International Journal of Contemporary Pediatrics
Mangshetty RB et al. Int J Contemp Pediatr. 2024 Nov;11(11):1569-1575
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20243083

Original Research Article

Enhancing neonatal sepsis outcomes: the role of ascorbic acid and thiamine as adjuvant therapies

Roopa B. Mangshetty, Apurva A. Binjanwadgi, Gayathri S. Gaddamanugu*

Department of Pediatrics, Mahadevappa Rampure Medical College, Kalaburagi, Karnataka, India

Received: 12 August 2024
Revised: 01 October 2024
Accepted: 02 October 2024

***Correspondence:**
Dr. Gayathri S. Gaddamanugu
E-mail: gayathri5sharanya@gmail.com

ABSTRACT

Background: Neonatal sepsis, a systemic infection affecting newborns under 28 days, remains a leading cause of global infant mortality and morbidity. It affects approximately 2.8% of live births and accounts for 18% of newborn deaths. Neonates are particularly vulnerable due to their immature immune systems. Current management primarily involves timely antibiotic therapy and supportive care. Emerging evidence suggests potential benefits of micronutrients like ascorbic acid (vitamin C) and thiamine in sepsis management, but research on their combined use in neonatal sepsis is limited.
Methods: This randomized controlled trial was conducted over 18 months involving 120 neonates with sepsis. The intervention group (n=60) received intravenous ascorbic acid (100 mg/day) and thiamine (4 mg/kg/day) for 5 days along with antibiotics, while the control group (n=60) received antibiotics alone. Clinical parameters, duration of hospital stay, NICU stay, antibiotic usage, ventilator support, vasopressor support, laboratory tests, and outcomes were compared between the two groups.
Results: The intervention group showed significantly shorter durations of antibiotic therapy (11.22 vs 13.06 days, p=0.035), NICU stay (7.73 vs 10.91 days, p=0.003), and total hospital stay (12.11 vs 14.55 days, p=0.013) compared to the control group. At discharge, the intervention group had lower C-reactive protein (19.04 vs 33.82, p=0.041) and serum lactate levels (2.55 vs 3.32, p=0.008).
Conclusions: Supplementation of ascorbic acid and thiamine as adjunctive therapy in neonatal sepsis appears to have potential benefits in reducing the duration of hospital stay and NICU stay, and improving certain biochemical markers, without any safety concerns.

Keywords: Neonatal sepsis, Ascorbic acid, Thiamine, Adjuvant therapy, NICU

INTRODUCTION

Neonatal sepsis, a systemic infection affecting newborns less than 28 days old, remains a leading cause of mortality and morbidity globally. It is estimated that approximately 2.8% of live births are affected by neonatal sepsis, which accounts for 18% of deaths among newborns.[1] The first month of life represents the most critical period, with a global average neonatal mortality rate of 17 deaths per 1,000 live births in 2022.[2] Neonates possess an immature immune system, with limited functionality of polymorphonuclear neutrophils, macrophages, and T lymphocytes, rendering them highly susceptible to invasive infections.[3] Despite advancements in neonatal care, managing neonatal sepsis remains challenging, as clinical presentation is often nonspecific, and rapid disease progression can occur. The mainstay of treatment involves timely initiating appropriate antibiotic therapy, along with supportive measures to maintain homeostasis.[4] Emerging evidence suggests that certain

micronutrients, such as ascorbic acid (vitamin C) and thiamine, may be beneficial in managing sepsis. While some studies have explored using these micronutrients in combination with hydrocortisone for sepsis patients in the PICU, research on using ascorbic acid and thiamine for neonatal sepsis remains limited.[5,6] Ascorbic acid, a water-soluble vitamin, provides several beneficial effects in the critical state of sepsis. It aids in neutralizing reactive oxygen species and modulating inflammatory mediators. Furthermore, as a cofactor for various biosynthetic and regulatory enzymes, it may influence gene transcription and affect multiple cells signaling pathway.[7] Thiamine, a water-soluble vitamin, is crucial for generating energy from glucose. It facilitates the conversion of pyruvate into acetyl-coenzyme A, which is necessary for the citric acid cycle. Without enough thiamine, this conversion is hindered, disrupting intermediate metabolism and resulting in lactic acidosis.[8]

Akhtar RJ et al, conducted a study demonstrating the effectiveness of intravenous vitamin C as adjunctive therapy for neonatal sepsis. The study concluded that intravenous ascorbic acid can be beneficial in treating neonatal sepsis.[4] Aly H et al, Sivanandan S et al, Mohite RV et al and Bass WT have explored the use of ascorbic acid as an adjunctive treatment for neonates with birth asphyxia and extreme preterm birth.[9-12] Gian PS et al, proposed that thiamine could act as a possible neuroprotective agent for newborns suffering from hypoxic-ischemic encephalopathy.[13] In a study of pediatric patients aged 0-16 years conducted by Lucile Equey et al., 72% (44/61) of the participants were found to have low circulating levels of ascorbic acid and thiamine.[14] The current data on the use of ascorbic acid and thiamine as adjunctive therapies for neonatal sepsis are limited. This randomized controlled trial was aimed to evaluate the effects of supplementing ascorbic acid and thiamine, in combination with standard antibiotic therapy, on clinical outcomes and biochemical parameters in neonates with sepsis.

METHODS

Study design

This study was a single-centered, randomized, controlled trial.

Study place

Study was conducted at the Neonatal Intensive Care Units (NICUs) of Basaveshwar Teaching and General Hospital and Sangameshwar Teaching and General Hospital, affiliated with Mahadevappa Rampure Medical College, Kalaburagi, Karnataka, India.

Study duration

Study was conducted over 18 months from August 2022 to January 2024.

Data collection

Data was collected after obtaining clearance from the Institutional Ethical Committee and informed consent from the attenders of the infants.

Inclusion criteria

Neonates diagnosed with neonatal sepsis in the NICU.

Exclusion criteria

Neonates with congenital malformations incompatible with life, Newborns transferred from another Intensive Care Unit or hospital with a diagnosis of septic shock for more than 24 hours, and Neonates discharged against medical advice.

Sample size

The study was conducted on 120 patients.

n=sample size for the study group (A) Interventional, (B) Control

In the reference study: Neonatal Sepsis in a Tertiary Care Hospital in South India: Bacteriological Profile and Antibiotic Sensitivity Pattern. Authors: Bambala Puthattayil, Vishanu Bhat.[15]

Prevalence rate of neonatal sepsis=41.6%
p=41.6 q=58.4
L=permissible error was 20% of P was 8.32 Power of study was 80.0
Sample size (n)=$Z2\alpha\ pq/L^2$
=(1.96)2×41.6×58.4/ (8.32)2
=3.84×2429.44/69.22
=134.8
Round figure sample size n=120

Neonates were randomly assigned by simple random technique to either the intervention group or the control group. The allocation was concealed in sequentially numbered, opaque, sealed envelopes. The study personnel involved in data collection and analysis were blinded to the group assignments.

Interventions

Intervention group

Neonates in the intervention group received intravenous ascorbic acid (100 mg/day) and thiamine (4 mg/kg/day) for 5 consecutive days, in addition to standard antibiotic therapy.

Control group

Neonates in the control group received standard antibiotic therapy alone, without any additional supplementation.

The antibiotic regimen for both groups was based on the local hospital protocol for the management of neonatal sepsis.

Outcomes

The outcomes were categorized as the primary outcome and secondary outcomes

Primary outcomes

Duration of hospital stay, duration of NICU stay, duration of antibiotic therapy, duration of ventilator support, duration of vasopressor support, mortality.

Secondary outcomes

Changes in laboratory parameters, Complete blood count (hemoglobin, total leukocyte count, platelet count), C-reactive protein (CRP), serum lactate

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 25.0. Continuous variables were presented as mean±standard deviation, and categorical variables were presented as frequencies and percentages. Comparisons between the intervention and control groups were made using the unpaired t-test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. A p value less than 0.05 was considered statistically significant.

RESULTS

A total 120 neonates were enrolled in the study, with 60 in the intervention group and 60 in the control group. The mean birth weight was 2.27±0.68 kg in the intervention group and 2.26±0.58 kg in the control group (p=0.926). The mode of delivery was similar between the groups, with 36.7% of neonates in the intervention group and 35.0% in the control group delivered via normal vaginal delivery (p=0.849). The distribution of gender was also comparable, with 63.3% male neonates in the intervention group and 61.7% in the control group (p=0.850). Based on the onset of sepsis, 71.7% of neonates in the intervention group and 85.0% in the control group had early-onset sepsis (p=0.076).

Clinical manifestations

The clinical characteristics of the study participants are presented in Table 5. The shock was present in 60.0% of neonates in the intervention group and 43.3% in the control group (p=0.067). Birth asphyxia was observed in 16.7% of neonates in the intervention group and 21.6% in the control group (p=0.796). Respiratory distress syndrome (RDS) was significantly more common in the control group (58.3%) compared to the intervention group (35.0%) (p=0.011). Seizures were present in 15.0% of neonates in the intervention group and 5.0% in the control group (p=0.067). Meconium-stained amniotic fluid (MSAF) was observed in 31.7% of the intervention group and 26.7% of the control group (p=0.546). Hyperbilirubinemia was present in 13.3% of the intervention group and 18.3% of the control group (p=0.453).

The changes in laboratory parameters between admission and discharge were compared (Table 6). In the intervention group, the mean haemoglobin decreased from 17.10±2.17 g/dl at admission to 13.93±3.38 g/dl at discharge (p<0.001). In the control group, the mean haemoglobin decreased from 17.83±2.50 g/dl to 14.18±2.53 g/dl (p<0.001). The total leukocyte count decreased significantly from admission to discharge in both the intervention group (21,111±12,727 to 11,106±3,223 cells/mm³, p<0.001) and the control group (17,202±10,630 to 11,378±3,635 cells/mm³, p<0.001). Platelet counts also decreased significantly from admission to discharge in both the intervention group (2.55±0.74 to 1.92±0.86 lakhs/mm³, p<0.001) and the control group (2.45±0.69 to 1.93±0.88 lakhs/mm³, p<0.001).

The erythrocyte sedimentation rate (ESR) decreased significantly from admission to discharge in the intervention group (11.46±5.52 to 9.26±3.78 mm/hr, p=0.003) but did not show a significant change in the control group (11.09±5.51 to 9.86±5.95 mm/hr, p=0.140). C-reactive protein (CRP) levels decreased significantly from admission to discharge in the intervention group (26.39±20.23 to 19.04 ± 32.04 mg/l, p=0.092), while they increased in the control group (24.82±19.82 to 33.82±45.26 mg/l, p=0.158). The difference in CRP levels at discharge between the two groups was statistically significant (p=0.041). Serum lactate levels decreased significantly from admission to discharge in both the intervention group (4.20±2.07 to 2.55±1.18 mmol/l, p<0.001) and the control group (4.19±2.48 to 3.32±1.84 mmol/l, p=0.028). The difference in serum lactate levels at discharge between the two groups was also statistically significant (p=0.008). The most common organisms isolated from blood cultures were Staphylococcus hominis (13.3% in the intervention group, 6.7% in the control group), Staphylococcus aureus (5.0% in both groups), and Candida species (6.7% in both groups). There was no statistically significant difference in the distribution of positive blood cultures between the two groups (p=0.268).

Outcome measures

The mean duration of antibiotic therapy was significantly shorter in the intervention group (11.22±3.99 days) compared to the control group (13.06±5.31 days) (p=0.035) (Table 7). In the intervention group, 24 neonates (40.0%) required ventilator support, with a mean duration of 4.50±3 days.[13] In the control group, 26 neonates (43.3%) required ventilator support, with a

mean duration of 4.30±3 days.[15] The difference in the need for and duration of ventilator support was not statistically significant between the two groups (p=0.830). The requirement for inotrope support was also similar between the intervention group (25 neonates, 41.6%) and the control group (29 neonates, 48.3%), with mean durations of 4.74±3.08 days and 4.48±2.01 days, respectively (p=0.697). The mean duration of NICU stay was significantly shorter in the intervention group (7.73±3.96 days) compared to the control group (10.91±6.01 days) (p=0.003). The mean duration of total hospital stay was also significantly shorter in the intervention group (12.11±4.56 days) compared to the control group (14.55±5.62 days) (p=0.013) (Table 9). Mortality In the intervention group, 3 neonates (5.0%) died, while in the control group, 8 neonates (13.3%) died. The difference in mortality between the two groups was not statistically significant (p=0.113) (Table 10).

Table 1: Birth weight-wise distribution of patients.

Birth weight	Group-A (Study group)		Group-B (Control group)	
	N	%	N	%
NBW≥2.5 kg	26	43.3	25	41.7
LBW 1.5-2.5 kg	22	36.7	28	46.6
VLBW 1.0-1.5 kg	12	20.0	7	11.7
ELBW<1.0 kg	0	0.0	0	0.0
Total	60	100.0	60	100.0
Mean±SD	2.27±0.68		2.26±0.58	

t-test and p value t=0.098, p=0.926, NS= not significant, S=significant, HS=highly significant

Table 2: Mode of delivery wise distribution of cases.

Mode of delivery	Group-A (Study group)		Group-B (Control group)	
	No.	%	No.	%
NVD	22	36.7	21	35.0
LSCS	38	63.3	39	65.0
Total	60	100.0	60	100.0

X2 test, p value, X^2=0.0362, P=0.849, NS= not significant

Table 3: Gender-wise distribution of cases.

Gender	Group-A (Study group)		Group-B (Control group)		Total	
	No.	%	No.	%	No.	%
Males	38	63.3	37	61.7	75	62.5
Females	22	36.7	23	38.3	45	37.5
Total	60	100.0	60	100.0	120	100.0

X^2=0.035, P=0.850, NS= not significant, S=significant, HS=highly significant

Table 4: Distribution based on onset of sepsis.

Parameters	Categories	Study group	Control group	Test value, P value
		No (%)	No (%)	
EOS/LOS	EOS	43 (71.7)	51 (85.0)	X^2=3.14, P=0.076, NS
	LOS	17 (28.3)	9 (15.0)	

Table 5: Clinical presentation-wise distribution of cases.

Parameters	Categories	Study group	Control group	Test value, P value
		No (%)	No (%)	
Shock	Present	36 (60.0)	26 (43.3)	X^2=3.33, P=0.067, NS
	Absent	24 (40.0)	34 (56.7)	
BA	HIE 1	10 (16.7)	13 (21.6)	X^2=0.545, P=0.796, NS
	HIE 2	5 (8.3)	6 (10.0)	
	HIE 3	3 (5.0)	2 (3.3)	
RDS	Present	21 (35.0)	35 (58.3)	X^2=6.562, P=0.011, S
	Absent	39 (65.0)	25 (41.7)	
Seizures	Present	9 (15.0)	3 (5.0)	X^2=3.332, P=0.0673, NS

Continued.

Parameters	Categories	Study group	Control group	Test value, P value
	Absent	51 (85.0)	57 (95.0)	
MSAF	Present	19 (31.7)	16 (26.7)	X^2=0.363, P=0.546, NS
	Absent	41 (68.3)	44 (73.3)	
Hyper bilirubinaemia	Present	8 (13.3)	11 (18.3)	X^2=0.562, P=0.453, NS
	Absent	52 (86.7)	49 (81.7)	

Table 6: Comparison of investigation parameters between the groups (study and controls).

Parameters	Time	Study group	Control group	t-test, P value
		Mean±SD	Mean±SD	
Hb	ADM	17.10±2.17	17.83±2.50	t=1.714, P=0.092, NS
	DIS	13.93±3.38	14.18±2.53	t=0.446, P=0.657, NS
TLC	ADM	21111.00±12727	17201.6±10630	t=1.801, P=0.0875, NS
	DIS	11106.33±3223	11378.33±3635	t=0.434, P=0.657, NS
Platelets	ADM	2.55±0.74	2.45±0.69	t=0.734, P=0.465, NS
	DIS	1.92±0.86	1.93±0.88	t=0.043, P=0.996, NS
ESR	ADM	11.46±5.52	11.09±5.51	t=0.837, P=0.404, NS
	DIS	9.26±3.78	9.86±5.95	t=0.643, P=0.521, NS
CRP	ADM	26.39±20.23	24.82±19.82	t=0.528, P=0.599, NS
	DIS	32.04±19.04	45.26±33.82	t=-2.064, P=0.041, S
Lactate	ADM	4.20±2.07	4.19±2.48	t=0.036, P=0.971, NS
	DIS	2.55±1.18	3.32±1.84	t=2.700, P=0.008, NS

Table 7: Comparison of antibiotics between the groups (study and controls).

Groups	No. of cases	Mean±SD	Unpaired t-test, P value
Study group	60	11.22±3.99	t=2.134, P=0.035, S
Control group	60	13.06±5.31	

Table 8: Comparison of ventilator support and inotrope between the groups (study and controls).

Parameters		Study group	Control group	Unpaired t-test, P value
		No. of days	No. of days	
Ventilator support	Required	24	26	t=0.216, P=0.830, NS
	Not required	36	34	
Mean±SD	--	4.50±3.13	4.30±3.15	
Inotrope	Required	25	29	t=0.391, P=0.697, NS
	Not required	35	31	
Mean±SD	--	4.74±3.08	4.48±2.01	

Table 9: Comparison of duration of NICU and hospital stays between the groups.

Variables	Study group	Control group	Unpaired t-test, P value 7 Significance
	Mean±SD	Mean±SD	
NICU stay	7.73±3.96	10.91±6.01	t=-3.424, P=0.003, S
Hospital stays	12.11±4.56	14.55±5.62	t=-2.602, P=0.013, S

Table 10: Comparison of study outcome between the groups.

Outcome	Study group		Control group	
	N	%	N	%
Discharged	57	95.0	52	86.7
Died	3	5.0	8	13.3
Total	60	100.0	60	100.0

DISCUSSION

This study included experimental and control groups that were well-matched in terms of demographic and clinical characteristics. There were no statistically significant differences between the groups in gestational age, mode of delivery, or birth weight. The mean birth weight was 2.27±0.68 kg in the intervention group and 2.26±0.58 kg in the control group. These figures differ from those reported in several other studies. For instance, Akhtar et al, reported mean birth weights of 2.8±0.29 kg for the study group and 2.9±0.29 kg for the control group, Aly et al found mean birth weights of 2.8±0.3 kg for the study group and 2.9±0.4 kg for the control group, while Bass et al, reported mean birth weight of 0.951±0.260 kg and 0.946±0.261 kg for the study and control group respectively.[4,9,12] In the present study, both the intervention group (38 male neonates) and the control group (37 male neonates) had a higher number of male neonates. This finding is consistent with Aly H et al, who reported 18 out of 30 neonates as male in the intervention group and 17 out of 30 in the control group.[9] Both the intervention group (43 neonates) and the control group (53 neonates) had a higher incidence of early-onset sepsis. In contrast, Akhtar et al, found a greater number of cases of late-onset sepsis, with 47 out of 61 neonates in the intervention group and 55 out of 63 neonates in the control group.[4]

Birth asphyxia was observed in 18 neonates with sepsis in the intervention group and 21 in the control group. This contrasts with the findings of Akhtar RJ et al, who reported 25 cases of birth asphyxia in the intervention group and 22 in the control group.[4] Sivanandan S et al, noted that 48 neonates in the intervention group and 47 in the control group had birth asphyxia, while Aly H et al, found 30 neonates with birth asphyxia in both the intervention and control groups.[9,10] RV Mohite et al, included 50 neonates each with birth asphyxia in both the study and the control groups.[11] 21 (35%) neonates in the intervention group and 35 (58%) neonates in the control group had respiratory distress syndrome.

This contrasts with the findings of Akhtar RJ et al who reported that 41 (67%) in the intervention and 40 (63%) in the control group had respiratory distress syndrome.[4] Bass ET et al included 51 preterm neonates in their study, with 18 in the study group and 20 in the control group showing respiratory distress syndrome.[12] The study compared pre-treatment and post-treatment CRP levels between the study and control groups. In the present study, the pre-treatment CRP levels were 26.39±20.23 in the study group and 24.82±19.82 in the control group. Post-treatment CRP levels were 32.04 ±19.04 in the study group and 45.26±33.82 in the control group. In Akhtar RJ et al study, pre-treatment CRP levels were 50.13±21.07 in the study group and 38.21±16.61 in the control group, while post-treatment levels were 7.69±7.48 in the study group and 23.82±19.01 in the control group.[4]

The duration of hospital stay was 10.21±4.47 days for the study group and 14.55±5.62 days for the control group. In Akhtar RJ et al4.'s study, the average hospital stay was 6.42±2.28 days for the study participants and 12.11±4.56 days for the control group. Additionally, in RV Mohite et al, study, 74% of the study participants were hospitalized for less than 5 days, while 88% of the control group had hospital stays exceeding 5 days.[11]

In this study, 24 neonates in the study group and 26 in the control group required ventilator support. In comparison, Sivanandan et al reported that 17 neonates in the study group and 18 in the control group needed ventilators. Aly H et al also found that 17 neonates in the study group and 15 in the control group required ventilator assistance.[9,10] 57 neonates in the study group and 52 in the control group were improved and discharged, with 3 deaths in the study group and 8 in the control group. In contrast, Bass WT et al12. observed that 23 neonates in the study group and 24 in the control group were improved and discharged, with 2 deaths in each group. Aly H et al found that 34 neonates in the study group and 24 in the control group improved and were discharged, but there were 14 deaths in the study group and 25 in the control group.[9]

According to Akhtar et al 56 neonates from the study group and 48 from the control group were discharged, with 2 deaths in the study group and 4 in the control group. Shivanandan S et al. reported that 19 neonates in the study group and 20 in the control group improved and were discharged, with 14 and 25 deaths in the study and control groups, respectively.[4,10] Mohite RV et al found that 48 neonates in the study group and 44 in the control group were discharged, with 2 deaths in the study group and 6 in the control group. The neonates who improved and were discharged were more in number in the study groups when compared to the control groups in the above-mentioned studies.[11]

This was a single-centered study with a relatively small sample size and the study did not assess baseline or post-intervention levels of vitamin C and thiamine in the neonate's blood

CONCLUSION

In this study, the intervention group showed promising results compared to the control group. Statistically significant reductions were observed in the duration of antibiotic therapy, NICU stay, and overall hospital stay. At discharge, the study group demonstrated significantly lower CRP and serum lactate levels. While there was a trend toward lower mortality in the intervention group, it was not statistically significant. The treatment appeared well-tolerated with no observed adverse effects. These findings align with some previous studies on vitamin C in neonatal sepsis, though direct comparisons are limited due to varying study designs. While the combination of ascorbic acid and thiamine as an adjunct to standard

antibiotic treatment shows potential benefits in managing neonatal sepsis, particularly in reducing hospital stays and improving certain biochemical markers, this study has limitations. Larger, multi-center trials are needed to confirm these findings and further explore the intervention's potential in neonatal sepsis management. In conclusion, this study provides preliminary evidence supporting the use of ascorbic acid and thiamine as adjunctive therapy in neonatal sepsis, but further research is required to establish its definitive role in standard care protocols.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Abbott MB, Classes CH. Nelson textbook of pediatrics. JAMA. 2019;306(21):400-1.
2. WHO. Neonatal mortality rate per 1,000 live births. World Health Organization. 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/maternal-mortalit. Accessed on 17th March 2024.
3. Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset neonatal sepsis. Clinical microbiology reviews. 2014;27(1):21-47.
4. Akhter RJ, Hoque MM, Yasmeen BN, Azad MA. Effect of vitamin C as an adjuvant therapy in neonatal sepsis. Ind J Tra Emerg Pediatrics. 2017;9(3):161.
5. Schlapbach LJ, Gibbons K, Ridolfi R, Harley A, Cree M, Long D, et al. Resuscitation in paediatric sepsis using metabolic resuscitation–a randomized controlled pilot study in the paediatric intensive care unit (respond picu): study protocol and analysis plan. Frontiers in Pediatrics. 2021;9:663435.
6. Mehta NM. Resuscitation with vitamins C and B1 in pediatric sepsis-hold on to your “HAT”. Pediatric Critical Care Medicine. 2022;23(5):385-9.
7. Carr AC. Vitamin C in pneumonia and sepsis. Vitamin C. 2020.
8. Mallat J, Lemyze M, Thevenin D. Do not forget to give thiamine to your septic shock patient. J Thorac Dis. 2016;8(6):1062.
9. Aly H, Abd-Rabboh L, El-Dib M, Nawwar F, Hassan H, Aaref M, Abdelrahman S, et al. Ascorbic acid combined with ibuprofen in hypoxic ischemic encephalopathy: a randomized controlled trial. J Perinatol. 2009;29(6):438-43.
10. Sivanandan S. First Day High Dose Vitamin C and Vitamin E in Hypoxic Ischemic Encephalopathy (following Birth Asphyxia) of Newborn: a Randomized Controlled Trial. Available at: https://papers.ssrn.com. Accessed on 17th March 2024.
11. Mohite RV, Kshirsagar VY, Rithika D. Effectiveness of vitamin C and E intervention on neurodevelopment of newborn baby with birth asphyxia: A randomized control trial. Curr Pediatr Res. 2024;28(03):2205-8.
12. Bass WT, Malati N, Castle MC, White LE. Evidence for the safety of ascorbic acid administration to the premature infant. Am J Perinatol. 1998;15(02):133-40.
13. Sechi GP, Bardanzellu F, Pintus MC, Sechi MM, Marcialis MA, Fanos V. Thiamine as a possible neuroprotective strategy in neonatal hypoxic-ischemic encephalopathy. Antioxidants. 2021;11(1):42.
14. Equey L, Agyeman PK, Veraguth R, Rezzi S, Schlapbach LJ, Giannoni E, Swiss Pediatric Sepsis Study Group. Serum ascorbic acid and thiamine concentrations in sepsis: secondary analysis of the Swiss pediatric sepsis study. Pedia Critic Care Med. 2022;23(5):390-4.
15. Zakariya BP, Bhat V, Harish BN, Arun Babu T, Joseph NM. Neonatal sepsis in a tertiary care hospital in South India: bacteriological profile and antibiotic sensitivity pattern. The Indian Journal of Pediatrics. 2011;78:413-7.

Cite this article as: Mangshetty RB, Binjanwadgi AA, Gaddamanugu GS. Enhancing neonatal sepsis outcomes: the role of ascorbic acid and thiamine as adjuvant therapies. Int J Contemp Pediatr 2024;11:1569-75.