Journal of Medicinal and Chemical Sciences 5 (2022) 129-136

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Cross Sectional Study

Indications and Outcome of Albumin Infusion in a Neonatal Population: A Cross Sectional Study

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ARTICLE INFO

Article history

Received: 2021-08-07
Received in revised: 2021-10-25
Accepted: 2021-11-02
Manuscript ID: JMCS-2108-1222
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Behrouz Jamalvandi
Editor who approved publication:
Dr. Ahmad Reza Moosavi-Zare

DOI:10.26655/JMCHEMSCI.2022.1.14

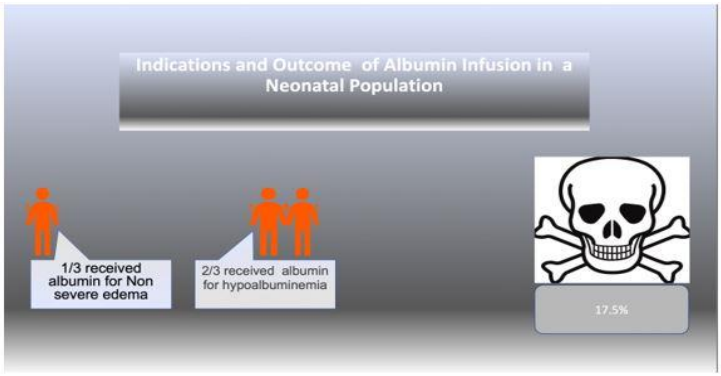
KEYWORDS

Newborn
Neonatal hypoalbuminemia
Albumin infusions

ABSTRACT

Objective: To determine the indications for human albumin infusion in neonatal units, as well as the neonatal outcomes after receiving human albumin.
Study design: A cross sectional study in neonatal ward at child's central teaching hospital in Baghdad conducted over 12 months period between December 2019 and December 2020 in Iraq. Infants who received albumin infusion for hypoalbuminemia or any other reason during study period were included in the study. Mortality and morbidities were recorded. Alterations in renal and liver function tests and serum albumin level before and after albumin infusion were recorded.
Results: 80 neonates required human albumin transfusion therapy 150 times during the study. In (31.25%) the indication for albumin transfusion was the presence of edema, while in (68.75%) the indication was hypoalbuminemia. During 30 days follow up, (82.5%) have survived and discharged well, while (17.5%) died during hospitalization. Four factors were found to be significantly associated with mortality in neonates undergoing albumin transfusion, which are prematurity, low birth weight, presence of comorbidity and higher number of albumin infusions. The mean urea concentration in deceased group was significantly higher than that of survived neonates. There was a significant reduction in blood urea after the last transfusion in survived neonates.
Conclusion: In the absence of evidence-based guidelines for albumin infusion in neonatal period, albumin used mainly to correct underlying hypoalbuminemia higher mortality rate was documented in neonate who received albumin infusions in higher number of times.

GRAPHICAL ABSTRACT



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Introduction

Over the last 50 years, human albumin has been employed as a therapeutic agent [1]. These solutions are expensive biological products derived from pooled human donors. It is available in three main types hypo- oncotic (4%), iso-oncotic (5%), or hyper-oncotic (20% or 25%) with various electrolyte concentrations [2]. In general practice, the key indications for its use are the restoration and maintenance of circulating blood volume in situations such as trauma, surgery and blood loss, burn management and during plasma exchange [1].

In currant neonatal practice there are no standard indications for the use of human albumin infusions. However, concentrated albumin solutions 20% are sometimes used to treat significant neonatal peripheral edema due to hypoalbuminemia but this practice still lacks evidence since even under this condition, the improvement of nutritional intake is the preferred choice of action [3].

In neonatal intensive care units, Human albumin infusions are frequently administered to correct low serum albumin level [4]. Normal albumin level in term infant (28-43 g/l) varies from that of preterm infants. In preterm infants, albumin increases with advancing gestational ages from (21-33) at 27 wks. to (22-36) at 35 weeks [5], As a result, serum albumin levels that are considered normal in preterm newborns should be determined according to gestational ages [6]. Lower albumin levels increase the risks of the later development of clinical disorders, which are common in premature infants [7]. It has been established that using albumin infusion routinely to increase albumin concentration in preterm newborns with hypoalbuminemia is not evidence-based [8].

Furthermore, it is now recommended that caution should be taken as an albumin infusion may be detrimental. Albumin infusion has been linked to considerable reduction in the body weight in the newborn. In addition, there is a risk of fluid overload following albumin administration [7].

Hypoalbuminemia may be viewed as a normal compensatory mechanism that does not require intervention due to its great frequency in a wide spectrum of pathologic situations [6]. Albumin appears to be being utilized for indications that have been considered unsupportable by literature-based guidelines [9]. Albumin was incorrectly given for 57.8% of adult patients and 52.2 percent of pediatric patients, according to a study of 53 hospitals in the United States [10].

Accordingly, we conducted a prospective study to assess the indications for the use of albumin infusion in neonatal wards and evaluate the effect of such infusion on neonatal outcomes.

Results and discussion

This was a cross-sectional study in neonatal wards of two Iraqi hospitals (Child's Central Teaching Hospital in Baghdad and Alramadi Teaching Hospital for Maternity and Childhood) conducted over 12 months period between December 2019 and December 2020 in Iraq. The infants were enrolled based on the following inclusion criteria: Admission to the neonatal ward, and infants who were given albumin infusion for any reason during any time of hospitalization.

Demographic data, perinatal history of infants, i.e. birth weight, gestational age, gender, Apgar scores, and maternal history, i.e. amnion abnormalities. The presence of other neonatal morbidities such as patent ductus arteriosus (PDA), indication of admission to hospital and laboratory tests (before and after albumin infusion; liver and renal function tests, serum albumin), long term outcomes, and mortality were all reported. Infants were classified into two groups: Survivors who received albumin infusions (Group I), and non-survivors who were given albumin infusion (Group II).

In term infants, hypoalbuminemia is defined as <20 g/L. In preterm, hypoalbuminemia was defined according to gestational age [7]. Albumin used in this study was in a dose of 1cc/kg of 20% albumin.

Statistical analysis

All statistical analyses were performed using SPSS software version 25.0 (SPSS, Chicago). Continuous data were presented as mean and standard deviation, and analyzed with independent-samples or paired-samples Student

t-test as required. Categorical variables were expressed as numbers and percentages and analyzed with the Chi-square test. A p-value less than 0.05 was considered to indicate a statistically significant difference.

Demographic and clinical characteristics of the patients

Over a period of 1-year (from December 2019 to December 2020), 80 neonates required human albumin transfusion therapy 150 times during the study. Females had a preponderance over males (58.75% versus 41.25%) with a male: Female ratio of 0.7:1. One-fourth of the neonate's mothers had a history of polyhydramnios, while 21.25% of them had oligohydramnios. The mean maternal age and birth weights were 27.83±7.77 years and 2.1±0.91 kg, respectively

Among the treated neonates (62.5%) were premature. Prematurity was the most common reason for hospitalization (40%), followed by jaundice (23.75%) and each sepsis and transient tachycardia of newborn (TTN) was diagnosed by 13.75%. Patent ductus arteriosus (PDA) was the most common comorbidity affecting 48.75% of neonates followed by sepsis (37.5%) and renal failure (13.75%). The mean APGAR score was 7.24±1.52 (ranging from 5-10). The frequency of transfusions was 1-2 times in 65% and 3-4 times in 35% of neonates (Table 1).

Table 1: Demographic and clinical characteristics of the patients (n=80)

Variables	Values
Gender	
Male	33(41.25%)
Female	47(58.75%)
Maternal history	
None	36(45%)
Polyhydramnios	20(25%)
Oligohydramnios	17(21.25%)
Others	7(8.75%)
Maternal age, years	
Mean±SD	27.83±7.77
Range	17-44
Birth weight	
Mean±SD	2.1±0.91
Range	1.1-4.0
Gestational age	
Preterm	50(62.5%)
Full-term	30(37.5%)
Mode of delivery	
Vaginal	26(32.5%)
Cesarean section	54(67.5%)
Diagnosis	
Prematurity	32(40%)
Jaundice	19(23.75%)
Sepsis	11(13.75%)
TTN	11(13.75%)
Others	7(8.75%)
Comorbidity	
No comorbidity	33(41.25%)
PDA	39(48.75%)
Sepsis	30(37.5%)
Renal failure	11(13.75%)
Others	8(10%)
APGAR score	
Mean±SD	7.24±1.52
Range	5-10
Frequency of infusion	
1-2	52(65%)
3-4	28(35%)

PDA: patent ductus arteriosus, TTN: transient tachypnea of newborns

Indications for albumin transfusion

In 25 neonates (31.25%), the indication for albumin transfusion was the presence of edema, while in the other 55 neonates (68.75%) the indication was hypoalbuminemia (Figure 1).

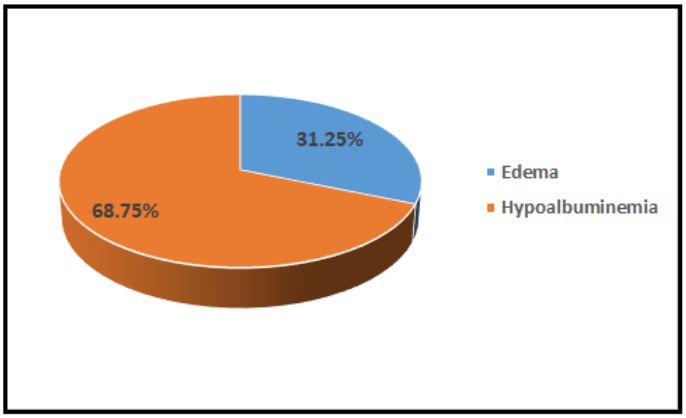

Figure 1: Indication for albumin transfusion

Mortality rate

During 30 days follow-up, 66 neonates (82.5%) were survived and discharged well, while 14 neonates (17.5%) unfortunately died (Figure 2).

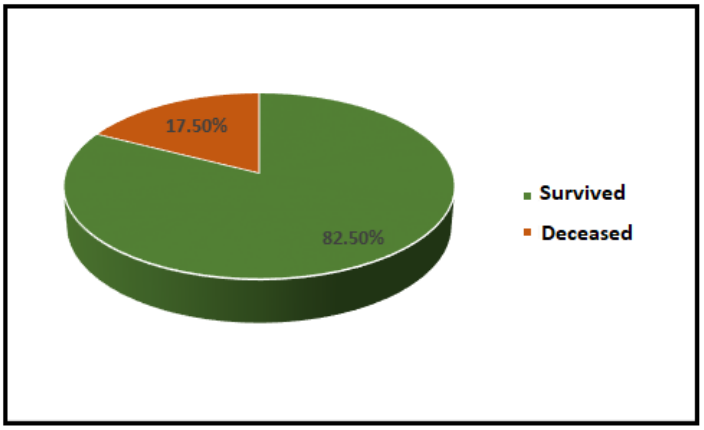

Figure 2: Mortality rate among neonates undergoing albumin transfusion

Association of demographic and clinical characteristics with patients' outcome

Four factors were found to be significantly associated with mortality in neonates undergoing albumin transfusion. The mean birth weight of survived neonates was 2.27±0.91 kg compared with 1.27±0.14 kg in deceased neonates with a highly significant difference. Similarly, prematurity was more common among the deceased than survived neonates (85.71% vs. 57.58%) with a significant difference. The presence of comorbidity, i.e. sepsis and renal failure, was reported in 57.14% and 35.71% of deceased neonates compared with 27.27% and 9.09% of survived neonates with significant differences. Finally, 64.29% of neonates in the deceased group were undergone 3-4 infusions compared with 28.79% in the survived group who had such an infusion rate, with a significant difference (Table 2).

Association of Liver and Kidney Function Tests before and after Treatment with Patients' Outcome

Generally, parameters related to liver function did not show significant variation between survived and deceased children. However, the mean serum concentration of albumin after the last infusion in survived and deceased neonates was 3.4±0.52 g/dl and 3.04±0.32 g/dl, respectively compared with 2.41±0.7 g/dl and 2.2±0.64 g/dl, respectively, before infusion with highly significant differences.

Table 2: Association of demographic characteristics with patients' outcome

Variables	Survived (n=66)	Deceased (n=14)	p-value
Gender			
Male	25(37.88%)	8(57.14%)	0.184
Female	41(62.12%)	6(42.86%)	
Maternal history			
None	31(46.97%)	5(35.71%)	0.131
Oligohydramnios	11(16.67%)	6(42.86%)	
Polyhydramnios	17(25.76%)	3(21.43%)	
Others	7(10.61%)	0(0%)	
Maternal age, years	28.28±7.81	25.21±7.42	0.168
Birth weight, kg	2.27±0.91	1.27±0.14	**<0.001**
Gestational age			
Preterm	38(57.58%)	12(85.71%)	**0.048**
Full-term	28(42.42%)	2(14.29%)	
Mode of delivery			
Vaginal	22(33.33%)	4(28.57%)	0.730
Cesarean section	44(66.67%)	10(71.43%)	
Diagnosis			
Premature	24(36.36%)	8(57.14%)	0.507
Sepsis	9(13.64%)	2(14.29%)	
Jaundice	16(24.24%)	3(21.43%)	
TTN	10(15.15%)	1(7.14%)	
Others	7(10.61%)	0(0%)	
Comorbidity	35(53.03%)	12(85.71%)	**0.024**
APGAR score (1st min)	7.26±1.77	6.57±1.34	0.177
Frequency of infusion			
1-2	47(71.21%)	5(35.71%)	**0.011**
3-4	19(28.79%)	9(64.29%)	
Indication for infusion			
Edema	23(34.85%)	2(14.29%)	0.132
Hypoalbuminemia	43(65.15%)	12(85.71%)	

TTN: Transient tachypnea of newborns

On the other hand, the mean urea concentration in deceased neonates before and after the last infusion was 85.93±37.96 mg/dl and 77.36±41.91 mg/dl, respectively, which was significantly higher than that of survived neonates (62.56±39.94 mg/dl and 54.14±36.34 mg/dl, respectively). It should be noted, there was a significant reduction in blood urea after the last transfusion in survived neonates but not in deceased neonates. Similarly, the mean serum creatinine in deceased neonates before and after the last transfusion was 1.82±1.21 mg/dl and 1.71-1.03 mg/dl, respectively, which was significantly higher than that of survived neonates (1.2±0.88 mg/dl and 1.04±0.93 mg/dl, respectively). However, there was no significant effect of albumin infusion on creatinine concentration neither in survived nor in deceased neonates (Table 3).

The vast majority of studies on albumin use were conducted with the adult population. Few Studies have investigated the indications for using albumin infusion in infants or the outcome of such therapy. This paper critically discussed the most common indications for albumin infusion in neonatal ward and consequences of such therapy. In this study, prematurity was the most frequent indication for hospitalization (40%), and 62.5% of neonates who received albumin infusions were premature, which goes in line with the result by Degirmencioglu H *et al*. [4]. Patent ductus arteriosus (PDA) was the most common comorbidity affecting (48.75%) neonates, which can be explained by the fact that PDA has a higher prevalence in preterm newborn [11].

The most common reason for albumin infusion in our cohort was to correct hypoalbuminemia (68.75%), which is consistent with Morris I *et al*.

finding [12]. On other hand, this percentage is much higher than the one obtained in a study done with the adult population finding that only (14.8%) of patients receive human albumin for correction of hypoalbuminemia [13]. It is most likely due to physician worrying about the inverse relationship between serum albumin level and clinical outcomes [14].

In our study, 30.4% of a neonate who received albumin the cause was non-severe edema without any other reason, which was not supported by any guideline. According to Leung AK et al, albumin may be useful for hospitalized children with severe edema due to nephrotic syndrome; however, this therapy carries potential risks and should not be given indiscriminately [15]. On the other hand, this could be attributed to the lack of a defined guidelines for albumin infusion in the neonatal period. Martelli et al. found that the adoption of guidelines may substantially reduce the inappropriate use of albumin [16].

In our study albumin infusion resulted in increased serum albumin levels in all of the cohort, which goes in line with a result by two major clinical trials SAFE [17] and ALBIOS [18] both documented a small but statistically significant increase in serum albumin level following albumin administration.

Table 3: Association of liver and renal function tests before and after treatment with patients' outcome

Variables	Discharged well (n=66)	Died (n=14)	p-value
Albumin before infusion, g/dl	2.41±0.7	2.2±0.64	0.304
Albumin after infusion, g/dl	3.4±0.52	3.04±0.32	0.504
P-value	**<0.001**	**<0.001**	-------
Urea before infusion, mg/dl	62.56±39.94	85.93±37.96	**0.040**
Urea after infusion, mg/dl	54.14±36.34	77.36±41.91	**0.037**
P-value	**<0.001**	0.404	**-------**
Creatinine before infusion, mg/dl	1.2±0.88	1.82±1.21	**0.028**
Creatinine after infusion, mg/dl	1.04±0.93	1.71-1.03	**0.017**
P-value	0.120	0.778	------
AST before infusion, U/L	28.91±16.95	33.57±14.32	0.341
AST after infusion, U/L	28.47±17.17	30.86±10.71	0.619
p-value	0.648	0.776	**------**
ALT before infusion, U/L	27.85±11.49	32.0±18.23	0.276
ALT after infusion, U/L	26.77±11.12	33.71±19.45	0.071
p- value	0.865	0.886	**------**

In this study, 17.5% of a neonate who received albumin infusion died during the study period. Four factors were found to be significantly associated with mortality in neonates undergoing albumin infusions (prematurity, low birth weight, comorbidities, albumin infusion for 3-4 times). One significant finding of this study is that neonates who received albumin infusions in higher numbers tend to have more mortality rates. Although a study by Vincent et al in acutely ill children showed that Albumin administration was associated with decreased survival, it was performed in older age group and did not relate the mortality with the number of times of albumin infusions [19].

Regarding the effect of human albumin infusion on renal function, the mean urea concentration in the deceased group was significantly higher than that of survived neonates, hence there was a significant reduction in blood urea after the last transfusion in survived neonates. This agrees with a study by Garcia-Martinez R *et al*. who found that albumin infusion leads to a shift in the renal blood flow autoregulation curve towards normalization; the result significantly increased renal blood flow and improved renal function [20]. On other hand, this is different from the result by Degirmencioglu *et al*. who found that albumin infusion resulted in worsening renal function, with worsening occurring more

frequently in infants who died during hospitalization.

Conclusion

In the absence of evidence-based guidelines for albumin infusion in the neonatal period, albumin was mainly used to correct underlying hypoalbuminemia. A higher mortality rate was documented in the neonate who received albumin infusions a higher number of times.

Acknowledgments

We appreciate Al Mustansiriyah University for continuous support.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

The authors declare that they have no competing interests.

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References

[1]. Matejtschuk P., Dash C.H., Gascoigne E.W., *Br. J. Anaesth.*, 2000, **85**:887 [Crossref], [Google Scholar], [Publisher]

[2]. Executive Committee of the German Medical Association on the Recommen- dation of the Scientific Advisory Board. *Transfus Med Hemother*, 2016, **43**:223 [Crossref], [Google Scholar], [Publisher]

[3]. Murray N.A., Roberts I.A., *Arch. Dis. Child Fetal Neonatal Ed., 2004*, **89**:F101 [Crossref], [Publisher]

[4]. Degirmencioglu H., Say B., Oguz S.S., *Obstet. Gynecol. Reprod. Med.*, 2018, **24**:47 [Crossref], [Google Scholar], [Publisher]

[5]. Rennie J.M., Roberton N.R.C., (Eds). *Textbook of Neonatology,* 5th edn. Churchill Livingstone, Edinburgh, 2012 [Google Scholar]

[6]. Vincent J.L., Dubois M.J., Navickis R.J., Wilkes M.M., *Ann. Surg.*, 2003, **237**:319 [Crossref], [Google Scholar], [Publisher]

[7]. Lee M., Yun S., Lim B.K., Kim J.S., *Korean J. Pediatr.*, 2005, **48**:148 [Google Scholar], [Publisher]

[8]. Jardine L.A., Jenkins-Marsh S., Davies M.W., *Cochrane Database Sys. Rev.*, 2004(3). [Crossref], [Google Scholar], [Publisher]

[9]. Fan C., Phillips K., Selin S., *B. C. Med. J.*, 2005, **47**:438 Google Scholar], [Publisher]

[10]. Tanzi M., Gardner M., Megellas M., Lucio S., Restino M.. *Am. J. Health. Syst. Pharm.*, 2003, **60**:1330 [Crossref], [Google Scholar], [Publisher]

[11]. Dice J.E., Bhatia J., *J. Pediatr. Pharmacol. Ther.*, 2007, **12**:138 [Crossref], [Google Scholar], [Publisher]

[12]. Morris I., Molloy E.J., Archives of Disease in Childhood - Fetal and Neonatal Edition., 2008, **93**:F326 [Crossref], [Google Scholar], [Publisher]

[13]. Roberton N.R., *Eur. J. Pediatr.*, 1997, **156**:428 [Crossref], [Google Scholar], [Publisher]

[14]. Margarson M.P., Soni N., *Anaesthesia*, 1998, **53**:789 [Crossref], [Google Scholar], [Publisher]

[15]. Leung A.K.C., Robson W.L.M., *R. Soc. Health. J.*, 2000, **120**:212 [Crossref], [Google Scholar], [Publisher]

[16]. Martelli A., Strada P., Cagliani I., Brambilla G., *Curr. Ther. Res.,* 2003, **64**:676 [Crossref], [Google Scholar], [Publisher]

[17]. Caironi P., Tognoni G., Masson S., Fumagalli R., Pesenti A., Romero M., Fanizza C., Caspani L., Faenza S., Grasselli G., Iapichino G., *N. Engl. J. Med.,* 2014, **370**:1412 [Crossref], [Google Scholar], [Publisher]

[18]. SAFE Study Investigators. *BMJ.*, 2006, **333**:1044 [Crossref], [Google Scholar], [Publisher]

[19]. Vincent J.L., Sakr Y., Reinhart K., Sprung C.L., Gerlach H., Ranieri V.M., *Crit. Care*., 2005, **9**:1 [Crossref], [Google Scholar], [Publisher]

[20]. Garcia-Martinez R, Noiret L, Sen S, Mookerjee R, Jalan R., *Liver Int.*, 2015, **35**:335 [Crossref], [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE
Nabeeha Najatee Akram, Maysam Yousif Abed. Indications and Outcome of Albumin Infusion in a Neonatal Population: A Cross Sectional Study, *J. Med. Chem. Sci*., 2022, 5(1) 129-136
DOI: 10.26655/JMCHEMSCI.2022.1.14
URL: http://www.jmchemsci.com/article_139700.html