EPIDEMIOLOGICAL ASPECTS OF THE LATE PRETERM VERSUS TERM BIRTH

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Keywords: *late preterm infant, premature birth, term birth, case-control study*

Abstract: *The rate of late premature births is increasing worldwide and in Romania. Purpose: To identify the particular epidemiological aspects associated with preterm compared to term birth. Materials and methods: The retrospective, case-control study included late preterm infants and term infants matched for birth weight (± 100 g). Results: The study group included 345 late preterm and 345 term neonates. Comparative analysis of the data of the two groups revealed: mothers of late preterm infants had a significantly higher mean age, higher number of previous pregnancies, originated more frequently from urban areas and had higher education background. Significant differences were also found as regards multiple pregnancies, pregnancies obtained by assisted reproductive techniques, and delivery circumstances. Conclusion: Late preterm birth is associated, in our study, with advanced maternal age, multiple pregnancy, use of assisted reproductive techniques, premature rupture of the amniotic membranes, and birth by caesarean section, consistent with data from the literature.*

INTRODUCTION

Until recently, no special attention was given by specialists to preterm infants with gestational ages of 34 0/7 -36 6/7 weeks, a category of neonates named "large preterm infants" or "moderate premature infants" or, more commonly, "near-term infants", but studies published in the literature after 2000 showed that these infants are, despite their physical appearance similar to term infants, particularly vulnerable since physically and functionally they are behaving as preterm infants. Already in 2005, the experts (1) decided to change the name of this category of newborns recommending naming them "late preterm" in order to underline the fact that they belong to the preterm infants' group. Also, the new terminology cautions about the increased risk of the late preterm infants for complications due to the immaturity of the organs and systems.

The continuously increasing rate of late prematurity in the entire world reveals more and more the problems and risks associated to late preterm birth on short and long term, suggesting that these infants may need special attention and care and even long term follow-up. Late preterm infants are representing the greatest proportion of the preterm infants - 63.2-79% of all preterm deliveries (2-5) and about 6% of all births.(2) Most of these late preterm infants are born in regional centers and industrialized countries and their number continuously increases mostly because of deliveries induced for maternal or fetal reasons.(6) In Romania, there are no specific data referring to late preterm births but, in 2010, preterm infants born at 32-36 weeks gestation comprised 6.4% of all preterm birth, a proportion similar with those reported by other countries.(7,8)

Multiple circumstances are responsible for the increasing number of late preterm deliveries: increased number of pregnancies interrupted for medical reasons - maternal and/or fetal; increased pregnancies obtained using assisted reproductive techniques - many of them being multiple pregnancies; more accurate identification of at risk pregnancies due to improved pregnancy monitoring; better diagnosis of conditions or complications with risk for preterm delivery - e.g. thrombophilia; increased number of deliveries by elective C-sections without clear maternal or fetal indication; increased number of C-sections performed on demand of the patients; errors in gestational age evaluation; increased maternal age, also associating more prenatal and pregnancy pathology.(2,6,9,10) The known circumstances of the spontaneous preterm birth are additional causes of the late preterm birth: spontaneous preterm rupture of the amniotic membranes, chorioamnionitis, multiple pregnancy, maternal hemorrhages, placental abruption, infections, pregnancy hypertension, eclampsia, previous and gestational diabetes, maternal age under 20 years or over 35 years, lack of prenatal care, smoking, previous preterm birth, reduced interval between pregnancies, multiparous women.(2,6,10,11)

PURPOSE

The purpose of the study was to identify the incidence and particular epidemiological aspects associated with preterm compared to term birth.

MATERIALS AND METHODS

The study is retrospective, case-control and included late preterm babies (34 0/7 - 36 6/7 weeks) admitted to Sibiu Maternity Hospital, a regional unit (level III), between 01.01.2013-30.06.2015 for whom it was possible to identify corresponding term newborns with ± 100 g birth weight compared to their pair late preterm infant. Exclusion criteria: death and late preterm infants for whom a pair term newborn with ± 100g birth weight could not be identified. Epidemiological information was gathered for the neonatal charts: gestational age, birth weight, ponderal index, maternal age, residence (urban or rural), maternal obstetrical history (number of pregnancies and deliveries), maternal level of education (categorized as no studies, elementary, medium or superior studies), follow-up of the current pregnancy (yes or not), type of pregnancy (singleton versus twin and natural versus

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Article received on 06.10.2015 and accepted for publication on 27.11.2015
ACTA MEDICA TRANSILVANICA December 2015;20(4):1-4

obtained using assisted reproductive techniques), details about labour (present or not, how it started - with uterine contractions or rupture of the amniotic membranes), delivery mode (vaginal, Caesarean section, or forceps delivery), indications for Caesarean section, presentation of the infant. The neonates included in the study were separated into two groups: late preterm infants and term infants (matched by birth weight).

Statistical analysis was performed using SPSS 10.0 for Windows, p was considered statistically significant at values below 0.05 (confidence interval - CI - 95%). Data are reported as values, mean values, standard deviations (SD), and percentages. Independent T-test was used to compare the scale variables, Fischer's exact test or chi square test were used (where appropriate) for the analysis of the categorial variables. We also calculated odds ratio, also using 95% confidence intervals.

RESULTS

During the study period, a total of 433 late preterm infants were admitted in the Sibiu Maternity Hospital, inborn or submitted from lower level hospital in the ascribed territory according to the regionalization of the mother and infant care in Romania. A total number of 6 558 newborns were born or admitted in our regional center during the study period. Of these infants, 433 were late preterm infants, representing 6.6 % of all admitted neonates.

The mean birth weight of the initial study group (433 late preterm neonates) was 2 373.8 ± 466.2 g (1 160-4 740 g) and the mean gestational age was 35.4 ± 0.75 weeks. Of these infants, 88 were excluded as we were not able to identify a matched term infant based on birth weight criteria (a birth weight ± 100g compared to the pair late preterm infant). Only one of the excluded late preterm infants had a birth weight higher than 2 240g (the one having 4 740g), all others had birth weights less than 2 240g.

Table no. 1. Baseline characteristics of the study groups

	LPI[2] vs T[3]	Mean ± SD	p
BW (g)	LPI	2493.7 ± 407.0	0.457
	T	2516.5 ± 397.9	
GA (weeks)	LPI	35.5 ± 0.7	0.000
	T	39.1 ± 0.9	
PI[1]	LPI	1.75 ± 0.76	0.957
	T	1.75 ± 0.68	

[1]Ponderal index; [2]LPI - late preterm infants; [3]T - term infants

Table no. 2. Maternal obstetrical history, residence, follow-up of the current pregnancy and maternal level of education

		LPI[1] vs T[2]	Mean ± SD/No (%)	p/OR [95%CI]
Maternal age (years)		LPI	28.3 ± 7.1	0.000
		T	25.9 ± 6.9	
Total number of pregnancies		LPI	2.7 ± 2.1	0.206
		T	2.5 ± 1.9	
Number of deliveries		LPI	2.1 ± 1.5	0.863
		T	2.1 ± 1.6	
Urban residence		LPI	180 (52.2)	0.005 OR 0.81 [0.69-0.94]
		T	144 (41.6)	
Follow-up of the pregnancy (yes)		LPI	280 (82.4)	0.000 OR 1.45 [1.17-1.80]
		T	240 (70.2)	
Maternal education	No studies	LPI	18 (5.3)	0.000
		T	31 (9.0)	
	Elementary education[3]	LPI	120 (35.1)	
		T	142 (41.4)	
	Medium level of education[4]	LPI	116 (33.9)	
		T	118 (34.4)	
	Superior education[5]	LPI	88 (25.7)	
		T	52 (15.2)	

[1]LPI - late preterm infants; [2]T - term infants; [3]Elementary education - first four grades; [4]Medium level of education - 4-12 grades of professional school graduates; [5]Superior education - university degree

The baseline characteristics of the two study groups - late preterm newborns and term newborns – are presented in table no. 1. As expected by patients' selection, the gestational age was significantly lower in the late preterm infants' group.

Maternal obstetrical history: number of pregnancies, number of deliveries, maternal age and residence, as well as information about current pregnancy monitoring and maternal education for both study groups are presented in table no. 2. When collecting the data regarding the follow-up of the current pregnancy, we assumed that the pregnancy was monitored if the mother was seen at least one time during pregnancy by an obstetrician or the family doctor, either as an outpatient or during a hospital admission.

The data regarding the type of pregnancy - singleton or multiple pregnancy and naturally occurring pregnancy versus pregnancy obtained using assisted reproductive techniques - are figured in table no. 3. During the study period, we did not register any neonate from pregnancies with more than two fetuses.

Table no. 3. Type of the pregnancies in the study groups

	LPI[2] vs T[3]	No/%	p/OR [95%CI]
Twin pregnancy	LPI	71 (20.6)	0.000 OR 0.67 [0.57-0.78]
	T	31 (9.0)	
Pregnancy after ART[1]	LPI	16 (4.6)	0.030 OR 0.67 [0.54-0.88]
	T	6 (1.7)	

[1]ART - assisted reproductive techniques; [2]LPI - late preterm infants; [3]T - term infants

Table no. 4 figures the collected information regarding labour: if present or not at delivery (indicating indirectly induced deliveries) and if the labour started with painful uterine contractions or with rupture of the amniotic membranes, and delivery: presentation of the fetus at birth and delivery mode: vaginal, Caesarean section, or instrumental delivery. Forceps delivery was performed in 4 infants: 2 in both study groups. Vacuum delivery is not used in our hospital.

Table no. 4. Labour and delivery information

		LPI[3] vs T[4]	No/(%)	p/OR [95%CI]
Labour		LPI	305 (88.7)	0.020 OR 1.32 [1.02-1.70]
		T	281 (82.4)	
Rupture of membranes[1]		LPI	185 (61.6)	0.000 OR 2.34 [1.76-2.65]
		T	77 (27.2)	
Delivery	Vaginal	LPI	224 (64.9)	0.013
		T	255 (73.9)	
	C-section	LPI	119 (34.5)	
		T	88 (25.5)	
	Forceps	LPI	2 (0.6)	
		T	2 (0.6)	
Presentation	Cranial	LPI	315 (91.3)	0.510
		T	311 (90.1)	
	Breech	LPI	27 (7.8)	
		T	30 (8.7)	
	Transverse	LPI	3 (0.9)	
		T	3 (0.9)	
	Other[2]	LPI	0 (0)	
		T	1 (0.3)	

[1]Rupture of the amniotic membranes as he beginning of labour; [2]Other presentations: facial, 1 case; [3]LPI - late preterm infant; [4]T - term infant

Multiple indications for C-section, maternal, fetal, placental, or labour related, were found after studying the

neonatal charts and all of these are presented, comparatively for late preterm infants and term infants, in table no. 5. In same cases - 13 of all studied cases, 11 late preterm deliveries and 2 term deliveries - no clear indication could be identified.

Table no. 5. Indications for Caesarean section deliveries

	LPI (no/%)	T (no/%)
Former C section	21 (18.4)	21 (23.9)
Twin pregnancy	21 (18.4)	11 (12.5)
No progression of labour	15 (13.2)	9 (10.2)
Maternal thrombophylia	12 (10.5)	3 (3.4)
No clear indication	11 (9.6)	2 (2.3)
Maternal hypertension	8 (7.0)	6 (6.5)
Fetal distress	4 (3.5)	9 (10.2)
Abnormal presentation	4 (3.5)	6 (6.8)
Maternal hepatitis B	3 (2.6)	2 (2.3)
Placental anomalies	3 (2.8)	2 (2.3)
Advanced maternal age	2 (1.8)	5 (5.7)
Maternal spinal abnormalities	2 (1.8)	1 (1.1)
Ophftalmological indication	2 (1.8)	3 (3.4)
Hydronephrosis with stenting	1 (0.9)	2 (2.3)
Maternal genital herpes	1 (0.9)	-
Maternal respiratory failure	1 (0.9)	-
Audiological indication	1 (0.9)	-
Maternal hemiparesis	1 (0.9)	-
Maternal depression	1 (0.9)	-
Maternal short stature	-	2 (2.3)
Maternal thrombopenia	-	2 (2.3)
Myomectomy	-	1 (1.1)

DISCUSSIONS

The incidence of late preterm delivery is continuously increasing in the latest years and, therefore, more and more, the specialists are recognizing that this category of preterm infants has an increased risk for postnatal morbidities and mortality. Immaturity of the organs and systems and insufficiently mature functionality of the organs are the main reasons for the increased risk for neonatal complications, as difficult adaptation to extrauterine life, deficient thermoregulation, perinatal hypoxia, increased need for resuscitation at birth, respiratory conditions, problems with cardiovascular adaptation, neonatal sepsis, electrolyte and metabolic disturbances, anemia, feeding difficulties, jaundice, necrotizing enterocolitis, cerebral hemorrhage.(2,6,11-16) Late preterm infants; morbidity rate is 3-9 times higher compared to term neonates (6,9,11), contributing significantly to the increased mortality rate - 3 times higher compared to term infants.(11)

Worldwide, the late preterm infants are representing the largest proportion of the preterm infants - 63.2-79% (2-5) - and about 6% of the all births.(2) During the study period, in our regional center, a total of 433 late preterm infants were admitted, representing 6.6 % of all admitted neonates. A slightly higher percentage of late preterm infants was registered in our unit, explained by the fact that our unit is a regional one, admitting newborns with various conditions from lower level units, according to Romanian regionalization criteria. An increased rate of late preterm infants in regional centers is cited by other authors.(6,15,17)

The baseline characteristics of the study groups (figured in table no. 1) confirms that the birth weight and ponderal index of the study groups are similar as the patients were matched based on birth weight in order to exclude birth weight as a possible confounding factor.

Same as our study, many studies in the recent years have identified increased maternal age as a risk factor for late preterm delivery.(1,2,6,10,18) An increased number of pregnancies and deliveries in the maternal obstetrical history are cited by some authors as risk factors for preterm delivery but not specifically for late preterm birth.(2,6) Similarly, the comparison of late preterm and term infants' data did not revealed any significant difference between the number of pregnancies (parity) and deliveries, even though mothers who delivered late preterm infants had a higher mean number of pregnancies and deliveries (table no. 2).

Significantly more mothers that gave birth to late preterm infants had an urban residence and even though we were not able to find references in the literature. These can be linked with significantly more often monitored pregnancies and higher degree of education observed in the mothers who delivered late preterm infants compared to those who delivered at term. Term deliveries occurred more often in mothers living in rural area, with no prenatal care, and lower level of education (table no. 2). These data are partially consistent with data in the literature that underline that mothers delivering preterm infants are more unlikely to benefit of prenatal care.(6,19) On the other hand, living in an urban area and having a higher education level increases significantly the likelihood for an improved prenatal care, as suggested by our data (table no. 2). We did not analyze the prenatal conditions and the conditions associated to the current pregnancy, but we cannot exclude that another reason for the better follow-up of the pregnancy may have been the co-existence of such conditions, as suggested by many authors.(2,6,9,10,20,21) This theory is, at least partially, sustained by the information collected regarding the C-section indications (presented in table no. 5), more often related to maternal conditions in the late preterm infants group compared to the term one.

As underlined by studies in the recent years, an important proportion of the increased rate of late preterm delivery is due to the increased number of multiple pregnancies seen in this category of newborns, an issue with strong correlation to the continuously increasing number of pregnancies after assisted reproductive techniques.(6,9,10) These pregnancies are also occurring usually in mothers with advanced age and higher degree of education, are better monitored and more likely to be terminated by C-section due to maternal and/or fetal indications.(1,2,6,9,10) Our data shows the late preterm births occurred significantly more often from twin pregnancies and from pregnancies obtained after assisted reproductive techniques (table no. 3).

Our results are demonstrating that a higher proportion of late preterm births occurred after the onset of labour and a significantly higher percentage of late preterm births occurred after preterm rupture of the amniotic membranes at the onset of the labour (p 0.000), the risk for late preterm delivery when labour starts with rupture of the membranes varying between 1.76 and 2.65 (table no. 4). These results are also consistent with data in the literature.(10,11,22) Also, significantly more late preterm infants were delivered by C-section compared to term infants and presentation at birth was not a reason for this difference as shown in table no. 4. A significantly increased rate of late preterm infants delivered by C-section is also reported by data in the literature (2,6,9,23,24) and authors are linking this to improved obstetrical care of the pregnancies allowing to better detect maternal or fetal conditions imposing the termination of pregnancy in maternal or fetal best interest.(2,9,23)

Various fetal, placental, and maternal conditions were identified as indications for C-section delivery both in term and late preterm infants in the study groups as presented in table no. 5. Analyzing this data, we saw that C-section had more maternal indications in the late preterm infants' group while fetal and placental indications were more frequently seen in term infants. Data is consistent with the other information obtained in this

study: mothers delivering late preterm infants had a better prenatal care, advanced maternal age, a higher proportion of twin pregnancies and pregnancies obtained after assisted reproductive techniques, situations with increased risk for C-section delivery. An interesting observation was the fact that a higher proportion of late preterm infants was born by C-section performed for no clear indication compared to term infants (9.6 versus 2.3%). We have no explanation for this finding but other authors are also citing this situation quite frequently (23) and explain that these situations may be elective interventions requested by the mother.

CONCLUSIONS

Consistent with data in the literature, late preterm birth was associated, in our study, with advanced maternal age, higher level of maternal education, multiple pregnancy, use of assisted reproductive techniques, better monitoring of the pregnancy, premature rupture of the amniotic membranes as onset of the labour, and delivery by caesarean section.

Identification of the epidemiological factors associated with late preterm delivery may help specialists to identify interventions to reduce the rate of late preterm delivery as studies are continuously demonstrating that late preterm delivery is associated with increased morbidity and mortality, therefore with increased emotional, social, medical, and financial costs.

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