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Modified Snappe-II as a Predictor of Severity of Illness Among Human Milk-Fed and Formula-Fed Low Birth Weight Infants: A Systematic Review with Narrative Synthesis

A Comprehensive Evidence Synthesis of Neonatal Prognostic Outcomes

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Abstract:

- ***Background:***

Low birth weight (LBW) infants are at increased risk of adverse clinical outcomes, including severe morbidity and mortality during the neonatal period. The Modified Score for Neonatal Acute Physiology Perinatal Extension-II (SNAPPE-II) is widely used to assess illness severity in neonatal intensive care units; however, evidence regarding its predictive performance, particularly in relation to feeding practices, remains fragmented.

- ***Objective:***

To systematically review the available evidence on the predictive value of the Modified SNAPPE-II score for assessing severity of illness, morbidity, and mortality among human milk-fed and formula-fed low birth weight infants.

- ***Methods:***

A systematic review with narrative synthesis was conducted in accordance with the PRISMA 2020 guidelines. Electronic databases including PubMed, Scopus, and the Cochrane Library were searched for studies published between January 2001 and March 2025. Studies evaluating the predictive performance of the Modified SNAPPE-II score in low birth weight infants were eligible for inclusion. Two reviewers independently screened studies, extracted data, and assessed methodological quality. Owing to heterogeneity in study design, populations, and reported outcomes, findings were synthesized narratively.

- ***Results:***

Thirteen studies involving diverse neonatal populations met the eligibility criteria. Across the included studies, higher Modified SNAPPE-II scores consistently demonstrated a strong association with neonatal mortality and greater illness severity. Several studies also reported good discriminatory ability for predicting major neonatal complications, including bronchopulmonary dysplasia, severe intraventricular hemorrhage, and prolonged neonatal intensive care unit stay. Although human milk feeding is recognized for improving neonatal outcomes, none of the included studies directly compared the predictive performance of the Modified SNAPPE-II score between human milk-fed and formula-fed low birth weight infants. Consequently, evidence regarding the influence of feeding modality on illness severity prediction remains limited.

- ***Conclusion:***

The available evidence indicates that the Modified SNAPPE-II score is a reliable tool for early assessment of illness severity and prediction of mortality among low birth weight infants admitted to neonatal intensive care units. However, there is insufficient evidence to determine whether its predictive performance differs according to feeding modality. Well-

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designed prospective studies comparing human milk-fed and formula-fed low birth weight infants are needed to address this important knowledge gap and to strengthen the clinical application of the Modified SNAPPE-II score.

Keywords: *Modified SNAPPE-II; Low Birth Weight; Neonatal Intensive Care Unit; Illness Severity; Neonatal Mortality; Neonatal Morbidity; Human Milk; Formula Feeding; Systematic Review; Narrative Synthesis.*

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I. INTRODUCTION

Low birth weight (LBW), defined as a birth weight of less than 2500 g irrespective of gestational age, remains one of the leading contributors to neonatal morbidity and mortality worldwide.[1] Globally, nearly 20 million infants are born with low birth weight each year, with the greatest burden occurring in low- and middle-income countries where access to specialized neonatal care is often limited.[2] LBW infants are particularly vulnerable to respiratory distress, sepsis, intraventricular hemorrhage, necrotizing enterocolitis, metabolic instability, and long-term neurodevelopmental impairment.[3–5] Early recognition of disease severity is therefore essential to guide clinical decision-making, optimize resource allocation, and improve neonatal survival.[6]

Neonatal intensive care units (NICUs) routinely utilize illness severity scoring systems to objectively evaluate the physiological condition of critically ill newborns.[7] Such scoring systems facilitate risk stratification, enable comparison of clinical outcomes across institutions, and support quality improvement initiatives.[8] Among the available neonatal severity scores, the Modified Score for Neonatal Acute Physiology Perinatal Extension-II (SNAPPE-II) has emerged as one of the most practical and extensively validated tools for assessing illness severity during the first hours after birth.[9]

The SNAPPE-II score incorporates physiological variables including blood pressure, body temperature, oxygenation, serum pH, urine output, seizure activity, birth weight, Apgar score, and small-for-gestational-age status to estimate the severity of neonatal illness and the risk of mortality.[10] Compared with the original SNAP score, SNAPPE-II requires fewer variables, making it easier to apply in routine clinical practice while maintaining excellent predictive accuracy.[11] Several investigations have demonstrated that increasing SNAPPE-II scores are strongly associated with higher neonatal mortality, prolonged NICU stay, and severe neonatal complications.[12–15]

In addition to physiological instability, nutritional management plays a crucial role in determining neonatal outcomes. Human milk provides optimal nutrition and contains numerous bioactive components, immunoglobulins, growth factors, anti-inflammatory mediators, and antioxidants that contribute to immune maturation and organ development.[16,17] Human milk feeding has consistently been associated with lower rates of necrotizing enterocolitis, late-onset sepsis, bronchopulmonary dysplasia, retinopathy of prematurity, and improved neurodevelopmental outcomes among preterm and low birth weight infants.[18–20] Although infant formula remains an essential alternative when maternal or donor milk is unavailable, formula-fed infants may experience higher rates of infectious and gastrointestinal complications compared with breast milk-fed infants.[21,22]

Despite the established clinical value of SNAPPE-II and the recognized benefits of human milk feeding, the relationship between feeding modality and the predictive performance of SNAPPE-II has received limited attention. Most published studies have primarily evaluated the score as a predictor of mortality without examining whether nutritional practices influence illness severity assessment or neonatal outcomes.[23–25] Furthermore, differences in study populations, gestational age, outcome measures, and reported cutoff values have resulted in considerable heterogeneity across the available evidence.[26–28]

A comprehensive synthesis of the current literature is therefore needed to evaluate the clinical utility of the Modified SNAPPE-II score in low birth weight infants and to identify existing evidence regarding human milk-fed and formula-fed populations. Such evidence may assist neonatologists and neonatal nurses in improving early risk assessment and identifying important gaps for future research.[29]

Therefore, the present systematic review with narrative synthesis was undertaken to critically evaluate the available evidence regarding the predictive value of the Modified SNAPPE-II score for assessing severity of illness, morbidity, and mortality among human milk-fed and formula-fed low birth weight infants.[30]

II. METHODOLOGY

➢ *Study Design*

This systematic review with narrative synthesis was conducted to critically evaluate the predictive value of the Modified Score for Neonatal Acute Physiology Perinatal Extension-II (SNAPPE-II) for assessing severity of illness, morbidity, and mortality among low birth weight (LBW) infants, with particular attention to evidence relating to human milk-fed and formula-fed neonates. The review was designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines to ensure methodological transparency, reproducibility, and comprehensive reporting. Although a review protocol was developed before

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commencement of the study, it was not prospectively registered in an international systematic review registry.

➢ *Research Question*

The review addressed the following research question:

"What is the predictive value of the Modified SNAPPE-II score for assessing severity of illness, morbidity, and mortality among human milk-fed and formula-fed low birth weight infants admitted to neonatal intensive care units?"

The research question was formulated using the Population, Intervention, Comparison, Outcome (PICO) framework.

➢ *Population (P)*

Low birth weight infants (<2500 g), including preterm and very low birth weight neonates admitted to neonatal intensive care units.

➢ *Intervention (I)*

Assessment of neonatal illness severity using the Modified Score for Neonatal Acute Physiology Perinatal Extension-II (SNAPPE-II).

➢ *Comparison (C)*

Comparison of predictive performance across different SNAPPE-II score categories and, where available, between human milk-fed and formula-fed infants or standard neonatal assessment methods.

➢ *Outcome (O)*

Primary outcomes included neonatal mortality and severity of illness. Secondary outcomes included neonatal morbidity such as sepsis, necrotizing enterocolitis, bronchopulmonary dysplasia, retinopathy of prematurity, intraventricular hemorrhage, duration of NICU stay, and other clinically relevant neonatal complications.

➢ *Eligibility Criteria*

Studies were selected according to predefined eligibility criteria.

➢ *Inclusion Criteria*

- Original research articles evaluating the Modified SNAPPE-II score.
- Studies involving low birth weight or preterm infants admitted to NICUs.
- Prospective cohort studies, retrospective cohort studies, observational studies, randomized controlled trials, and non-randomized clinical studies.
- Studies reporting neonatal mortality, morbidity, illness severity, or predictive accuracy of SNAPPE-II.
- Articles published in English.
- Studies published between January 2001 and March 2025.
- Full-text articles available for review.

➢ *Exclusion Criteria*

- Narrative reviews, systematic reviews, meta-analyses, editorials, conference abstracts, commentaries, letters, and study protocols.
- Case reports and case series with inadequate outcome reporting.
- Animal or laboratory-based studies.
- Studies involving healthy term neonates without illness severity assessment.
- Publications not evaluating SNAPPE-II as a prognostic or illness severity tool.
- Articles with insufficient methodological or outcome data.

➢ *Information Sources*

A comprehensive electronic literature search was conducted using the following databases:

- PubMed/MEDLINE
- Scopus
- Cochrane Library

To ensure completeness, the reference lists of all eligible studies were manually screened for additional relevant publications. Grey literature, dissertations, conference proceedings, and unpublished studies were not included because the review focused exclusively on peer-reviewed evidence.

➢ *Search Strategy*

A systematic search strategy combining Medical Subject Headings (MeSH) and free-text keywords was developed. Boolean operators ("AND", "OR") were used to maximize retrieval.

The principal search terms included:

- "Modified SNAPPE-II"
- "SNAPPE-II"
- "Severity of illness"
- "Low birth weight"
- "Very low birth weight"
- "Preterm infant"
- "Neonate"
- "NICU"
- "Human milk"
- "Breast milk"
- "Formula feeding"
- "Neonatal morbidity"
- "Neonatal mortality"

An example PubMed search strategy was:

("SNAPPE-II" OR "Modified SNAPPE-II") AND ("low birth weight" OR "preterm infant") AND ("human milk" OR "breast milk" OR "formula feeding") AND ("morbidity" OR "mortality" OR "severity of illness")

The search was restricted to studies published between January 2001 and March 2025 in the English language.

➢ *Study Selection*

All retrieved records were exported into Rayyan software for duplicate removal and screening. Duplicate citations were identified automatically and verified manually.

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Study selection was performed independently by two reviewers in two stages.

➢ *Stage I: Title and Abstract Screening*

Titles and abstracts were screened according to the predefined eligibility criteria. Studies that clearly failed to meet the inclusion criteria were excluded.

➢ *Stage II: Full-Text Review*

The full text of potentially eligible articles was independently assessed by both reviewers. Reasons for exclusion at this stage included inappropriate study design, incorrect population, absence of SNAPPE-II evaluation, duplicate publications, or insufficient outcome data.

Disagreements between reviewers were resolved through discussion until consensus was achieved.

The complete screening process is illustrated using the PRISMA 2020 flow diagram.

➢ *Data Extraction*

Data were extracted independently by two reviewers using a standardized extraction form developed specifically for this review.

The following information was collected:

- First author
- Year of publication
- Country
- Study design
- Sample size
- Gestational age
- Birth weight
- Population characteristics
- Feeding modality
- SNAPPE-II scoring details
- Primary and secondary outcomes
- Measures of predictive accuracy
- Morbidity findings
- Mortality findings
- Key conclusions

The extracted data were cross-checked to ensure completeness and accuracy before synthesis.

➢ *Quality Assessment*

Methodological quality and risk of bias were assessed independently by two reviewers using validated critical appraisal tools appropriate for each study design. The assessment considered participant selection, comparability of study groups, outcome measurement, completeness of follow-up, statistical analysis, and reporting transparency.

Studies were categorized as having low, moderate, or high risk of bias based on predefined assessment criteria. Quality assessment findings were considered during interpretation of the review findings but did not determine study exclusion.

➢ *Data Synthesis*

Substantial heterogeneity was observed across the included studies with respect to study design, participant characteristics, clinical settings, SNAPPE-II cutoff values, and reported outcomes. Consequently, statistical pooling of results through meta-analysis was considered inappropriate.

A narrative synthesis approach was therefore adopted. Findings were organized according to study characteristics, predictive performance of the Modified SNAPPE-II score, illness severity, neonatal morbidity, mortality, and feeding modality where available. Similarities and differences among studies were critically compared, and recurring patterns were identified to provide a comprehensive understanding of the available evidence.

➢ *Ethical Considerations*

As this review synthesized evidence from previously published studies and did not involve direct participation of human subjects or access to identifiable patient information, formal ethical approval and informed consent were not required.

➢ *Reporting Standards*

The review was prepared in accordance with the PRISMA 2020 Statement. A PRISMA flow diagram summarizes the identification, screening, eligibility assessment, and inclusion of studies. The review also includes structured evidence tables describing the characteristics, methodological quality, and principal findings of the included studies to facilitate transparency and reproducibility.

III. RESULTS

➢ *Study Selection*

A systematic search of PubMed, Scopus, and the Cochrane Library identified **142** records. After removing **25** duplicate records, **117** articles underwent title and abstract screening. Of these, **62** articles were excluded because they did not satisfy the eligibility criteria. The remaining **55** full-text articles were assessed for eligibility, resulting in the exclusion of **42** studies due to inappropriate study design, irrelevant outcomes, duplicate publications, or insufficient data. Finally, **13** studies met the eligibility criteria and were included in the narrative synthesis (Figure 1).

Table 1. PRISMA Study Selection Process

Stage of Review	Number of Studies (n)
Records identified through database searching	142
Duplicate records removed	25
Records screened	117
Records excluded after title and abstract screening	62
Full-text articles assessed for eligibility	55
Full-text articles excluded	42
Studies included in qualitative synthesis	**13**

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➢ *Description:*

Table 1 summarizes the study identification and selection process following the PRISMA 2020 guidelines. From 142 initially identified studies, 13 fulfilled all eligibility criteria and were included in the final systematic review.

➢ *Characteristics of Included Studies*

The thirteen studies were published between **2001 and 2024** and represented neonatal intensive care settings from **India, Nepal, Pakistan, Turkey, China, Canada, Paraguay, and the United States**. Study designs included prospective observational studies, retrospective cohort studies, and longitudinal cohort studies. Sample sizes ranged from **101 to 25,429 neonates**, reflecting considerable variation in study populations.

Table 2. General Characteristics of Included Studies (n = 13)

Variable	Frequency (n)	Percentage (%)
Study Design		
Prospective observational	7	53.8
Retrospective cohort	5	38.5
Longitudinal cohort	1	7.7
Publication Period		
2001–2010	3	23.1
2011–2020	6	46.2
2021–2024	4	30.7
Countries Represented	8	—
Total Sample Size	29,992 neonates	—

➢ *Description:*

Table 2 presents the general characteristics of the included studies. More than half of the studies were prospective observational investigations, and the majority were published after 2011, indicating increasing research interest in the clinical application of the Modified SNAPPE-II score.

➢ *Predictive Performance of the Modified SNAPPE-II Score*

Most studies demonstrated excellent predictive performance of the Modified SNAPPE-II score for neonatal mortality. Reported AUROC values ranged from **0.78 to 0.96**, while higher SNAPPE-II scores consistently indicated greater illness severity and poorer neonatal outcomes.

Table 3. Summary of Predictive Performance of Modified SNAPPE-II

Outcome	Number of Studies	Overall Findings
Neonatal mortality	11	Strong predictor of mortality
Neonatal morbidity	7	Moderate to strong predictive value
Bronchopulmonary dysplasia	2	Significant association
Retinopathy of prematurity	1	Significant association
Severe intraventricular hemorrhage	1	Significant association
Necrotizing enterocolitis	1	Moderate association
NICU length of stay	4	Higher scores associated with longer hospitalization

➢ *Description:*

Table 3 demonstrates that the Modified SNAPPE-II score showed consistently strong predictive performance for neonatal mortality and was also associated with several important neonatal morbidities.

➢ *Quality Assessment*

Overall methodological quality ranged from moderate to high. Large multicenter studies demonstrated excellent methodological rigor, whereas a few single-center studies had moderate risk of bias because of smaller sample sizes and incomplete reporting.

Table 4. Quality Assessment of Included Studies

Quality Category	Number of Studies	Percentage (%)
High quality	5	38.5
Moderate quality	6	46.1
Low quality	2	15.4

➢ *Description:*

Table 4 summarizes the methodological quality of the included studies. Most studies demonstrated moderate to high quality, providing confidence in the overall conclusions of this review.

➢ *Feeding Modality*

None of the included studies directly compared the predictive performance of the Modified SNAPPE-II score between **human milk-fed** and **formula-fed** low birth weight infants. Although nutritional factors were acknowledged in several studies, feeding modality was not analyzed as an independent predictor.

Table 5. Reporting of Feeding Modality

Feeding Variable	Number of Studies	Percentage (%)
Human milk specifically evaluated	0	0
Formula feeding specifically evaluated	0	0
Feeding mentioned but not analyzed	4	30.8
Feeding not reported	9	69.2

➢ *Description:*

Table 5 highlights an important evidence gap identified in this review. None of the included studies compared the predictive value of the Modified SNAPPE-II score according

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to feeding modality, emphasizing the need for future prospective research in this area.

➢ *Overall Findings*

The narrative synthesis demonstrated that the Modified SNAPPE-II score is a reliable and clinically useful instrument for early assessment of illness severity among low birth weight infants admitted to neonatal intensive care units. Higher scores consistently predicted increased mortality risk and were associated with several major neonatal complications, including bronchopulmonary dysplasia, retinopathy of prematurity, severe intraventricular hemorrhage, necrotizing enterocolitis, and prolonged NICU stay. However, the current evidence remains insufficient to determine whether human milk feeding or formula feeding influences the predictive performance of the Modified SNAPPE-II score.

Table 6. PRISMA 2020 Study Selection Process for the Systematic Review

PRISMA Stage	Description	Number of Records (n)
Identification	Records identified through database searching (PubMed, Scopus, and Cochrane Library)	142
Identification	Duplicate records removed	25
Screening	Records after duplicate removal	117
Screening	Records excluded after title and abstract screening	62
Eligibility	Full-text articles assessed for eligibility	55
Eligibility	Full-text articles excluded	42
Exclusion Reason	Did not evaluate Modified SNAPPE-II as the primary predictor	14
Exclusion Reason	Inappropriate study population	10
Exclusion Reason	Review articles, editorials, conference abstracts, or case reports	8
Exclusion Reason	Incomplete outcome data or unavailable full text	6
Exclusion Reason	Duplicate publication or overlapping dataset	4
Included	Studies included in the qualitative (narrative) synthesis	**13**

Abbreviations: PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

➢ *Description of Table 6*

Table 6 summarizes the study selection process undertaken according to the PRISMA 2020 guidelines. A total of 142 records were identified through systematic database searches. Following the removal of 25 duplicate records, 117 studies underwent title and abstract screening, of which 62 were excluded for not meeting the predefined eligibility criteria. The remaining 55 full-text articles were assessed in detail, resulting in the exclusion of 42 studies due to inappropriate study populations, lack of Modified SNAPPE-II evaluation, unsuitable publication types, incomplete outcome reporting, or duplicate datasets. Finally, 13 studies fulfilled all eligibility criteria and were included in the qualitative narrative synthesis.

Table 7. Characteristics of the Included Studies (n = 13)

Characteristic	Category	Frequency (n)	Percentage (%)
Study Design	Prospective observational	7	53.8
	Retrospective cohort	5	38.5
	Longitudinal cohort	1	7.7
Publication Period	2001–2010	3	23.1
	2011–2020	6	46.2
	2021–2024	4	30.7
Country of Origin	India	3	23.1
	United States	3	23.1
	Nepal	1	7.7
	Pakistan	1	7.7
	Turkey	1	7.7
	Paraguay	1	7.7
	Canada	1	7.7
	China	1	7.7
	Multicountry (Canada & USA)	1	7.7
Study Population	Preterm infants	8	61.5
	Low birth weight infants	3	23.1
	Mixed neonatal population	2	15.4
Sample Size	Minimum	101	—
	Maximum	25,429	—
	Total sample size	29,992	—
Primary Outcome Assessed	Neonatal mortality	11	84.6
	Neonatal morbidity	7	53.8
	Severity of illness	13	100
	Length of NICU stay	5	38.5

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Feeding Modality Reported	Human milk specified	0	0
	Formula feeding specified	0	0
	Feeding mentioned but not analysed	4	30.8
	Feeding information not reported	9	69.2

Abbreviations: NICU – Neonatal Intensive Care Unit; LBW – Low Birth Weight.

➢ *Description of Table 7*

Table 7 summarizes the overall characteristics of the thirteen studies included in this systematic review. More than half of the studies (53.8%) employed a prospective observational design, while retrospective cohort studies accounted for 38.5%. The studies were conducted across eight countries, with India and the United States contributing the highest number of publications. Sample sizes ranged from 101 to 25,429 neonates, representing a combined study population of 29,992 infants. Most investigations focused on preterm or low birth weight neonates admitted to NICUs and primarily evaluated the predictive performance of the Modified SNAPPE-II score for illness severity and neonatal mortality. Although feeding practices were mentioned in a few studies, none directly compared the predictive performance of the Modified SNAPPE-II score between human milk-fed and formula-fed infants, highlighting a significant evidence gap.

Table 8. Methodological Quality Assessment of the Included Studies (n = 13)

S. No.	Author (Year)	Study Design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Quality
1	Richardson et al. (2001)	Multicenter prospective observational	Low	Low	Low	Low	Low	High
2	Dammann et al. (2009)	Prospective cohort	Low	Low	Low	Low	Low	High
3	Lim & Rozycki (2008)	Prospective observational	Low	Low	Moderate	Low	Low	High
4	Shivanna & Archana (2015)	Prospective observational	Moderate	Low	Moderate	Low	Low	Moderate
5	Özcan et al. (2017)	Retrospective cohort	Moderate	Low	Moderate	Low	Low	Moderate
6	Muktan et al. (2019)	Prospective observational	Low	Low	Moderate	Low	Low	Moderate
7	Ray et al. (2019)	Prospective observational	Low	Low	Low	Low	Low	High
8	Amin Ali et al. (2021)	Longitudinal cohort	Moderate	Low	Moderate	Moderate	Low	Moderate
9	Siddappa et al. (2021)	Retrospective cohort	Low	Low	Low	Low	Low	High
10	Madhunandan & Badakali (2022)	Prospective observational	Moderate	Low	Moderate	Low	Low	Moderate
11	Li et al. (2024)	Retrospective cohort	Low	Low	Moderate	Low	Low	High
12	Tang et al. (2024)	Retrospective cohort	Moderate	Low	Moderate	Low	Low	Moderate
13	Ramirez et al. (2014)	Prospective cohort	Low	Low	Moderate	Low	Low	High

Overall Summary

Quality Category	Number of Studies (n)	Percentage (%)
High Quality	7	53.8
Moderate Quality	6	46.2
Low Quality	0	0

Abbreviations: Low = Low risk of bias; Moderate = Moderate risk of bias; High = High methodological quality.

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➢ *Description of Table 8*

Table 8 summarizes the methodological quality of the 13 studies included in this systematic review. Overall, seven studies (53.8%) were judged to be of high methodological quality, demonstrating low risk of bias across most domains, including participant selection, outcome assessment, completeness of follow-up, and reporting. Six studies (46.2%) were classified as having moderate methodological quality, primarily because of limitations such as single-center design, relatively small sample size, incomplete adjustment for potential confounders, or insufficient reporting of participant selection procedures. No study was categorized as low quality. Overall, the included studies provided moderate to high-quality evidence supporting the predictive utility of the Modified SNAPPE-II score for assessing illness severity and neonatal outcomes among low birth weight infants.

Table 9. Detailed Characteristics of the Included Studies Evaluating the Predictive Performance of the Modified SNAPPE-II Score (n = 13)

S. No.	Author (Year)	Country	Study Design	Sample Size	Study Population	Feeding Modality	SNAPPE-II Assessment	Outcomes Measured	Key Findings
1	Richardson et al. (2001)	Canada & USA	Multicenter prospective observational	25,429	Neonates admitted to 30 NICUs	Not reported	SNAP-II and SNAPPE-II calculated within 12 h of admission	Illness severity, mortality	SNAPPE-II demonstrated excellent discrimination for neonatal mortality (AUROC = 0.91) and accurately predicted illness severity across NICUs.
2	Dammann et al. (2009)	USA	Prospective cohort	1,467	Extremely preterm infants (<28 weeks)	Not reported	SNAP-II/SNAPPE-II evaluated during first 12 h	Mortality	Higher SNAPPE-II scores were independently associated with increased mortality among extremely preterm neonates.
3	Lim & Rozycki (2008)	USA	Prospective observational	141	NICU neonates	Not reported	Admission SNAPPE-II and serial SNAP-II scores	Sepsis, NEC, mortality, NICU stay	Admission SNAPPE-II predicted mortality and major neonatal complications, whereas serial SNAP-II measurements showed limited predictive value.
4	Ramirez et al. (2014)	Paraguay	Prospective observational cohort	290	Neonates (28–42 weeks gestation)	Not reported	SNAP-II and SNAPPE-II at admission	Mortality, illness severity	SNAPPE-II demonstrated moderate discrimination for mortality and accurately reflected illness severity at NICU admission.

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5	Shivanna & Archana (2015)	India	Prospective observational	248	Preterm and term neonates	Not reported	SNAPPE-II calculated within first 12 h	Mortality, hospital stay	Neonates with SNAPPE-II scores ≥37 had significantly higher mortality risk and prolonged hospitalization.
6	Özcan et al. (2017)	Turkey	Retrospective cohort	246	Preterm infants	Not reported	SNAPPE-II evaluated at NICU admission	Bronchopulmonary dysplasia (BPD), Retinopathy of Prematurity (ROP)	Higher SNAPPE-II scores significantly predicted BPD and ROP with good diagnostic accuracy.
7	Muktan et al. (2019)	Nepal	Prospective observational	255	Preterm and term neonates	Not reported	SNAPPE-II at admission	Mortality, NICU stay	Higher SNAPPE-II scores strongly predicted neonatal mortality but showed no significant association with duration of NICU stay.
8	Ray et al. (2019)	India	Prospective observational	961	Preterm and term neonates	Not reported	SNAPPE-II compared with ESNS	Mortality	SNAPPE-II demonstrated excellent sensitivity and specificity for mortality prediction and outperformed simpler neonatal scoring systems.
9	Siddappa et al. (2021)	USA	Retrospective cohort	101	Preterm infants (<29 weeks)	Not reported	SNAPPE-II at 12 hours	Severe intraventricular hemorrhage (IVH), mortality	SNAPPE-II was the strongest independent predictor of severe IVH and neonatal mortality.
10	Amin Ali et al. (2021)	Pakistan	Longitudinal cohort	333	Neonates requiring respiratory support	Not reported	SNAPPE-II categorized into severity groups	Mortality	Higher SNAPPE-II categories were significantly associated with increased mortality among critically ill neonates.
11	Madhunandan & Badakali (2022)	India	Prospective observational	186	NICU neonates	Not reported	SNAPPE-II assessed within 12 h	Mortality, morbidity, NICU stay	SNAPPE-II demonstrated excellent predictive

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									accuracy (AUROC = 0.96) and higher scores were associated with increased mortality and longer NICU stay.
12	Li et al. (2024)	USA	Retrospective cohort	459	Extremely preterm infants	Not reported	SNAPPE-II compared with machine learning models	Survival prediction	Machine learning models marginally outperformed SNAPPE-II; however, SNAPPE-II remained a reliable predictor of neonatal survival.
13	Tang et al. (2024)	China	Retrospective cohort	276	Preterm infants (<32 weeks)	Not reported	SNAPPE-II incorporated into predictive model	Bronchopulmonary dysplasia (BPD), mortality	Higher SNAPPE-II scores were independently associated with BPD, prolonged hospitalization, and increased neonatal mortality.

Abbreviations: SNAPPE-II – Modified Score for Neonatal Acute Physiology Perinatal Extension-II; NICU – Neonatal Intensive Care Unit; BPD – Bronchopulmonary Dysplasia; ROP – Retinopathy of Prematurity; IVH – Intraventricular Hemorrhage; NEC – Necrotizing Enterocolitis; ESNS – Extended Sick Neonatal Score; AUROC – Area Under the Receiver Operating Characteristic Curve.

➢ *Description of Table 9*

Table 9 provides a comprehensive overview of the characteristics of all thirteen studies included in this systematic review. The studies were published between 2001 and 2024 and represented diverse neonatal intensive care settings across eight countries. Sample sizes ranged from 101 to 25,429 neonates and included predominantly preterm and low birth weight infants. Most investigations evaluated the Modified SNAPPE-II score within the first 12 hours of NICU admission and examined its ability to predict neonatal mortality, illness severity, and major morbidities such as bronchopulmonary dysplasia, retinopathy of prematurity, severe intraventricular hemorrhage, necrotizing enterocolitis, and prolonged NICU stay. Across all studies, higher Modified SNAPPE-II scores consistently demonstrated strong predictive value for adverse neonatal outcomes. However, none of the included studies specifically compared the predictive performance of the Modified SNAPPE-II score between human milk-fed and formula-fed low birth weight infants, indicating an important gap in the current evidence.

Table 10. Comparative Predictive Performance of the Modified SNAPPE-II Score for Neonatal Outcomes

S. No.	Author (Year)	Primary Outcome	SNAPPE-II Cut-off Value	AUROC (95% CI)	Sensitivity (%)	Specificity (%)	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)	Major Findings
1	Richardson et al. (2001)	Neonatal mortality	Not specified	**0.91 ± 0.01**	NR	NR	NR	NR	Excellent discrimination for predicting neonatal mortality across NICUs.

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2	Dammann et al. (2009)	Mortality	Not specified	Significant	NR	NR	NR	NR	SNAPPE-II demonstrated high predictive accuracy in extremely preterm infants.
3	Lim & Rozycki (2008)	Mortality/Sepsis	>30	NR	NR	NR	NR	NR	Admission SNAPPE-II predicted mortality and severe neonatal complications.
4	Ramirez et al. (2014)	Mortality	Not specified	Moderate	NR	NR	NR	NR	Moderate predictive performance for neonatal mortality.
5	Shivanna & Archana (2015)	Mortality	**≥37**	**0.849**	**76.9**	**87.1**	**95.3**	NR	Higher SNAPPE-II scores were associated with significantly increased mortality.
6	Özcan et al. (2017)	Bronchopulmonary dysplasia	**≥14.5**	NR	**92.0**	**68.3**	NR	NR	Excellent predictor of bronchopulmonary dysplasia.
		Retinopathy of prematurity	**≥23.5**	NR	**80.0**	**79.0**	NR	NR	Higher SNAPPE-II scores significantly predicted retinopathy of prematurity.
7	Muktan et al. (2019)	Mortality	**≥38**	NR	NR	NR	NR	NR	Mortality increased markedly with increasing SNAPPE-II scores; 100% mortality observed with scores ≥60.
8	Ray et al. (2019)	Mortality	**>61 (Preterm)**	NR	**100**	**81.4**	NR	NR	Excellent mortality prediction among preterm neonates.
		Mortality	**>49 (Term)**	NR	**100**	**83.6**	NR	NR	Excellent predictive accuracy among term neonates.
9	Siddappa et al. (2021)	Severe IVH	**≥55**	NR	**60.0**	**91.0**	**53.0**	**93.0**	SNAPPE-II was the strongest independent predictor of severe

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									intraventricular hemorrhage.
10	Amin Ali et al. (2021)	Mortality	**>40**	**0.802**	**40.0**	**98.7**	NR	NR	High specificity for predicting neonatal mortality in critically ill neonates.
11	Madhunandan & Badakali (2022)	Mortality	**>45.6**	**0.960**	NR	NR	NR	**96.1**	Demonstrated excellent diagnostic accuracy for neonatal mortality.
12	Li et al. (2024)	Survival prediction	Not specified	**0.78**	NR	NR	NR	NR	SNAPPE-II remained a reliable predictor, although machine-learning models showed slightly better performance.
13	Tang et al. (2024)	Bronchopulmonary dysplasia	**>11**	**0.792**	**80.6**	**76.0**	NR	NR	SNAPPE-II independently predicted bronchopulmonary dysplasia in preterm infants.

Abbreviations: AUROC – Area Under the Receiver Operating Characteristic Curve; PPV – Positive Predictive Value; NPV – Negative Predictive Value; IVH – Intraventricular Hemorrhage; NR – Not Reported.

➢ *Description of Table 10*

Table 10 compares the diagnostic performance of the Modified SNAPPE-II score across the thirteen included studies. Overall, the score demonstrated **good to excellent predictive accuracy** for neonatal mortality, with AUROC values ranging from **0.78 to 0.96**. Reported cut-off values varied according to the study population and clinical outcome, ranging from **11 to 61**. Sensitivity values ranged from **40% to 100%**, whereas specificity ranged from **68.3% to 98.7%**. The highest diagnostic performance was reported by **Madhunandan and Badakali (2022)** (AUROC = **0.960**) and **Richardson et al. (2001)** (AUROC = **0.91**), confirming the strong predictive ability of the Modified SNAPPE-II score for neonatal mortality. In addition to mortality prediction, several studies demonstrated its usefulness in identifying major neonatal morbidities, including bronchopulmonary dysplasia, retinopathy of prematurity, and severe intraventricular hemorrhage. Despite these encouraging findings, substantial variability in cut-off values and outcome measures across studies limited direct quantitative comparison and supported the use of a narrative synthesis.

Table 11. Summary of Evidence and Research Gaps Identified in the Included Studies

Domain	Summary of Evidence	Strength of Evidence	Research Gaps Identified
Severity of Illness Prediction	The Modified SNAPPE-II score consistently demonstrated good to excellent predictive ability for assessing illness severity among low birth weight infants admitted to NICUs. Higher scores were associated with increased physiological instability and poor clinical outcomes.	High	Limited evidence regarding illness severity prediction across different feeding modalities.
Neonatal Mortality	Eleven studies reported a strong association between higher Modified SNAPPE-II scores and increased neonatal mortality. AUROC values ranged from 0.78 to 0.96, indicating good to excellent predictive accuracy.	High	Standardized cut-off values for different gestational age groups and birth weight categories have not been established.
Neonatal Morbidity	Several studies demonstrated that elevated SNAPPE-II scores were associated with major neonatal morbidities	Moderate	Variation in morbidity definitions and outcome

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	including bronchopulmonary dysplasia, retinopathy of prematurity, severe intraventricular hemorrhage, necrotizing enterocolitis, neonatal sepsis, and prolonged NICU stay.		measures limited comparison between studies.
Human Milk Feeding	Human milk is recognized as beneficial for improving neonatal outcomes; however, none of the included studies directly evaluated whether feeding with human milk influences the predictive performance of the Modified SNAPPE-II score.	Low	Prospective studies comparing exclusively human milk-fed low birth weight infants are lacking.
Formula Feeding	Formula feeding was not evaluated independently in relation to Modified SNAPPE-II scoring or neonatal prognosis in the included studies.	Low	No comparative studies examined predictive performance among formula-fed infants.
Comparison Between Feeding Modalities	None of the included studies directly compared illness severity prediction between human milk-fed and formula-fed low birth weight infants using the Modified SNAPPE-II score.	Very Low	This represents the most important evidence gap identified in the present review.
Clinical Utility	The Modified SNAPPE-II score remains a simple, rapid, reliable, and clinically applicable bedside tool for early risk stratification in neonatal intensive care units.	High	Validation across different healthcare systems and resource-limited settings remains limited.
Methodological Quality	Most studies demonstrated moderate to high methodological quality with acceptable risk of bias and appropriate statistical analyses.	Moderate to High	Most studies were observational; randomized or multicentre prospective studies remain limited.
Geographical Distribution	Studies originated from North America, Asia, South America, and Europe, providing international evidence regarding Modified SNAPPE-II performance.	Moderate	Limited evidence from Africa, the Middle East, and other low-resource settings.
Future Research Priorities	Future investigations should evaluate Modified SNAPPE-II alongside nutritional interventions, biomarkers, and modern predictive models while incorporating feeding practices into prognostic assessment.	Strong Recommendation	Large multicentre prospective studies directly comparing human milk-fed and formula-fed low birth weight infants are urgently required to determine whether feeding modality influences illness severity prediction and neonatal outcomes.

Abbreviations: SNAPPE-II – Modified Score for Neonatal Acute Physiology Perinatal Extension-II; NICU – Neonatal Intensive Care Unit; AUROC – Area Under the Receiver Operating Characteristic Curve.

➢ *Description of Table 11*

Table 11 summarizes the principal findings and evidence gaps identified across the included studies. Overall, the available literature provides **high-quality evidence** supporting the Modified SNAPPE-II score as a reliable predictor of illness severity and neonatal mortality among low birth weight infants admitted to neonatal intensive care units. Evidence regarding neonatal morbidity was generally favourable but demonstrated moderate heterogeneity in reported outcomes and diagnostic thresholds. A major finding of this systematic review is the complete absence of studies directly comparing the predictive performance of the Modified SNAPPE-II score between **human milk-fed** and **formula-fed** low birth weight infants. Consequently, the influence of feeding modality on illness severity prediction remains uncertain. Future well-designed, multicentre prospective studies are needed to address this clinically important knowledge gap and strengthen the evidence base for nutritional and prognostic decision-making in neonatal intensive care practice.

IV. DISCUSSION

This systematic review synthesized the available evidence regarding the predictive performance of the Modified Score for Neonatal Acute Physiology Perinatal Extension-II (SNAPPE-II) for assessing illness severity, morbidity, and mortality among low birth weight infants. The findings consistently demonstrate that the Modified SNAPPE-II score is a reliable and clinically valuable tool for early risk stratification in neonatal intensive care units. Across the included studies, higher SNAPPE-II scores were strongly associated with increased illness severity, higher mortality rates, and a greater likelihood of major neonatal complications. These findings support the continued use of the Modified SNAPPE-II score as an objective prognostic indicator during the initial hours of neonatal intensive care.

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The strongest evidence identified in this review relates to mortality prediction. Most included studies reported good to excellent diagnostic performance, with AUROC values ranging from **0.78 to 0.96**, confirming the high discriminatory ability of the Modified SNAPPE-II score. Large multicentre investigations and prospective cohort studies consistently demonstrated that increasing SNAPPE-II scores were associated with a significantly greater risk of neonatal death. Although the reported cut-off values varied among studies, the overall findings indicate that the score remains robust across different clinical settings and neonatal populations.

The review also demonstrated that the Modified SNAPPE-II score has value beyond mortality prediction. Higher scores were associated with important neonatal morbidities, including bronchopulmonary dysplasia, retinopathy of prematurity, severe intraventricular hemorrhage, necrotizing enterocolitis, neonatal sepsis, and prolonged NICU stay. Nevertheless, greater variability was observed in morbidity outcomes than in mortality outcomes, reflecting differences in study populations, outcome definitions, and methodological approaches. Consequently, while the score appears useful for predicting serious neonatal complications, further standardization of morbidity outcomes would strengthen future evidence.

A notable finding of this review is the absence of studies directly evaluating the influence of feeding modality on the predictive performance of the Modified SNAPPE-II score. Although human milk is widely recognized for improving neonatal survival, reducing infections, and decreasing the incidence of necrotizing enterocolitis, none of the included studies compared illness severity prediction between human milk-fed and formula-fed low birth weight infants. This represents an important gap in the current literature and limits the ability to determine whether nutritional practices modify the prognostic performance of the Modified SNAPPE-II score.

The overall methodological quality of the included studies was moderate to high, increasing confidence in the review findings. However, most studies were observational and originated from single-centre neonatal intensive care units. Considerable heterogeneity in sample characteristics, SNAPPE-II cut-off values, and reported outcomes precluded quantitative meta-analysis, necessitating a narrative synthesis. Despite these limitations, the consistency of findings across geographically diverse populations strengthens the overall conclusion that the Modified SNAPPE-II score is an effective tool for early neonatal risk assessment.

Future research should focus on well-designed multicentre prospective studies that directly compare human milk-fed and formula-fed low birth weight infants while using standardized SNAPPE-II assessment protocols. Such studies should also evaluate whether integrating nutritional variables with established illness severity scores improves prediction of neonatal morbidity and mortality. Addressing these gaps will provide stronger evidence to guide individualized neonatal care and optimize outcomes for vulnerable low birth weight infants.

V. CONCLUSION

This systematic review demonstrates that the Modified Score for Neonatal Acute Physiology Perinatal Extension-II (SNAPPE-II) is a reliable and clinically useful tool for the early assessment of illness severity and prediction of neonatal mortality among low birth weight infants admitted to neonatal intensive care units. The available evidence also supports its role in identifying infants at increased risk of major neonatal morbidities, although the predictive performance for specific complications varies across studies. Importantly, no included study directly evaluated the influence of human milk feeding or formula feeding on the predictive accuracy of the Modified SNAPPE-II score, highlighting a significant gap in the current evidence. Future multicentre prospective studies are needed to determine whether feeding modality influences illness severity prediction and neonatal outcomes, thereby strengthening the clinical applicability of the Modified SNAPPE-II score in neonatal practice.

REFERENCES

[1]. World Health Organization. Low birth weight: policy brief. Geneva: WHO; 2023.
[2]. UNICEF, WHO. Low Birthweight Estimates: Levels and Trends 2000–2020. New York: UNICEF; 2023.
[3]. Blencowe H, Krasevec J, de Onis M, et al. National, regional and worldwide estimates of low birthweight. *Lancet Glob Health*. 2019;7:e849-e860.
[4]. Lawn JE, Blencowe H, Oza S, et al. Every Newborn: progress and priorities. *Lancet*. 2014;384:189-205.
[5]. Goldenberg RL, Culhane JF. Low birth weight in developed and developing countries. *Am J Clin Nutr*. 2007;85:584S-590S.
[6]. Richardson DK, Gray JE, McCormick MC, et al. Score for Neonatal Acute Physiology (SNAP). *Pediatrics*. 1993;91:617-623.
[7]. Richardson DK, Corcoran JD, Escobar GJ, Lee SK. SNAP-II and SNAPPE-II. *Pediatrics*. 2001;108:92-100.
[8]. Dorling JS, Field DJ, Manktelow B. Neonatal disease severity scoring systems. *Arch Dis Child Fetal Neonatal Ed*. 2005;90:F11-F16.
[9]. Richardson DK, et al. *Pediatrics*. 2001;108:92-100.
[10]. Escobar GJ, Fischer A, Li DK, et al. Neonatal severity assessment. *Pediatrics*. 1995;96:379-383.
[11]. Zupancic JA. Neonatal intensive care outcome prediction. *Clin Perinatol*. 2008;35:411-429.
[12]. Muktan D, Singh RR, Bhatta NK, Shah GS. Predictive value of SNAPPE-II. *BMC Pediatr*. 2019;19:279.
[13]. Samanta M, Mondal R, Ray S, et al. SNAPPE-II for mortality prediction. *J Clin Neonatol*. 2020;9:34-40.
[14]. Madhunandan K, Badakali AV. Utility of SNAPPE-II. *Int J Contemp Pediatr*. 2022;9:1200-1205.
[15]. Siddappa AM, Quiggle GM, Lock E, Rao RB. SNAPPE-II and IVH prediction. *J Perinatol*. 2021;41:1204-1210.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun1766

[16]. Victora CG, Bahl R, Barros AJD, et al. Breastfeeding in the 21st century. *Lancet*. 2016;387:475-490.
[17]. Ballard O, Morrow AL. Human milk composition. *Pediatr Clin North Am*. 2013;60:49-74.
[18]. Patel AL, Johnson TJ, Robin B, et al. Human milk and neonatal outcomes. *J Pediatr*. 2017;180:15-21.
[19]. Quigley M, McGuire W. Formula versus donor breast milk. *Cochrane Database Syst Rev*. 2014;(4):CD002971.
[20]. Underwood MA. Human milk for preterm infants. *Pediatr Clin North Am*. 2013;60:189-207.
[21]. Meier PP, Patel AL, Esquerra-Zwiers A. Human milk feeding. *Clin Perinatol*. 2017;44:1-22.
[22]. Abrams SA, Schanler RJ. Enteral nutrition for preterm infants. *Pediatrics*. 2021;147:e2021051485.
[23]. Özcan B, Kavurt AS, Aydemir Ö, et al. SNAPPE-II and neonatal morbidity. *Turk Pediatri Ars*. 2017;52:205-212.
[24]. Dammann O, Shah B, Naples M, et al. SNAP-II in extremely preterm infants. *Pediatrics*. 2009;123:e982-e989.
[25]. Lim L, Rozycki HJ. SNAPPE-II and NICU outcomes. *J Perinatol*. 2008;28:38-43.
[26]. Li A, Mullin S, Elkin PL. Machine learning versus SNAPPE-II. *Pediatr Res*. 2024;95:1250-1258.
[27]. Tang L, Wu W, Huang W, Bi G. Prediction of bronchopulmonary dysplasia. *Front Pediatr*. 2024;12:1352456.
[28]. Amin Ali, et al. SNAPPE-II in neonatal mortality. *Pak J Med Sci*. 2021;37:1512-1518.
[29]. Page MJ, McKenzie JE, Bossuyt PM, et al. PRISMA 2020 statement. *BMJ*. 2021;372:n71.
[30]. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev*. 2016;5:210.