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RESEARCH

Comparison of serum albumin level and lactate for predicting preterm morbidities and mortality

Preterm morbiditeleri ve mortalitesinin tahmininde serum albümini ile laktat düzeyinin karşılaştırılması

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Abstract

Purpose: We aimed to comparison of serum albumin and lactate level for predicting neonatal morbidities and mortality in preterm infants < 32 weeks of gestation.

Materials and Methods: The medical records of babies were retrospectively analyzed. Patients were divided into three groups; plasma albumin levels ≤ 2.5 g/dL were defined as Group 1, 2.6-3 g/dL as Group 2 and ≥ 3 g/dL as Group 3. The babies < 28 weeks of gestation were analysed as a subgroup.

Results: 300 infants with mean gestational age of 28.7 ± 2.4 weeks and mean birth weights 1240 ± 405 grams were included. In predicting mortality; the sensitivity of the albumin level within the first three days was 74.4% and the specificity was 73.2% (cut-off < 2.9 g/dL), the sensitivity of the lowest albumin level was 90.7% and the specificity was 70.1% (cut-off < 2.65 g/dL), the sensitivity of the lactate level was 67.4% and the specificity was 63.3% (cut off > 3.1 mmol/L). Analysis of < 28 weeks babies; the sensitivity of lowest albumin level was 80% and the specifity was 66.7% (cut-off < 2.45 g/dL) and the sensitivity of the albumin level within the first three days was 74.3% and the specificity was 72.6% (cut-off < 2.8 g/dL), and the sensitivity of lactate was 74.3% and the specifity was 64.2% (cut-off > 3.1mmol/L).

Conclusion: Low serum albumin level appears to be more specific and sensitive than lactate in predicting mortality and may be considered to be added to mortality prediction scores.

Keywords: Hypoalbuminemia, morbidity, mortality, preterm, newborn

Öz

Amaç: 32 haftadan küçük preterm bebeklerde neonatal morbiditeleri ve mortaliteyi öngörmede serum albumin ve laktat düzeylerini karşılaştırmayı amaçladık.

Gereç ve Yöntem: Bebeklerin tıbbi kayıtları retrospektif olarak incelendi. Hastalar üç gruba ayrıldı; plazma albümin düzeyi ≤ 2.5 g/dL olanlar Grup 1, 2.6-3 g/dL olanlar Grup 2 ve ≥ 3 g/dL olanlar Grup 3 olarak tanımlandı. < 28 gebelik haftası olan bebekler alt grup olarak analiz edildi.

Bulgular: Ortalama gebelik yaşı 28.7 ± 2.4 hafta ve ortalama doğum ağırlığı 1240 ± 405 gram olan 300 bebek dahil edildi. Mortaliteyi öngörmede; ilk üç gün içindeki albümin düzeyi duyarlılığı %74.4 ve özgüllüğü %73.2 (cut-off < 2.9 g/dL), en düşük albümin seviyesinin duyarlılığı %90.7 ve özgüllüğü %70.1 (cut-off < 2.65 g/dL), laktat seviyesinin duyarlılığı %67.4 ve özgüllüğü %63.3 (cut-off > 3.1 mmol/L) idi. < 28 hafta bebeklerin analizinde; en düşük albümin seviyesinin duyarlılığı %80 ve özgüllüğü %66.7 (cut-off < 2.45 g/dL), ilk üç gün içindeki albümin seviyesinin duyarlılığı %74.3 ve özgüllüğü %72.6 (cut-off < 2.8 g/dL), laktatın duyarlılığı %74.3 ve özgüllüğü %64.2 (cut-off > 3.1 mmol/L) idi.

Sonuç: Düşük serum albumin düzeyi mortaliteyi öngörmede laktata göre daha özgül ve duyarlı görünmektedir ve mortalite tahmin skorlarına eklenmesi düşünülebilir.

Anahtar kelimeler: Hipoalbüminemi, morbidite, mortalite, preterm, yenidoğan

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INTRODUCTION

Most of preterms in the neonatal intensive care unit have low albumin levels. Actually, fetus is capable of endogenous albumin synthesis from early pregnancy and albumin cannot be transported through the placenta. But critically ill preterms have low albumin levels due to redistrubition, increased catabolism, or both[1]. Albumin plays an important role in binding and transporting proteins, maintaining colloid osmotic pressure, scavenging free radicals, suppressing platelet functions, providing antithrombotic effect and changes in vascular permeability[2]. There is strong evidence that hypoalbuminemia is important in predicting mortality in adult patients[3]. In Acute Physiology and Chronic Health Evaluation III (APACHE III) score, serum albumin level is a component of the scoring system[4]. There are few studies evaluating the prognostic value of serum albumin in neonates and pediatric patients[5,6].

Lactate is a terminal product of the anaerobic metabolism of glucose. It is increased in situations of tissue hypoxia-ischemia which may result from respiratory or circulatory disorders. Studies have shown that lactate levels have correlated with mortality in critically ill infants and preterms[7-9]. However, both lactate and albumin levels are not included in mortality scoring systems.

We hypotesized that; low albumin synthesis due to immaturity in preterm infants contributes to their preterm morbidity and mortality by causing insufficient intravascular volume and therefore reduced blood flow to the end organs. We aimed to investigate the relationship between serum albumin levels and mortality and preterm morbidities in preterm infants. For this purpose; we compared lactate, which is claimed to be important in predicting preterm mortality and morbidity, with albumin level.

MATERIALS AND METHODS

Sample

The study was conducted retrospectively in Neonatal Intensive Care Unit of Health Sciences University, Adana City Training and Research Hospital. The records of 300 infants born before 32 weeks of gestation who were hospitalized between March 2017 and March 2020 were analyzed. Approval was obtained from the local ethics committee of the Adana City Training and Research Hospital (Number of meetings: 45, Date: 04.12.2019, Decission no: 627). The cases were obtained from the hospital database. In our clinic, all data of babies are recorded in the electronic information system. The daily clinical course and diagnoses of babies are recorded in the system by neonatal specialists.

Congenital malformation or chromosomal anomaly, hydrops fetalis, chylothorax, congenital heart and kidney disease, suspected metabolic and genetic disease, babies who died within the first week of life, babies whose albumin levels were not measured within the first three days of life and babies born outside were excluded from the study.

Procedure

The mothers' diagnoses of hypertension, gestational diabetes mellitus, preeclampsia-eclampsia, preterm rupture of membranes (rupture of membranes before 37 gestational week, PROM), preterm and prolonged rupture of membranes (time from rupture of membranes to birth > 18 hours, PPROM) and giving antenatal corticosteroid (ANC) to the mother were recorded. The babies gestational age (as confirmed by last menstrual period and/or ultrasonography), birth weight, sex, fifth minute Apgar score, presence of small for gestational age (SGA), blood gases at admission, hematological and biochemical parameters, albumin values, presence of respiratory distress (RDS) and degree, need of surfactant treatment and numbers of surfactant administration, need of mechanical ventilation and duration of ventilation, premature morbidity [(sepsis, patent ductus arteriosus (PDA) which required treatment, bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), periventricular leucomalasia (PVL)], duration of total parenteral nutrition (TPN) and death before discharge were recorded.

Serum albumin measurement and selection of groups

Serum albumin concentration was measured with bromocresol green binding method (Beckman Coulter, Beckman Coulter Inc., USA). In our clinic, the earliest biochemical test is performed within the first three days. The patients were divided into three groups according to albumin level. Plasma albumin levels ≤ 2.5 g/dL were defined as Group 1, between

2.6 and 3 g/dL as Group 2 and > 3 g/dL as Group 3[6]. The babies born before 28 weeks of gestation were analysed as a subgroup. Groups were compared in terms of preterm morbidity and mortality.

Statistical analysis

Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean and standard deviation and as median and IQR where appropriate. Chi-square test was used to compare categorical variables between the groups. The normality of distribution for continuous variables was confirmed with the Shapiro Wilk test. For comparison of continuous variables between two groups (i.e., mortality status), the Student's t-test (albumin, lowest albumin) or Mann-Whitney U test (base excess, lactate, C-reactive protein, procalcitonin) was used depending on whether the statistical hypotheses were fulfilled or not. For comparison of continuous variables between Albumin groups, Oneway ANOVA (pH, albumin, gestational week, birth weight) or Kruskal Wallis test (base excess, lactate, C-reactive protein, procalcitonin) was used depending on whether the statistical hypotheses were fulfilled or not. For normally distributed data, regarding the homogeneity of variances, Tukey or Games-Howell tests were used for multiple comparisons of groups. For non-normally distributed data, Bonferroni adjusted Mann Whitney U test was used for multiple comparisons of groups. A receiver operator characteristic (ROC) curve analysis was performed in order to identify the optimal cut-off points for the lowest albumin, Albumin and Lactate levels to predict mortality. All analyses were performed using IBM SPSS Statistics Version 20.0 statistical software package. The statistical level of significance for all tests was considered to be 0.05.

RESULTS

During the period of study, it was determined that the 476 babies born before 32 weeks of gestation in our hospital. 101 were referred to other hospitals, 14 were missing data, 24 were excluded due to congenital malformation and 37 were excluded because they were dead within the first week of life. Therefore, study group included 300 patients who met the inclusion criteria and had full data (Figure 1).

The mean gestational age of the infants was 28.7 ± 2.4 weeks, birth weight was 1240 ± 405 grams, and the mean albumin value in the first three days was 3.04 ± 0.50 g/dL. Birth weight, gestational age and giving ANC to the mother were found to be higher and mortality was lower for babies in Group 3 compared to other groups ($p < 0.001$ for all) (Table 1).

Table 1. Characteristics of groups

Measurements	Group 1 (n = 51)	Group 2 (n = 63)	Group 3 (n = 186)	p
Gestational age*, (weeks)	27.6 ± 3.1	27.8 ± 2.4	29.3 ± 2.0	< 0.001[b,c]
Birth weight*, (gram)	1032.9 ± 433.4	1070.5 ± 337.8	1354.8 ± 376.2	< 0.001[b,c]
Albumin in first three days*, (g/dL)	2.24 ± 0.21	2.74 ± 0.11	3.36 ± 0.30	< 0.001[a,b,c]
Female, n (%)	24 (47.1)	28 (44.4)	79 (42.5)	0.835
APGAR at 5th minute > 7, n (%)	25 (49)	31 (49.2)	143 (76.9)	< 0.001[b,c]
ANC, n (%)	14 (27.5)	19 (30.2)	96 (51.6)	< 0.001[b,c]
Preeclampsia, n (%)	2 (3.9)	10 (15.9)	25 (13.4)	0.118
PROM, n (%)	3 (5.9)	5 (7.9)	23 (12.4)	0.315
PPROM n (%)	2 (3.9)	2 (3.2)	24 (12.9)	0.027
Chorioamnionitis, n (%)	3 (5.9)	3 (4.8)	4 (2.2)	0.299
Gestational diabetes, n (%)	0 (0.0)	2 (3.2)	8 (4.3)	0.419

a: p<0.05 for Group1 vs Group2, b: p<0.05 for Group1 vs Group3, c: p<0.05 for Group2 vs Group3.
* Mean ± Standart deviation,
ANC: Antenatal corticosteroid (defined as receiving full-dose antenatal corticosteroid therap), PROM: Preterm rupture of membranes, PPROM: Preterm and prolonged rupture of membranes.

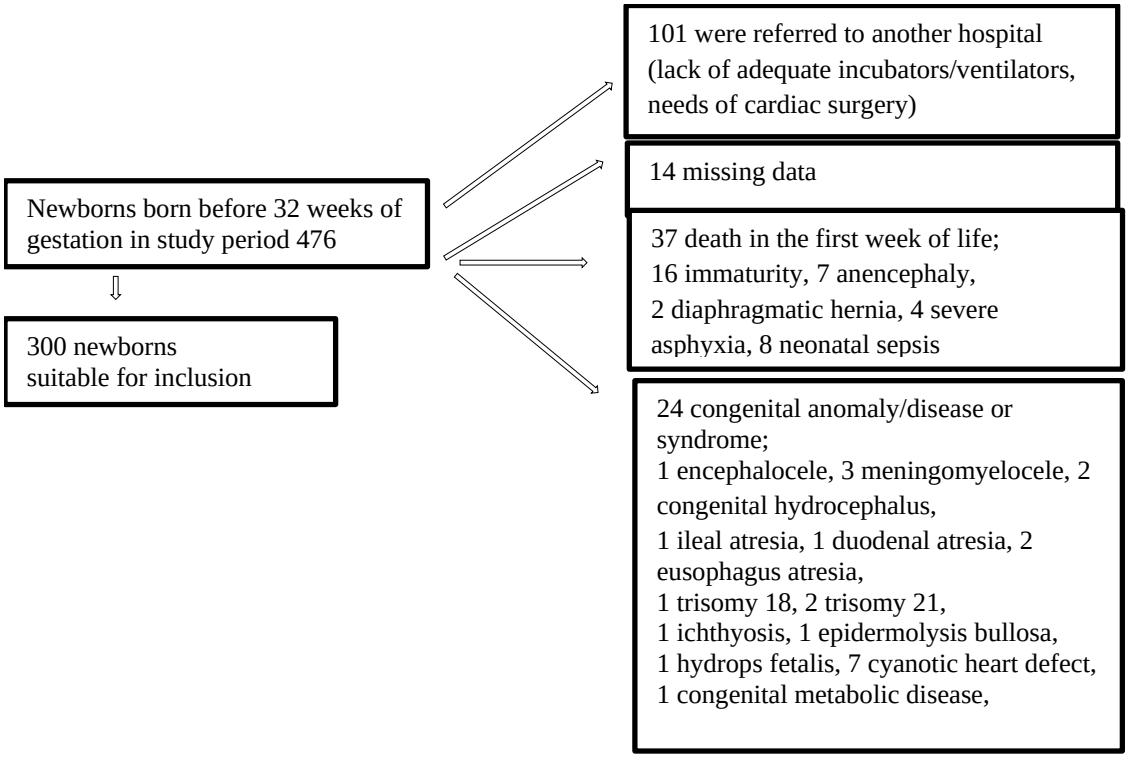

Figure 1. Flow chart of patient selection

Table 2. Laboratory results of the groups based on the albumin level at day 0-3

Measurements *	**Group 1 (n = 51)**	**Group 2 (n = 63)**	**Group 3 (n = 186)**	**P**
Blood gases at 1st hour				
pH	7.24 ± 0.14	7.24 ± 0.11	7.27 ± 0.11	0.079
Base excess	-5.62 ± 4.45	-4.17 ± 4.87	-2.36 ± 4.52	< 0.001[a,b]
Lactate (mmol/L)	5.17 ± 3.86	4.55 ± 4.36	3.22 ± 2.52	< 0.001[b]
2-3. day				
Albumin (g/dL)	2.24 ± 0.21	2.74 ± 0.11	3.36 ± 0.30	< 0.001
CRP (mg/L)	11.1 ± 29.7	4.6 ± 7.5	3.3 ± 12.8	< 0.001[b,c]
PCT (ng/mL)	23.1 ± 25.4	13.6 ± 17.0	10.2 ± 19.6	0.013[b]
Lowest albumin (g/dL)	2.17 ± 0.29	2.51± 0.30	3.11 ± 0.45	< 0.001[a,b,c]

a: p<0.05 for Group1 vs Group2, b: p<0.05 for Group1 vs Group3, c: p<0.05 for Group2 vs Group3
*Mean ± Standard deviation
CRP: C-reactive protein, PCT: Procalcitonin

The relationship between lactate, which is an important indicator in mortality, and the albumin values within the first three days and the lowest albumin value, were calculated with the ROC curve. It was observed that lowest albumin level was more sensitive in monitoring the clinical course than lactate (Figure 2).

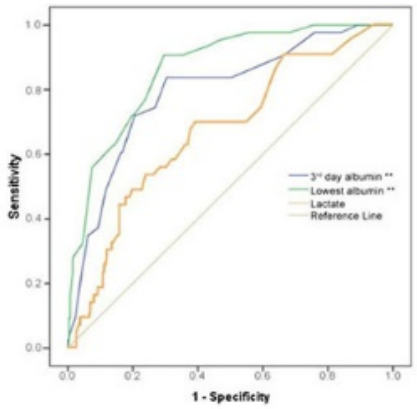

Figure 2. ROC curve of serum albumin and lactate level to evaluate the probability of mortality (AUC for albumin level measured within the first three days 0.794, AUC for lowest albumin level 0.863, AUC for serum lactate level 0.67).

In predicting mortality, it was obtained that the sensitivity of the albumin level in the first three days was 74.4% and the specificity was 73.2% (cut-off < 2.9 g/dL), the sensitivity of the lowest albumin level was 90.7% and the specificity was 70.1% (cut-off < 2.65 g/dL), the sensitivity of the lactate level was 67.4% and the specificity was 63.3% (cut of > 3.1 mmol/L). According to that, although albumin appears to be more sensitive and specific than lactate in predicting mortality, additional analyzes were performed to evaluate whether the mortality was related to albumin level or to the fact that the mean gestational age and birth weight of the babies of Group 3 who were higher than the other groups. The mean of albumin levels in the first three days and the mean of the lowest albumin values were significantly lower in dead babies, but the birth weight and gestational age of the babies who dead were significantly lower than the surviving babies ($p < 0.001$ for all) (Table 3 and 4).

Table 3. Examining the relationship between mortality and albumin level

Measurements	Discharged (n = 257)	Exitus (n = 43)	P
Lowest albumin level (g/dL)*	2.93 ± 0.5	2.20 ± 0.4	< 0.001
Albumin level on third day (g/dL)*	3.12 ± 0.5	2.57 ± 0.46	< 0.001
Lactate on admission (mmol/L)**	2.5 (2.15)	4.2 (4.7)	< 0.001
Birth weight (gram)*	1315.2 ± 372.4	793.3 ± 291.3	< 0.001
Gestational week (week)*	29.2 ± 2.0	25.8 ± 2.7	< 0.001

*Mean ± Standard deviation
** median (IQR)

Table 4. Sensitivity and specificity of lowest albumin in predicting mortality, based on albumin level in the first three days and lactate level

Measurements	Cut-off value	Sensitivity (%)	Specificity (%)	AUC (95% CI for AUC)
Whole group Lowest albumin (g/dL)	< 2.65	90.7	70.1	0.863 (0.811-0.916)
Albumin in the first three days (g/dL)	< 2.9	74.4	73.2	0.794 (0.720-0.867)
Lactate (mmol/L)	> 3.10↑	67.4	63.3	0.670 (0.583-0.756)
≤28 gestational week Lowest albumin (g/dL)	< 2.45	80.0	66.7	0.814 (0.733-0.894)
Albumin in the first three days (g/dL)	< 2.8	74.3	72.6	0.753 (0.657-0.850)
Lactate (mmol/L)	> 3.10	74.3	64.2	0.713 (0.617-0.809)

In the analysis of infants born before 28 weeks of gestation showed that the sensitivity of the albumin level in the first three days was 74.3% and the specificity was 72.6% (cut-off < 2.8 g/dL), the sensitivity of the lowest albumin level was 80% and specificity was 66.7% (cut-off < 2.45 g/dL), the sensitivity of the lactate level was 74.3% and the specificity was 64.2% (cut-off > 3.1 mmol/L) in predicting mortality (Table 4). The mean albumin level of 130 infants < 28 weeks was 2.88 ± 0.49 g/dL. Of these, 95 (73%) were discharged and their mean albumin value was 2.73 ± 0.46 g/dL, 35 (27%) babies were died and their mean albumin value was 2.17 ± 0.41 g/dL (p < 0.001) (Table 5 and 6).

Table 5. Examining the infants born ≤ 28 gestational week

Measurements	Group 1 (n = 33)	Group (n = 36)	Group 3 (n = 61)	p
Gestational age, weeks*	25.7 ± 1.9	26.1 ± 1.5	27.0 ± 1.3	< 0.001[b,c]
Birth weight*, gram	815.5 ± 213.1	901.7 ± 231.9	1057.2 ± 262.6	< 0.001[b,c]
Albumin in the first three days*, (g/dL)	2.21 ± 0.23	2.75 ± 0.11	3.31 ± 0.23	< 0.001[a,b,c]
Lowest albumin level (g/dL)	2.12 ± 0.24	2.45 ± 0.35	2.91 ± 0.48	< 0.001[a,b,c]
Lactate (mmol/L) **	4.3 (4.85)	2.85 (4.27)	2.5 (2.2)	0.231
Mortality, n (%)	19 (57.6)	10 (27.8)	6 (9.8)	< 0.001[a,b]

a: p<0.05 for Group1 vs Group2, b: p<0.05 for Group1 vs Group3, c: p<0.05 for Group2 vs Group3
*Mean ± Standard deviation
** median (IQR)

Table 6. Examining the relationship between mortality and albumin level in babies ≤ 28 gestational week

Measurements	Discharged (n = 95)	Exitus (n = 35)	p
Lowest albumin level (g/dL)*	3.00 ± 0.46	2.56 ± 0.47	< 0.001
Albumin level in the first three days (g/dL)*	2.73 ± 0.46	2.17 ± 0.41	< 0.001
Lactate on admission (mmol/L)**	2.4 (2.5)	5.1 (4.2)	< 0.001
Birth weight (gram)*	1042.5 ± 230.2	709.1 ± 174.3	< 0.001
Gestational week (week)	27.0±1.1	24.8 ± 1.8	< 0.001

In infants who died, albumin level was found to be lower and lactat level was higher but, the gestational age and birth weight of these babies were also low significantly. The relationship between lactate and albumin levels in the first three days in these infants was calculated with the ROC curve (AUC for albumin level measured in the first three days: 0.753, AUC for the lowest albumin level: 0.814, AUC for serum lactate level: 0.713) (Figure 2).

In Group 3, the rate of infants receiving TPN, presence of early and late neonatal sepsis, RDS, PDA, and BPD were found to be lower compared to other groups (p < 0.001 for all). In terms of severe IVH development, the groups were found to be similar. The rate of PVL in Group 3 was lower than that of the other groups (p < 0.001).

NEC rate in Group 3 was found to be significantly lower than the other groups (p < 0.001). The 15 patient which had a history of NEC, five (9.8%) were in Group 1, six (9.5%) were in Group 2, and four (2.2%) were in Group 3.

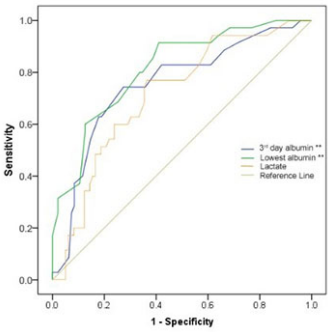

Figure 3. ROC curve of serum albumin and lactate level to evaluate the probability of mortality in infants < 28 weeks (AUC for albumin level measured within the first three days 0.753, AUC for lowest albumin level 0.814, AUC for serum lactate level 0.713).

All five (100%) patients with a history of NEC surgery were identified as patients in Group 1. In Group 3 the ROP rate was found to be significantly lower than the other groups (p = 0.002). However, there was no ROP stage 3 and 4 in the whole group (Table 7).

Table 7. Comparison of morbidity of the groups and albumin level in the first three days

Measurements	Group 1 (n = 51)	Group 2 (n = 63)	Group 3 (n = 186)	p
RDS, n (%)	39 (76.5)	47 (74.6)	67 (36)	<0.001[b,c]
Surfactant (≥ 2 dose), n (%)	9(24.3)	9(19.1)	8(12.1)	0.099
Severe IVH, n(%)	16 (72.7)	5 (41.7)	6 (60)	0.205
NEC, n (%)	5 (9.8)	10 (15.9)	5 (2.7)	0.001[c]
PDA, n (%)	28 (54.9)	26 (41.3)	11 (5.9)	<0.001[b,c]
Invasive MV, n (%)	41 (80.4)	51 (81)	52 (28)	<0.001[b,c]
Duration MV, day (median, IQR)	7 (13)	4 (11)	2 (4)	<0.001[b,c]
Early sepsis, n (%)	48 (94.1)	61 (96.8)	145 (78)	<0.001[b,c]
Early culture positive, n (%)	4 (7.8)	6 (9.5)	5 (2.7)	0.059
Late sepsis, n (%)	28 (54.9)	43 (68.3)	44 (23.7)	<0.001[b,c]
Late culture positive, n (%)	3 (5.9)	13 (20.6)	13 (7)	0.004[c]
PVL, n (%)	16 (31.4)	7 (11.1)	9 (4.8)	<0.001[a,b]
BPD, n (%)	9 (17.6)	20 (31.7)	18 (9.7)	<0.001[c]
ROP (stage 1-2), n (%)	11 (21.6)	14 (22.2)	14 (7.5)	0.002[b,c]
TPN, n (%)	42 (82.4)	56 (88.9)	114 (61.3)	<0.001[b,c]
TPN duration, days (median, IQR)	11 (11)	9.5 (11)	5 (5)	<0.001[b,c]

b: p<0.05 for Group1 vs Group3, c: p<0.05 for Group2 vs Group3
RDS: Respiratory distress syndrome, IVH: Intraventicular hemorrhage, NEC: Necrotising enterocolitis, PDA: patent ductus arteriosus, MV: Mechanical ventilation, PVL: Periventricular leucomalasia, BPD: Bronchopulmonary dysplasia, ROP: Retinopathy of prematurity, TPN: Total parenteral nutrition.

DISCUSSION

In this study, we evaluated the relationship between serum albumin levels and preterm morbidity and mortality in preterm infants. Main findings; Both the albumin level in the first three days of life and the lowest albumin level seem to be more sensitive and specific than lactate in predicting preterm mortality.

There are few studies in the literature showing that serum albumin level in the first days of life can be used as an indicator of prognosis in preterm infants[6,10]. In our study, it was determined that the rate of ANC application was the lowest in Group 1, and rate of RDS was higher than normo-albuminemic group. Low albumin level may cause increased alveolo-capillary permeability and increased protein leakage into the alveolar space. ANC treatment improves cytostructural maturation of the lungs and reduces pulmonary protein leakage. Ying et al.[11] reported in their study that the decrease in serum albumin within the first day of life was related to the occurrence of RDS in late-preterm infants. They claimed that the rate of ANC therapy and albumin level higher in non-RDS infants. Bunt et al.[12] reported that after ANC administration, albumin level was higher in the postnatal period, the synthesis capacity of the liver was well developed in these babies and prenatal ANC had a tendency to increase albumin synthesis.

In the analysis of other morbidities of premature babies it was observed; in the Group 3 the rates of sepsis, RDS, NEC, BPD, ROP and the duration of invasive mechanical ventilation were lower. Torer et al.[6] showed that a significant relationship between serum albumin level and mortality in babies born before the 32nd week of gestation. In the same study, there were no significant relationship found between serum albumin levels and the duration of mechanical ventilation and oxygen support, the frequency of PDA, IVH, NEC, ROP, PVL, BPD and the duration of hospital stay.

In our study, the early and late onset neonatal sepsis rates were found to be lower in Group 3, which they had the highest albumin level measured in the first three days, compared to other groups. In the comparison of babies who had culture-positive early

onset sepsis rates were similar between groups, while culture-positive late onset sepsis was found to be higher in Group 2. Culture positivity can be detected in about 33% of neonatal sepsis; the amount of blood taken for culture is important for the growth of microorganisms and the number of microorganisms that cause sepsis in the newborn is low. Therefore, we think that it is more important to evaluate clinical sepsis outcomes than the culture positive sepsis. We found; CRP, PCT and lactate values were lower in Group 3, which had higher gestational age, birth weight, and albumin level than the other groups. Yang et al.[5], in their retrospective studies in which they examined late preterm infants, showed that serum albumin levels were significantly lower in infants with sepsis and infants who died, and low serum albumin was associated with severe adverse outcomes. They reported that this relationship is more important than other acute phase reactants (CRP, PCT, platelet, leukocyte count). Abdelaal et al.[13] reported that in newborns with sepsis, hypoalbuminemia is common and low albumin levels may be associated with poor prognosis. In the same study, they showed that albumin levels are also a suitable indicator for the diagnosis and prognosis of preterm babies with sepsis, and hypoalbuminemia may be associated with poor clinical course. Akram et al.[14] reported that in the first day of life, low serum albumin level in preterm neonate significantly correlate with sepsis and indicate higher risk of mortality. El-Lahony et al.[15] found a significant relationship between neonatal sepsis and serum albumin levels. They showed that significant correlation between serum albumin levels and both clinical and hematological sepsis scores.

In our studty, the lower mortality rate in Group 3, may be due to the higher gestational age and birth weight of Group 3 babies. For this reason, albumin values in the first three days and the lowest albumin values were compared between dead and alive babies and found to be similar. Park et al.[16] reported the birth weight, Apgar scores at 1 and 5 minute, and serum albumin levels in first days of life were significantly higher, while the clinical risk index for babies II score (CRIB II) was significantly lower in survival group, and gestational age and lowest serum albumin level in survival group were significantly higher than infants who died after first week of life. Contrary to our study, Morris et al.[17] evaluated the relationship between the lowest serum albumin level and mortality in 107 preterm extremely low birth weight (ELBW) babies. They reported that, there was a significant relationship between the lowest albumin level and mortality, which continued even when birth weight and gestational age were adjusted. However, this is a retrospective study and albumin measurements were not made at standard times.

In our study, all babies in Group 1 who developed NEC were found to be in an advanced stage (stage 3-4) NEC and all of them required surgery. Recent study by Amin et al.[18] reported the serum CRP/Albumin ratio has a prognostic value in predicting surgery and mortality in neonates with NEC. They showed the CRP/Albumin ratio of ≥ 3 on second day after NEC diagnosis, was associated with a statistically signifcant higher likelihood for surgery.

High serum lactat level in critically ill children is associated with worse outcome in critically ill patient in pediatric intensive care unit. There are few publications evaluating the relationship of lactate with mortality in preterms. In a recent study by Tuten et al.[19] they evaluated the effect of serum lactate and perfusion index on predicting mortality and morbidity in very low birth weight infants. They showed that ROP was significantly higher in the patients with high lactate levels (> 4 mg/dL) at 1st hour and low-perfusion index levels (< 0.5) at 12th hour of life, BPD was significantly higher in the patients with low perfusion index (< 0.5) at 1st hour. Lactate and perfusion index values were not significantly correlated with NEC, IVH, PDA, sepsis and mortality. In our study; the area under the curve (AUC) for albumin and lactate was calculated as a mortality determinant and it was observed that albumin level was more sensitive in monitoring the clinical course than lactate. We detected; both the first three days and lowest albumin levels of the patients were found to be significant in all groups in terms of mortality and morbidity. However, it was also considered that this difference could be due to the higher gestational age and birth weight of Group 3 babies. Mortality was found to be higher in infants born before 28 weeks, with lower birth weight and gestational age.

The limitations of our study were the fact that it is retrospectively designed, the gestational age and weight of the groups are different, and long-term morbidities could not be followed.

In conclusion, our study showed that low serum albumin level in the first three days of life is associated with the development of preterm

morbidities such as RDS, PVL, NEC, BPD, ROP in preterm infants, and there is a relationship between low albumin and mortality. It may be beneficial to consider to add the serum albumin level to physiological scores such as SNAPPE II, which determine disease severity. Prospective studies with homogeneous groups and higher patient numbers are needed to determine the importance of adding albumin to risk estimation scores.

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