# Short-Term Complications and Mortality of late Preterm Infants

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## ABSTRACT

**Objectives:** To identify the short-term complications and mortality of late preterm infants (34 0/7-36 6/7 weeks gestation) comparing to term infants (37 0/7-41 6/7 weeks gestation) who were admitted to the neonatal intensive care unit (NICU) and special care nursery (SCN) at King Hussein Medical Center (KHMC).

**Methods:** This study was a retrospective chart review of all late preterm and term infants who were born at KHMC in Jordan and admitted to NICU and SCN of KHMC from January first 2018 to December 31st, 2018. The authors formulated a data sheet for late preterm and term infants that contains the following information; Clinical characteristics of each late preterm and term infants admitted to NICU and SCN including gestational age, birth weight, gender, mode of delivery, maternal diseases around the time of delivery like preeclampsia, diabetes, and prolonged rupture of membranes (PROM). Morbidities involving both groups were documented including respiratory distress syndrome of newborn (RDS), transient tachypnea, hypoglycemia, hypothermia, jaundice needed phototherapy, sepsis, feeding problems, requirement of ventilation, surfactant, length of admission, and death.

**Results:** The total number of deliveries was 9195 singleton live births during the period of study. Term babies' birth rate was 90.8 %( 8352) and preterm babies <37 weeks gestation birth rate was 9.2 %( 843). The birth rate of late preterm infants was 5.5% (510) out of them 252 babies admitted to NICU and SCN. Late preterm infants compared to control group (term infants) had obviously more statistical significant complications such as RDS (P=0.000), transient tachypnea of newborn (P=0.001), hypoglycemia, (P=0.001), hypothermia (P=0.010), jaundice needed phototherapy (P=0.001), feeding problems (P=0.000) and sepsis (P=0.001). Late preterm infants with respiratory distress required more respiratory support with nasal continuous positive airway pressure (nCPAP) (p=0.000) and mechanical ventilator (p=0.001).Surfactant given to 12(4.7%) late preterm babies compared to 3(0.7%) term babies. Hospital stay was longer in late preterm infants and mortality rate was also significantly higher among late preterm infants ($t_{691}$=7; p= 0.000).

**Conclusion:** Late preterm infants had increased duration of hospital stay, significant neonatal morbidity and higher mortality in comparison to term infants.

**Key words:** Late preterm infants, short-term, complications, mortality

**JRMS December 2020; 27(3): 10.12816/0057182**

## Introduction

Late preterm infants are defined as infants born at gestational age from 34 0/7 to 36 6/7 weeks (239 days to 259 days) of gestation. [(1)] These infants usually have more short-term complications and long term effect on Neurodevelopment in comparison to term infants.[(4-6,14-16,21-26)] Large number of late preterm infants need

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Admission to NICU and SCN than term infants due to respiratory problems, feeding difficulties, jaundice, sepsis, and hypoglycemia. [11-18]

Late preterm infants used to be called near-term infants because they have nearly the same appearance, size, and weight of the term infants.[6] In 2005 a workshop held by the National Institute of Child Health and Human Development (NICHD) changed this concept to late preterm infants.[10] Those have higher risk of morbidity and mortality than term babies due to immature and underdeveloped functions of immunologic, respiratory, neurologic, and metabolic systems as a result of prematurity.[3,10]

It is crucial to emphasize on the risks that facing late preterm infants either acutely after delivery during their hospitalization in NICU and SCN or later due to long term effects on neurodevelopment. [23, 24]It is important to avoid premature delivery if there are no fetal risks or maternal indications for early delivery to avoid the morbidities and complications of prematurity. Another important issue of preterm delivery that those babies require more respiratory and nutritional support which increase the financial burden on the hospital. [10]

Limited available studies in our country about complications and morbidity of late preterm infants. [11]This is the first study in our hospital concerning the short term complications and mortality of late preterm infants in comparison to term infants admitted to NICU and SCN in the same period.

## Materials and methods

This retrospective study was carried out in the NICU and SCN of KHMC over one year duration between January first 2018 and December 31st, 2018. KHMC is the biggest tertiary referral military hospital in Jordan. Late preterm infants of gestational age from 34 0/7 to 36 6/7 weeks considered as cases and term infants delivered from 37 0/7 to 41 6/7 weeks of gestation considered as control group. Gestational age was calculated according to the first day of last menstrual period and new Ballard score estimation. [1, 28]

For each neonate included in this study consent was obtained and signed by his/her parents and an ethical committee approval from our hospital was granted before starting the study. Neonates with major congenital abnormalities were excluded from this study.

Clinical characteristics of each late preterm infant and term infant admitted to NICU and SCN were recorded. These data included birth weight at time of delivery, gender, mode of delivery, obstetrical complications including preeclampsia, premature rupture of membranes(PROM), placenta Previa, and diabetes either type I and II diabetes or gestational diabetes.

Morbidities and complications were recorded and analyzed for both late preterm infants and term infants during hospitalization after delivery including respiratory distress syndrome (RDS), transient tachypnea of newborn (TTN), hypoglycemia with blood glucose level <40 mg/dl, hypothermia with core temperature <36.0ºC, feeding problems, neonatal jaundice needed phototherapy according to American Academy of Pediatrics guidelines (AAP).[27] Culture proven sepsis either early onset or late onset sepsis, respiratory support assistance either nasal continuous positive airway pressure (nCPAP) or ventilator use and surfactant administration. Also, Length of hospital stay and mortality rate were recorded and analyzed.

## Data analysis

Descriptive statistics were utilized to draw summary measures of central tendency and frequencies. Means and standard deviations of the dependent variables estimated and compared among different groups of the study population. An inferential statistical test was used as the independent t test to test the differences between two independent group means, the late preterm infants group compared with the control term infants group. The researchers considered p value $\leq 0.01$ significant results.

## Results

The total number of babies delivered was 9195 singleton live births during the study period. 843 babies out of the total were preterm babies< 37 weeks gestational age included 510 (60%) late preterm babies and 333(40%) babies preterm <34 weeks gestation (Figure 1). Moreover, 8352 (90.8%) of the total born babies were term babies, however, 510 babies (5.5%) were late preterm and 333 (3.7%) were preterm <34 weeks gestational age (Figure 2).

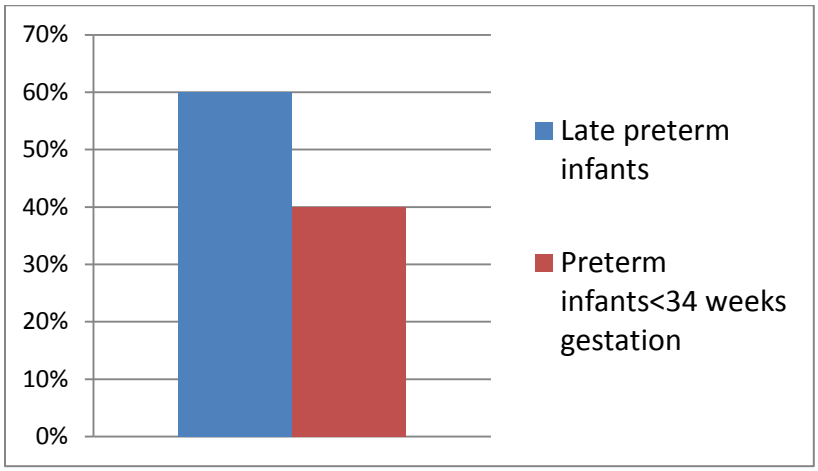


**Figure 1:** The distribution of 843 premature live births to late preterm infants and preterm infants <34 weeks gestation

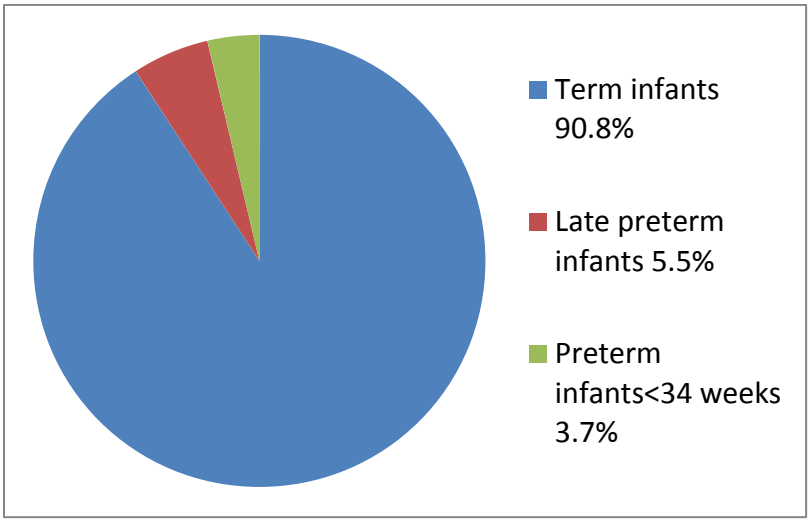


**Figure 2:** The distribution of gestational age of 9195 total live deliveries

During the study period, 252 out of 510 (49.4%) late preterm infants admitted to NICU and SCN while 441 out of 8352 (5.2%) term infants admitted to NICU and SCN. Clinical characteristics of both groups of babies are illustrated in (Table I). Birth weight of late preterm infants in grams was 2364 ± 322 (mean ± SD) and for term infants 3131 ± 452. According to babies' gender, there were 138 males (55%) among late preterm and 228 male (52%) term infants. Majority of babies admitted to NICU or SCN for both late preterm and term infants were born by cesarean section (62% vs. 63%).

Maternal risk factors for both groups admitted to NICU or SCN which are shown in (Table I) were more significant in late preterm infants like preeclampsia (PET) (9.5% vs. 2.7%, p=0.001) and premature rupture of membranes (PROM) (8% vs. 0.7%, p=0.000), while placenta Previa (4.7% vs. 1.4%, p=0.000) and diabetes (8 % vs. 2.2 %, p=0.001).

Neonatal morbidities for both late preterm and term babies during their hospitalization are shown in (Table II).

The most common cause of NICU and SCN admission for late preterm infants was RDS (40% vs. 4.5%, p=0.000) while the commonest cause of admission for term infants was TTN 43% against 35% late preterm. Significant number of term infants admitted due TTN as a result of higher rate of cesarean section delivery (63%). Late preterm required respiratory support either by nCPAP (69% vs. 38%, p=0.000) or by mechanical ventilator (7% vs. 3.4%, p= 0.001). Surfactant administered mainly for RDS in 12 (4.7%) late preterm babies vs. 3 (0.7%) term babies.

Morbidities observed more often in late preterm infants during their hospitalization (Table II). Hypoglycemia (6% vs. 0.7%, p=0.001), Hypothermia developed in 3 late preterm babies (1.2%) while no term baby suffered from hypothermia. 30% of late preterm and 13.3% of term babies developed neonatal jaundice required phototherapy. Difficulty with feeding was more prominent in late preterm infants (37.6% vs. 4.5%). Moreover, Sepsis with positive culture results was much higher in late preterm (7.2% vs. 1.8%).

The mean length of hospitalization was significantly higher in late preterm babies compared to term babies (12 days vs. 4 days, p=0.001). Obviously the mortality rate was much higher in late preterm 15 (6%) against 3 (0.7%) term babies during the study period (p=0.000). These data are illustrated in
(Table III).

**Table I:** Clinical characteristics of late preterm and term infants admitted to the neonatal unit

| Parameter | Late preterm infants ( Number: 252) | Term infants ( Number: 441) | t | P value |
|---|---|---|---|---|
| Birth weight (g) mean±SD | 2364±322 | 3131±452 | 5 | 0.000** |
| Gender | | | | |
| Male, n (%) | 138(55) | 228(52) | 1 | 0.477 |
| Female, n (%) | 114(45) | 213(48) | 1 | 0.477 |
| Mode of delivery | | | 0.5 | 0.744 |
| Cesarean section, n (%) | 156(62) | 279(63) | 0.5 | 0.744 |
| Vaginal delivery, n (%) | 96(38) | 162(37) | | |
| Preeclampsia, n (%) | 24(9.5) | 12(2.7) | 5 | 0.001** |
| Premature rupture of membranes | 21(8) | 3(0.7) | 12 | 0.000** |
| Placenta Previa, n (%) | 12(4.7) | 6(1.4) | 6 | 0.000** |

| | | | | |
|---|---|---|---|---|
| Diabetes, n (%) | 20(8) | 10(2.2) | 4.8 | 0.001** |

**p value ≤0.01

**Table II:** morbidities of late preterm term infants during their admission to the neonatal unit

| Morbidities | Late preterm infants Number (%) | Term infants Number (%) | t | P value |
|---|---|---|---|---|
| Respiratory distress syndrome | 100(40) | 20(4.5) | 12 | 0.000** |
| Transient tachypnea of newborn | 89(35) | 189(43) | 3.5 | 0.001** |
| nCPAP | 174(69) | 168(38) | 8 | 0.000** |
| Ventilator | 18(7) | 15(3.4) | 3.8 | 0.001** |
| Surfactant | 12(4.7) | 3(0.7) | 4 | 0.001** |
| Hypoglycemia | 15(6) | 3(0.7) | 4.5 | 0.001** |
| Hypothermia | 3(1.2) | 0(0) | 3 | 0.010** |
| Feeding problems | 95(37.6) | 20(4.5) | 7.5 | 0.000** |
| Neonatal jaundice needed phototherapy | 75(30) | 59(13.3) | 5.5 | 0.001** |
| Culture proven sepsis | 18(7.2) | 8(1.8) | 6 | 0.001** |

**p value ≤0.01
nCPAP: Nasal continuous positive airway pressure

Table III: Length of hospital stay and mortality rate of term and late preterm infants admitted to the neonatal unit

| | Late preterm infants | Term infants | t | P value |
|---|---|---|---|---|
| Length of hospital stay(days) | 12(3-30) | 4(2-8) | 4.5 | 0.001** |
| Death, n (%) | 15(6) | 3(0.7) | 7 | 0.000** |

**p value ≤0.01

## Discussion

The study confirmed that late preterm infants who were delivered with a gestational age of 34 0/7 to 36 6/7 and required admission to NICU and SCN of KHMC are prone to short term morbidities and have higher mortality rate as reported by other studies carried out in different countries. [1-9] In this study, the authors noticed that almost half of the babies who were born late preterm needed admission (49.4%) due to high

number of high risk deliveries transferred to our tertiary NICU from other peripheral hospitals in the country. In other studies the number of late preterm infants needed admission was less than the number of patients in this study as in Tsai M N, et al. study in Taiwan which showed that 36% late preterm infants vs. 2 % term infants required hospitalization. [3] In Begun L N, et al. study in Bangladesh only 12.9% of late preterm admitted to NICU. [12]

Before 2005, late preterm infants were called near term, because of nearly same size and appearance as term babies, so it was thought that those babies behave as term babies without any short term or long term adverse consequences due to prematurity.[8,10] The guidelines of American College of Obstetrics and Gynecology (ACOG) do not recommend delivery before 39 weeks gestation for elective deliveries if there is no clear obstetric or fetal indications to avoid possible preterm birth complications.[1,9] Even babies born early term (37 0/7 through 38 6/7) gestation have some risks especially if delivered by elective cesarean section mainly due to respiratory morbidity.[1] The benefits of avoiding preterm delivery should outweigh the maternal and neonatal risks.

Maternal risk factors and medical diseases like diabetes, preeclampsia, and placenta previa were more frequent in late preterm infants which contribute to early delivery. [1, 13-16] PROM was an important factor for preterm birth. [9,16] Tsai M N, et al. showed that the commonest cause of late preterm birth is the spontaneous onset of labor and amniotic fluid rupture.[3] Haroon A, et al**.** proved that maternal diseases and medical status like hypertension, diabetes, urinary tract infection and PROM increased the risk of preterm birth.[16] Because the present study is a retrospective study not all perinatal records were available to determine exactly the causes of preterm birth and the adverse effects of maternal obstetrical complications on babies delivered late preterm. Shapiro-Mendoza C K, et al. indicated that late preterm birth morbidity was seven fold that of term infants and the risks of preterm delivery aggravated by maternal medical diseases. [17]

In our study late preterm babies suffered more neonatal morbidities compared to term babies. Most of late preterm needed hospitalization due to respiratory distress mainly diagnosed as RDS or TTN as shown in other studies as a result of immaturity of lung tissues, relative surfactant deficiency and delayed absorption of lung fluid. [2-6, 18] We noticed that in the present study large number of late preterm babies diagnosed as RDS (40%) followed by TTN (35%). In other studies like Savitha M R, et al. 28.2% of late preterm infants admitted to hospital had respiratory distress and 3.7% of term infants admitted to hospital due to respiratory distress.[2] In comparison to other studies, larger number of preterm babies delivered by cesarean section delivery (62%) which increased the risk of respiratory distress.[8,9] Antenatal corticosteroids are very effective in reducing severe RDS and improving survival rate for preterm babies <34 weeks gestation.[1] Due to large number of late preterm babies admitted to hospital due to RDS in our study this guide us to consider giving antenatal steroids in cases of elective late preterm deliveries in the future to decrease the respiratory morbidities in these babies. Late preterm babies required more respiratory support than term babies either by non invasive nCPAP in around one third of cases or invasive mechanical ventilation in 7%. Surfactant administered more to late preterm babies 4.7% while just 3(0.7%) term babies required surfactant because RDS is more common in preterm babies. Surfactant given just to 6 late preterm babies out of 100 babies with RDS because in our unit we apply nCPAP immediately after birth for babies with moderate to severe respiratory distress which improved their lung functional residual capacity and decreased the requirement for surfactant and invasive ventilation. Late preterm infants are liable for apnea of prematurity due to immaturity of central nervous system and pulmonary receptors. [1, 6] They are also more liable in infancy to get respiratory syncytial virus (RSV) and recurrent wheezy chest in childhood with the later development of bronchial asthma. [19]

In our study late preterm babies had more feeding difficulties 37.6% compared to 4.5% term infants as evidenced in other studies due to immaturity of neurodevelopment system to coordinate sucking-swallowing-breathing process, respiratory distress which interferes with feeding and longer sleeping time. [2, 3, 9] The rate of breast feeding is less in late preterm infants, because large number needs NICU admission with longer duration of hospital stay so the mothers' of late preterm neonates require more support for establishment of breast feeding.

Hypoglycemia is more frequent in late preterm due to limited stores of glycogen, inadequate glycogenolysis and gluconeogenesis with impaired ketogenesis.[5,6,18] Hypoglycemia has subsequent adverse neurological effects.[5,8,9] Hypothermia is more frequent in late preterm babies due to large surface area and less subcutaneous brown fat.[3,5,8] In our study 3 (3%) late preterm babies had hypothermia while no term baby experienced hypothermia. Savitha M R, et al. also found that hypothermia was very significant in late preterm infants 41 babies vs. 9 term babies. [2]

In our study the risk of jaundice which required phototherapy was higher in late preterm in comparison to term 30% vs. 13.3%. Same results were shown in other studies.[6,12,13] Jakiel G, et al. showed that jaundice was the most common morbidity of late preterm babies during their hospital stay affecting around 50% of cases.[14] Also Visruthan N K, et al. study concluded that late preterm babies were 3 to 6 times more vulnerable to have jaundice than term babies.[9] This is due to immaturity of liver enzymes with subsequent decrease in bilirubin conjugation and excretion.[2,6] Feeding difficulty and immaturity of gastrointestinal system of late preterm infants increase the enterohepatic circulation which aggravates the risk of hyperbilirubinemia in these babies .[5,6,9] They are at high risk for developing kernicterus. As obtained in Begum L N. et al. study Jaundice was the most common cause of readmission to hospital in the neonatal period of late preterm babies. [12] Close follow up is mandatory in all late preterm babies especially in the neonatal period to detect jaundice early and start phototherapy if needed to avoid the risks of kernicterus and the exchange transfusion requirement although it is rarely needed.[9]

Culture proven sepsis in late preterm infants is about four times term infants in the present study 7.2% vs. 1.8%. Wagh A S, et al. revealed that nearly the same results of sepsis frequency in the present study 9.6% vs. 0.9%.[25] Bulut C, et al. reported the incidence of sepsis of late preterm babies twice that of term babies (21.1% vs. 11.1%). [5] The higher incidence of sepsis in late preterm babies is due to immaturity of immune system, longer hospital stay, and the passage of maternal immunoglobulin IgG antibodies occur after 34 weeks gestation. [12, 20]

In the present study the length of hospitalization is much longer in late preterm babies three times that of term babies as shown in other studies. [2, 6, 12, 26] This will add a burden to health resources because these babies need extra care during their hospitalization including nutrition, antibiotics and respiratory support. Equivalent results were obtained by Bulut C, et al. in their study that the median duration of hospital admission of late preterm infants was 7 days while in term babies 4 days. [5] Readmission is more common in late preterm babies due to jaundice, feeding problems and suspected sepsis. [6, 7]

In our study, the mortality rate was obviously higher in late preterm in comparison to term infants 6% vs. 0.7%. Similar results were obtained in other studies. [1-3, 12, 13]) Bulut C, et al. reported that the mortality rate as 1.4%, 0.9%, and 0.6% for 34, 35 and 36 weeks gestation late preterm infants respectively while in term babies 0.3%.[5] The rate of mortality is higher in our hospital could be due to more high risk deliveries referred to our tertiary unit for more evaluation and care including preterm deliveries.

Our study has some limitations because of the retrospective nature of the study. The medical records did not include all the information about the circumstances of delivery and not all maternal risk factors were documented. So it was difficult to determine the exact causes of late preterm delivery. And we couldn't assess the neurodevelopment complications due to inadequate and incomplete follow up.

## Conclusion

Late preterm infants suffer from short term morbidities, complications, required longer hospital stay and have higher mortality rate when compared to term neonates. Late preterm infants require special care and

attention since birth. Further research should be carried out to evaluate the role and safety of antenatal corticosteroids in improving lung maturity and decreasing the incidence of RDS in late preterm infants.
Obstetricians should pay attention to the risks of the late preterm neonates whether acute or long term when they decide to deliver a preterm baby when there is no clear maternal or fetal indications for early delivery.

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