

Original Research

Is it Good to be Born as a Late Preterm Infant?

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Abstract

Background: This study conducted at the Clinic for Children's Diseases of the University Clinical Hospital Mostar, aims to highlight the characteristics, frequency, course, most common complications and treatment outcomes of pregnant women and their late preterm infants according to gestational age. **Methods:** This study is a retrospective epidemiologic study for the period from 1/1/2018 to 31/12/2021. The study included all the preterm infants who were born at a gestational age from 34^{+0/7} to 36^{+6/7} weeks and their mothers. **Results:** In the period under study, a total of 7178 infants were born, of which 253 (3.52%) were late preterm infants. The results show that most mothers were between 30 and 39 years of age, pregnant for the first time with a single pregnancy, delivered by caesarean section, with complications in 53.1% of the pregnancies. All the analyzed pathological conditions were more common in the pregnancies which ended at 34 weeks. Our results indicate that the late preterm babies had a good birth weight (53.8%) and high vitality scores (93%) at birth, but these scores were not confirmed on the first day of life. A significant number of late preterm infants had some pathological condition which was treated in the intensive care units (ICU) ($p < 0.001$). **Conclusions:** The study concludes that half of the pregnant women had risk factors which were the basis for the preterm births and the development of complications in the late preterm infants. Furthermore, despite good birth weight and vitality scores at birth, only one fifth of the late preterm infants were not treated with medications or developed pathological conditions, whereas only one third required no intensive care treatment. It is, therefore, necessary to improve the monitoring and understanding of such pregnancies, implement antenatal corticosteroid therapy, and increase parental awareness to ensure long-term and frequent monitoring of late preterm infants by pediatricians.

Keywords: late preterm infant; pregnancy; gestational age; outcome

1. Introduction

Late preterm infants are premature infants who frequently resemble full-term newborn in size and birth weight, but who tend to be susceptible to various medical complications due to their metabolic and physiological immaturity. Late preterm infants constitute 75% of preterm babies and 20–25% of admissions to intensive care units [1]. The reason for the increased proportion of late preterm infants lies in the fact that, in certain situations, a preterm delivery is the optimal outcome for a pregnancy. It is important to realize that some preterm births benefit the mother, baby or both [2]. This makes them a high-risk group of infants who require special care during their hospital stay, and who also frequently require pediatric monitoring upon discharge from hospital [3]. Conducted studies suggest that late preterm infants with a lower birth weight are more susceptible to early sepsis, whereas neonates whose mothers had previously been treated with antibiotics are less susceptible to it [4]. The brain of a late preterm newborn is

still undeveloped and is therefore susceptible to detrimental stimuli that can arise from complications after birth, such as respiratory distress syndrome, hypoglycemia, hyperbilirubinemia, or apnea [5], and from poor or insufficient feeding and breastfeeding difficulties after birth [6]. Although many studies indicate that late preterm infants have more developmental issues, they are, nevertheless, a group that is not subject to routine check-ups following discharge unless they had been treated in intensive care units (ICU) [1]. These newborn infants are sorted into different gestational categories and identified by different descriptive terms. Unfortunately, these terms do not satisfactorily encompass the important specificity of these infants, that is, they are still preterm infants and belong to a vulnerable category [7]. Pediatricians should explain to parents that delivery before the gestational age of 39 weeks is accompanied by health and neuro-developmental risks which may extend into childhood and later into adulthood [8]. Failure to recognize specific characteristics, a superficial assessment of their devel-



opment, early discharge and inadequate monitoring could have far-reaching consequences for the infants and their families [9]. Therefore, detailed pediatric guidelines and recommendations about the care of such infants should be issued. All early interventions and recommendations will reduce subsequent readmittance to hospital and help to improve early and late outcomes and reduce respiratory disorders in early childhood [10]. These studies have reawakened scientific interest in this category of preterm infants, and point to the significance of this, the largest, group of preterm infants for public health.

The aim of this study at the Clinic for Children's Diseases is to highlight the characteristics, frequency, course, most common complications and treatment outcomes of the pregnant women and their late preterm infants according to gestational age.

2. Materials and Methods

This study is a retrospective epidemiologic study conducted over a four-year period. The study was conducted at the Neonatal and Preterm Intensive Care Unit (ICU) and the Department of Neonatology of the Clinic for Children's Diseases, University Clinical Hospital Mostar (UCH). The study encompassed all the preterm infants who were born at a gestational age from $34^{+0/7}$ to $36^{+6/7}$ weeks at the Clinic for Gynecology and Obstetrics of UCH. It also included the preterm infants transferred to the Department of Neonatology from maternity wards which gravitate towards the Clinic for Children's Diseases UCH. The course and outcome of treatment during their stay in the maternity ward were analyzed retrospectively from data in the medical documentation at the Clinic. The data were collated from the delivery register, containing evidence of all deliveries at the Clinic, the history of illness and electronic medical documentation of newborn from the hospital information system. The data were analyzed in three groups according to the gestational age of the preterm infant (the first group $34^{0/7}$ - $34^{6/7}$, the second group $35^{0/7}$ - $35^{6/7}$, and the third group $36^{0/7}$ - $36^{6/7}$). The parameters analyzed in the pregnant women were age, parity, mode of delivery, medication, pathological conditions (hypertension, diabetes, infections prior to delivery), and pregnancy type (single or multiple pregnancy). The following parameters were analyzed in the newborn infants: gender, gestational age, birth weight, vitality score, pathological conditions (jaundice, infections, sepsis, respiratory disorders, brain hemorrhage), mechanical ventilation, the use of antibiotics, other types of therapy, the duration of treatment in intensive care in days, the outcome of treatment.

The statistical analysis was conducted by IBM SPSS Statistics for Windows, (version 25, IBM Corp, Armonk, NY, USA). The results are expressed as absolute and relative frequencies. The χ^2 test was used to determine statistical significance of difference (the Fisher exact test was used where expected frequencies were lacking). The sta-

tistical significance limit was set at $p = 0.05$. p values that could not be expressed up to three decimal places were expressed as $p < 0.001$.

3. Results

In the four-year period, a total of 7178 infants were born at the UCH Mostar, of which 253 (3.52%) were late preterm infants. 2044 newborn infants were treated in the Department of Neonatology. Of these, 12.38% were late preterm infants. Twenty-five sets of twins were among the late preterm infants (Table 1).

The results show that most of the mothers were between 30 and 39 years of age, pregnant for the first time with a single pregnancy, with complications. Of the total 228 pregnant women, 121 (53.1%) had pathological conditions during pregnancy, and 115 (50.3%) of the pregnant women delivered via Caesarean section. The results show that the most common complication was hypertension, whilst other complications were anaemia, cholestasis, and epilepsy. The characteristics of the mothers show no statistically significant difference according to gestational age of the late preterm infants. Despite this, the results indicate that pathological pregnancies ended earlier. All the analyzed pathological conditions were more common in the pregnancies which ended in gestational week 34, compared to the analyzed pregnancies that were longer. Of the total 228 pregnant women, 80 (35%) received antenatal corticosteroid therapy, most frequently in gestational week 34 (Table 2).

The results indicate that significantly more male late preterm infants ($p < 0.001$) were born. There was a total of 22 (8.7%) low-birth-weight babies in all three groups under analysis. More than 90% of the preterm infants from all three groups had good vitality scores, whereas lower vitality scores were significantly frequent amongst the late preterm infants born at the gestational age of 36 weeks. A significant number of late preterm infants had some pathological condition (204/253; $p < 0.001$). The most common was jaundice, whereas the analysis of gestational age indicates significantly more respiratory difficulties amongst the late preterm infants born at the gestational age of 36 weeks. The analysis showed that the occurrence of respiratory disorders does not depend on the type of delivery in late preterm infants at the gestational age of 36 weeks. Brain hemorrhages were confirmed in 39/253 late preterm infants, which is the same with the late preterm infants born at all gestational ages. 17.8% of them were diagnosed with multiple pathological conditions (e.g., jaundice and infection), which is 45/204 of the late preterm infants. A significant number of late preterm infants, 200 of them ($p < 0.001$), underwent treatment: 75 of them were administered a single type of treatment, and 125 of them were administered multiple treatments. Of the latter, 59 (60%) were born at the gestational age of 36 weeks. Supportive therapy (oxygen, blood transfusions) and cardiotonic agents (dopamine,

Table 1. The distribution of characteristics of the pregnant women according to the gestational age of the preterm infant.

		Number (%) of mothers				
	Total (n = 228)	<i>p</i> ^A	Gestational age			<i>p</i> ^A
			34 ^{+0/7} -34 ^{+7/7} (n = 52)	35 ^{+0/7} -35 ^{+7/7} (n = 76)	36 ^{+0/7} -36 ^{+7/7} (n = 100)	
Age years		<0.001				0.977 ^B
<20	6 (2.6)		1 (1.9)	3 (3.9)	2 (2)	
20–30	91 (39.9)		20 (38.5)	29 (38.2)	42 (42)	
30–40	120 (52.6)		28 (53.8)	40 (52.6)	52 (52)	
40–50	11 (4.8)		3 (5.8)	4 (5.3)	4 (4)	
Pregnancy		<0.001				0.458
1	105 (46.1)		29 (55.8)	37 (48.7)	39 (39)	
2	54 (23.7)		9 (17.3)	20 (26.3)	25 (25)	
3	47 (20.6)		10 (19.2)	12 (15.8)	25 (25)	
4+	22 (9.6)		4 (7.7)	7 (9.2)	11 (11)	
Mode of delivery		0.895				0.100
Vaginal	113 (49.6)		19 (36.5)	40 (52.6)	54 (54)	
Cesarean	115 (50.4)		33 (63.5)	36 (47.4)	46 (46)	
Pregnancy type		<0.001				0.368
Single	203 (89.0)		44 (84.6)	67 (88.2)	92 (92)	
Multiple pregnancy	25 (11.0)		8 (15.4)	9 (11.8)	8 (8)	
Pathological conditions*		<0.001				0.096
No	107 (46.9)		18 (34.6)	38 (50)	51 (51)	
Hypertension	33 (14.5)		7 (13.5)	8 (10.5)	18 (18)	
Diabetes	15 (6.6)		6 (11.5)	4 (5.3)	5 (5)	
Infections	21 (9.2)		6 (11.5)	4 (5.3)	11 (11)	
Other	52 (22.8)		15 (28.8)	22 (28.9)	15 (15)	
Medication*		0.085				0.062
No	127 (55.7)		22 (42.3)	48 (63.2)	57 (57)	
Yes	101 (44.3)		30 (57.7)	28 (36.8)	43 (43)	

*Manifested in pregnancy.

^AChi-Square test; ^BFisher's exact test

dobutamine) were more frequent in the treatment of late preterm infants of a gestational age of 36 weeks. Two hundred and ten of the 253 late preterm infants did not require mechanical ventilation, which is statistically significant ($p < 0.001$).

Significantly more late preterm infants were treated in the ICU ($p < 0.001$). Only 43 (40%) of the late preterm infants in the third group did not require intensive monitoring in the ICU. Nearly 84% of the preterm infants started tolerating milk perorally on the first day. Only 49 (19.4%) of the late preterm infants did not develop a pathological condition. A fatal outcome was more frequent among the infants born at the gestational age of 36 weeks.

4. Discussion

Although the proportion of late preterm infants in the general premature baby population is above 70% worldwide [11–13], as is the case in our country, the care and monitoring of these infants has not been taken seriously enough because of the prevailing attitude that they were born “a bit” before full-term. However, the most recent studies in the field of neonatology have provided more ev-

idence indicating that late preterm infants are at a greater risk of developing various pathological conditions [14,15]. Our results indicate that pathological pregnancies ended in gestational week 34, whereas the health of the infants born at 36 weeks was unexpectedly poorer. These findings may be the result of a superficial understanding of such pregnancies, a lack of critical supervision of them and a lack of foresight for potential poor outcomes. The incidence of premature births is on the rise across the globe, mostly due to an ever-higher frequency of induced preterm deliveries [16], most frequently at the gestational age of late preterm [17], which coincides with our results where half the pregnancies were pathological, and 50% of the late preterm infants were delivered by Caesarean section. It is, therefore, necessary to make informed decisions and to educate parents on the eventual risks involved in continuing a pregnancy or delivering preterm [2]. The experiences of neonatologists to date suggest that parents' lack of awareness leads to unreal expectations of the outcome of late preterm infants. Since 2006, late preterm birth rates have decreased in Norway and the United States, whereas clinician-initiated obstetric interventions have increased among late preterm births in Ca-

Table 2. Distribution of characteristics of the late preterm infants according to gestational age.

	Number (%) newborn				<i>p</i> ^A	
	total (n = 253)	<i>p</i> ^A	Gestational age			
			34+0/7-34+7/7 (n = 60)	35+0/7-35+7/7 (n = 86)		36+0/7-36+7/7 (n = 107)
Gender		0.001				0.717
Male	153 (60.5)		35 (58.3)	55 (64)	63 (58.9)	
Female	100 (39.5)		25 (41.7)	31 (36)	44 (41.1)	
Birth weight (g)		<0.001				<0.001 ^B
1000–1499	4 (1.6)		2 (3.3)	0	2 (1.9)	
1500–1999	29 (11.5)		9 (15)	11 (12.8)	9 (8.4)	
2000–2499	84 (33.2)		27 (45)	34 (39.5)	23 (21.5)	
2500–2999	111 (43.9)		22 (36.7)	32 (37.2)	57 (53.3)	
3000–4500	25 (9.9)		0	9 (10.5)	16 (15)	
APGAR		<0.001				0.724 ^B
8–10	236 (93.3)		58 (96.7)	81 (94.2)	97 (90.7)	
4–7	14 (5.5)		2 (3.3)	4 (4.7)	8 (7.5)	
0–3	3 (1.2)		0 (0)	1 (1.2)	2 (1.9)	
Patological condition		<0.001				0.045
No	49 (19,4)		5 (8,3)	19 (21,1)	25 (23,4)	
Yes	204 (80,6)		55 (91,7)	67 (77,9)	82 (76,6)	
Perinatal infection	30 (11,9)		11 (18,3)	11 (12,8)	8 (7,5)	
Respiratory disorders	43 (17,0)		9 (15,0)	11 (12,8)	23 (21,5)	
Brain hemorrhage	39 (15,4)		10 (16,7)	16 (18,6)	13 (12,1)	
Jaundice	114 (45,1)		35 (16,4)	36 (41,9)	43 (10,2)	
Therapy		<0.001				0.058
No	52 (20.9)		6 (10.0)	21 (24.4)	26 (24.3)	
Yes	200 (79.1)		54 (90.0)	65 (75.6)	81 (75.7)	
Antibiotics	153 (60.5)		47 (78.3)	49 (57.0)	57 (53.3)	
Supportive therapy	72 (28.5)		14 (23.3)	22 (25.6)	36 (33.6)	
Cardiotonic	26 (10.3)		7 (11.7)	6 (7.0)	13 (12.1)	
Phototherapy	114 (45.1)		35 (16.4)	36 (41.9)	43 (10.2)	
Mechanical ventilation		<0.001				0.249
Yes	43 (17.0)		9 (15.0)	11 (12.8)	23 (21.5)	
No	210 (83.0)		51 (85.0)	75 (87.2)	84 (78.5)	
Duration of treatment in intensive care (days)		<0.001				0.010
No	92 (36.4)		12 (20.0)	37 (43.0)	43 (40.2)	
Yes	161 (63.6)		48 (80.0)	49 (57.0)	64 (59.8)	
<7	76 (30.0)		13 (21.7)	23 (26.7)	40 (37.4)	
8–14	46 (18.2)		20 (33.3)	12 (14.0)	14 (13.1)	
>15	39 (15.4)		15 (25.0)	14 (16.3)	10 (9.3)	
Start tolerating meals (hours)		<0.001				0.946 ^B
0–24 h	213 (84.2)		47 (81)	72 (85.7)	86 (83.5)	
25–72 h	32 (12.6)		9 (15.5)	10 (11.9)	13 (12.6)	
>73 h	8 (3.2)		2 (3.4)	2 (2.4)	4 (3.9)	
Outcome of treatment		<0.001				0.594 ^B
Positive outcome	245 (96.8)		59 (98.3)	84 (97.7)	102 (95.3)	
Fatal outcome	8 (3.2)		1 (1.7)	2 (2.3)	5 (4.7)	

^AChi-Square test; ^BFisher's exact test.

nada, Denmark, and Finland [18]. In specific situations, such as hypertension in pregnancy [19] and gestational diabetes [20], a preterm birth is the optimal outcome to pregnancy [2]. Our results indicate that the late preterm infants were more susceptible to developing pathological parameters because of the mother's risk factors, as 53% of the pregnant women in our study had pathological pregnancies. However, despite the large percentage of older pregnant women, and those with pathological pregnancies, along with those who underwent medical treatment during pregnancy, our results show that the late preterm infants had a good birth weight (53.8%) and high vitality scores (93%) at birth, but these scores were not confirmed on the first day of life. Nearly 17% of our late preterm babies were admitted to the ICU in the first hours after birth due to a deterioration of respiratory functions, a larger percentage of them were born at 36 weeks irrespective of mode of birth. This contradicts the conclusions of other studies [16,21]. This is partially a consequence of the non-implementation of antenatal protection during pregnancy, which has proven to be significant in the reduction of the incidence of respiratory disorders in late preterm infants [21]. This concurs with the conclusions that infants born before 39 weeks are at a higher risk of developing pathological conditions [22,23]. This is similar to our findings where only 19% of the late preterm infants had no pathological conditions and required no therapy. Studies indicate that 47% of newborn born at the gestational age of 34 weeks and 11% of those born at 36 weeks were admitted to ICUs [24,25], whereas our study shows that only 40% of the third group did not require intensive care. Hyperbilirubinemia was the most frequent pathological condition in our study, which is similar to the findings of other studies [1] and was most probably the result of milk intolerance. While this is the most common reason for readmittance to hospital [26], suspected milk aspiration was the most frequent reason for readmittance to hospital in our study. Furthermore, a factor for concern is the finding that 15% of the late preterm infants had brain hemorrhaging of different degrees, diagnosed across all gestational ages. A possible explanation for this lies in the infants' undeveloped brain, and its vulnerability to harmful factors which affect critical phases of development, and which can result in different neurological outcomes later in life [27]. The third group sample was most frequently treated with a combination of medications (antibiotics and other supportive therapy). A possible explanation of such a result could be that the course of the pregnancy may not have been considered risky, nor was a deterioration of the clinical state of the infants born at 36 weeks expected. Possible reasons for such poor outcomes can be identified in the better care and monitoring of risky pregnancies before 34 weeks in comparison to the pregnancies at 36 weeks of gestation where a good outcome is expected. This may likely be the result of a superficial understanding of such pregnancies, a lack of critical supervision of them and the lack of foresight for

potential poor outcomes. However, our findings suggest that late preterm infants are a group at risk, irrespective of their gestational age, because they behave like premature infants born before 34 weeks. The conclusion of the 2022 study is that the risk of iatrogenic preterm birth <37 weeks in singleton pregnancies achieved after in vitro fertilization (IVF/ICSI) is significantly greater than that occurring in spontaneous conceptions [28]. In our study, this parameter was not analyzed due to insufficient data in the perinatal history. Thus, it is vital to acknowledge the late preterm infant as a premature infant, and that it requires significant medical monitoring by obstetricians and pediatricians. The limitations of our study are a lack of data on the pathological conditions of individual mothers, lack of data on assisted reproduction, the short period of the study and the fact that there is no control group for late preterm infants.

5. Conclusions

The study concludes that half of the pregnant women had risk factors which were the bases for preterm delivery and the development of complications in their late preterm infants. Furthermore, despite good birth weight and vitality scores at birth, only one fifth of the late preterm infants were not administered medication or developed pathological conditions, and only one third required no intensive care treatment. Therefore, it is necessary to monitor and understand these pregnancies better, to administer antenatal corticosteroid protection, to educate parents and to provide long-term and more frequent pediatric monitoring of late preterm infants.

Author Contributions

MJR, KŠ, ŽP, VM, TB and SG designed and wrote the research study. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

This retrospective study was conducted according to all the ethical principles of the University Clinical Hospital Mostar. Ethical Approval was obtained from the Ethics Committee of the Clinical Hospital Center Mostar (reference number 1071/22, dated 07/03/2022).

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Conflict of Interest

The authors declare no conflict of interest.

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