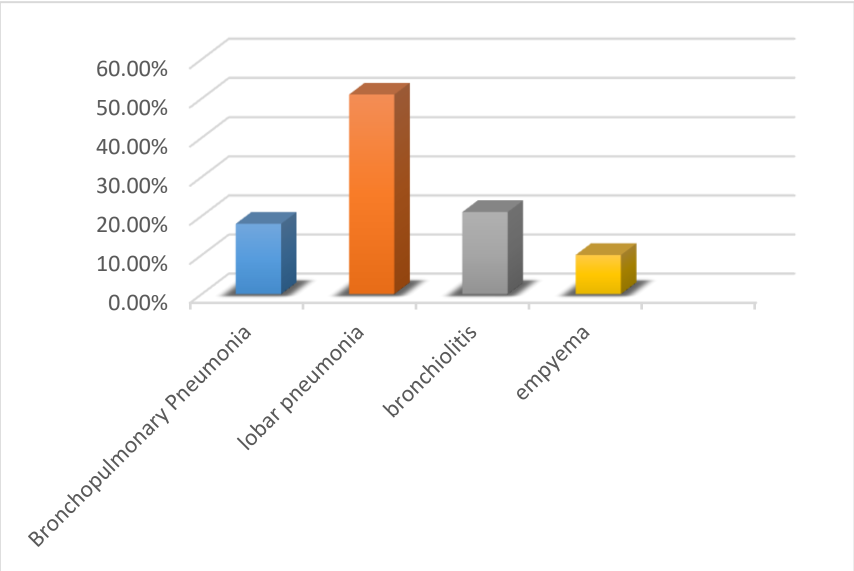

Figure 1. Shows the overall distribution of studied groups

Table 1: Sodium status as regards to Complete blood count parameters & arterial blood gases parameters and electrolytes

		Sodium status		Test	P value
		<135 N=32 %	=>135 N=68 %		
Hemoglobin	**Mean ±SD**	**10.5±0.8**	**10.7±1.1**	**t=0.49**	**0.59**

(mg/dl)	**Range**	**8.4-11.8**	**8.5-13.2**		
TLC ($x10^3$/L)	**Mean ±SD**	**19.6±8.7**	**17.3±9.2**	**t=1.1**	**0.11**
	Range	**2.1-29.3**	**2.5-25.7**		
Lymphocytes	**Mean ±SD**	**17.5±11.8**	**24.5±9.4**	**t=2.6**	**0.006***
(%)	**Range**	**6.5-37.6**	**9.7-49.2**		
Neutrophils (%)	**Mean ±SD**	**77.3±13.3**	**68.8±11.8**	**t=3.1**	**<0.001***
	Range	**52.1-90.2**	**42.1-89.5**		
Platelets	**Mean ±SD**	**192±89**	**199±96**	**t=0.89**	**0.36**
($x10^3$/L)	**Range**	**25-320**	**45-325**		
C-reactive	**Mean ±SD**	**52.9±27.4**	**41.8±24.7**	**t=2.1**	**0.044***
protein (mg/dl)	**Range**	**24-192**	**3-192**		
PH	**Mean ±SD**	**7.24±0.09**	**7.28±0.07**	**t=1.1**	**0.26**
	Range	**7.14-7.37**	**7.14-7.37**		
CO_2	**Mean ±SD**	**53.4±9.5**	**49.9±7.1**	**t=2**	**0.07**
	Range	**41-66**	**40-65**		
HCO_3	**Mean ±SD**	**16.8±3.9**	**18.7±2.3**	**t=3.1**	**0.016***
	Range	**4.1-21**	**13.2-22.5**		
Potassium (mmol/L)	**Mean ±SD**	**3.9±0.8**	**5.1±0.7**	**t=1.2**	**0.22**

t: Student t-test, *: significant,

Table 2: Sodium status in the studied group

		Study group N= 100	**%**
Sodium status	**Severe hyponatremia (<125)**	**3**	**3.0%**
	Moderate hyponatremia (125-129)	**10**	**10.0%**
	Mild hyponatremia (130-134)	**19**	**19.0%**
	Normal sodium (135-145)	**63**	**63.0%**
	Hypernatremia (>145)	**5**	**5.0%**

Table 3: Correlation between serum sodium status andother clinical data in the studied group

	Sodium	
	r	**P value**
Age/years	-0.120	0.235
RR	0.070	0.486
HR	0.195	0.052

SPO2	0.205	0.049*
CRT	-0.080	0.427
Weight	-0.131	0.192
Height	-0.135	0.179
BMI	-0.157	0.118
HEMOGLOBIN	-0.028	0.782
WBC	-0.015	0.881
Neutrophils	-0.156	0.121
Lymphocytes	0.084	0.408
PLATELET	0.062	0.538
CRP	-0.212	0.035*
PH	0.241	0.016*
CO2	-0.342	<0.001*
Hco3	0.244	0.014*
Potassium	0.084	0.407
PRESS	-0.335	0.001*

Table 4: Sodium status as regards to chest examination

		Sodium status				**Test**	**P value**
		<135		**=>135**			
		N=32	**%**	**N=68**	**%**		
Respiratory distress grade	**I**	1	3.1%	12	17.6%	X^2=16.4	0.001*
	II	14	43.8%	41	60.3%		
	III	6	18.8%	11	16.2%		
	IV	11	34.4%	4	5.9%		
Crepitations	**No**	15	46.9%	31	45.6%	X^2=0.02	0.91
	Yes	17	53.1%	37	54.4%		
Wheezes	**No**	13	40.6%	28	41.2%	X^2=0.03	0.96
	Yes	19	59.4%	40	58.8%		
	Yes	15	46.9%	48	70.6%		
Air entry	**Normal**	18	56.3%	36	52.9%	X^2=0.1	0.76
	Decrease	14	43.8%	32	47.1%		
PRESS score	**Mean ±SD**	4.5±0.5		4.2±0.4		t=3.1	0.006*
	Range	4-5		4-5			
Oxygen support	**Nasal oxygen**	7	21.9%	44	64.7%	X^2=43.1	<0.001*
	HFNC	5	15.6%	15	22.1%		
	CPAP	8	25.0%	7	10.3%		
	MV	12	37.5%	2	2.9%		
Duration of hospital stay/days	**Mean ±SD**	10.1±4.1		8.1±3.4		t=2.6	0.020*
Duration of oxygen support/days	**Mean ±SD**	9.7±4		6.7±1.9		t=5.2	<0.001*
Death	**No**	22	68.8%	68	100.0%	X^2=23.6	<0.001*
	Yes	10	31.3%	0	0.0%		

X^2: Chi-square test, t: Student t-test, *: significant

Discussion

In our study, most cases had normal sodium (63%), 3% had severe hyponatremia, 10% had moderate hyponatremia, 19% had mild hyponatremia, and 5% had hypernatremia.

In the same line, Yılmaz et al., (8)**,** found one patient in group 1 of severe hyponatremia (Na <125mmol/dl), nine in group 2 of moderate hyponatremia (Na 126-130mmol/dl) , 90 in group 3 of mild hyponatremia (Na 131-134) , 446 in group 4 of normal sodium level (Na 135-145mmol/dl) , and three in group 5 of hypernatremia (Na>146mmol/dl). And in the study by Mahapatra et al., (9)**,** the prevalence of hyponatremia was found to be 58.9% (Out of 231 cases, hyponatremia was present in 136 cases and absent in 95 cases). Mild hyponatremia was the most common (83.8%) followed by moderate (13.2%) and then by severe hyponatremia (2.9%). However, our results weren’t matched with Parekh et al., (10)**,** who reported that prevalence of Hyponatremia in LRTI children was 66.6% (90/135).

Hyponatremia is one of the most diagnosed electrolyte disorders in clinical medicine. Because it is often an indicator of an underlying disease, the diagnosis of hyponatremia is important in preventing morbidity and mortality. Pediatric hyponatremia is usually caused by an excess of ADH. Recent studies have demonstrated that ADH secretion increases during inflammation (11)**.** Hyponatraemia in association with LRI’s may occur due to many reasons, such as salt deficit, or excess of water. Other contributory factors may be primary illness, impaired water excretion, improper release of vasopressin, use of hypotonic fluids, redistribution of sodium and water, sick cell syndrome, and numerous drugs (12)**.**

In our study, sodium had significant positive correlations with (SPO2, PH, HCO3) and had significant negative correlations with (CRP, CO2).

Yılmaz *et al.*, (8)**,** found a statistically significant negative correlation between serum sodium levels and CRP levels, WBC counts, and absolute neutrophils count. In the same way, Pintaldi et al., (13)**,** found that the mean CRP level was more than three times higher in the hyponatremic children compared to normonatremic children (61.3 mg/L vs. 19.9 mg/L). Moreover, there was a negative linear correlation between higher levels of CRP and hyponatremia (r -0.351; $p < 0.001$).

In our study, there was no statistical difference between children with hyponatremia and patients with normal sodium as regards to age, sex, and history of NICU or PICU admission. Children with hyponatremia had statistically lower weight, height and BMI compared to patients with normal sodium. Moreover, most patients with hyponatremia (68.8%) were underweight, while most patients in normal sodium group were of normal range weight (86.8%).

This was in agreement with Yılmaz *et al.*, (8)**,** who reported that there was no difference between the hyponatremic and normonatremic groups for mean age. The 100 hyponatremic patients comprised 39 females and 61 males. The 446 normonatremic patients comprised 167 females and 279 males. There was no statistically significant difference between the hyponatremic and normonatremic groups with respect to gender distribution. In the same way, Sakellaropoulou et al. (14) found no significant difference in the gender distribution of children having hyponatremia. While Mahapatra et al., (9)**,** reported that the prevalence of hyponatremia was highest in the age group 10-12 years (100%) and lowest in the age group 1-12 months (53.8%). However, as the number of cases was only three in the age group 10-12 years, they cannot make any conclusion on this basis. Prevalences in the 6-10 years group, the 1-3 years group and the 3-6 years group were 83.3%, 61.7% and 56.2% respectively. The prevalence of hyponatremia was 4.29 times higher in the 6-10 years group than the 1-12 months group (OR=4.29, 95% CI=0.90-20.45, p<0.05). Moreover, they reported that the prevalence of hyponatremia was higher in females (66.7%) than males (53%) with a significantly higher risk (OR=0.56, 95% CI=0.32-0.96, p=0.03).

In our study, children with hyponatremia had statistically higher frequencies of MV, mortality and statistically longer duration of oxygen support and hospital stay compared to children with normal sodium.

This was in agreement with Lamichhane et al., (15)**,** reported that the association of hyponatremia with the need of non-rebreathing facemask (p=0.001) and mechanical ventilation (p=0.009) was significant. Moreover, a significant association of hyponatremia with outcome was statistically significant (P=0.047). Similarly, Singh et al., (12) observed that children with hyponatremia had longer hospital stay and there was statistically significant difference of hospital stay between hyponatremic v/s isonatremic groups (p<0.01). In the same way, Al-Sofyani, (16)**,** reported that in children admitted to PICU, hyponatremia was also associated with increased length of stay ($p = 0.04$) and a trend of increased mortality ($p = 0.05$).

Conclusion

Hyponatremia was found in 32% of children with severe lower respiratory tract infection. 3% had severe hypernatremia, 10% had moderate hyponatremia, 19% had mild hyponatremia. Children with hyponatremia had statistically higher grades of respiratory distress, PRESS score compared to children with normal sodium. Hyponatremia was significantly associated with the need of ventilator, prolonged hospital stay and mortality.

References

1. Mahashur A. Management of lower respiratory tract infection in outpatient settings: Focus on clarithromycin. Lung India Off Organ Indian Chest Soc. 2018;35(2):143.
2. Pak A, Adegboye OA, Eisen DP, McBryde ES. Hospitalisations related to lower respiratory tract infections in Northern Queensland. Aust N Z J Public Health. 2021;45(5):430–6.
3. Calderaro A, Buttrini M, Farina B, Montecchini S, De Conto F, Chezzi C. Respiratory tract infections and laboratory diagnostic methods: a review with a focus on syndromic panel-based assays. Microorganisms. 2022;10(9):1856.

4. Meena AK, Nanda PM, Sharma R, Chakrabarty B, Gulati S. Tolvaptan for treatment of syndrome of inappropriate antidiuretic hormone secretion (SIADH) in a child with corpus callosum agenesis. Indian J Pediatr. 2024;91(2):188–90.

5. Reddy P. Clinical approach to euvolemic hyponatremia. Cureus. 2023;15(2).

6. Tzoulis P, Grossman AB, Baldeweg SE, Bouloux P, Kaltsas G. MANAGEMENT OF ENDOCRINE DISEASE: Dysnatraemia in COVID-19: prevalence, prognostic impact, pathophysiology, and management. Eur J Endocrinol. 2021;185(4):R103–11.

7. Miyaji Y, Sugai K, Nozawa A, Kobayashi M, Niwa S, Tsukagoshi H, et al. Pediatric respiratory severity score (PRESS) for respiratory tract infections in children. Austin Virol Retrovirol. 2015;2(1):1009.

8. Yılmaz Y, Candar T, Kara F, Ustebay S, Ustebay DÜ, Aydın E, et al. Serum sodium levels in children with lung infections. J Pediatr Inf. 2016;10:10–3.

9. Mahapatra C, Sharma VK, Singhal S, Jangid RK, Laxminath TK. Risk factors of hyponatremia in children with lower respiratory tract infection (LRTI). J Pediatr Res. 2021;8:479–84.

10. Parekh AN, Patel D, Parekh AN. A Prospective Observational Study Of Hyponatremia In Lower Respiratory Tract Infection In Children Admitted In Tertiary Care Teaching Hospital. Natl J Integr Res Med. 2019;10(6).

11. Królicka AL, Kruczkowska A, Krajewska M, Kusztal MA. Hyponatremia in infectious diseases—A literature review. Int J Environ Res Public Health. 2020;17(15):5320.

12. Singh P, Attri HK, Sodhi MK, Singh V, Chopra L, Neki NS. A Study of Hyponatremia in Lower Respiratory Infections in Children Aged 2months to 5 Years. 2019;

13. Pintaldi S, Zago A, Pizzolon C, Magni E, Cozzi G, Andrade S, et al. Children with mild hyponatremia at the emergency department are at higher risk of hospitalization. BMC Pediatr. 2023;23(1):318.

14. Sakellaropoulou A, Hatzistilianou M, Eboriadou M, Athanasiadou-Piperopoulou F. Hyponatraemia in cases of children with pneumonia. Arch Med Sci. 2010;6(4):578–83.

15. Lamichhane M, Shrestha L, Bajracharya L, Bagale A. Hyponatremia as a Predictor of Adverse Outcome in Children with Severe Lower Respiratory Tract Infection in Tribhuvan University Teaching Hospital (TUTH), Nepal. 2020;

16. Al-Sofyani KA. Prevalence and clinical significance of hyponatremia in pediatric intensive care. J Pediatr Intensive Care. 2019;8(03):130–7.

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