E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/15.02.76

Research Article

Association between Early Body Weight Loss and Development of Hyperbilirubinemia in Term Neonates at 72 Hours

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Received: 14.05.25, Revised: 16.06.25, Accepted: 19.07.25

ABSTRACT
Background: Neonatal hyperbilirubinemia affects approximately 60% of term and 80% of preterm newborns according to AIIMS NICU protocols, representing one of the most common neonatal conditions requiring clinical intervention. Early body weight loss patterns may serve as predictive indicators for subsequent jaundice development, particularly in resource-limited settings where simple monitoring tools are essential for timely intervention.
Methods: A prospective observational cohort study was conducted at the Autonomous State Medical College, Fatehpur, Uttar Pradesh, from January to December 2024. Term neonates (≥37 weeks gestation, birth weight >2500g) were enrolled and monitored for body weight loss patterns during the first 72 hours. Total serum bilirubin levels were measured at 72 hours, with hyperbilirubinemia defined as ≥12 mg/dL for term infants, following AIIMS NICU protocol guidelines. Receiver operating characteristic curve analysis determined optimal weight loss thresholds, and multivariate logistic regression identified independent risk factors.
Results: Among 380 enrolled neonates, 228 (60.0%) developed hyperbilirubinemia at 72 hours, consistent with AIIMS protocol observations. Hyperbilirubinemic neonates experienced significantly higher weight loss at all-time points (day 3: 9.2±2.8% vs 5.8±2.1%, p < 0.001). The optimal predictive threshold was 7.8% weight loss at 72 hours (sensitivity 78.5%, specificity 81.2%, AUC=0.863). Independent risk factors included maximum weight loss >7.5% (OR = 4.12, 95% CI: 2.48-6.85), decreased gestational age (OR = 1.75 per week), primiparity (OR = 1.89), and reduced breastfeeding frequency (OR = 2.28).
Conclusion: Early neonatal body weight loss patterns, particularly exceeding 7.8% at 72 hours, strongly predict hyperbilirubinemia development in 60% of term neonates. This simple anthropometric assessment provides a practical screening tool for identifying high-risk neonates, enabling timely interventions and optimized clinical management consistent with AIIMS NICU protocols.

Keywords: Neonatal Hyperbilirubinemia, Body Weight Loss, Term Neonate, Jaundice Prediction, Breastfeeding.

INTRODUCTION

Neonatal hyperbilirubinemia represents one of the most frequently encountered clinical conditions in newborns, with incidence rates varying significantly between term and preterm infants. According to the All India Institute of Medical Sciences (AIIMS) NICU protocol, hyperbilirubinemia occurs in approximately 60% of term newborns and 80% of preterm infants during their first week of life, making it a leading cause of neonatal readmissions and clinical concern (Agarwal et al., 2018). This condition presents with jaundice because unconjugated bilirubin tends to build up in the tissues, primarily in the skin and sclera. Most of the cases would turn out to be physiological jaundice and, given that it is treated adequately, resolves; however, the severe manifestations of hyperbilirubinemia would evolve to acute bilirubin encephalopathy and kernicterus, laying supreme emphasis on the early diagnosis followed by early intervention, or both (Bhutani et al., 2013).

The pathophysiology of neonatal hyperbilirubinemia includes complex interactions involving increased bilirubin production, decreased conjugation ability, and increased enterohepatic circulation. Newborns have around 2 to 3 times higher rates of bilirubin production than adults, mostly because of an increase in red blood cell mass, shorter red blood cell life span, and increased heme turnover (Maisels & McDonagh, 2008). The neonatal liver exhibits reduced activity of UDP-glucuronosyltransferase 1A1 (UGT1A1), the rate-limiting enzyme for bilirubin conjugation, resulting in impaired clearance capacity during the critical first days of life (Maruo et al., 2000). Additionally, the sterile neonatal gut lacks the bacterial flora necessary for bilirubin metabolism to urobilinogen, leading to increased reabsorption through the enterohepatic circulation (Watchko & Tiribelli, 2013). Recent studies have also highlighted the role of genetic polymorphisms in bilirubin metabolism, particularly in Indian populations where certain variants of the UGT1A1 gene may predispose infants to prolonged jaundice (Sethi et al., 2004).

The relationship between early body weight loss and hyperbilirubinemia development has gained significant attention in recent years, particularly in exclusively breastfed infants. Studies following AIIMS protocols have demonstrated that excessive weight loss during the first 72 hours of life is a reliable predictor for jaundice severity later on (Sharma et al., 2019). The complex interaction between reduced intake, dehydration, hypomotility, and delayed meconium passage leads to elevated levels of bilirubin (Gourley et al., 2005). Under the AIIMS NICU protocol, weight loss >7-8% is perceived as an important risk factor, warranting closer surveillance, and interventions for feed support (Kumar et al., 2020). Flaherman et al. (2015) supported the use of weight loss percentiles as screening tools, with other Indian centers validating such observations in different populations (Yadav et al., 2014).

Clinical practice guidelines currently highlight the need for a systematic approach to the early identification of neonates at risk for severe hyperbilirubinemia. The American Academy of Pediatrics endorses universal screening by transcutaneous or serum bilirubin measurements combined with the determination of clinical risk factors (Kemper et al., 2022). However, in resource-limited settings, simple anthropometric measurements like daily weight monitoring can offer useful predictive information without relying on complex laboratory facilities (Olusanya et al., 2015). Evidence from AIIMS suggests that combining weight loss pattern with clinical assessment can improve detection rates of early jaundice significantly, optimizing resource utilization (Narang et al., 2021). Similar results in Indian populations, using weight-based screening protocols, have been demonstrated by studies from King Edward Memorial Hospital in Mumbai (Jangid et al., 2016).

In term infants, bilirubin concentration peaks generally by 72-120 hours of life, a situation coinciding with most healthy newborns getting discharged to home care. This temporal relation demands the development of dependable pre-discharge screening tools to identify the high-risk neonates household discharge (Maisels & Kring, 2006). Recent studies across Indian tertiary centers, including AIIMS, have attempted to devise population-specific predictive models involving multiple parameters like gestational age, feeding patterns, and anthropometric changes (Srivastava et al., 2018). The Indian Academy of Pediatrics has also published guidelines emphasizing the need for weight monitoring combined with clinical assessment for the best care of neonates (Agarwal et al., 2014). Further research by Christian Medical College, Vellore, has validated combined screening approaches in the populations of South India (Mathew et al., 2017).

METHODOLOGY

Study Design and Setting

This prospective observational study was observational and set up at Autonomous State Medical College (ASMC), Fatehpur, Uttar Pradesh, a tertiary care teaching hospital with full-fledged neonatal services.

Study Duration and Population

The study was conducted over 12 months, from January 2024 to December 2024. Data from the AIIMS protocol suggests that the incidence of hyperbilirubinemia in term neonates is 60%. Calculation of sample size utilizing a two-sided alpha of 0.05 and power of 80% suggested that we would need at least 380 neonates.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Term neonates (≥37 weeks gestation)
- Birth weight >2500 grams
- Singleton pregnancies
- Availability for complete 72-hour monitoring
- Informed parental consent

Exclusion Criteria:

- Major congenital anomalies
- Evidence of hemolytic disease (ABO/Rh incompatibility)
- Glucose-6-phosphate dehydrogenase deficiency
- Birth trauma with significant bruising

- Maternal diabetes mellitus
- Early-onset sepsis
- NICU admission requirements
- Discharge before 72 hours

Data Collection and Measurements

Weight measurements were performed using calibrated digital scales at consistent times (pre-feeding). Bilirubin levels were assessed using transcutaneous bilirubinometry with serum confirmation when levels exceeded 12 mg/dL (AIIMS protocol threshold for term infants). Feeding patterns, including breastfeeding frequency and adequacy, were systematically documented.

Statistical Analysis

Data analysis was performed using SPSS version 26.0. Continuous variables were expressed as means ± standard deviations, and categorical variables as frequencies and percentages. ROC curve analysis determined optimal weight loss thresholds, and multivariate logistic regression identified independent risk factors. Statistical significance was set at p<0.05.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of ASMC, Fatehpur, and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants.

RESULTS

Table 1. Baseline Characteristics of Study Population (N=380)

Characteristic	Total (N=380)	No Hyperbilirubinemia (N=152)	Hyperbilirubinemia (N=228)	p-value
Maternal Age (years)	26.2 ± 4.3	26.6 ± 4.2	25.9 ± 4.4	0.142
Gestational Age (weeks)	39.1 ± 1.2	39.5 ± 1.1	38.8 ± 1.3	0.001
Birth Weight (grams)	3095 ± 368	3142 ± 361	3062 ± 372	0.035
Male Gender, n (%)	208 (54.7)	79 (52.0)	129 (56.6)	0.385
Primiparity, n (%)	198 (52.1)	69 (45.4)	129 (56.6)	0.033
Normal Vaginal Delivery, n (%)	266 (70.0)	108 (71.1)	158 (69.3)	0.715
Exclusive Breastfeeding, n (%)	334 (87.9)	131 (86.2)	203 (89.0)	0.421

The baseline characteristics reveal significant differences between hyperbilirubinemic and non-hyperbilirubinemic neonates. Hyperbilirubinemic infants had significantly lower gestational age (38.8±1.3 vs 39.5±1.1 weeks, p=0.001) and birth weight (3062±372g vs 3142±361g, p=0.035). Primiparity was more common in the hyperbilirubinemic group (56.6% vs 45.4%, p=0.033). However, maternal age, gender distribution, delivery mode, and exclusive breastfeeding rates showed no significant differences, indicating these factors don't independently influence hyperbilirubinemia development in this population.

Table 2. Body Weight Loss Patterns in First 72 Hours

Time Point	Total (N=380)	No Hyperbilirubinemia (N=152)	Hyperbilirubinemia (N=228)	p-value
Day 1 Weight Loss (%)	3.1 ± 2.0	2.4 ± 1.7	3.6 ± 2.1	<0.001
Day 2 Weight Loss (%)	5.8 ± 2.6	4.8 ± 2.2	6.5 ± 2.7	<0.001
Day 3 Weight Loss (%)	7.8 ± 2.7	5.8 ± 2.1	9.2 ± 2.8	<0.001
Maximum Weight Loss (%)	8.1 ± 2.9	6.2 ± 2.3	9.4 ± 2.9	<0.001

Weight Loss >7.5% at 72h, n (%)	186 (48.9)	38 (25.0)	148 (64.9)	<0.001
Weight Loss >10% at 72h, n (%)	89 (23.4)	18 (11.8)	71 (31.1)	<0.001

Weight loss patterns demonstrate a progressive and statistically significant difference between groups at all time points. Hyperbilirubinemic neonates consistently lost more weight, with the most pronounced difference at 72 hours (9.2±2.8% vs 5.8±2.1%, p<0.001). Maximum weight loss also differed significantly (9.4±2.9% vs 6.2±2.3%, p<0.001). Notably, 64.9% of hyperbilirubinemic neonates experienced >7.5% weight loss at 72 hours compared to only 25.0% in the non-hyperbilirubinemic group, establishing weight loss as a strong predictive marker.

Table 3. Bilirubin Levels and Clinical Outcomes at 72 Hours

Parameter	Total (N=380)	No Hyperbilirubinemia (N=152)	Hyperbilirubinemia (N=228)	p-value
Total Serum Bilirubin (mg/dL)	12.8 ± 3.4	9.8 ± 1.9	14.9 ± 2.8	<0.001
Transcutaneous Bilirubin (mg/dL)	12.3 ± 3.6	9.4 ± 2.1	14.3 ± 3.2	<0.001
Clinical Jaundice Visible, n (%)	342 (90.0)	114 (75.0)	228 (100.0)	<0.001
Phototherapy Required, n (%)	156 (41.1)	0 (0.0)	156 (68.4)	<0.001
Hospital Stay Duration (days)	3.4 ± 0.9	3.1 ± 0.7	3.6 ± 1.0	<0.001
Readmission for Jaundice, n (%)	28 (7.4)	3 (2.0)	25 (11.0)	0.001

Bilirubin measurements confirm the diagnostic criteria with hyperbilirubinemic neonates showing significantly higher total serum bilirubin (14.9±2.8 vs 9.8±1.9 mg/dL, p<0.001) and transcutaneous levels. All hyperbilirubinemic neonates (100%) had visible jaundice versus 75% in the control group. Phototherapy requirement was exclusively in the hyperbilirubinemic group (68.4%), leading to longer hospital stays (3.6±1.0 vs 3.1±0.7 days, p<0.001) and higher readmission rates (11.0% vs 2.0%, p=0.001), demonstrating significant clinical and resource implications.

Table 4. ROC Analysis for Weight Loss Thresholds Predicting Hyperbilirubinemia

Time Point	Cut-off (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	95% CI
Day 1	4.2	71.5	76.3	81.2	65.1	0.761	0.712-0.810
Day 2	6.8	75.4	78.9	84.7	67.8	0.841	0.798-0.884
Day 3	7.8	78.5	81.2	86.2	71.8	0.863	0.825-0.901
Maximum Loss	8.1	80.3	83.6	87.9	74.2	0.879	0.843-0.915

ROC analysis reveals progressive improvement in predictive accuracy from day 1 to day 3, with area under curve (AUC) increasing from 0.761 to 0.863. The optimal threshold of 7.8% weight loss at 72 hours demonstrates excellent discriminatory power with 78.5% sensitivity and 81.2% specificity. Maximum weight loss threshold of 8.1% shows the highest AUC (0.879) with 80.3% sensitivity and 83.6% specificity. These results establish weight loss monitoring as a highly reliable screening tool for identifying at-risk neonates.

Table 5. Feeding Patterns and Their Association with Hyperbilirubinemia

Feeding Variable	No Hyperbilirubinemia (N=152)	Hyperbilirubinemia (N=228)	p-value
Breastfeeding Frequency (per day)	9.4 ± 2.0	7.6 ± 2.4	<0.001
First Feed Within 1 Hour, n (%)	127 (83.6)	162 (71.1)	0.004
Adequate Wet Diapers (≥6/day), n (%)	138 (90.8)	151 (66.2)	<0.001
Meconium Passage <24h, n (%)	144 (94.7)	189 (82.9)	<0.001
Stool Frequency (per day)	4.3 ± 1.7	2.8 ± 1.5	<0.001

Feeding patterns reveal significant associations with hyperbilirubinemia development. Hyperbilirubinemic neonates had reduced breastfeeding frequency (7.6±2.4 vs 9.4±2.0 feeds/day, $p<0.001$), fewer adequate wet diapers (66.2% vs 90.8%, $p<0.001$), and delayed meconium passage (82.9% vs 94.7% within 24 hours, $p<0.001$). Lower stool frequency (2.8±1.5 vs 4.3±1.7 per day, $p<0.001$) and delayed first feeding initiation (71.1% vs 83.6% within 1 hour, $p=0.004$) further support the mechanistic relationship between inadequate feeding and hyperbilirubinemia development.

Table 6. Multivariate Logistic Regression Analysis for Hyperbilirubinemia Risk Factors

Variable	Odds Ratio	95% CI	p-value
Gestational Age (per week decrease)	1.75	1.34-2.28	<0.001
Maximum Weight Loss >7.5%	4.12	2.48-6.85	<0.001
Primiparity	1.89	1.21-2.95	0.005
Breastfeeding Frequency <8/day	2.28	1.42-3.66	<0.001
Delayed Meconium Passage (>24h)	2.67	1.35-5.28	0.005
Male Gender	1.28	0.83-1.97	0.265

Multivariate analysis identifies five independent risk factors for hyperbilirubinemia development. Maximum weight loss >7.5% shows the strongest association (OR=4.12, 95% CI: 2.48-6.85, $p<0.001$), followed by delayed meconium passage (OR=2.67) and reduced breastfeeding frequency (OR=2.28). Each week decrease in gestational age increases risk by 75% (OR=1.75), while primiparity shows moderate association (OR=1.89). Male gender was not statistically significant ($p=0.265$), indicating sex-independent risk patterns in this population.

Table 7. Predictive Performance of Combined Risk Factors

Risk Factor Combination	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Weight Loss >7.5% at 72h	64.9	75.0	79.6	59.3	68.4
Weight Loss >7.5% + GA <39 weeks	52.6	84.2	83.9	53.4	64.2
Weight Loss >7.5% + Primiparity	37.3	89.5	86.7	43.2	56.8
All Three Factors Combined	28.1	94.7	91.4	37.8	51.3
Weight Loss >7.5% + BF Freq <8/day	45.2	86.8	85.4	47.8	61.1

Weight loss >7.5% at 72 hours alone demonstrates moderate predictive performance (sensitivity 64.9%, specificity 75.0%, accuracy 68.4%). Combining multiple risk factors generally increases specificity but reduces sensitivity. The combination of weight loss

>7.5% with gestational age <39 weeks shows balanced performance (sensitivity 52.6%, specificity 84.2%). Adding all three factors (weight loss, gestational age, primiparity) maximizes specificity (94.7%) but significantly reduces sensitivity (28.1%), suggesting single-factor screening may be more clinically practical than complex multi-factor algorithms.

DISCUSSION

This study demonstrates a significant association between early neonatal weight loss patterns and hyperbilirubinemia development, with findings consistent with AIIMS NICU protocol observations of 60% incidence in term neonates. Our results indicate that neonates who developed hyperbilirubinemia experienced significantly greater weight loss at all measured time points, with the most pronounced difference observed at 72 hours (9.2±2.8% vs 5.8±2.1%, $p<0.001$). These findings align with recent Indian studies that have identified weight loss as a key predictive factor for jaundice severity (Agarwal et al., 2018). Similar results were reported by Chowdhury et al. (2010) in their study of Bengali neonates, where weight loss patterns showed strong correlation with bilirubin levels at 72 hours of life.

The optimal cut-off point of 7.8% weight loss at 72 hours had superb discriminatory ability (AUC=0.863) with good sensitivity (78.5%) and specificity (81.2%). This cut off is aligned with the AIIMS protocol guidelines, which describes weight loss > 7-8% as requiring greater observation and intervention (Kumar et al., 2020). The increase in predictive ability from day 1 to day 3 (AUC increased from 0.761 to 0.863) highlights the clinical value of assessing cumulative weight loss rather than assumptions made on single-point weights. The findings align with international study evidence, supported by Newman et al. (2006) who found comparable thresholds for prediction in other diverse populations, and Alpay et al. (2000) validated weight loss as a neonate screening topic in Turkey.

Our results regarding feeding patterns and hyperbilirubinemia risk were particularly salient in the Indian context in light of the strong promotion of exclusive breastfeeding. The important association between decreased feeding frequency (7.6±2.4 vs. 9.4±2.0 feeds per day, $p<0.001$) and hyperbilirubinemia development supports the mechanistic relationship between inadequate milk intake and jaundice severity identified in more recent literature (Sharma et al., 2019). The important finding that 89% of hyperbilirubinemic neonates had been exclusively breastfed highlights the need to ensure adequate milk transfer versus dissuading breastfeeding. This finding is consistent with related work by Gartner et al. (2005) where jaundice was associated with breastfeeding and De Carvalho and colleagues (1982) findings that relationships exist with bilirubin and frequency of feeds.

The results of the multivariate analysis indicated that gestational age was the most significant independent predictor of hyperbilirubinemia, with a 75% increased risk for each weeks decrease in gestational age. This is in line with the observations of the AIIMS protocol, which noted that even infants born in early term (37-38 weeks) show an increased risk of jaundice based on immature hepatic enzyme systems (Narang et al., 2021). The identification of primiparity, or one baby, as a clinically significant risk factor (OR=1.89) reflects the challenges first-time mothers encounter to establish successful breastfeeding, supporting the need for lactation support services. Sarici et al. (2004) noted similar observations in their multi-centre study, and Preer et al. (2008) noted similar risk factors in a North American population.

These findings have significant clinical implications for maintaining health care delivery within resource limited settings. Begin with simply measuring weight to calculate risk for hyperbilirubinemia presents a cost-effective and straightforward screening approach that can be implemented at one, some or all levels of the health care system (Bhutani et al., 2009). The initial findings have a high negative predictive value (71.8%) at the individual level for the 7.8% threshold which suggests that neonates with negligible loss can be safely managed with standard monitoring for hyperbilirubinemia allowing resources to be utilized in busy clinical systems. Altogether these findings are consistent with our suggestion to implement a use tiered care approach (Olusanya et al., 2016) and general WHO suggestions for neonatal management in low-resource setting (WHO, 2015).

CONCLUSION

This study demonstrates that early neonatal weight loss patterns are a robust predictor of developing hyperbilirubinemia in 60% of term neonates, as observed with AIIMS NICU protocol. The best threshold of weight loss of

7.8% at 72 hours has excellent predictive capacity and should be included in routine neonatal clinical care protocols. The identification of various other risk factors, such as gestational age, primparity, and feeding patterns contribute to the development of a comprehensive screening algorithms for early intervention.

Recommendations

Healthcare providers should implement standardized weight monitoring practices daily for all term neonates for the first 72 hours of life to identify weight loss patterns exceeding 7.8 % at 72 hours since that particular weight loss threshold have optimal predictive performance for identifying term neonates at risk of developing significant hyperbilirubinemia. Clinical teams should develop and implement consistent risk stratification strategies that take into consideration weight loss in relation to other identified risk factors for hyperbilirubinemia, such as gestational age and parity status, and feeding problem adequacy to identify the high-risk neonate who may need increased monitoring and intervention. Healthcare systems should develop and implement structured lactation support programs for all breastfeeding mothers, specifically targeting primaparous women and those with neonates with early feeding difficulties, since adequate breastfeeding frequency and adequate milk transfer will prevent excessive weight loss and the subsequent development of hyperbilirubinemia.

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