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ASSESSING NEONATAL COMPLICATIONS IN LATE PRETERM INFANTS RELATIVE TO TERM BIRTHS

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Abstract

Late preterm infants (34–36 weeks gestation) are physiologically immature, increasing their risk of morbidity and mortality compared to term infants. This study evaluated neonatal outcomes and mortality risk factors in late preterm infants.A prospective cohort study was conducted on 200 neonates (100 late preterm, 100 term). Clinical and demographic variables were analyzed using chi-square and t-tests, while logistic regression identified predictors of mortality ($p < 0.05$).Late preterm infants had lower birth weights (2.18 ± 0.53 kg vs. 2.97 ± 0.58 kg, $p < 0.01$) and APGAR scores ($p < 0.01$). Morbidities—including sepsis, respiratory distress, hypoglycemia, perinatal asphyxia, and need for mechanical ventilation—were significantly higher ($p < 0.01$). Mortality was also elevated (48% vs. 12%, $p < 0.01$). Mechanical ventilation emerged as a strong independent predictor of mortality (OR: 0.027, $p < 0.001$), while late preterm birth showed a non-significant trend ($p = 0.094$).Late preterm infants experience substantially higher morbidity and mortality. Close monitoring and timely interventions, particularly regarding respiratory support, are essential to improve outcomes.

INTRODUCTION

Preterm birth, defined as delivery before 37 weeks of gestation, continue to be one of the notable sources of newborn morbidity and mortality globally, responsible for 35% of neonatal deaths worldwide [1,2]. As reported by the World Health Organization (WHO), approximately 15 million infants are born preterm every year, and more than 1 million of them die because of complexities related to prematurity [3]. Late preterm infants (LPIs); those born between 34+0- and 36+6-weeks' gestation account for nearly 75% of all preterm births and 9% of total live births internationally [4-6].

Regardless of their near-term appearance, LPIs are biologically undeveloped and practically remains at an inflated risk of neonatal complexities in comparison to term infants. Their organ systems, together with the respiratory, metabolic, thermoregulatory, hepatic, and immune systems, remain immature leaving them to detrimental neonatal outcomes [7-8]. These newborns have an augmented frequency of respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), feeding disorders,hypoglycemia, hyperbilirubinemia, infections, and delays in developments of neurological system resulting in extended hospitalization, excessive cost of neonatal intensive care unit (NICU) admissions, and escalated medical care expenses [9-10].

Over the past few decades, the prevalence of late preterm births has climbed globally [11] which is mainly motivated due to breakthrough in maternal-fetal technology, evolving obstetric practices, and enhanced prenatal management [1]. The increasing utilization of elective cesarean sections, induction of

labor and early term deliveries due to maternal or fetal distress has resulted into a higher section of medically indicated late preterm births [12-13].

In modern settings, rigorous maternal-fetal surveillance and improvements in perinatal care enable timely recognition of at-risk pregnancies encouraging deliberated late preterm deliveries [11]. However, such intensified medicalization of pregnancy has given rise to unwanted unnecessary early term mediation, increasing induced late preterm births in some settings [12].

Although developed countries have comprehensively investigated late preterm outcomes and enforced structured neonatal handling decorum, evidence from developing countries remain insufficient [14]. The burden of neonatal morbidity and mortality is distinctly immense in Asian countries, where restricted healthcare facilities and hampered maternal care access promote inferior outcomes among LPIs [15].

In a country such as Pakistan, preterm birth complexities are a major source of newborn deaths, accounting for approximately 36% of neonatal fatalities [16]. A study conducted in Karachi revealed that LPIs attributed to 95.5% of all preterm births and 12.7% of total neonatal admissions [14]. However, due to limited resources, neonatal care facilities for LPIs are often poor, with several patients of avoidable difficulties such as sepsis, jaundice, and respiratory distress developing into deadly outcomes [17]. Moreover, the early discharge of LPIs to avoid congestion in the hospital escalates their likelihood of postnatal issues such as hypoglycemia, feeding difficulties, and untreated hyperbilirubinemia [18]. Scarcity of parental awareness, insufficient follow up care and prolong detection of neonatal ailment further promote high frequency of readmission and newborn deaths in Pakistan [19]. A study indicated that LPIs had a 2-3 times higher likelihood of growth delays and learning Impairment in comparison to term born adults [20]. These persistent implications highlight the urgency for timely neurodevelopmental screening and devoted interventions for LPIs [21].

Despite the increasing research on late preterm birth in developed nations, insufficient data exist from low income country such as Pakistan. The escalated neonatal mortality rate in South Asia emphasizes the necessity to examine the morbidity and mortality among late preterm infants (LPIs) in the region. This study aimed at addressing this gap by investigating the morbidity and mortality patterns of LPIs admitted to Civil Hospital Karachi. By determining high risk factors, neonatal complexities, and survival outcomes, this study will offer opportunities for development of evidence-based clinical protocols and improving neonatal care facilities in Pakistan. The objective of this study is to compare neonatal morbidity and mortality among late preterm and term infants and identify risk factors associated with mortality.

Literature Review

Respiratory difficulties are the most frequent morbidities in LPIs, mainly due to undeveloped lung function and procrastinated surfactant production (7, 22). Studies have shown that that a sizeable segment of LPIs need interventions including continuous positive airway pressure (CPAP) or mechanical ventilation because of their immature lungs and elevated threat of respiratory distress syndrome (23-25). The most dominant respiratory situation in this group includes respiratory distress syndrome (RDS), transient tachypnea (TTN) and pneumonia. RDS is often related to surfactant inadequacy whereas TTN arise from delayed lung fluid clearance. Moreover, cesarean delivery in the absence of labor has been associated with a excessive risk of RDS and TTN, as labor plays a vital part in lung fluid absorption (26). The utilization of antenatal corticosteroids for reducing respiratory difficulties in LPIs stays a topic of concern, as findings demonstrate contradictory results concerning their effectiveness (10).

Metabolic complexities, specifically hypoglycemia is another notable issue in LPIs. These newborns have restricted glycogen stores and undeveloped glucose regulation, making them more susceptible to hypoglycemia, which appears in 23-47% of LPIs (18). Regular blood glucose surveillance and timely nutritional assistance are decisive in handling this ailment. Furthermore, hypothermia is a primary risk due to an enlarged body surface area-to-weight ratio and undeveloped thermoregulatory process (15). Literature underscores that kangaroo mother care

(KMC), incubators, and warmers remarkably assist in maintaining thermal reliability and reducing energy loss in LPIs (27).

Jaundice is also frequent in LPIs attributable to undeveloped liver function and enhanced bilirubin formation, influencing 50% of LPIs in contrast to 23% of term infants (28). Many needs phototherapy or exchange transfusion to avoid kernicterus, a serious neurological problem (29). Premature discharge without bilirubin screening augments the risk of unidentified acute jaundice (28). The American Academy of Pediatrics (AAP) advocates delayed discharge and timely screening to avoid complexities (30).

Infections and sepsis are primary issues related to LPIs due to undeveloped immune defences and lower maternal antibody transfer, making them 2-3 times more vulnerable to ailment than term infants (31). Sepsis influences 30-50% of LPIs with early occurring cases associated with Group B Streptococcus (GBS) whereas late occurring infections induced by hospital acquired pathogens (32). Early antibiotic treatment, infection management, and exclusive mother feeding assist in lowering these potential outcomes (14).

LPIs also experience extended neurodevelopment threats as a results of partial brain growth, with cortical volume accumulating about 50% between 34 and 40 weeks (21). Studies advocate that they have 2-3 times higher probability of cognitive delays, ADHD, and learning challenges as compared to term infants (33). Timely diagnosis and treatment strategies are crucial to improve extended mental and behavioural outcomes (21).

Largely, LPIs continue to be a vulnerable group demanding special neonatal facilities, timely diagnosis, and continual follow-up to lessen complexities and enhance survival outcomes. The increasing identification of their distinctive susceptibility emphasizes the necessity for evidence-based neonatal care approaches adapted to manage their particular risks and augment postnatal support procedures.

Material And Methods

Study Design and Setting: This was a prospective cohort study conducted at the Department of Paediatrics, Dr. Ruth K.M. Pfau Civil Hospital Karachi. The data collection lasted for six months from 24th December 2017 to 23rd June 2018.

Sample Size:

OpenEpi version 3.01 was used to calculate sample size by using 15.3% of jaundice in non-exposed versus 41.6% in exposed groups respectively (34) with confidence interval of 95% and absolute precision 5% resulted in the sample size of 100 for each group (200 neonates)

Sampling Technique: Non probability convenience sampling technique was employed to recruit participants.

Inclusion Criteria:

- Exposed Group: Late preterm infants (34+0 to 36+6 weeks of gestation).
- Non-exposed Group: Term infants with gestational age > 37 weeks.

Exclusion Criteria:

- Multiple gestation infants.
- Infants with major congenital anomalies and clinically identified chromosomal syndromes.

Data Collection Procedure: The study was initiated after getting approval from College of Physicians and Surgeons Pakistan. Patients visiting the Department of Paediatrics, Dr Ruth K.M Pfau Civil Hospital Karachi (CHK) meeting the inclusion criteria were registered in the study. Informed consent was obtained from all the parents. Neonates were categorized into **two groups** as:

- Exposed group: LPIs
- Unexposed group: Term Infants

A structured proforma was utilized to get demographic details and other information such as maternal history, gestational age, and perinatal records. Gestational age was determined by employing the last menstrual period (LMP). Enrolled neonates were closely observed for seven days to assess their morbidity and mortality outcomes. Clinical examination and laboratory investigations were carried out as follows:

Vital signs monitoring (temperature, heart rate, respiratory rate, oxygen saturation) at regular intervals.

Blood sugar levels testing was inspected 6-hourly for the first 24 hours, followed by 12-hourly monitoring up to 72 hours and as needed depending on clinical presentation. Serum bilirubin levels were checked at 24, 48, and 72 hours to monitor jaundice. Complete blood count (CBC), C-reactive protein (CRP), and blood culture and sensitivity were performed for suspected sepsis cases. Chest X-rays were performed for neonates presenting with respiratory distress to assess situation like respiratory distress syndrome (RDS) or pneumonia. Serum electrolytes and renal function tests were conducted in neonates presenting signs of metabolic instability. Morbidity patterns and mortality outcomes were analysed at the end of the seven-day of follow-up. Neonates discharged earlier were followed up by means of hospital records to ensure data completeness.

Data Analysis

SPSS Version 26 was used to analyse data. Descriptive statistics were used to summarize data as mean ± standard deviation (SD) for continuous variables whereas frequencies and percentages were used to summarize categorical variables. To compare morbidity and mortality among groups, Chi-square test (for categorical variables) and independent sample t test (for continuous variables) were applied. A multivariable logistic regression model was used to determine independent predictors of mortality. A p-value ≤0.05 was considered statistically significant for the analyses.

Results:

Demographic and Clinical Characteristics of Study Population

The study included a total of 200 infants with 100 in the Late Preterm group whereas 100 in the Term group. The distribution of gender was similar between the two groups ($p = 0.887$), indicating no significant difference. In LPIs, the mean birth weight was significantly smaller (2.177 ± 0.531 kg) as compared to the term group (2.966 ± 0.584 kg) ($p < 0.01$). The mean Apgar scores were significantly smaller in the LPIs as compare to term infants: at 1 minute (5.97 ± 1.632 vs 6.75 ± 1.395, $p < 0.01$) and at 5 minutes (7.35 ± 1.320 vs 8.02 ± 1.189, $p < 0.01$)

Neonatal Morbidity in Late Preterm and Term Infants

Morbidities were found to be significantly more dominant between LPIs in comparison to term infants as sepsis was identified in 99% of LPIs versus 82% of term infants ($p < 0.01$). Likewise, jaundice was more frequent in the LPIs (51% vs. 23%, $p < 0.01$). Hypoglycemia was also significantly found in higher frequency among LPIs (47% vs. 23%, $p < 0.01$). Similarly, respiratory distress was detected in majority of LPIs (89% vs 65%, $p < 0.01$). The frequency of perinatal asphyxia was significantly prominent in LPIs (46% vs. 24%, $p = 0.001$) whereas the need for mechanical ventilation was noticeably higher in the late preterm group (37% vs. 11%, $p < 0.01$).

Mortality Outcomes in Late Preterm and Term Infants

It was revealed that mortality rates were significantly higher for LPIs as compared to term infants ($p < 0.01$). Among LPIs , 48% expired, while merely 12% of term infants did not survive. On the other hand, the survival frequency was substantially lower in LPIs (52%) in contrast to term infants (88%).

Association of Morbidities with Mortality Status

Table 4 shows the association among different neonatal morbidities and mortality status. Respiratory distress showed a strong association with mortality ($p = 0.001$) as 91.67% of expired neonates having respiratory distress compared to 70.71% of survivors. Perinatal asphyxia also revealed a strong relationship with mortality ($p < 0.001$) as 53.33% of expired neonates affected in comparison to 27.14% of survivors. Similarly, mechanical ventilation also indicated significant relationship with mortality ($p < 0.001$) with 70% of expired neonates required ventilation as compared to only 4.29% of survivors. However, jaundice and hypoglycemia were not significantly related to mortality ($p = 0.225$ and $p = 0.332$, respectively).

Risk Factors Associated with Mortality

The multivariable logistic regression model was employed to determine the relationship between different risk factors and mortality. Mechanical ventilation emerged as a significant predictor of

mortality (Exp(B) = 0.027, 95% CI: 0.008–0.094, $p < 0.001$), demonstrating a noticeably elevated risk among ventilated infants. Other factors, suh as late preterm birth, low birth weight, sepsis, jaundice, and respiratory distress, did not exhibit significant relationship with mortality.

Discussion

This study intended at comparing neonatal outcomes among late preterm and term infants, concentrating on morbidity and mortality rates and to determine significant factors related to neonatal mortality. The findings highlight the elevated susceptibility of LPIs to detrimental outcomes and emphasize mechanical ventilation as a pivotal predictor of mortality.

Neonatal Characteristics and Outcomes

The results exhibited that LPIs had significantly lesser birth weights and APGAR scores at both 1 and 5 minutes in contrast to term infants. Particularly, the mean birth weight for LPIs was 2.177 ± 0.531 kg, noticeably lower than the 2.966 ± 0.584 kg found in term infants ($p < 0.01$). Equivalently APGAR scores were significantly lesser in the LPIs ($p < 0.01$) at 1 minute (5.97 ± 1.632 vs. 6.75 ± 1.395) and 5 minutes (7.35 ± 1.320 vs. 8.02 ± 1.189). These results accord with current literature demonstrating that LPIs frequently have decreased physiological reliability at birth making them vulnerable to various complexities [28].

Morbidity Profiles

LPIs showed elevated frequency of various morbidities compared to their term infants. The occurrence of presumed sepsis was higher in LPIs (99% vs. 82%, $p < 0.01$). Moreover, conditions such as jaundice (51% vs. 23%), hypoglycaemia (47% vs. 23%), respiratory distress (89% vs. 65%), perinatal asphyxia (46% vs. 24%), and the need for mechanical ventilation (37% vs. 11%) were all significantly more frequent in the LPIs ($p < 0.01$). These results are compatible with previous findings that have reported elevated likelihood of neonatal complexities in LPIs together with respiratory distress syndrome and sepsis [28].

Mortality Rates

The mortality rates were considerably higher among LPIs with 48% dying in contrast to 12% of term infants ($p < 0.01$). This significant variation highlights the increased likelihood of mortality correlated with late preterm birth. Earlier studies have also revealed that elevated mortality in this population frequently associated with their physiological immaturity and the enhanced incidence of serious conditions demanding critical care [35].

Risk Factors for Mortality

Univariate analysis detected respiratory distress, perinatal asphyxia, and the need for mechanical ventilation as factors significantly associated with escalated mortality. Particularly, 91.67% of expired neonates suffered from respiratory distress in contrast to 70.71% survivors ($p = 0.001$). Perinatal asphyxia was found in 53.33% of non-survivors as compared to 27.14% of survivors ($p < 0.001$). While mechanical ventilation was needed in 70% of expired infants, on the other hand 4.29% of survivors required this intervention ($p < 0.001$). These results emphasize the crucial description of respiratory complications and the relevant interventions in finding neonatal outcomes.

Multivariable Logistic Regression Analysis

The results of a multivariable logistic regression showed that mechanical ventilation was the most significant predictor ($p < 0.001$). This specify that infants in need of mechanical ventilation had a distinctly escalated chance of mortality. Other factor including late preterm birth, low birth weight (≤2.5 kg), sepsis, jaundice, and respiratory distress, did not achieve statistically significance with mortality in the multivariable model. The importance of mechanical ventilation as a mortality predictor aligns with recent studies that have reported its relationship with raised morbidity and mortality attributable to the seriousness of the underlying conditions demanding its use [36].

Limitations and Future Research

While this study imparts important insights, some limitations must be acknowledged. The study did not

consider possible confounding factors like mother health, quality of prenatal care, and sociodemographic factors that may impact neonatal outcomes. Moreover, few factors that exhibited statistical significance in univariate analysis did not achieve statistical significance in logistic regression probably due to interactions among risk factors. Further research must take into account a more comprehensive evaluation of maternal and perinatal factors to better deduce their influence on neonatal morbidity and mortality. Studies with more contrasted populations and increased follow-up duration may further justify these findings and offer extensive insights into long-term outcomes.

Conclusion

Late preterm infants are at substantially elevated risk for different morbidities and mortality compared to term infants. Mechanical ventilation appears as a decisive independent predictor of mortality in this population. These results underline the requirement for focussed clinical plans incorporating increased surveillance, precautionary measures and resource assigning to revamp outcomes for late preterm infants.

Table-01: Baseline Characteristics of Neonates

Characteristic	Late Pre-Term	Term	p-value
Gender			
Male	52	51	0.887
Female	48	49	
Birth Weight (kg)	2.177±0.531	2.966±0.584	<0.01
Mode of Delivery			
Vaginal	38	67	<0.01
Cesarean	62	33	
APGAR Score at 1 min	5.97±1.632	6.75±1.395	<0.01
APGAR Score at 5 min	7.35±1.320	8.02±1.189	<0.01

Table-02: Comparison of Neonatal Morbidities Between Exposed and Unexposed Groups

Morbidity	Late Pre-Term	Term	p-value
Presumed Sepsis			
Yes	99	82	<0.01
No	1	18	
Jaundice			
Yes	51	23	<0.01
No	49	77	
Hypoglycemia			
Yes	47	23	<0.01
No	53	77	
Respiratory Distress			
Yes	89	65	<0.01
No	11	35	
Perinatal Asphyxia			
Yes	46	24	0.001
No	54	76	

Mechanical Ventilation			
Yes	37	11	<0.01
No	63	89	

Table-03: Comparison of Mortality Between Exposed and Unexposed Groups

Mortality	Late Pre-Term (%)	Term (%)	p-value
Survived	52	88	<0.01
Expired	48	12	

Table-04: Association Between Neonatal Characteristics and Mortality

Factor	Survived n(%)	Expired n(%)	p-value
Presumed Sepsis			
Yes	123 (87.86)	58 (96.67)	0.052
No	17 (12.14)	2 (3.33)	
Jaundice			
Yes	48 (34.29)	26 (40)	0.225
No	92 (65.71)	34 (60)	
Hypoglycemia			
Yes	46 (32.86)	24 (40)	0.332
No	94 (67.14)	36 (60)	
Respiratory Distress			
Yes	99 (70.71)	55 (91.67)	0.001
No	41 (29.29)	5 (8.33)	
Perinatal Asphyxia			
Yes	38 (27.14)	32 (53.33)	<.001
No	102 (72.86)	28 (46.67)	
Mechanical Ventilation			
Yes	6 (4.29)	42 (70)	<.001
No	134 (95.71)	18 (30)	

Table-05: Logistic Regression Analysis of Risk Factors for Neonatal Mortality

Risk factor	Exp(B)	Sig.	95% C.I
Late pre term	0.312	0.094	0.08-1.219
Birthweight (≤2.5)	1.974	0.308	0.534-7.294
Sepsis	0.778	0.807	0.103-5.859
Mechanical Ventilation	0.027	0	0.008-0.094
Jaundice	0.967	0.957	0.286-3.265
Respiratory Distress	0.974	0.969	0.256-3.707

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