BREASTFEEDING LATE PRETERM INFANTS - CAN WE DO BETTER?

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Abstract: *Lower rates of breastfeeding are significant contributors to neonatal morbidity both on short and long term in late preterm infants (LPI). The authors evaluated the factors associated with lower rates of breastfeeding at discharge in LPI. Materials and methods: We analyzed maternal and neonatal factors that may affect breastfeeding rates in the LPI born 2013- 2015. Maternal and neonatal data were comparatively analyzed between exclusively breastfed, partially breastfed, and formula fed LPI. Results: The study group comprised 60 exclusively breastfed, 335 partially breastfed, and 40 formula fed infants at discharge. Compared to the infants exclusively breastfed, the infants fed exclusively with formula had significantly lower gestational age, birth weight, Apgar scores at 1 minute, higher incidence of maternal fetal-infections, and increased hospitalization length ($p<0.05$). Also, their mothers were more often multiparous, resident in rural areas, without prenatal care, and less educated ($p<0.05$). Compared to infants partially breastfed, the infants exclusively breastfed had lower Apgar scores, increased rates of anemia at birth, and longer admissions in neonatal intensive care unit ($p<0.05$). Conclusions: Identification of factors that affect breastfeeding rates may help professionals to implement effective strategies for breastfeeding success in LPI infants.*

INTRODUCTION

Late preterm infants (LPI) - born between 34 weeks 0 days and 36 weeks 6 days (1) - are representing the largest proportion of preterm infants - between 55 (2) and 79% (3) of all preterm births. Studies published after 2000s have shown that despite their general resemblance to term infants, late preterm infants have increased risks for neonatal and postneonatal morbidity (4-12) and mortality (6,8,11-18) compared to term infants. Therefore, in 2005, experts from Eunice Shriver National Institute of Child Health and Human Development called for abandonment of the term "near-term" for describing these preterm infants, proposing the term "late preterm" as it better warns about risks and vulnerability associated with late preterm delivery and avoids treating these infants as almost mature infants.(1)

In newborns, gestational age (GA) is the most important predictor of short and long term health. (19) The last six gestational weeks up to term are extremely important as they are demonstrated as a critical developmental period for the brain and lung.(3,10) Physiological and metabolic immaturity is responsible for all the adaptation difficulties to extrauterine life - respiratory, neurological, metabolic, thermal, renal, etc. - despite the general look of relatively mature infants.(2,13,20-22) Immaturity of all organs and systems and increased incidence of neonatal pathology may negatively influence the long term outcome and, in the recent years, studies are reporting and increased risk for growth deficiencies, neurological, cognitive, and sensorial impairment, behaviour disturbances, and medical conditions (respiratory infections, asthma, diabetes) in former LPI.(4,6,19,22-27)

Breastfeeding and breast milk has numerous advantages - protection against gastrointestinal, respiratory and ear infections, allergy, malnutrition, obesity, stimulation of motor and cognitive development, prevention against sudden infant death syndrome, psychological and relational benefits, etc. (28-34) - ensuring an optimal nutritive intake for an appropriate growth and development.(28,32,35,36) The unique character of breast milk is due to its content in nucleotides, oligosaccharides, immunoglobulins, immune cells, antioxidants, cytokines, growth factors, byoactive proteins, enzymes, and hormones that are never found in formula.(29,30,33,37,38) In preterm infants, breastfeeding is also improving thermoregulation, glycemic control, breathing and cardiac rhythm regulation, stimulates postnatal intestinal growth, protects against oxidative stress.(39-44) Therefore, breastfeeding is considered the optimal feeding option also in preterm infants (29,34,38) while breast milk fortification and supplementation are recommended in preterm infants with increased nutritional and energy needs.(34)

Breastfeeding difficulties are frequently reported in LPI compared to term infants (11,13,20,45-47) due to immaturity of the oral-motor reflexes, difficulties in coordinating sucking with deglutition and breathing, hypotonia, immaturity of state control, and perinatal associated comorbidities.(11,13,17,38,44,46,48-54) Nutritional needs of the LPI are increased compared to those of the term infant and breastfeeding is even more important in LPI than in term infants.(44,51,55,56) Studies have consistently reported in LPI an increased risk for lack of breastfeeding initiation and shorter duration of breastfeeding.(8,17,46,50,57-59) Delayed lactogenesis II, due either to maternal conditions or treatments during labor either to prematurity itself, is an important factor contributing to breastfeeding difficulties in LPI.(17,51,60-62)
Also, in LPI, breastfeeding difficulties are important risk factors for hypoglycemia (11) and severe jaundice (7,63), conditions imposing formula or parenteral nutritional supplementation

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and/or separation of mother and child for therapy and consequently impeding successful breastfeeding.(17,44,48,49,51) In fact, breastfeeding difficulties and severe jaundice are the most frequent reasons for readmission of LPI (14,64-66) while breastfeeding and exclusive breastfeeding is one of the most important risk factors for LPI readmission after discharge from maternity compared to term infants and LPI infants fed with formula.(8,17,67,68)

Late preterm delivery rate is continuously increasing worldwide due to multiple factors: increased rate of multiple pregnancies, increased incidence of pregnancies associated with health conditions since advanced maternal age is also rising, increased preference of both professionals and mothers for elective induced labor and cesarean section, avoiding obstetric malpractice litigation etc.(69,70) Experts are talking now about the paradox of breastfeeding association with increased morbidity in LPI (17) searching for guidelines for feeding these infants that would improve their short and long term outcome.

PURPOSE

Faced also with these realities in the latest years, we aimed, in this study, to search for risk factors for breastfeeding difficulties and lower rates of breastfeeding in our population of LPI as a first step of a planned intervention for improvement of breastfeeding promotion and support for mothers of newborns at risk, including LPI.

MATERIALS AND METHODS

The retrospective study aimed to analyze maternal and neonatal factors that may affect partial and exclusive breastfeeding rates in the LPI (34^0-36^6 weeks gestation) born between January 1, 2013 and December 31, 2015 in the maternity of the Clinical County Emergency Hospital Sibiu, a level III regional unit. The protocol of our unit imposes initiation of breastfeeding and first related counselling in the first 30 minutes up to 2 hours of life whenever the neonatal and maternal condition allows it. All infants are cared in rooming-in if both mother and newborn don't need special care in intensive care units. A separation of no more than 24 hours occurs in the case of cesarean section delivery after the first breastfeeding due to institutional particularities and lack of sufficient nurses. No pacifiers are offered in the unit. Freshly expressed breast milk is preferred for nutritional supplementation instead of formula and is administered by spoon or cup. Bottle is offered only when mother leaves the hospital or in special medical situations. Gavage feeding is used only in the neonatal intensive care unit (NICU) for feeding sick newborns, irrespective of GA. A psychologist trained as consultant in lactation is available during week days for all mothers that need supplementary advice and guidance for breastfeeding. Maternal and neonatal characteristics, epidemiological, and clinical data were extracted from neonatal charts and comparatively analyzed between exclusively breastfed LPI and those partially breastfed and formula fed LPI. In the absence of maternal and/or neonatal conditions, during the study period newborns were discharged after 48-72 hours after vaginal delivery and after 72-96 hours after cesarean section. Statistical analysis was performed using SPSS for Windows 10.0; p was considered statistically significant if < 0.05.

RESULTS

During the study period a total number of 7953 live births were counted in our unit, of whom 435 were LPI (5.47%) - 60 exclusively breastfed (13.8%), 335 partially breastfed (77.0%), and 40 formula fed infants (9.2%) at discharge.

The LPI exclusively breastfed were compared both to those partially breastfed and to those fed only with formula. Since prenatal characteristics and delivery may influence decision to breastfeed and breastfeeding rates we first compared the maternal baseline characteristics of the study groups. Significantly more LPI partially breastfed and fed only with formula were born by mothers living in rural areas ($p<0.05$) (Table no. 1). Also, mothers of PLI exclusively fed with formula more often lacked prenatal care (52.5% compared to 20% in the group exclusively breastfeeding and 16.2% in the group partially breastfeeding; $p=0.001$) and had significantly increased number of pregnancies and deliveries (multiparous mothers) (table no. 1). No significant differences were found as regards maternal age (although slightly decreased), prenatal pathology, multiple pregnancies, type of pregnancy (naturally occurring versus assisted reproductive techniques), and mode of delivery (vaginal delivery versus cesarean section, planned cesarean section versus cesarean section after beginning of labor) (table no. 1)

No difference between LPI exclusively breastfed and those partially breastfed as regards was found as regards GA and BW ($p>0.05$) but LPI fed exclusively with formula were had significantly lower GA and BW compared to exclusively breastfed LPI ($p<0.05$) (table no. 2). No gender differences were found between study groups (table no. 2). More exclusively formula fed LPI needed resuscitation at birth (2.5% compared to 16.% in exclusively breastfed PLI and 11.9% in partially breastfed LPI) and their mean Apgar score at 1 minute was significantly lower compared to the other two LPI groups ($p<0.05$) (table no. 2). This group had also a significantly increased rate of maternal-fetal infections (22.5% versus 6.7 and 6.6%, respectively; $p<0.05$) and significantly increased total length of hospitalization ($p<0.05$) (table no. 2).

Table no. 1. Maternal baseline characteristics

	BF[1]		*p*[2]	PBF[3]		F[4]		*P*[5]
	No.	Value		No.	Value	No.	Value	
Rural residence (no/%)	60	22 (36.7)	0.033	335	173 (51.6)	40	24 (60)	0.022
Twins (no/%)	60	12 (20)	0.195	335	94 (28.1)	40	10 (25)	0.559
ART pregnancies[5] (no/%)	60	2 (3.3)	0.413	335	30 (6)	40	2 (5)	0.681
No prenatal care (no/%)	60	12 (20)	0.465	335	54 (16.2)	40	21 (52.5)	0.001
Maternal age (mean±SD)	60	28.5±7.0	0.749	335	28.2±7.0	40	27.7±7.8	0.613
No of pregnancies (mean±SD)	60	2.3±1.7	0.289	335	2.6±1.9	40	4.1±2.9	0.001
No of deliveries (mean±SD)	60	2.0±1.4	0.816	335	2.1±1.4	40	3.4±2.4	0.001
Antenatal pathology (no/%)	60	7 (11.7)	0.779	335	35 (10.4)	40	4 (10)	0.797
Pathology during pregnancy	60	18 (30)	0.168	335	132 (39.4)	40	11 (27.5)	0.790
C-section (no/%)	60	22 (36.7)	0.766	335	112 (33.4)	40	19 (47.5)	0.285
Labor prior C-section (no/%)	60	7 (11.7)	0.735	333	34 (10.2)	40	10 (25)	0.084

Legend: [1]BF - breastfeeding; [2]*p* - comparison between BF and PBF; [3]PBF - partial breastfeeding; [4]F - formula; [5]*p* - comparison between BF and F

Table no. 2. Neonatal baseline characteristics and neonatal conditions

	BF[1]		p[2]	PBF[3]		F[4]		P[5]
	No.	Value		No.	Value	No.	Value	
GA (mean±SD)(weeks)	60	35.4±0.8	0.922	335	35.4±0.7	40	35.1±0.7	0.043
BW (mean±SD(g)	60	2433.0±486.8	0.558	335	2392.1±485.0	40	2091.7±347.7	0.000
PI[5] (mean±SD)	60	1.72±0.78	0.632	335	1.77±0.73	40	1.92±0.54	0.152
Male gender (no/%)	60	31 (51.7)	0.769	335	180 (53.7)	40	25 (62.5)	0.290
Apgar score at 1 min (mean±SD)	60	8.4±1.2	0.156	335	8.6±1.0	40	7.8±1.5	0.029
Apgar score at 5 min (mean±SD)	60	8.9±1.2	0.005	335	9.3±0.8	40	8.9±0.8	1
Resuscitation at birth (no/%)	60	10 (16.7)	0.312	335	40 (11.9)	40	11(27.5)	0.196
RDS[6] (no/%)	60	18 (30)	0.516	335	87 (26)	40	13 (32.5)	0.794
Maternal-fetal infections (no/%)	60	4 (6.7)	0.977	335	22 (6.6)	40	9 (22.5)	0.021
Jaundice[7] (no/%)	60	47 (79.7)	0.711	335	258 (77.5)	40	31 (81.6)	0.819
Weight loss (mean±SD) (g)	60	132.8±54.6	0.235	335	142.3±58.6	40	113.6±52.3	0.083
Anemia at birth (no/%)	51	20 (39.2)	0.009	284	63 (22.2)	39	22 (30.8)	0.413
Hemoglobin (mean±SD) (g)	51	15.8±2.4	0.012	284	16.7±2.3	39	16.2±2.8	0.495
NICU admission (no/%)	60	29 (48.3)	0.034	335	114 (34)	40	27 (67.5)	0.059
NICU hospitalization (mean±SD) (days)	60	7.5±10.4	0.012	335	4.4±3.4	40	6.8±9.5	0.803
Hospitalization length (mean±SD) (days)	60	14.7±14.2	0.239	335	13.1±9.2	40	24.2±15.4	0.002

Legend: [1]BF - breastfeeding; [2]*p* - comparison between BF and PBF; [3]PBF - partial breastfeeding; [4]F - formula; [5]*p* - comparison between BF and F; [6]RDS - respiratory distress syndrome; [7]Jaundice needing phototherapy, except pathological jaundice

No significant differences were found between study groups when comparing the rates of respiratory distress syndrome and jaundice needing phototherapy. Interestingly, PLI exclusively breastfed had significantly increased rates of birth anemia and mean lower hemoglobin levels at birth, were more often admitted to intensive neonatal care unit (NICU), and had a longer stay in NICU compared to those partially breastfed LPI ($p<0.05$) (table no. 2).

DISCUSSIONS

Immaturity of the oral-motor reflexes, difficulties in coordinating sucking with deglutition and breathing, hypotonia, dependency of intestinal motility on neurological maturation, transient interruption of intestinal maturation at birth due to preterm delivery, immaturity of status regulation, and perinatal associated comorbidities are well-known important factors contributing to increased rates of breastfeeding difficulties reported in LPI compared to term infants.(11,13,17,38,44,46,48-54) Delayed lactogenesis II, due either to maternal conditions or treatments during labor either to prematurity itself, is also an important factor contributing to breastfeeding difficulties in LPI.(17,44,51,60-62) Inefficient sucking reflex, attachment difficulties, neonatal fatigue, longer sleep duration, behavioral difficulties, need for nutritional supplements, more intense jaundice are additional factors contributing to decreased breastfeeding rates in LPI.(13,39,44,71) All these factors are responsible for the increased risk for lack of breastfeeding initiation, breastfeeding difficulties, and shorter duration of breastfeeding in LPI.(17,44,46,50,51,57,58)

We aimed to identify maternal and neonatal risk factors for breastfeeding difficulties and for lower rates of breastfeeding in LPI as the first step of a planned intervention for improvement of breastfeeding promotion and support in newborns at risk, including LPI. We therefore compared the maternal and neonatal characteristics and perinatal data of three groups of LPI born during a period of two years: exclusively breastfed (60 infants), partially breastfed (335 infants), and exclusively fed with formula (40 infants). Our data regarding the rates of exclusive and partial breastfeeding, and exclusive formula feeding at discharge are similar to the few data reported in the literature. The study performed by Lee and Jang (72) in 106 LPI reported that 77.4 of them were breastfed during hospitalization, while only 5.7% were exclusively breastfed and 67% were partially breastfed at the end of the first week of life. Others reported 59-70% breastfeeding rates lower in LPI compared to term infants.(8,46,59) No data are available for Romania except the study published by Stoicescu and Ciochina (73) in 2011, a multicentric study of 13770 newborns aged 22-43 weeks gestation, 11.4% of them preterm infants. The study reported a breastfeeding rate at discharge of 89%, decreasing with decreased birth weight (BW).

Maternal age, education, prenatal care, prenatal pathology, and delivery mode are known all factors influencing breastfeeding rates.(12,17,44,51,68,74-79) Compared to mother of LPI partially breastfed, mothers of exclusively breastfed infants were more often living in urban areas ($p<0.05$), had lower rates of complications during pregnancy but these differences were not significant ($p>0.05$). This is in contradiction with data reported by Romania in 2005 to World Health Organization (80): no differences were reported between urban and rural areas as regards early initiation of breastfeeding (10.5 versus 13.5%), any breastfeeding (88.0 versus 88.5%), and exclusive breastfeeding at 6 months (14.5 versus 17.3%). Complications during pregnancy - as obesity, cesarean delivery, pregnancy-induced hypertension, diabetes, drugs administered during labor - may delay prolactin release and initiation of lactogenesis II phase, according to data in the literature (17,44,51,54,60-62) explaining an increased rate of breastfeeding failure in such situations.

No other differences were found between these two groups - exclusive versus partial breastfeeding - as regards maternal age (although slightly increased in exclusively breastfeeding mothers), type of pregnancy (singleton versus multiple pregnancy, natural versus assisted reproductive techniques), parity, number of deliveries, prenatal pathology, type of delivery (vaginal versus cesarean section, elective cesarean section versus cesarean section after labour onset). Studies are suggesting that advanced maternal age is associated with increased rates of breastfeeding and lower maternal age is associated with decreased breastfeeding rates.(74,79,81-83) According to these data, we can conclude most probably unexplored maternal variables - such as educational level, attendance to prenatal courses, prenatal intention to breastfeed, previous positive or negative breastfeeding experiences, anxiety, stress, marital status, peer or family support, maternal self-confidence in her breastfeeding abilities, financial familial

resources, cultural norms and values, personal believes, etc. - may have influence the mothers in their decision to use or not supplemental formula. Such information, although known to influence breastfeeding decision in term infants (12,17,77-79,84) is not available in the maternal and neonatal charts and evaluation of these factors was not targeted by our study.

Mothers of LPI exclusively fed with formula were living more often in rural areas (60% versus 36.7%; p=0.022), lacked more often prenatal care (52.5% versus 20%; p=0.001), had an lower mean maternal age (p>0.05), and had more pregnancies and deliveries in their obstetric history (p<0.05) compared to those exclusively breastfed LPI (table no. 1). Residence in rural areas is the only result of this comparison conflicting current evidence in Romania, as stated above.(73) Lack of prenatal care and prenatal education are reported as breastfeeding barriers, higher educational level and attendance to prenatal courses being associated with increased rates of breastfeeding in term infants (77,79,85-89) and LPI.(90) Conflicting data are published in the literature as regards links between breastfeeding success and parity.(74,76,77) Even though data on maternal education were not studied, our results are suggesting that these mothers most probable had lower educational levels than the mothers of exclusively breastfed infants. Living in rural areas hinder access to both prenatal care, parental classes, information about breastfeeding having a dominant negative effect on breastfeeding rate despite the fact that breastfeeding was a century-old habit in Romanian rural areas. Association with lower maternal age and increased multiparity warns about possible social and economic familial problems. Another important observation is the increased number of deliveries by cesarean section (47.5% versus 36.7%), an important proportion of them performed after the labor onset, suggesting emergency interventions (since complications before and during pregnancy had the lowest rates in these mothers). Delivery by cesarean section is may impede breastfeeding initiation, rate, and duration as demonstrated by some studies.(17,44,51,75,77,82,90) but there also studies suggesting the delivery mode does not influence breastfeeding rates.(91) No references were found in the literature as regards breastfeeding rates after assisted reproductive techniques or related to presence or absence of labor prior to cesarean section.

Breastfeeding rates are undoubtedly influenced by neonatal characteristics and conditions. Comparison of LPI exclusively breastfed with those partially showed no difference in mean GA, BW, and ponderal index, gender, Apgar score at 1 minute, incidence of RDS, maternal-fetal infections, jaundice severe enough to necessitate phototherapy, and physiological weight loss (p>0.50) (table no. 2). Surprisingly, LPI exclusively breastfed had significantly lower Apgar scores at 5 minutes, higher incidence of anemia at birth (including lower mean values of hemoglobin at birth), were more often admitted to NICU, and longer NICU hospitalization stay (p<0.05). Except the fact that birth hypoxia and anemia are more often reported in LPI (2-4,6,8) compared to term infants we have not found any reference in the literature to explain this association. Increased rates of exclusive breastfeeding in infants admitted in NICU are in accordance with data from studies reporting that NICU hospitalization is associated with increased rates and duration of breastfeeding.(9,14,18,46,90) Additional guidance and breastfeeding support offered during NICU hospitalization may explain this finding.

Compared to LPI exclusively breastfed, those fed exclusively with formula at discharge had significantly lower GA and BW, lower Apgar score at 1 minute, increased incidence of maternal-fetal infections (OR 1.94 [95% CI 1.22-3.08]), and increased duration of hospitalization (p<0.05). Also, in this group were more male infants, as expected, resuscitation at birth was needed more often, and more infants were admitted to NICU (although the mean NICU stay was shorter than in LPI exclusively breastfed) (p>0.05). Lower GA and BW are associated with increased immaturity and more frequent complications associated to prematurity (46,73,77), therefore it is not unexpected that lower GA and BW are also associated with breastfeeding difficulties. Birth hypoxia and maternal-fetal infections - as any other severe neonatal disease - are associated with increased rate and duration of mother-infant separation, situation that hinders breastfeeding promotion, neonatal attachment at breast, and lactogenesis. Increased nutritional needs, decreased feeding tolerance, and nutritional enteral and/or parenteral supplementation are contributing risk factors for breastfeeding difficulties in these situations.(48,49,53,72) No difference was found between exclusively breastfed infants and those fed exclusively with formula as regards RDS (the most severe complication in LPI), jaundice, and anemia rates, and physiological weight loss. Surprisingly, event though no significant difference was found for the rates of most of the neonatal complications, LPI fed only with formula at discharge had a significantly prolonged duration of hospitalization. We believe that, most probably maternal factors - medical or social - have contributed to prolonged hospitalization. It is not unusual, unfortunately, that multiparous women leave the hospital if their child is sick in order to take care of minor children at home and return for the newly born (thus fed with formula) after days or even weeks. Yet, no such data were collected, even if available in neonatal charts, for this study.

The results of our study are limited by the retrospective design and relatively low number of cases. Also, data not collected, intentionally or unintentionally, may limit the interpretation of the study results. The two years duration of the study may also affect the results as protocols may change during such a long time, according to new evidence or recommendations. Although only minor changes occurred between 2013 an 2015 in our breastfeeding protocol and these changes were made to strengthen the recommendations. Also, evaluation of ethnic differences in breastfeeding was not performed and it is known that cultural norms and values considerably influence breastfeeding rates.(92) Maternal health status after delivery was not recorded and this also may limit interpretation of results, mostly in situations when formula is offered for nutritional supplementation as maternal diseases may negatively affect lactation.

CONCLUSIONS

Faced with increased incidence of late preterm deliveries and the continuously accumulating evidence that breastfeeding is an important contributor both to increased shirt and long-term morbidity in LPI despite numerous known advantages of breastfeeding, we attempted to find factors that can be addressed in order to improve breastfeeding rates in LPI. We found fair good rates of breastfeeding at discharge, better than reported in the literature for exclusive breastfeeding, in our study group but we have also found areas that can be improved. Development and implementation of a multidisciplinary hospital based prenatal training for parents is the first step done by professional in our unit in order to improve both maternal and neonatal outcome but this program, even if it is free of charge - will still not cover at risk mothers as defined by our study - young mothers, from rural areas, often multiparous, lacking or not attending any prenatal care. Solutions must be found for a better health education and prenatal care of these women, most probably supported at national level.

Periodic training of the professionals - obstetricians,

midwifes, neonatologists, pediatricians, neonatal and pediatric nurses - for breastfeeding support is an already proved intervention that increases both breastfeeding rates and duration (93) and may help improve exclusive breastfeeding rates at discharge in LPI admitted to normal nursery, one of the deficits found by our study. In our unit, almost all of the steps required by Baby Friendly Hospital Initiative are already implemented. Strengthening of these recommendations may also improve the initial rates of breastfeeding, as already demonstrated.(94)

Continuous evaluation of breastfeeding practices in vulnerable categories of neonates helps us to offer them adequate nutritional support for an optimal growth and development and for a better long term outcome.

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