Curr Pediatr Res 2021; 25 (11): 1082-1088 *ISSN 0971-9032*
www.currentpediatrics.com

Significance of measuring serum albumin in preterm neonates during 1st day of life.

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Abstract

Aims: serum albumin has been used in the neonatal population to assess for the presence of inflammation and predict mortality. In preterm low level of albumin level on the 1st day of life significantly increase the risks of the later development of clinical disorders. The aim of this study was to assess the value of measuring serum albumin level on the 1st day of life in detecting severity, morbidity, and mortality of preterm infants

Patients and Methods: A prospective, cross sectional study was conducted on 82 preterm neonates (GA<37 weeks), who had been admitted to the neonatal ward at the child's central teaching hospital within 24 hours after birth, from the 1st of Jan to the 31st of June 2020. For all cases, detailed history and full examination was done and. Laboratory tests were send according to presumed diagnosis but in all cases, serum albumin was sent within first 24 hours of life. All survived cases followed for 30 days following discharge.

Results: A total of 82 patients, birth weight were 2.11 ± 0.74 g, gestational age was 33.49 ± 2.74 weeks and 58.45% were male. 22 neonates (26.8%) were in the low albumin group. From preterm with hypoalbuminemia 45.45% of patients develop RDS, 40.91% sepsis, and 13.64% develop pneumonia, sepsis was significantly higher in preterm with hypoalbuminemia (p-value 0.001). The laboratory parameters in this study do not show any significant correlation with low serum albumin level. The median duration of CPAP and total O2 were higher in neonates with hypoalbuminemia (2.0 hours and 4.5 hours respectively) than those with normal albumin level. Low albumin level had no significant correlation with duration of mechanical ventilation or length of hospital stay but show significant correlation with mortality of preterm babies.

Conclusion: In the first day of life, low serum albumin level in preterm neonate significantly correlate with sepsis and indicate higher risk of mortality. Albumin level has no relation to duration of hospitalization or mechanical ventilation.

Keywords: Hypoalbuminemia, Preterm, Sepsis, Serum albumin.

Accepted on 15th November, 2021

Introduction

Albumin is the most abundant plasma protein which account for almost two third of total protein in human plasma [1,2]. Normal neonatal concentration of albumin rise with increasing gestational and post-natal age, a more rapid turnover of the albumin pool and slower rate of synthesis by the immature liver both explain the lower albumin level in preterm infants [3]. In preterm infants a low serum albumin level in the 1st day of life significantly increase the risks of the later development of clinical disorders, which are common in premature infants like hyaline membrane disease, intraventricular hemorrhage, retinopathy of prematurity, apnea and bronchopulmonary dysplasia [4].

Due to the fact that albumin levels are reduced in the presence of inflammation regardless of nutritional condition, some physicians now employ albumin and prealbumin to detect inflammation. Level of serum albumin decrease during acute phase response to infection, it's one of the so called negative acute phase proteins. During times of stress, the body may need to enhance the production of immune mediators while decreasing the production of other proteins that aren't necessary for immune function. This could result in a fall in albumin levels [5,6]. In addition to its role in prediction of presence of inflammation, in adult patients, low serum albumin has been shown to be a significant predictor of mortality. The predictive value of serum albumin in neonates, on the other hand, remains unclear. There is a paucity of data evaluating serum albumin level on admission as a predictor of outcome in critically ill children [7,8]. The aim of this study was to assess the value of measuring serum albumin level in the 1st day of life in detecting severity, morbidity and mortality of preterm infants.

Patients and Methods

A prospective, cross sectional study was conducted on 82 late preterm neonates (GA 34 week to 36+6 weeks), who had been admitted to the neonatal ward at child central teaching hospital within 24 hours. After birth from the 1st January 2020 to the 31st June 2020. The study population was randomly selected and informed consent was taken from their parents. Exclusion criteria include:

- Neonates older than 24 hour when the blood sample was taken.

- Fetal-maternal blood incompatibility.
- Patients who had received human albumin infusions or other blood products.
- Neonates with gross anomalies.

Those whose parents refuse to sign the consents. A detailed history was taken regarding: Gender, mode of delivery, maternal diseases (like DM, HTN, PROM), and if the mother had received antenatal steroids or not. Clinical examination was done by the pediatrician on call, gestational age was measured using the new Ballard scoring system, and the birth weight was measured for each patient.

Blood samples were taken in the first 24 hours of life and sent for measurement of serum albumin, CBC, CRP, and Blood culture. Serum albumin concentration was measured by the Bromocresol green method. All patients in the study were not received human albumin infusion or other blood products. All patients were followed during hospitalization and for 30 days following discharge. The duration of Mechanical Ventilation (MV), Continuous Positive Airway Pressure (CPAP), and non-invasive O2, final diagnosis, outcomes and the duration of hospitalization had been documented. Hypoalbuminemia was considered in patients who had serum albumin level ≤ 25 g/L, so the study population was categorized into 3 groups: High (>30 g/L), moderate (25-30 g/L), and low albumin level (≤ 25 g/L). Sepsis was diagnosed depending on the results of blood cultures or on clinical assessment supported by other laboratory results.

Statistical Analysis

All statistical analyses were performed using SPSS software version 25.0 (SPSS, Chicago). Continuous data were subjected to normality test (Shapiro Wilk test). Data with normal distribution were presented as mean and standard deviation, and analyzed with Analysis of Variance (ANOVA). Those with non-normal distribution were presented as median and range, and analyzed with Kruskal Wallis. Categorical variables were expressed as number and percentage and analyzed with Chi-square test. Receiver Operating Characteristic (ROC) curve was used to find the predictive value of albumin in predicting death of premature neonates. A p-value less than 0.05 were considered to indicate a statistically significant difference.

Results

Demographic and clinical characteristics of the patients

Table 1 shows that males had preponderance over females (58.45% *versus* 41.46%) with male: female ratio of 1.4:1. A 17.07% of the neonate's mothers had a history of hypertension, while 13.41% of them were diabetic. Eleven (13.41%) of neonate's mother received antenatal steroids, while the PROM was reported in 9 mothers (10.98%). The mean birth weight of the patients was 2.11 ± 0.74 grams. All neonates were premature with a mean gestational age of 33.49 ± 2.74 weeks (range 25 weeks-36 weeks). The modes of delivery in more than two-third of the neonates (69.51%) were cesarean section. The mean duration of NIV O2, CPAP, MV was 2.46 ± 1.7 hours, 1.19 ± 1.35 hours, 0.2 ± 0.92 hours respectively. Hospital stay of the neonates ranged from 1 to 35 days with a mean of 6.09 ± 5.05 days. Respiratory distress syndrome was the most common morbidity encountered in 36 neonates (43.9%), followed by sepsis (19.51%) and pneumonia (17.07%). Non-infectious diseases were reported in 16 neonates (19.51%).

Variables	Values
Gender	
Male	48(58.45%)
Female	34(41.46%)
Maternal history	
None	57(69.51%)
HTN	14(17.07%)
DM	11(13.41%)
Birth weight	
Mean ± SD	2.11 ± 0.74
Range	0.9-5.0
Gestational age	
Mean ± SD	33.49 ± 2.74
Range	25.0-36.0
Mode of delivery	

Vaginal	25(30.49%)
Cesarean section	57(69.51%)
Duration of NIV O2, hours	
Mean ± SD	2.46 ± 1.7
Range	0.0-10
Duration of CPAP	
Mean ± SD	1.19 ± 1.35
Range	0.0-5.0
Duration of MV, hours	
Mean ± SD	0.2 ± 0.92
Range	0.0-6.0
Hospital stay	
Mean ± SD	6.09 ± 5.05
Range	1.0-35
Antenatal steroids	
Received	11(13.41%)
Undeceived	71(86.59%)
Diagnosis	
RDS	36(43.9%)
Sepsis	16(19.51%)
Pneumonia	14(17.07%)
Non-infectious*	16(19.51%)

Table 1. Demographic and clinical characteristics of the patients (n=82). CPAP: Continuous Positive Airway Pressure; MV: Mechanical Ventilation; NIV: Non-Invasive Ventilation; RDS: Respiratory Distress Syndrome; *: Non-infectious diseases include coronary heart disease, necrotizing enterocolitis, hydrocephalus and omphalocele.

In Table 2 laboratory characteristics of the patients the mean albumin level was 34.33 ± 5.24 g/L. The mean White Blood Cell (WBC) and platelets count was 6.79 ± 6.15 × 103/ml and 201.67 ± 62.73 × 103/ml, respectively. The vast majority of the neonates were non-anemic with a mean Hb and PCV of 16.4 ± 2.02 g/dl and 50.84 ± 6.84%, respectively. C-reactive protein was positive in 23 neonates (28.05%), with a total mean of 7.29 ± 14.97 mg/dl.

Variables	**Values**
Albumin, g/L	
Mean ± SD	34.33 ± 5.24
Range	23-46
WBC × 103/ml	
Mean ± SD	6.79 ± 6.15
Range	3.3-30.0
PLT × 103/ml	
Mean ± SD	201.67 ± 62.73

Range	54.0-362
Hb, g/dl	
Mean ± SD	16.4 ± 2.02
Range	11.0-22.0
PCV, %	
Mean ± SD	50.84 ± 6.84
Range	33.0-66.0
CRP, mg/dl	
Mean ± SD	7.29 ± 14.97
Range	0.0-81.0
CRP positivity	
Yes	23(28.05%)
No	59(71.95%)

Table 2. Laboratory characteristics of the patients (n=82).

During 30 days follow up, 66 neonates (82.5%) have survived and discharged well, while 14 neonates (17.5%) unfortunately deceased. Table 3 shows the Association of Demographic and Clinical Characteristics with Albumin levels. Six demographic and clinical factors were significantly associated with albumin levels. Neonates with hypoalbuminemia demonstrated lower birth weight and gestational age (1.45 kg and 30.68 ± 2.63 weeks, respectively) than those with normal albuminemia in both categories with highly significant differences. In contrast, the median duration of CPAP and total O2 were higher in neonates with hypoalbuminemia (2.0 hours and 4.5 respectively) than those with normal albuminemia in both categories with highly significant differences. Furthermore, 27.27% of neonates with hypoalbuminemia had a history of PROM compared with only 4% and 5.71% of neonates with 25-30 g/L and >30 g/L albumin, respectively who had such a history, with significant difference. The incidence of difference diseases also associated significantly with albumin level. In particular, about half of neonates with hypoalbuminemia were diagnosed with sepsis compared with only 12% and 11.43% of neonates with 25-30 g/L and >30 g/L albumin, respectively with significant difference. In contrast, non-infectious disease was more common among 30 g/L group (37.14%) than either those with 25-30 g/L albumin level or those with ≤ 25 g/L (12% and 0%, respectively) with a significant difference. Finally, mortality rate in neonates with hypoalbuminemia was 31.82% compared with 20% in those with 25-30 g/L albumin and 0% in those with >30 g/L albumin level with a highly significant difference.

Variables	**Albumin level**			**p-value**
	≤ 25 g/L (n=22)	25-30 g/L (n=25)	>30 g/L (n=35)	
Gender				
Male	14(63.64%)	18(72%)	16(45.71%)	0.107
Female	8(36.36%)	7(28%)	19(54.29%)	
Maternal history				
None	17(77.27%)	17(68%)	23(65.71%)	0.96
HTN	2(9.09%)	3(12%)	5(14.29%)	
DM	3(13.64%)	5(20%)	7(20%)	
Birth weight				
Median(range)	1.51 ± 0.43a	2.16 ± 0.84b	2.45 ± 0.6b	<0.001
Gestational age				
Mean ± SD	30.68 ± 2.63	33.68 ± 2.51	35.11 ± 1.15	<0.001
Mode of delivery				

Vaginal	11(50%)	7(28%)	7(20%)	0.054
Cesarean section	11(50%)	18(72%)	28(80%)	
Duration of NIVO2,hours				
Median (range)	3.0(0.0-10)	2.0(0.0-7.0)	2.0(0.0-5.0)	0.107

Table 3: Association of demographic and clinical characteristics with albumin levels different small letters indicates significant differences.

Table 4 shows the association of laboratory parameters with albumin levels. All included laboratory parameters were comparable between the three groups with no significant differences. Although positivity for CRP was less frequent among neonates with with >30 g/L albumin level (17.14%) than either those with hypoalbuminemia (36.36%) or those with 25-30 g/L albumin (36%), the difference was not significant.

Variables	**Albumin level**			**p-value**
	≤ 25 g/L (n=22)	25-30 g/L (n=25)	>30 g/L (n=35)	
WBC × 103/ml				
Median(range)	14.45(3.1-22.4)	14.3(3.0-33)	14.4(4.0-30)	0.978
PLT × 103/ml				
Median(range)	190(109-362)	185(54-312)	191(88-322)	0.816
Hb, g/dl				
Mean ± SD	15.71 ± 2.26	16.35 ±1.18	16.88 ± 1.94	0.104
PCV,%				
Mean ± SD	49.15 ± 7.47	51.23 ± 6.89	51.63 ± 6.4	0.394
CRP, mg/dl				
Median(range)	1.0(0.0-58)	1.0(0.0-81)	1.0(0.0-40)	0.253
CRP positivity				
Yes	14(63.64%)	16(64%)	29(82.86%)	0.165
No	8(36.36%)	9(36%)	6(17.14%)	

Table 4. Association of laboratory characteristics with albumin levels.

Predicative value of hypoalbuminemia

Receiver operating characteristic curve was used to find to find the predictive value of albumin in predicting death of premature neonates.

The Area Under the Curve (AUC) was 0.824, 95% CI=0.734-0.914.

The sensitivity of specificity of test at cut off value of albumin = 24.05 g/L was 81% and 58%, respectively (Figure 1).

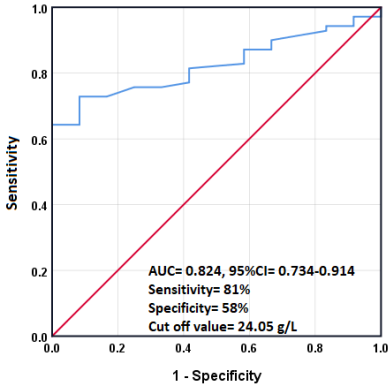

Figure 1. Receiver operating characteristic curve for albumin in predicting death of premature neonates.

Discussion

Serum albumin level is widely utilized as nonspecific marker for inflammation and as a prognostic factor in adult. However, its role as predictive factor for disease severity and mortality in

neonatal population and especially in preterm is still subject of interest. This paper critically discusses the usefulness of measuring serum albumin in the 1st day of life in predicting severity, morbidity and mortality of preterm infants. In this study, Neonates with hypoalbuminemia demonstrated lower birth weight and gestational age (1.45 kg and 30.68 ± 2.63 weeks, respectively) than those with normal albuminemia in both categories with highly significant differences (p value 0.001). This explained by the fact that normal serum albumin level is lower in preterm neonate and vary greatly with gestational age and albumin levels steadily increasing approaching time of delivery.

In current study (40.9%) of preterm babies with laboratory finding of hypoalbuminemia in the first day of life develop sepsis. This was significantly higher than those with moderate or high albumin levels with p value (0.001). This finding is in line with that of Abdelaal et al. Furthermore, (56.25%) of preterm with sepsis had low serum albumin. This percentage is lower than that seen in earlier studies by Abdelaal et al. and Yang et al. who found that hypoalbuminemia was seen in (86%) and (70%) of preterm with sepsis, respectively. The laboratory parameters in this study including CRP, WBC, PLT, HB does not show any correlation with low serum albumin level. On the other hand Abdelaal et al. [9] and Yang et al. [10] found a significant correlation between platelet count and S. albumin level. This could be explained by the difference in the underlying diagnosis in the sample of the study as all of the cases in Abdelaal et al. and Yang et al. carry diagnosis of sepsis, which is a known cause of thrombocytopenia. Whereas, in this study only 19.5% from sample carry diagnosis of sepsis.

In this study there was no significant relation between serum albumin level and Length of Stay (LOS) in hospital. This match result by Abdelaal et al. who found that in preterm infant with sepsis low albumin level does not affect length of hospital stay. The median duration of CPAP and total O2 were higher in neonates with hypoalbuminemia (2.0 hours and 4.5 hours, respectively) than those with normal albumin level in both categories with highly significant differences. The reason for this is unknown; however it could be linked to an increase in complications and comorbidity, which were not addressed in this study. In this study, Preterm with Hypoalbuminemia did not require longer duration of mechanical ventilation than those with normal albumin levels which agree with Horowitz et al. in a study on critically ill patients found no significant association between hypoalbuminemia and length of ventilatory support. In the current study lack of antenatal corticosteroids was not significantly related to hypoalbuminemia in the 1st day of life. This in contradict the finding of Iacobelli et al. [11] and Bunt et al [12]. Iacobelli et al. found that the lack of antenatal corticosteroids was an independent variable associated with hypoproteinemia, and this is in line Bunt et al findings, which showed that albumin synthesis in preterm infants on the first day of life tended to increase after antenatal corticosteroids were given.

In fact, only 13.4% of mothers of preterm babies in this study received prenatal steroid. This can be explained by the fact that this study was conducted during the COVID19 quarantine which may have limited pregnant women's access to prenatal care. In this study, 31.82% of the low serum albumin group died during hospitalization, but no death was recorded in the high albumin group, indicating that low albumin levels had a significant positive predictive value for premature infant mortality. This is in line with the findings of Torer et al. who discovered that a low blood albumin level on the first day of life is an independent predictor of preterm infant death [13]. Hypoalbuminemia has also been linked to negative outcomes, according to Abdelaal et al.

Conclusion

In the first day of life, low serum albumin level in preterm neonate significantly correlate with sepsis and indicate higher risk of mortality. Albumin levels have no relation to duration of hospitalization or mechanical ventilation.

Acknowledgement

To our beloved university; Al Mustansiriyiah for continuous support.

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