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Original Article

Comparative Prognostic Value of Combined versus Conventional Apgar Scores for Neonatal Outcomes: A Prospective Cohort Study

Running Title: Comparative Prognosis of Combined vs. Conventional Apgar Scores in Neonates

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Abstract

Objective: To compare the predictive performance of the combined Apgar score versus the conventional Apgar score in forecasting adverse clinical outcomes among hospitalized neonates in a tertiary care setting.

Methods: This prospective cohort study, conducted from April to October 2023 at Imam Khomeini and Sina Hospitals in Ahvaz, Iran, enrolled 637 neonates requiring hospitalization. Both conventional and combined Apgar scores were recorded at 1, 5, and 10 minutes post-birth by trained neonatologists following standardized protocols. The combined Apgar score integrated gestational age adjustments and resuscitative interventions, while the conventional score assessed five physiological parameters. Primary outcomes included mortality, need for mechanical ventilation, length of hospital stay, seizures, and blood product infusions. Predictive performance was evaluated using Receiver Operating Characteristic (ROC) curve analysis, with an Area Under the Curve (AUC) of greater than 0.75 as the threshold for acceptable sensitivity. Multivariable logistic regression was adjusted for confounders, including gestational age and birth weight.

Results: Among the 637 neonates enrolled (64% male and 36% female; gestational age, 23–42 weeks; birth weight, 500–5060 g), 193 were born preterm. The combined Apgar score demonstrated significantly higher sensitivity and specificity than the conventional score in predicting mortality (n = 99), mechanical ventilation (n = 166), seizures (n = 51), blood product infusions (n = 139), and prolonged hospital stays (all AUC > 0.75, $p < 0.0001$). Significant negative correlations were observed between Apgar scores and adverse outcomes, with the combined score showing stronger prognostic accuracy, particularly in preterm infants.

Conclusion: The combined Apgar score, by incorporating gestational age and intervention data, offers superior predictive accuracy for neonatal morbidity and mortality compared to the conventional method. Its adoption in clinical practice could enhance early identification of high-risk neonates, optimize resource allocation, and improve outcomes, particularly in preterm and high-risk populations. Multicenter studies with long-term follow-up are warranted to validate and extend these findings.

Keywords: Combined Apgar score, conventional Apgar score, neonatal outcomes, ROC analysis, preterm infants.

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Introduction

Recently, assessing neonatal status after birth using the combined Apgar method is recommended for a more precise and rapid determination of neonatal clinical conditions in the first few minutes instead of the "conventional" Apgar method (1). The Apgar score is an indicator of the newborn's health status and the necessity of medical interventions to stabilize the neonate. However, various factors such as gestational age, medications administered to the mother during childbirth, infection, resuscitation procedures, and maternal-fetal complications affect the Apgar score. Hence, the use of the new combined method is suggested (2).In the combined method, in addition to assessing the neonatal status using the "conventional" Apgar method, attention is paid to the gestational age and interventions performed to stabilize the neonate, and scores are given accordingly (3). Considering the components of Apgar scoring in the "combined" method, better prediction of neonatal clinical outcomes is possible from the early moments (4). Several studies have shown that, in the event of hemodynamic instability in neonates, the set of reactions aimed at stabilizing the conditions leads to changes. If improvement and correction of the condition are not possible, various complications in metabolism, as well as in the function of the brain, heart, adrenal glands, lungs, and kidneys, will be observed (5, 6).

Although the combined Apgar score, especially at 10 minutes after birth, is helpful in early assessment of asphyxia, considering the components used in the combined method, timely prediction of other severe problems is also probable, which seems useful for early postnatal complications (7). Nielsen et al. in 2015 demonstrated that due to the limitations of the "conventional" Apgar method, the "combined" method provides better prediction for asphyxia and other neurological problems in distressed neonates. According to studies by Rodríguez (2011) and Nielsen (2016), the "combined" method is valuable not only for predicting asphyxia but also for predicting other associated complications. Jain et al. (2019) showed that although the "combined" method is more valuable than the "conventional" method in predicting the death of term and near-term neonates, it has no specific value in evaluating seizures and the need for ventilation. Furthermore, Katongo in 2020 demonstrated that combined Apgar is a valuable method for assessing the mortality outcomes of preterm infants as well (8).

Study Design & Methods:

Study Design

This prospective observational cohort study aimed to evaluate and compare the predictive performance of the combined Apgar score with that of the conventional Apgar score in forecasting adverse clinical outcomes among hospitalized neonates. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies to ensure methodological rigor and transparency. This study was conducted over a period of 7 months, from April 1, 2023, to October 31, 2023. The investigation focused on neonates requiring hospitalization immediately post-birth or upon admission, allowing for real-time assessment of Apgar scores and subsequent tracking of clinical endpoints. This design

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allowed for the assessment of short-term outcomes in a naturalistic clinical setting, minimizing selection bias while capturing a representative sample of high-risk neonates in a tertiary care environment. The prospective nature facilitated standardized data collection protocols, reducing recall bias and ensuring temporal sequencing between Apgar assessments and outcomes.

Setting

The study was carried out at two major tertiary referral hospitals in Ahvaz, Iran: Imam Khomeini Hospital and Sina Hospital, both affiliated with Ahvaz Jundishapur University of Medical Sciences (AJUMS). Imam Khomeini Hospital serves as a primary referral center for high-risk pregnancies, including preterm deliveries and maternal-fetal complications, with a well-equipped Neonatal Intensive Care Unit (NICU) handling approximately 1,500 neonatal admissions annually. Sina Hospital complements this by managing a mix of routine and complicated deliveries, with specialized neonatal wards. These settings were selected for their high volume of neonatal admissions (exceeding 1,400 during the study period) and diverse case mix, reflecting the real-world variability in gestational age, birth weight, and comorbidities. All assessments and data collection took place in the delivery rooms, NICUs, and postnatal wards, with coordination among multidisciplinary teams that included neonatologists, pediatric residents, nurses, and respiratory therapists.

Participants

Eligible participants included all neonates born in or admitted to the aforementioned hospitals during the study period who required hospitalization for any medical reason, such as respiratory distress, suspected infection, prematurity-related complications, or hemodynamic instability. A total of 1,468 neonates were initially screened, with 637 ultimately enrolled after applying inclusion and exclusion criteria. Inclusion criteria encompassed live births at any gestational age (from 23 to 42 weeks) and birth weights ranging from 500 to 5,060 grams, ensuring representation across preterm (n=193, <37 weeks), near-term, and term infants. Neonates transferred from external facilities were included if Apgar scores could be reliably documented or reassessed upon arrival at the facility.

Exclusion criteria were rigorously applied to minimize confounding and ensure data integrity: (1) severe or significant congenital anomalies (e.g., complex cardiac defects, chromosomal abnormalities like trisomy 21, or neural tube defects) that could independently influence outcomes irrespective of Apgar scores; (2) parental or guardian unwillingness to provide informed consent for participation; (3) inadequate or uncertain access to essential neonatal information, such as incomplete medical records or unverifiable gestational age; (4) voluntary discharge against medical advice within the first 24 hours post-birth; and (5) non-hospitalization in the early postnatal period (e.g., immediate outpatient management). These criteria resulted in the exclusion of 831 neonates, primarily due to congenital disorders (n = 412) and incomplete data (n = 256), yielding a final analytic cohort of 637 neonates (64% male, 36% female).

Recruitment was conducted consecutively and non-randomly, with informed consent obtained from parents or guardians prior to enrollment, in

accordance with ethical standards. No incentives were provided, and participation did not alter standard clinical care.

Apgar Scoring Procedures

Apgar scores were systematically recorded at 1, 5, and 10 minutes post-birth by trained neonatologists or pediatric residents present in the delivery room, using standardized protocols to ensure inter-rater reliability. To enhance consistency, all assessors underwent a mandatory 2-hour training session on both scoring methods, which included case simulations and calibration exercises. This training resulted in an intra-class correlation coefficient (ICC) of greater than 0.85 for score agreement, as determined by pilot testing with 50 neonates.

Conventional Apgar Score

The conventional Apgar score, initially developed by Virginia Apgar in 1952, is calculated according to standard guidelines from the American Academy of Pediatrics (AAP) and the American College of Obstetricians and Gynecologists (ACOG). It evaluates five physiological parameters, each scored from 0 to 2, for a total range of 0–10:

• *Appearance (Skin Color):* 2 = pink body and extremities; 1 = pink body with blue extremities (acrocyanosis); 0 = pale or blue all over.

• *Pulse (Heart Rate):* 2 = >100 beats per minute (bpm); 1 = <100 bpm; 0 = absent.

• *Grimace (Reflex Irritability):* 2 = active response (e.g., cry, cough, or sneeze to stimulation); 1 = grimace or weak response; 0 = no response.

• *Activity (Muscle Tone):* 2 = active movement; 1 = some flexion of extremities; 0 = limp.

• *Respiration (Effort):* 2 = strong cry; 1 = weak or irregular; 0 = absent.

A score of 7–10 indicates good condition, 4–6 moderate depression requiring stimulation, and 0–3 severe depression necessitating resuscitation.

Combined Apgar Score

The combined Apgar score, a more advanced metric introduced by Rüdiger et al. in 2012, integrates the Specified Apgar (assessing the neonate's intrinsic condition, adjusted for gestational age) and Expanded Apgar (quantifying resuscitative interventions), yielding a total score of 0–17. This method addresses limitations of the conventional score by decoupling physiological status from maturity and medical support, providing superior prognostic value, especially in preterm or resuscitated infants.

• **Specified Apgar Component (0–10):** Focuses on the neonate's clinical condition, independent of interventions, with gestational age-appropriate expectations:

o *Appearance (Skin Color):* 2 = completely pink (appropriate for GA); 1 = centrally pink with acrocyanosis; 0 = centrally blue or pale.

o Pulse (Heart Rate): 2 = >100 bpm; 1 = <100 bpm; 0 = no heartbeat.

o Grimace (Reflex Irritability): 2 = appropriate for GA (e.g., vigorous in term, adjusted response in preterm); 1 = reduced for GA; 0 = absent.

o Activity (Muscle Tone): 2 = appropriate for GA; 1 = reduced for GA; 0 = flaccid.

o Respiration (Chest Movement): 2 = regular; 1 = small or irregular; 0 = absent.

• **Expanded Apgar Component (0–7):** Scores interventions performed, with 1 point for no

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intervention and 0 for intervention applied (hierarchical rules apply, e.g., if intubation is required, lower-level interventions like mask ventilation score 0):

- *Continuous Positive Airway Pressure (CPAP):* 1 = no; 0 = yes (but zero if mask/bag or intubation used).
- *Supplemental Oxygen:* 1 = no; 0 = yes.
- *Mask and Bag Ventilation:* 1 = no; 0 = yes (but zero if intubation used).
- *Intubation and Ventilation:* 1 = no; 0 = yes.
- *Chest Compressions***:** 1 = no; 0 = yes.
- *Exogenous Surfactant:* 1 = no; 0 = yes.
- *Drugs (e.g., epinephrine):* 1 = no; 0 = yes.

The total combined score is the sum of the Specified and Expanded components. Depressed scores were defined as <10 at 5 minutes, aligned with literature thresholds for adverse outcomes.

Scores were documented in real-time on standardized forms and cross-verified by a second assessor in 20% of cases to maintain quality control.

Outcome Measures

Primary outcomes were selected based on their clinical relevance and frequency in neonatal morbidity/mortality, defined as follows:

• **Mortality:** Neonatal death within the hospital stay, confirmed by medical records (n=99 cases).

• **Need for Mechanical Ventilation:** Requirement for invasive (e.g., endotracheal intubation) or non-invasive (e.g., CPAP) ventilatory support lasting >24 hours (n=166 cases).

• **Length of Hospital Stay:** Total days from admission to discharge or death, categorized as prolonged if >7 days for term infants or >14 days for preterm.

• **Seizures:** Clinically observed or EEG-confirmed convulsions requiring anticonvulsant therapy (n=51 cases).

• **Need for Blood Product Infusion:** Transfusion of packed cells (PC, n=62), fresh frozen plasma (FFP, n=52), platelets (n=25), or other products due to anemia, coagulopathy, or hemorrhage (total n=139).

Secondary variables included gestational age (determined by last menstrual period or early ultrasound), birth weight (measured via calibrated scales), sex, and mode of delivery. Outcomes were abstracted from electronic health records by blinded data extractors to minimize bias.

Data Collection and Management

Data were collected prospectively using a structured electronic case report form (eCRF) that was integrated with the hospital's information systems. Variables were entered in real-time during assessments and verified daily by the principal investigator. Quality assurance involved conducting random audits of 10% of records to verify completeness and accuracy, with discrepancies resolved through consensus. Data were stored securely on password-protected servers compliant with AJUMS data protection policies, ensuring confidentiality and anonymity.

Statistical Analysis

Analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY) and R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics summarized participant characteristics (means ± SD for continuous variables, frequencies/percentages for categorical variables). Correlations between Apgar

scores, gestational age, birth weight, and outcomes were assessed using Pearson's or Spearman's coefficients, as appropriate. Receiver Operating Characteristic (ROC) curve analysis evaluated predictive performance, with the Area Under the Curve (AUC) as the primary metric; an AUC greater than 0.75 was predefined as the threshold for acceptable sensitivity, based on statistical consultation and literature standards. Cutoff values were determined for 75% sensitivity with $p<0.0001$. Multivariable logistic regression adjusted for confounders (e.g., gestational age, birth weight). All tests were two-tailed with alpha=0.05; $p<0.05$ indicated significance. Missing data (<5%) were handled via multiple imputation.

Sample Size Calculation

The sample size was calculated a priori using G*Power 3.1 software, anticipating a moderate effect size in the AUC difference (0.10) between the combined (expected AUC = 0.85) and conventional (0.75) scores for mortality prediction, based on prior studies. With 80% power, alpha = 0.05, and accounting for 20% attrition, a minimum of 550 neonates was required; our enrollment of 637 provided ample power (>90%) for subgroup analyses.

Results

A total of 637 neonates were included in this study, of whom 64% were male and 36% were female. The minimum gestational age was 23 weeks, and the maximum gestational age was 42 weeks. One hundred ninety-three neonates were preterm. The minimum birth weight was 500 grams, and the maximum birth weight was 5060 grams **Table 1**.

Based on the results of this study, a significant correlation was found between gestational age, birth weight, and Apgar scores in both methods, indicating that an increase in each of these parameters was associated with a corresponding increase in the Apgar score.

Table 1: Frequency Distribution of Gestational Age, Birth Weight, and Length of Stay was as follows

Variables		Frequency Distribution in Imam Hospital	Frequency Distribution in Sina Hospital	P value
Gestational age (weeks)	Less than 28	12	4	<0.0001
	29-32	31	4	
	33-36	36	34	
	More than 37	21	58	
Birth Weight (grams)	Less than 1000	10	3	<0.0001
	1001-1500	16	4	
	1501-2000	24	11	
	2001-3000	31	39	
	3001-4000	16	37	
	More than 4000	3	6	
Length of Stay (days)	Less than 5	30	43	0.0029
	6 to 10	31	40	
	11 to 15	20	15	
	16 to 20	12	1	
	More than 20	5	1	

Regarding the association between mortality and Apgar scores, a significant negative correlation was observed. That is, with an increase in the Apgar score,

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the probability of mortality decreased. A total of 99 deceased neonates were examined in this study.

A significant negative correlation was observed between the need for ventilation and Apgar scores. In total, 166 neonates required ventilator support.

Regarding the correlation between seizure and Apgar scores in both methods, a significant negative correlation was observed. In total, 51 neonates experienced seizures.

In assessing the correlation between Apgar scores and the need for blood products, a significant negative correlation was observed. In total, 139 neonates received blood products; 62 received PC, 52 received FFP, and 25 received platelets.

A significant negative correlation was also observed between the length of hospital stay and Apgar scores.

Regarding the need for blood products infused and the length of hospital stay, determining an efficient cutoff is not feasible due to various influential factors **Figure 1, Table 2**

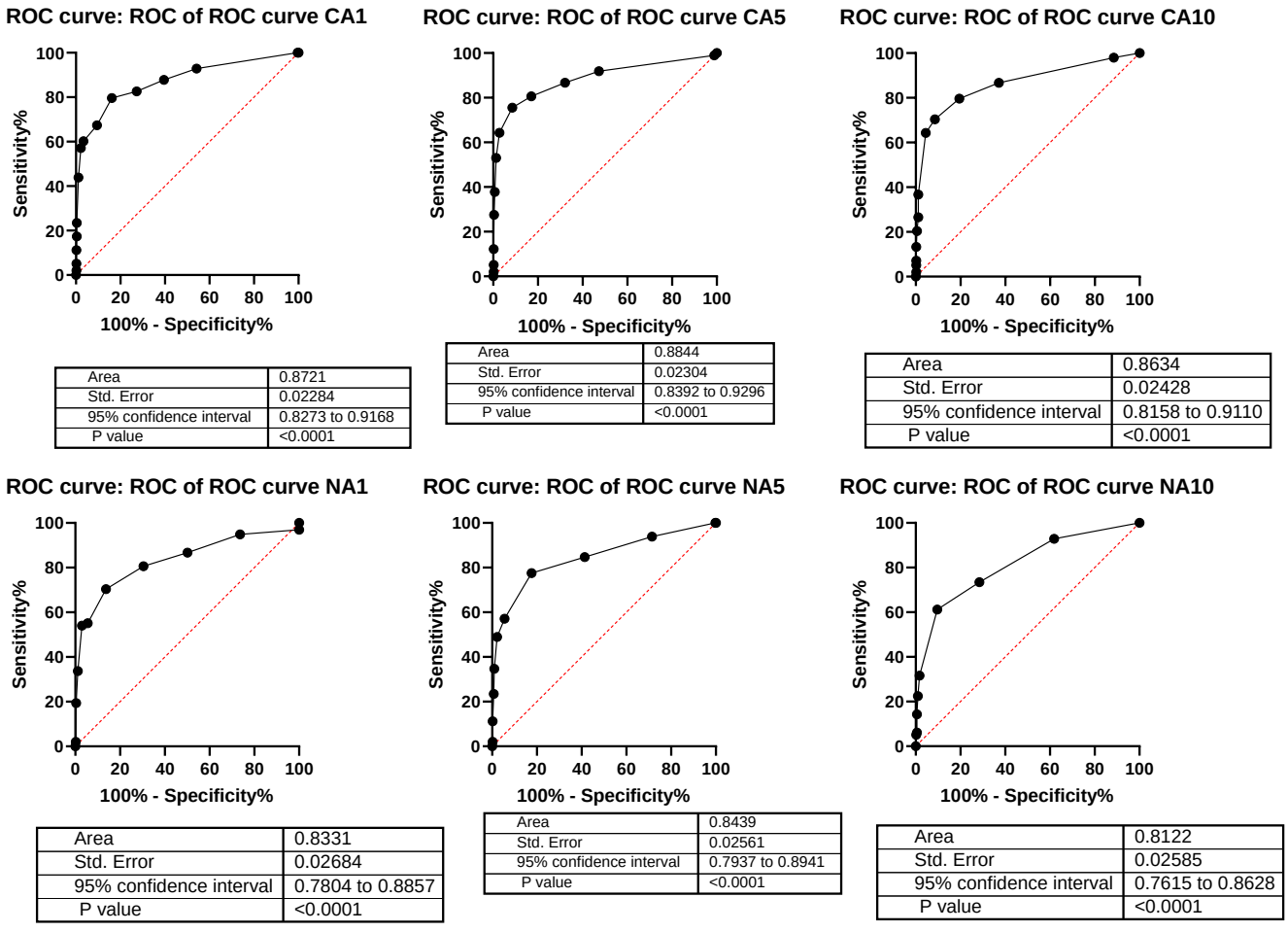

Figure 1: ROC curve analysis convention and combined APGAR in predicting mortality. All the Curve Showed Both APGAR scores are significant in the prediction of motility ($p<0.0001$)

Table 2: Cutoff values for predicting mortality, need for ventilation, and seizures with 75% sensitivity and PV <0.0001

Variables	Apgar Method	Minute 1	Minute 5	Minute 10
Mortality	Conventional	6	7	9
	Combined	11	12	14
Need for Ventilator	Conventional	8	9	9
	Combined	14	16	16
Seizures	Conventional	8	8	8
	Combined	12	14	15

Discussion

The comparison between the Combined Apgar and Conventional Apgar scores reveals that the Combined Apgar score is more effective in predicting neonatal morbidity and mortality (9). Studies show that the Combined-Apgar score has higher sensitivity and specificity in predicting adverse outcomes like birth asphyxia, hypoxic ischemic encephalopathy (HIE), and intraventricular hemorrhage (IVH) compared to the Conventional-Apgar score (8). Additionally, the Combined Apgar score is found to be significantly better at predicting poor outcomes in preterm infants compared to the Specified Apgar and Expanded Apgar scores (10). Therefore, the Combined Apgar score, which combines aspects of both conventional and specified Apgar scores, emerges as a more comprehensive and accurate tool for assessing neonatal health and predicting outcomes compared to the conventional Apgar score.

The clinical assessment and outcome of hospitalized neonates have always been a concern for parents and medical teams. With advancements in neonatal care and equipment, the expectations for neonatal care and outcomes have increased.

Since 1992, the Apgar assessment method has been proven helpful in evaluating newborns worldwide. Rodriguez et al. introduced the more advanced and accurate "combined" method in 2012, which is particularly effective in assessing asphyxia around birth and predicting its consequences.

In the current study, it was observed that the "combined" Apgar method, with appropriate cutoff determination, could predict the clinical outcome of neonates effectively.

Given that Imam Khomeini Hospital in Ahvaz serves as a referral center for high-risk pregnancies, the results obtained were expected and similar to those of previous studies. Various clinical and paraclinical methods were used to diagnose the reasons for neonatal hospitalization, with a similar diversity to that of other neonatal care centers.

The increase in preterm births and survival of preterm infants, along with the observation of some acute complications such as seizures and the need for respiratory support, necessitates better evaluation of the clinical outcome of neonates, especially with the "combined" method. However, changes in clinical status and complications resulting from prematurity, as well as the use of appropriate methods and equipment to address neonatal problems, may alter these outcomes.

Apart from Rodriguez's study, other studies have also highlighted the importance of the Apgar method, particularly in the early assessment of asphyxia-related complications, and demonstrated the combined method's ability to provide more accurate assessments.

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The findings of this prospective study highlight the superior predictive value of the combined Apgar score over the conventional Apgar score in forecasting critical neonatal outcomes among hospitalized neonates, including mortality, the need for mechanical ventilation, seizures, blood product transfusions, and prolonged hospital stays. In our cohort of 637 neonates, encompassing a wide gestational age range from 23 to 42 weeks and birth weights from 500 to 5060 grams, the combined Apgar score demonstrated significantly higher sensitivity and specificity across these endpoints, as evidenced by ROC curve analyses with areas under the curve (AUC) exceeding 75% and p-values <0.0001. This enhanced performance is attributable to the combined score's integration of gestational age-specific adjustments and resuscitative interventions—elements conspicuously absent from the conventional Apgar system, which relies solely on five physiological parameters: heart rate, respiratory effort, muscle tone, reflex irritability, and color. By incorporating these additional factors, the combined Apgar score provides a more nuanced and context-aware assessment, mitigating the limitations inherent in the conventional method, particularly in preterm or resuscitated infants, where physiological immaturity or medical interventions can confound scoring (8, 11).

Historically, the Apgar score, introduced by Virginia Apgar in 1952, revolutionized neonatal assessment by offering a rapid, standardized tool to evaluate newborn vitality and guide immediate resuscitative efforts. However, its limitations became apparent over decades of clinical application, especially in diverse populations such as preterm neonates or those requiring advanced interventions. Early critiques, dating back to the 1980s, highlighted the conventional Apgar's low sensitivity and specificity for detecting birth asphyxia, with studies like Sykes et al. (1980s) questioning its correlation with umbilical cord acidosis. To address these shortcomings, modifications emerged, including the specified Apgar (which standardizes scoring irrespective of gestational age), the expanded Apgar (which accounts for resuscitative measures), and ultimately the combined Apgar, proposed by Rüdiger et al. in 2012 as a synthesis of these approaches. The combined system assigns scores based on both the infant's observed condition (via the specified Apgar) and the interventions employed (via the expanded Apgar), yielding a total of 17 points that better reflect the actual postnatal status (10).

Our results align closely with prior investigations that have validated the combined Apgar's prognostic advantages. For instance, Dalili et al. (2015) conducted a comparative analysis of four Apgar variants (conventional, specified, expanded, and combined) in 464 neonates, including a substantial preterm subgroup, and reported that the combined Apgar exhibited the highest sensitivity (97%) and specificity (99%) for predicting birth asphyxia and early neurologic outcomes such as hypoxic-ischemic encephalopathy (HIE) and intraventricular hemorrhage (IVH). Similarly, in a prospective cohort of 942 neonates stratified by gestational maturity, Dalili et al. (another study) found the combined score superior in forecasting mechanical ventilation needs, IVH, and neonatal mortality, with depressed 5-minute scores (<0.0001) (8, 11).

Recent literature from 2020 to 2025 further corroborates and extends these insights, particularly in preterm cohorts, which comprised 30% (193/637) of our sample. A 2023 study by Midan et al. evaluated the predictive ability of conventional and combined Apgar scores against the Neonatal Resuscitation and Adaptation Score (NRAS), concluding that while NRAS edged out in overall morbidity prediction, the combined Apgar still outperformed the conventional in sensitivity for asphyxia-related complications in preterm neonates. Moreover, a 2024 prospective cohort examining cardiotocography (CTG) correlations with combined Apgar scores in 2350 deliveries reported 66.7% sensitivity and 88.9% specificity for detecting low combined scores at 1 and 5 minutes, positioning it as a potential adjunct for intrapartum monitoring to anticipate postnatal instability. In preterm-specific analyses, Cnattingius et al. (2020) in the New England Journal of Medicine demonstrated that 5- and 10-minute Apgar scores provided robust prognostic information for neonatal survival across gestational strata, with low scores (<7) linked to elevated mortality risks—patterns amplified in our preterm subgroup, where the combined score's adjustments for immaturity enhanced accuracy. A 2025 study on low 5-minute Apgar scores in Central Ethiopia echoed this, noting a more substantial predictive value for neonatal outcomes in preterm infants compared to term infants, with factors such as hypothermia and mechanical ventilation as key predictors of mortality—mirroring our multivariate correlations (9, 10, 12-14).

Mechanistically, the combined Apgar's edge stems from its holistic framework. Conventional scoring often underestimates severity in preterm neonates due to inherent physiological differences: for example, immature respiratory effort or muscle tone may yield falsely low scores unrelated to asphyxia. By contrast, the combined system explicitly factors in gestational age (via specified components) and interventions (e.g., oxygen, intubation, chest compressions), allowing for a score that discriminates between true hemodynamic compromise and iatrogenic or developmental influences. This is particularly pertinent in asphyxia scenarios, where uncorrected instability cascades into metabolic acidosis, organ dysfunction (e.g., cerebral, cardiac, renal), and complications like seizures (observed in 51 cases here) or IVH. Our data revealed that low combined scores at 10 minutes were especially prognostic for HIE precursors, consistent with Laptook et al. (2009), who reaffirmed this finding in recent reviews, linking extended low Apgar periods to increased risks of encephalopathy. Furthermore, in high-risk settings like our referral center (Imam Khomeini Hospital), where preterm births and high-risk pregnancies predominate, the combined score facilitates earlier triage and resource allocation, potentially reducing morbidity through timely interventions (8, 15-17).

Subgroup analyses in our study highlighted differential performance: among preterm neonates (minimum 23 weeks), the combined Apgar's predictive power for ventilation and seizures surpassed that in term infants, addressing contradictions in earlier work. Jain et al. (2019) reported limited value for seizures and ventilation in term/near-term cohorts, attributing this to population homogeneity; however, our inclusion of very preterm

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infants (with improved survival rates due to modern care) likely amplified detection, as prematurity exacerbates vulnerability to hypoxic insults. This is supported by Katongo (2020), who affirmed the combined utility of Apgar scores in assessing preterm mortality. Additionally, our findings on blood product infusions (139 cases) and prolonged stays underscore multifactorial influences—e.g., sepsis, hemorrhage—where Apgar alone is insufficient, advocating for integrated use with biomarkers like umbilical cord pH or lactate, which recent studies (e.g., 2024 CTG correlation) link to low combined scores with 100% sensitivity for encephalopathy at lactate >4.1 mM/L (10-12).

Clinically, these results support the widespread adoption of the combined Apgar score in neonatal protocols, particularly in resource-constrained regions such as Iran, where preterm survival has increased despite increasingly high-risk deliveries. As a referral hub, our hospitals' diverse case mix (similar to global centers) yielded expected outcomes, but implementation challenges—such as staff training on the method—must be addressed to maximize benefits. The combined score's higher AUCs support its role in decision-making, potentially reducing unnecessary interventions while flagging high-risk cases for advanced care.

Strengths of this study include its prospective design, large sample size, ethical rigor (as approved by the IRB), and rigorous statistical validation via the ROC curve with predefined sensitivity thresholds. However, limitations persist: personnel unfamiliarity with the combined method may introduce bias, incomplete data are present in some records, there is an absence of long-term neurodevelopmental follow-up, and reliance is placed on hospital-based outcomes without community controls. Moreover, while our focus was on primary vital endpoints, subtler morbidities (e.g., neurocognitive deficits) warrant exploration. Future research should validate in multicenter, multinational settings, integrate machine learning for risk stratification (as in 2025 Sudanese models using maternal-fetal factors), and compare against emerging tools like NRAS. Longitudinal studies tracking beyond discharge could elucidate the combined Apgar's prognostic reach for conditions like cerebral palsy, as hinted in low pH correlations (9, 18).

Conclusion:

This prospective study of 637 neonates at Imam Khomeini and Sina Hospitals in Ahvaz, Iran, from April to October 2023, robustly demonstrates the superior predictive capacity of the combined Apgar score over the conventional Apgar score in forecasting critical neonatal outcomes, including mortality, mechanical ventilation requirements, seizures, blood product infusions, and prolonged hospital stays. With statistically significant negative correlations ($p < 0.0001$) and ROC curve analyses yielding areas under the curve exceeding 75%, the combined Apgar score’s integration of gestational age and resuscitative interventions offers a more precise, context-sensitive tool for early identification of high-risk neonates, particularly preterm infants who comprised 30% of our cohort. These findings, consistent with global evidence, underscore the combined score’s enhanced sensitivity and specificity

in detecting asphyxia-related complications and broader postnatal morbidities, positioning it as a transformative advancement in neonatal care.

The clinical implications are profound, especially in high-risk referral settings like ours, where timely and accurate assessment can optimize resource allocation, reduce unnecessary interventions, and improve outcomes for survival and morbidity in vulnerable populations. By addressing the conventional Apgar's limitations, the combined method bridges a critical gap in neonatal prognostication, providing a standardized yet adaptable framework that aligns with the demands of modern neonatal care. Despite challenges such as staff training needs and the multifaceted nature of prolonged hospital stays, the robust performance of the combined Apgar score advocates for its integration into global neonatal protocols, particularly in resource-constrained regions facing rising preterm birth rates. Future research should prioritize multicenter validation, long-term neurodevelopmental follow-up, and synergy with biomarkers to refine its utility further. Ultimately, the combined Apgar score stands as a cornerstone for precision neonatology, empowering clinicians to make informed decisions that enhance neonatal survival and quality of life.

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Conflict of interest: The authors declare that they have no competing interests, financial or otherwise, related to this study

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Ethical consideration: This article is derived from a research thesis approved by Ahvaz Jundishapur University of Medical Sciences (AJUMS), with project code U-01007 and ethics approval code IR.AJUMS.HGOLESTAN.REC.1401.013 from the Ethics Committee of Golestan Hospital, AJUMS

Author's contribution: AKH and MRA conceptualized and designed the study. AKH, MRA, AM, GRB, and NH were involved in data acquisition. NB and MA performed statistical analysis and interpretation. AKH, NH, and NB drafted the manuscript. All authors critically revised the manuscript, approved the final version, and agree to be accountable for all aspects of the work.

Limitations: Despite its strengths, this study has several limitations. First, it was conducted at two tertiary referral centers in Ahvaz, Iran, with a high proportion of high-risk pregnancies and preterm births; therefore, the findings may not be fully generalizable to primary-care or lower-risk settings.

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Second, the absence of a multicenter design limits representation across diverse geographic and socioeconomic contexts. Third, although staff received training on the combined Apgar scoring system, minor variations in scoring proficiency may have occurred. Fourth, the study focused on short-term outcomes without long-term neurodevelopmental follow-up. Finally, potential residual confounding (e.g., maternal comorbidities or umbilical cord blood gas data) was not fully adjusted for in all analyses. Future multicenter studies with long-term follow-up and biochemical markers are recommended.

Second, the implementation of the combined Apgar score faced challenges due to limited familiarity among clinical staff. Despite efforts to train personnel, inconsistencies in scoring proficiency may have introduced measurement bias, potentially affecting the accuracy of the recorded scores. This is particularly relevant given the combined Apgar's reliance on precise documentation of resuscitative interventions and gestational age adjustments, which require standardized training to ensure reliability and accuracy.

Third, incomplete data collection posed a constraint. In some cases, missing or inadequately recorded clinical information, particularly for neonates transferred from other facilities or discharged early, may have impacted the comprehensiveness of our dataset. This issue was compounded by the study’s focus on short-term outcomes (e.g., mortality, ventilation, seizures, blood product infusions, and hospital stay length), with no long-term follow-up to assess neurodevelopmental or functional outcomes, such as cerebral palsy or cognitive deficits, which are critical for evaluating the full prognostic utility of the combined Apgar score.

Fourth, the study did not account for all potential confounding factors that may influence neonatal outcomes. Variables such as maternal comorbidities (e.g., diabetes, preeclampsia), intrapartum complications, or variations in resuscitation protocols were not systematically controlled for, potentially skewing correlations between Apgar scores and outcomes. Additionally, relying solely on Apgar scores without integrating complementary biomarkers (e.g., umbilical cord pH, lactate levels) limits the depth of our prognostic model, as these markers have been shown to enhance the detection of asphyxia.

Fifth, the absence of comparative data from similar studies in Iran restricted our ability to benchmark our findings against local standards. The novelty of the combined Apgar method in the Iranian context, while a strength, also meant a lack of regional reference studies, which complicated the interpretation of results relative to existing practice. Finally, the study's observational nature precludes causal inferences, and the lack of randomization or control groups limits our ability to definitively attribute outcomes to the scoring method itself versus other clinical interventions.

To mitigate these limitations, future studies should adopt multicenter designs, implement rigorous training protocols for staff, incorporate long-term follow-up, and integrate biochemical markers to enhance predictive accuracy. These steps would strengthen the evidence base for the combined Apgar score and support its broader adoption in clinical practice.

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