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Neonatal Morbidity in Late Preterm Infants Associated with Intrauterine Growth Restriction

Evelina Kreko[1*], Ermira Kola[2], Festime Sadikaj[2], Blerta Dardha[2], Eduard Tushe[1]

[1]Service of Neonatology, University Hospital of Obstetrics and Gynecology "Koço Gliozheni", Tirana, Albania; [2]Department of Pediatrics, University Hospital Center "Nene Tereza", Tirana, Albania

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***Correspondence:** Evelina Kreko. Service of Neonatology, University Hospital of Obstetrics and Gynecology "Koço Gliozheni", Tirana, Albania. E-mail: evelinakreko@yahoo.com

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Abstract

AIM: This study aims to compare the neonatal morbidity of Intrauterine growth restricted (IUGR) Late Preterm (LP) babies, to those born Late Preterm but evaluated as Appropriate for Gestational Age (AGA).

METHODS: The study is a 2-year prospective one that used data from the Neonatal Intensive Care Unit (NICU) charts of LP neonates born in our tertiary maternity hospital "Koço Gliozheni" in Tirana. Congenital anomalies and genetical syndromes are excluded. Neonatal morbidity of IUGR Late Preterm is compared to those born Late Preterm but evaluated as AGA. OR and CI, 95% is calculated.

RESULTS: Out of 336 LP babies treated in NICU, 88 resulted with IUGR and 206 AGA used as a control group. We found significantly higher morbidity in the IUGR group for hypoglycemia, polycythemia, feeding intolerance, birth asphyxia and seizures, secondary sepsis have higher morbidity but the difference is not significant. No differences were found for hyperbilirubinemia in both groups. No neonatal deaths were observed in both groups.

CONCLUSION: Our study showed that late preterm IUGR has a significantly higher risk for neonatal morbidity when compared to late preterm AGA babies.

Introduction

Late preterm birth is defined as birth between 34 0/7 weeks and 36 6/7 weeks of gestation [2].

They are the fastest-growing in the preterm group in the last decade. In the United States in 2005, LP births account for more than 70% of all preterm births [15]. The number increased from 10.9% in 1990 in 12.8% in 2007 [3]. Now it is known that in the late preterm infants, the morbidity and mortality are higher than in term neonates. In Albania, there are no official data published about the late preterm birth rate and their morbidity and mortality.

IUGR is the term used to designate a fetus that has not reached its potential growth [1]. Intrauterine growth restriction is one of the causes of late preterm delivery, and it occurs more often in late preterm infants than term ones. IUGR itself is associated with perinatal morbidities and contributes to increased metabolic disease and poor neurodevelopmental outcome.

IUGR is an important cause of high-risk pregnancies and elective preterm deliveries. IUGR is present only in a small percentage of deliveries, but an increased frequency has been observed among women who go into preterm labour followed by premature delivery. Preterm infants and with intrauterine growth restriction are vulnerable to the complications of prematurity and IUGR as well, though there are conflicting findings in the literature about late preterm IUGR and AGA morbidity [7]. It appears normal, unchanged in the IUGR group compared to AGA LP infants [5] suggesting an advantage to the stress of poor growth.

The objective of this study is to compare

neonatal morbidity between late preterm IUGR and AGA infants with the same gestational age to better understand the neonatal outcomes of these infants for both complications of IUGR and prematurity.

Methods

Our study analysed the prospectively gathered data of babies born late preterm in two years from January 2014 – December 2015 in our tertiary maternity hospital "Koço Gliozheni" in Tirana. We analysed the data from medical charts of late preterm infants born in our hospital who entered NICU and compared the morbidity of IUGR LP, with the AGA as a control group. Gestational age at delivery was determined by mothers last menstrual period and or confirmed by early ultrasound examination. The evaluation of IUGR is done by calculating 3 growth indexes (Ponderal Index, that is an index of weight-related to length; the ratio of Head Circumference to Abdominal Circumference (HC/AC); and the difference between Chest Circumference with Abdominal Circumference ≥ 3 cm) after anthropometric measurements in the respective charts. In case 2 or more indexes result not normal the baby is identified as IUGR. AGA are babies whose birth weight is above the 11th to 89th percentile of birth weight in the growth curve of Alexander et al., [14]. Pregnancies with congenital anomalies or with unknown data criteria were excluded. Delivery characteristics included gestational age at birth, route of delivery, birth, Apgar scores. Neonatal data included respiratory morbidity with, (transient tachypnea of the newborn and respiratory distress), neonatal sepsis, sepsis follow up, birth depression with Apgar score < 7 the 5th minute, seizures and metabolic disorders as hyperbilirubinemia, hypoglycemia, polycythemia, and feeding intolerance [8]. Diagnosis and treatments are done by using the NICU protocol for every disorder and the criteria outlined in Standard Textbooks of Neonatology.

Hypoglycemia: defined as a blood glucose level less than 40 mg/dl in the first 24 hours and less than 45 mg/dl after 24 hours.

Hyperbilirubinemia: Clinically visible jaundice requiring phototherapy or exchange transfusion as per hour specific total serum bilirubin nomogram (AAP chart) [19].

Sepsis :Probable sepsis :positive septic screen (two of the five parameters, total white blood count < 5000/mm^3 or > 15000/mm^3, immature to total polymorph ratio ≥ 0.2, absolute neutrophil count less than 1750/mm^3 or > 7200/mm^3, C reactive protein > 1 mg/dl, platelets < 100.000/mm^3), and proven sepsis: Isolation of pathogens from blood or Cerebrospinal fluid [17], [18].

Feeding intolerance: Inability to digest enteral feedings associated with increased gastric residuals, abdominal distension and or emesis, often leading to a disruption of the feeding plan.

Polycythemia: Hematocrit or haemoglobin concentration > 2 SD above the normal value for gestational and postnatal age associated with clinical findings resulting from hyperviscosity [16].

Statistical data were collected into the database. The difference in morbidity between two groups is compared by calculating the OR and confidence interval 95% using the Fisher exact test for statistical analysis. The result is considered significant at $p < 0.05$.

Results

During the 2-year study period, 1334 babies entered the NICU. Of those admissions, 336 or 25% were babies born late preterm i.e. 34 0/7 – 36 6/7 weeks of gestational age. 3 infants are excluded from the study as they were born with a congenital anomaly. IUGR late preterms treated in the NICU were 88 babies and AGA 206 babies.

Gestational age at delivery ranged from 34 to 36.9 weeks, with a median of 35.1 and did not differ between the two groups. Mode of delivery was 78% cesarean section in the IUGR group vs 50% in the AGA group with a significant difference. The length of stay of the newborn in the NICU differed significantly as well between the two groups (Table 1).

Table 1: The length of stay of the newborn in the NICU

	IUGR LP	AGA LP	OR	CI 95%
Median Gestational age	35.1	35.07		
SD	± 0.8	± 0.8		
Mode of delivery (CS)	78% 61	50% 97	2.5	1.49-4.3 p = 0.002
Length of NICU stay	9.45	5.5		
Median weight	1871.9 gr	2500.05 gr		
SD	± 318.5	± 382.1		

LP-late preterm; IUGR-Intrauterine growth-restricted; AGA-appropriate for gestational age.

The neonatal morbidity: we found a slight difference between the two groups as it concerns overall respiratory morbidity (Transient Tachypnea, Respiratory Distress Syndrome) where IUGR LP is less vulnerable to this morbidity compared to AGA LP. No difference was found about, hyperbilirubinemia and sepsis workup. We found a significant difference between the two groups about hypoglycemia, where IUGR LP suffer more than AGA. For polycythemia, feeding problems, birth depression APGAR score < 7, 5th minute of life, seizures and secondary sepsis IUGR LP are more vulnerable, but the difference is not significative (Table 2).

Table 2: There are no deaths registered in either group

	IUGR LP N = 88, 26%		AGA LP N = 206, 61%		OR	CI 95%	p-value
Respir. Morbidity	38	43%	115,	55%	0.6	0.37-0.99	P = 0.05
Hyperbilirubinemia	49	55%	112,	54%	1	0.8-1.2	P = 0.5
Apgar score < 7, 5Th min	6	6.8%	7,	3.3%	2.1	0.68-6.38	P = 0.19
Seizures	3	3.4%	1,	0.4%	7.2	0.74-70.5	P = 0.08
Hypoglycemia	9	10%	3,	1.4%	7.7	2-29.2	P = 0.0013
Polycythemia	3	3.4%	1,	0.4%	7.2	0.74-70.5	P = 0.08
Feeding problems	2	2.2%	3,	1.4%	1.57	0.26-9.6	p=0.6
Neonatal sepsis	3,	3.4%	2,	0.9%	3.6	0.6-21.9	P = 0.16
Sepsis follow up	6,	6.8%	44,	21%	0.27	0.11-0.66	P = 0.002

LP-late preterm; IUGR-Intrauterine growth-restricted; AGA-appropriate for gestational age.

Discussion

Late preterm births are an increasing problem in the world nowadays. They account for 70% of all preterm births. They experience a higher incidence of neonatal morbidity and mortality compared to term neonates [7]. On the other hand, IUGR is a problem that complicates their prematurity situation, contributing to an increased morbidity and mortality observed among late preterms.

Although there is a lack of studies about IUGR late preterms, as in other studies, we found a slight difference for respiratory morbidity, probably this a contribution to their inutero stress that leads to an early pulmonary maturity and the high incidence of CS for AGA LP (50%). We did not observe severe complications as Necrotizing Enterocolitis NEC, Pulmonary Hemorrhage, and death perhaps because these are rare findings in this gestational group [15].

Problems like hypoglycemia, polycythemia and feeding intolerance are common in the IUGR preterm group, and neonatal sepsis is found more in this group rather than AGA because we did not exclude women with preterm premature rupture of membranes from our study [9]. As found in other studies Laptook and Jackson [20], hypoglycemia has an elevated incidence in late preterm infants as a result of deficient neoglycogenesis, hepatic glycogenolysis and hormonal irregularities. Finding seizures more often in IUGR group is linked to metabolic problems like hypoglycemia, but birth asphyxia as well, which is linked to the emergency of Cesarian Section interventions in IUGR Late Preterms in our hospital as a reference hospital in Albania.

Our study is focused on the early morbidity of late preterm infants, and we don't have evidence about their long-term consequences in later life.

In conclusion, IUGR late preterm infants have higher morbidity compared to AGA LP, and IUGR is a major cause for late preterm delivery and CS delivery. A better understanding and evaluation of their problems is very important [12], [13].

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