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Original Article

Correlation between Serum Albumin Level and Respiratory Distress in Preterm Infants

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ABSTRACT

Background: Although hypoalbuminemia predicts mortality in adults, its prognostic relevance in neonates is unclear. It is suggested that, serum albumin levels in the first day after birth can predict premature births.

Aim of the work: This study aimed to evaluate the correlation between serum albumin level and respiratory distress in preterm infants.

Patients and methods: This prospective cross-sectional study included 75 patients which was carried out at Neonatal Intensive Care Unit [NICU] of Pediatric Department, Al-Azhar University Hospital at New Damietta. The Primary outcome of the study was: The incidence of respiratory distress syndrome [RDS] in preterm infants and their correlation with neonatal serum albumin levels. Secondary outcomes included: Mortality: The study measured the mortality rate of infants diagnosed with RDS.

Results: According to the serum albumin level of the patients; the median and IQR was 3.6 [3.2– 3.9] gm/dl with a range of 2– 4.5 gm/dl. The normal level of albumin was reported in 58.7% of the studied patients, However the low level was reported in 41.3% of the patients. The mortality rate of the studied patients was 21.3% [Table 5]. A comparison between the normal and low albumin level as regards different study variables were done. The gestational age and the birth weight of the patients with low albumin level was significantly lower than the patients with high albumin level [P = 0.001 for both].

Conclusion: There is a significant correlation between the low serum albumin level and the gestational age and also the low birth weight.

Keywords: Albumin; Neonate; Preterm; Respiratory Distress.

INTRODUCTION

Serum albumin, a protein in newborn blood, indicates the baby's health and nutrition. Low serum albumin levels may indicate malnutrition, illness, or other health concerns [1]. Preterm infants often have respiratory distress, which causes breathing problems and a shortage of oxygen to tissues. Brain injury, lung damage, and death can result [2]. Research has linked low serum albumin levels to respiratory discomfort in premature newborns. The newborn may have trouble breathing because serum albumin maintains the body's fluid balance, and low levels can cause fluid accumulation in the lungs [3]. In addition, low serum albumin levels may suggest insufficient nutrition, which can cause respiratory distress. Preterm newborns are at a higher risk of malnutrition due to their tiny size and undeveloped digestive systems, making it crucial to regularly monitor their nutrition and supplement as necessary [4]. To prevent respiratory distress in preterm newborns, monitor serum albumin levels and correct irregularities. This may involve adding protein and other nutrients to the baby's food, addressing illnesses, and monitoring breathing and oxygen levels [5]. In cases of respiratory distress, treatment may include oxygen, a mechanical ventilator, or bronchodilators to open airways. The newborn may need specialized treatment in a neonatal critical care unit [6]. In severe circumstances, Preterm newborns must consider neonatal serum albumin and respiratory distress. Low infant serum albumin levels may suggest malnutrition or respiratory distress. Close monitoring, therapy, and treatments can prevent and control respiratory distress and improve preterm baby outcomes [7].

This study aims to evaluate the correlation between serum albumin level and respiratory distress in preterm infants.

PATIENTS AND METHODS

This prospective cross-sectional study included 75 patients which was carried out at Neonatal Intensive Care Unit [NICU] of Pediatric Department, Al-Azhar University Hospital at New Damietta. Sample was collected by the systematic random method and the study protocol was approved by the Local Ethics Committee and written informed consents were obtained from the parents of the patients. **The Inclusion criteria were preterm with the following:** Gestational age less than 37 weeks; Respiratory distress within 72 hours of birth; and parents have signed an informed consent to participate in the study.

The Exclusion criteria: **Preterm with one or more of the following:** Major congenital anomalies or chromosomal abnormalities; Known history of in utero exposure to drugs or alcohol; Sepsis or meningitis; Receiving any form of mechanical ventilation or surfactant therapy before inclusion in the study; Persistent pulmonary hypertension of the newborn [PPHN], and parents did not give the consent to participate in the study.

Data collection

All included neonates were subjected to the following:

Careful history taking from the caregiver which included 1] Prenatal history; Maternal diseases, drugs or irradiation exposure; 2] Natal history; Time, type and site of delivery, complicated or not; 3] Postnatal history; Crying, cyanosis, convulsions, jaundice and resuscitative measures, and consanguinity.

Clinical examination, which included 1] vital signs; heart rate, respiratory rate, blood pressure and temperature; 2] Birth weight; 3] Chest examination: by inspection [shape of the chest, signs of respiratory distress as tachypnea, nasal flaring, retraction, grunting and cyanosis]; By palpation [palpable wheezes or rales]; By auscultation [air entry and additional sounds as wheezes or rales] and 4] Examination of other systems [nervous system, heart and abdomen].

Investigations that included complete blood count [CBC], arterial blood gases and measurement of serum albumin level. For determination of the serum albumin level, the sample was drawn into gel barrier tubes from preterm infants within 24 hours of birth and albumin levels was measured using the bromocresol green method. The results were expressed as g/dL [Normal range is 3.32-3.56 g/dL in full term babies]

Outcomes

The Primary outcome of the study was the incidence of RDS in preterm infants and their correlation with neonatal serum albumin levels. **Secondary outcomes included** mortality rate in neonates with RDS.

Statistical analysis: The collected data were coded, processed and analyzed using SPSS program [Version 26] for windows. Descriptive statistics was included medians, ranges, and percentages. Qualitative variables were expressed as Median and Interquartile range [IQR] and were compared using the Chi square test. Quantitative variables were checked for normality firstly by Kolmogorov-Smirnov test, and as all data were not normally distributed, we described it as median and IQR, and were compared by using the Mann Whitney U test.

RESULTS

A total number of 75 preterm labors were included in this study. The median gestational age of the babies was 34 [31 – 36] weeks with a range of 27 – 36 weeks. Fifty sex percentage [56%] of them were male and 44% were female. The median birth weight was 2.3 [1.6 – 2.8] Kg with a range of 8 – 2.9 kg. Nineteen patients [25.3%] were small for gestational age. Six patients [9.8%] were delivered by normal delivery, and 55 patients [90.1%] were delivered by CS method [Table 1].

As regards the mother's data, their median age was 27 [24 – 31] years with a range of 18 – 43 years. Twenty-three of them were primiparas. According to their comorbidities, 44.2% were diabetic, 49.1% were hypertensive, and 90.1% were anemic [Hb is < 11.5 g/dL]. In terms of pregnancy complications, 1.6% of them developed placental abruption, 6.5% developed placenta previa, and 18% of them developed PROM [Table 2].

As regards the grades of RDS in the patients, 2.7% were grade 1, 50.7% were grade 2, 14.7% were grade 3, and 32% were grade 4. According to the serum albumin level of the patients; the median and IQR was 3.6 [3.2– 3.9] gm/dl with a range of 2– 4.5 gm/dl. The normal level of albumin was reported in 58.7% of the studied patients, However the low level was reported in 41.3% of the patients [Table 3]. The mortality rate of the studied patients was 21.3% [Table 4]. A comparison between the normal and low albumin level as regards different study variables were done. The gestational age and the birth weight of the patients with low albumin level were significantly lower than the patients with high albumin level [P = 0.001 for both]. Furthermore, there was significant differences between normal and low levels albumin as regard to Degree of RDS and mortality [Table 5]. A statistically significant positive correlation was found between the serum albumin level and the gestational age [r= 0.5, P =0.001], and also the birth weight [r= 0.4, P =0.001] [Table 6 and [Figures 1 and 2]. A statistically significant negative correlation was found between the serum albumin level and the degree of RDS and also the mortality rate, in which the lower the albumin level, the higher the degree of the RDS, and the higher the mortality rate [r= -0.55, P =0.001, r= -0.42, P =0.001 respectively] [Table 6 and Figure 3, 4].

Table [1]: Demographic data of the studied patients

Variables		N [%] or Median [IQR]
Gestational age [weeks]	Median [IQR]	34 [31 – 36]
	Range	[27 – 36]
Gender [n=75] [n,%]	Male	42 [56%]
	Female	33 [44%]
Birth weight [Kg] [n=75]	Median [IQR]	2.3 [1.6 – 2.8]
	Range	[0.8 – 2.9]
Small for gestational age [n,%]		19 [25.3%]
Large for gestational age [n,%]		0 [0%]
Mode of delivery [n=61] [n,%]	NVD	6 [9.8%]
	CS	55[90.1%]
Number of births [n=61] [n,%]	Single	47 [81.3%]
	Twins	14 [18.7%]

Table [2]: Baseline clinical data of the mother.

Variables		N [%] or mean ± SD [N=61]
Age [years]	Median [IQR]	27 [24 – 31]
	Range	[18 – 43]
Primipara		23 [37.7%]
Comorbidities	GDM	27 [44.2%]
	HTN	30 [49.1%]
	Anemia	55 [90.1%]
Pregnancy complications	Placental abruption	1 [1.6%]
	Placenta previa	4 [6.5%]
	PROM	11 [18%]

Table [3]: Grades of RDS and serum albumin levels among study participants

Variables		N [%] [n=75]
RDS grades	Grade 1	**2** [2.7%]
	Grade 2	**38** [50.7%]
	Grade 3	**11** [14.7%]
	Grade 4	**24** [32%]
Serum albumin level [g/dl]	Median [IQR]	3.6 [3.2– 3.9]
	Range	[2– 4.5]
	Normal level	44 [58.7%]
	Low level	31 [41.3%]

IQR: Inter quartile range.

Table [4]: Mortality rate of the studied patients

Mortality rate	N [%] [n=75]
Live	**59** [78.7%]
Died	**16** [21.3%]

Table [5]: Association between the Serum Albumin Level and other variables.

Variables		Normal level [N=44]	Low level [N=31]	P value
Gestational age [weeks]	Median [IQR]	**35 [33 – 36]**	**31 [29 – 34]**	0.001*
Gender	Male	**23 [52.2%]**	**19 [61.2%]**	0.44
	Female	**21 [47.7%]**	**12 [38.7%]**	
Birth weight [kg]	Median [IQR]	**2.8 [2.1 – 2.9]**	**1.6 [1.1 – 2.3]**	0.001*
	Small for gestational age	**6 [13.6%]**	**13 [41.9%]**	0.006*
Degree of RDS	Grade 1	2 [4.5%]	0 [0%]	0.001*
	Grade 2	30 [68.1%]	8 [25.8%]	
	Grade 3	8 [18.1%]	3 [9.6%]	
	Grade 4	4 [9%]	20 [64.5%]	
Mortality	Died	2 [4.5%]	14 [45.1%]	0.001*
	Alive	42 [95.4%]	17 [54.8%]	

Table [6]: Correlation between the Serum Albumin Level and Gestational Age

Variables	Serum Albumin Level	
	r	P value
Gestational Age [Weeks]	0.55	0.001*
Birth weight	0.42	0.001*
RDS grades	-0.55	0.001*
Mortality	-0.42	0.001*

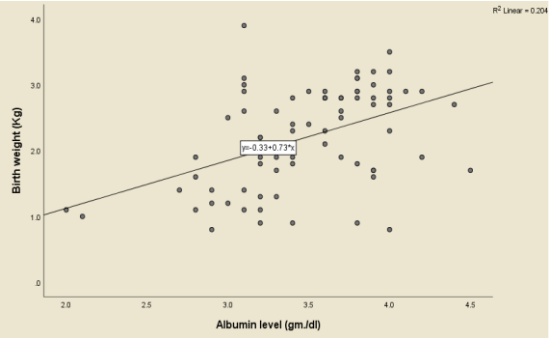

Figure [1]: Correlation between Albumin level and Birth weight.

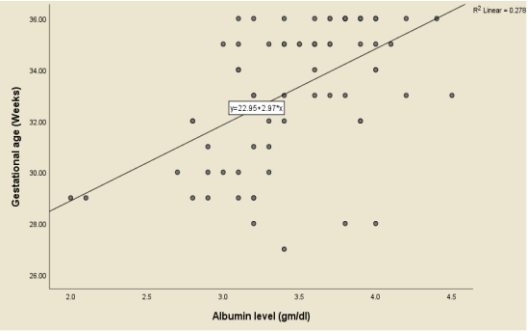

Figure [2]: Correlation between Albumin level and Gestational age.

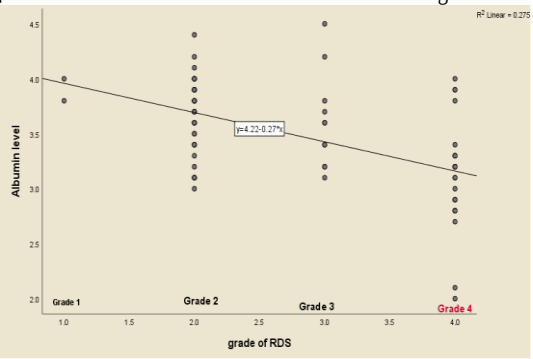

Figure [3]: Correlation between Albumin level and the degree of RDS.

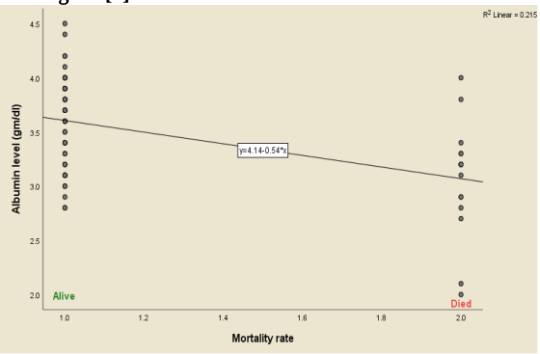

Figure [4]: Correlation between Albumin level and the Mortality rate.

DISCUSSION

Neonatal respiratory distress syndrome [RDS] is common and deadly. Early postpartum respiratory difficulties, blue skin, and inability to breathe are typical RDS symptoms. Severe respiratory distress syndrome [RDS] necessitates immediate medical treatment and breathing support [8]. RDS is widely linked to preterm. It mostly affects preterm newborns under 34 weeks old with undeveloped lungs and low pulmonary surfactant production. Recent research shows that 34-36 week-old babies had a higher rate of respiratory distress syndrome [RDS] than full-term babies. RDS at this stage increases the risk of health issues [9]. Protein binding and transport, colloid osmotic pressure maintenance, free radical scavenging, and vascular permeability change are all performed by serum albumin. Many pathophysiological pathways can lower serum albumin, resulting in a poor prognosis [10].

Although hypoalbuminemia predicts mortality in adults, its prognostic relevance in neonates is unclear. Serum albumin levels in the first day after birth can predict premature births, according to several research [11].

Our goal was to examine premature babies' blood albumin levels and respiratory distress syndrome [RDS]. In line with our results, **Ying *et al.*** [8] found that the mean serum albumin of 112 pregnant women was 33.49 ± 3.30 g/L, while the mean serum albumin of 112 neonates was 34.18 ± 3.25 g/L. In addition, the records of 208 neonates born between 23 and 41 weeks were retrospectively analyzed by **Ge *et al.*** [12]. The mean albumin concentrations and reference ranges by gestational age were calculated. Comparisons were made between group statistics. Albumin concentration in newborns increased from 2.36 g/dL in 23-24-week gestation kids to 3.43 g/dL in full term babies. The serum albumin concentration reference ranges [95% confidence limits] were 1.74-2.94 g/dL in 23-24 week-olds and 3.32-3.56 in full-term newborns. Both our and their studies show that preterm lower albumin levels.

Our investigation showed that 21.3% patient mortality. Many study criteria were studied between normal and low albumin levels. Low albumin levels lowered gestational age and birth weight [P = 0.001]. Our study found a significant positive correlation between serum albumin levels, gestational age, and birth weight. The analysis revealed that albumin concentration increased with longer gestation periods. **Jang *et al.*** [11] found no significant changes in mean albumin concentrations between the clinical and control groups for respiratory distress syndrome [clinical group, 2.36±0.42 g/dL, n=54; control group, 2.64±0.34 g/dL, n=7].

Our study established a statistically significant negative association between serum albumin level, RDS severity, and mortality rate. The lower the albumin level, the higher the RDS severity and mortality rate. **Ying *et al.*** [8] Researchers showed that after controlling for gestational age, newborn blood albumin levels, placenta previa, and delivery style independently affected late-term preterm infants' respiratory distress syndrome [RDS]. Albumin levels were unrelated to RDS severity, surfactant use, or ventilation type.

As in our study, **Jang *et al.*** [11] found that premature newborns with low serum albumin concentrations had higher rates of respiratory distress syndrome, intraventricular hemorrhage, retinopathy of prematurity, apnea, and bronchopulmonary dysplasia. After weight adjustment, preterm fetuses had the highest albumin synthesis rate, followed by term and pregnant women [13]. This finding supports **Ying *et al.*** [8]. According to research, albumin levels at birth

are connected to pregnancy length and newborn age. Albumin rises with gestational age and birth weight. In addition, prenatal corticosteroids can boost albumin levels in neonates by stimulating liver production. Ying et al. found that the control group had more prenatal corticosteroid medication and albumin than the RDS group. Albumin levels can be used to assess acute respiratory distress syndrome in adults, however newborns have less studies. In their research of 2200 babies, **Bland *et al.*** [14] found that 33 of 34 idiopathic RDS children had cord-blood total protein concentrations of 4.6 g per 100 ml or lower. They suggested that a large or mature newborn with low cord protein levels and respiratory difficulty is likely to have RDS. **Moison *et al.*** [15] found that RDS babies have less albumin than well-preterm newborns. **Jang *et al.*** [11] examined the nutritional indicators of 94 newborns hospitalized to the NICU soon after birth. For every 1 g/dL increase in albumin levels, the need for respiratory support on the first day of life decreased by 0.001 [95%CI, 0.000–0.136, P = 0.009]. They concluded that birth nutrition affects the need for respiratory support on the first day. **Park *et al.*** [16] analyzed the medical records of 564 infants who were born with an abnormally low birth weight. The researchers suggested that the lowest serum albumin level was the best predictor of newborn mortality after 7 days. Blood albumin levels can predict premature neonatal death, especially in instances with respiratory problems, according to these studies. **Ying *et al.*** [8] reported that RDS neonates had lower albumin levels than controls. Although not statistically significant, the RDS group exhibited more hypoalbuminemia.

Respiratory distress syndrome [RDS] increases capillary permeability, leaking albumin into the alveolar space [14,17]. In addition, inflammatory mediators can directly inhibit albumin gene transcription, limiting albumin synthesis in illness. Prioritizing protein synthesis increases acute response protein production. Consequently, albumin declines. The serum albumin content of 199 preterm neonates was examined within 24 hours of birth by **Torer *et al.*** [17]. The researchers found that albumin levels below the 25th percentile predicted mortality regardless of other covariates. Albumin concentration below 27.2 g/L was associated with death with 71% sensitivity and 86% specificity. **Watchko et al.** [18] examined 382,190 albumin and bilirubin levels in 164,401 infants. Newborns with serum albumin levels <2.5 g/dL had a higher mortality rate. A research of healthy people and patients with acute or chronic illnesses found that serum albumin concentration is inversely connected to mortality risk across its whole range **Nomura et al.** [19]. They suggested that albumin concentration is a sensitive indication of preclinical disease and severity and might be used to quantify risk in many clinical and research situations.

Study Limitations: We initially studied 34- and 36-week-olds and found that respiratory distress syndrome [RDS] is rare in them. Our study has a small sample size; thus we need to enlarge it to boost statistical significance. Our study also only considered the initial albumin level, not the minimum or fluctuating pattern. However, correctly pinpointing the timing of the lowest albumin level throughout disease development is difficult, making comparison less beneficial. The first-day albumin level is more important in clinical practice. Later examinations can use albumin changes in the first three days as a trustworthy marker.

Conclusion: This study concluded that, there is a significant correlation between the low serum albumin level and the gestational age and also the low birth weight.

Disclosure: None to be disclosed.

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