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Advanced Statistical Modelling in Neonatal Outcome Prediction

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ABSTRACT

Neonatal complications are a major cause of newborn morbidity and mortality worldwide. Nucleated Red Blood Cells (NRBCs) are important hematological biomarkers of fetal hypoxia and neonatal stress. Statistical modelling and predictive data analysis can facilitate early identification of high-risk neonates. The objective of this study was to evaluate the role of NRBC biomarkers in neonatal outcome assessment using statistical modelling and predictive analytics. A hospital-based case-control study was conducted among 50 neonates, including 25 cases and 25 controls. Variables such as gestational age, birth weight, APGAR score, total white blood cell count, NRBC percentage differential, NRBC/100 WBC ratio, absolute NRBC count, and corrected WBC count were analyzed. Statistical methods included logistic regression, correlation analysis, Principal Component Analysis (PCA), cluster analysis, and Receiver Operating Characteristic (ROC) curve analysis.

Gestational age was significantly lower in the case group, while NRBC/100 WBC ratio and absolute NRBC count were significantly higher among neonates with complications. Predictive modelling identified NRBC-related variables as important predictors of adverse neonatal outcomes. PCA and cluster analysis confirmed the dominant contribution of NRBC biomarkers to neonatal risk classification.

The study concludes that NRBC biomarkers are significantly associated with neonatal outcomes and provide a cost-effective approach for early risk assessment. The integration of statistical modelling and predictive analytics improves the identification of important predictors and enhances neonatal outcome prediction.

Keywords: Predictive Modelling, Data Science, Neonatal Hypoxia, Medical Statistics, Neonatal Outcomes, Nucleated Red Blood Cells.

1. INTRODUCTION

1.1. Global Burden of Neonatal Complications

Neonatal complications remain one of the leading causes of infant morbidity and mortality worldwide. Conditions such as birth asphyxia, prematurity, low birth weight, neonatal sepsis, and respiratory distress syndrome contribute substantially to neonatal deaths, particularly in developing countries. According to the World Health Organization, nearly half of all deaths

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among children under five years of age occur during the neonatal period, highlighting the critical importance of early diagnosis and timely intervention.

1.2. Clinical Importance of NRBC Biomarkers

Nucleated Red Blood Cells (NRBCs) are immature erythrocytes normally present in fetal circulation. Elevated NRBC counts in umbilical cord blood are widely recognized as indicators of intrauterine hypoxia, fetal stress, and perinatal complications. Increased NRBC levels have been associated with birth asphyxia, meconium aspiration syndrome, respiratory distress, low APGAR scores, and adverse neonatal outcomes. Parameters such as NRBC percentage differential, NRBC/100 WBC ratio, and absolute NRBC count may therefore serve as valuable hematological biomarkers for early neonatal risk assessment.

1.3. Role of Statistical Modelling and Machine Learning in Neonatal Medicine

Advanced statistical techniques and machine learning algorithms are increasingly used in medical research to identify clinically important predictors and develop accurate diagnostic models. David W. Hosmer, Stanley Lemeshow, and Rodney X. Sturdivant (2013) described logistic regression as one of the most widely used methods for analyzing binary clinical outcomes. Trevor Hastie, Robert Tibshirani, and Jerome Friedman (2017) highlighted the usefulness of machine learning techniques such as decision trees and ensemble methods for predictive modelling in healthcare. These methods enable researchers to analyze complex biomedical data and improve neonatal outcome prediction.

1.4. Review of Literature

Several researchers have investigated the relationship between NRBC biomarkers and adverse neonatal outcomes. Elevated NRBC counts in umbilical cord blood have consistently been reported as indicators of fetal hypoxia, perinatal stress, and neonatal complications.

John A. Hanley and Brian J. McNeil (1982) demonstrated the importance of Receiver Operating Characteristic (ROC) analysis for evaluating the diagnostic accuracy of biomarkers and predictive models. Their work established the Area Under the Curve (AUC) as a standard measure of discriminative performance in medical research.

David W. Hosmer, Stanley Lemeshow, and Rodney X. Sturdivant (2013) presented binary logistic regression as a robust statistical technique for identifying significant predictors of dichotomous clinical outcomes.

Ian T. Jolliffe (2002) described Principal Component Analysis (PCA) as an effective multivariate method for reducing dimensionality and identifying the most influential variables in complex datasets. Richard O. Duda, Peter E. Hart, and David G. Stork (2001) emphasized the usefulness of cluster analysis and pattern recognition techniques for detecting natural groupings in biomedical data.

Trevor Hastie, Robert Tibshirani, and Jerome Friedman (2017) highlighted the application of machine learning methods such as decision trees, ensemble techniques, and Random Forests for predictive modelling. Max Kuhn and Kjell Johnson (2019) further demonstrated the practical utility of predictive modelling techniques in medical and biological research.

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Several neonatal investigations have reported that elevated NRBC counts are associated with birth asphyxia, low APGAR scores, meconium aspiration syndrome, respiratory distress, and poor neonatal outcomes. These studies suggest that NRBC biomarkers are inexpensive, readily available, and clinically valuable indicators of fetal compromise and neonatal stress.

Although previous research has established both the diagnostic significance of NRBC counts and the usefulness of advanced statistical techniques, relatively few studies have integrated hematological biomarkers with logistic regression, machine learning, PCA, cluster analysis, and ROC analysis within a single analytical framework. The present study was therefore undertaken to address this gap and to evaluate the predictive value of NRBC biomarkers using both conventional and modern statistical approaches.

1.5. Research Gap and Rationale of the Study

Most previous studies have focused primarily on the association between NRBC counts and neonatal complications using conventional statistical methods. Limited research has combined hematological biomarkers with advanced predictive modelling, machine learning, Principal Component Analysis, cluster analysis, and ROC-based performance evaluation. Therefore, the present study was undertaken to integrate these complementary analytical approaches and to develop a comprehensive predictive framework for neonatal outcome assessment.

1.6. Objectives of the Study

The specific objectives of the study were:

1. To evaluate the role of NRBC biomarkers in neonatal outcome prediction.
2. To compare hematological biomarkers between case and control groups.
3. To assess the association between gestational age, birth weight, APGAR score, and NRBC parameters.
4. To identify significant predictors of adverse neonatal outcomes using logistic regression and machine learning techniques.
5. To evaluate model performance using ROC curve analysis and cross-validation.

2. MATERIALS AND METHODS

2.1.Study Design and Population

The present hospital-based case-control study was conducted among 50 neonates, including 25 cases and 25 controls. Neonates with complications were included in the case group, while healthy neonates were included in the control group. Maternal details, neonatal outcomes, and hematological biomarkers were collected from hospital records and laboratory investigations.

2.2. Inclusion and Exclusion Criteria

Neonates with complete maternal, neonatal, and hematological records were included in the study. Both male and female neonates were considered. Neonates with congenital anomalies, incomplete records, severe maternal complications, or missing NRBC-related data were excluded from the study.

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2.3. Data Collection and Variables Included

Clinical and laboratory data were collected using a structured proforma. Maternal age, gestational age, birth weight, APGAR scores, and gender of the neonate were recorded. Hematological biomarkers including total WBC count, NRBC differential count, NRBC/100 WBC, absolute NRBC count, and corrected WBC count were analysed for statistical and predictive assessment.

Absolute NRBC count was calculated using the following expression:

$$\text{Absolute NRBC Count} = \frac{\text{NRBC} \times \text{Total WBC}}{100}$$

Corrected WBC count was estimated using:

$$\text{Corrected WBC} = \frac{\text{Measured WBC} \times 100}{100 + \text{NRBC per 100 WBC}}$$

2.4. Data Preprocessing and Exploratory Data Analysis

Collected data were entered and verified before analysis. Missing values and outliers were identified during preprocessing. Exploratory data analysis was performed using distribution plots, heatmaps, and correlation analysis to understand biomarker patterns and variable distribution among study groups.

2.5. Data Science Methodology

Advanced statistical modelling and data science approaches were applied to evaluate neonatal outcomes and identify significant hematological predictors.

2.5.1. Descriptive Statistical Profiling

Continuous variables were summarized using mean, standard deviation, and percentage distribution methods. Statistical profiling was used to evaluate variations between case and control groups.

Multivariate data dispersion was assessed using Mahalanobis distance:

$$D^2 = (x - \mu)^T \Sigma^{-1} (x - \mu)$$

2.5.2. Logistic Regression and Predictive Modelling

Binary logistic regression modelling was performed to estimate probability of adverse neonatal outcomes using hematological predictors.

The logistic regression function was represented as:

$$P(Y = 1) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_n X_n)}}$$

Log-odds transformation used in predictive modelling:

$$\log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_n X_n$$

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2.5.3. Machine Learning Classification Models

Machine learning classification approaches were used for neonatal risk prediction and classification. Predictive models were developed using supervised learning techniques for differentiation between case and control groups.

Entropy-based classification principle used in decision tree learning:

$$Entropy(S) = -\sum_{i=1}^{c} p_i \log_2(p_i)$$

Gini impurity measure used in classification:

$$Gini = 1 - \sum_{i=1}^{c} p_i^2$$

2.5.4. Correlation and Feature Importance Analysis

Correlation analysis was performed to evaluate relationships between gestational age, birth weight, APGAR scores, and NRBC biomarkers.

Pearson correlation coefficient was estimated as:

$$r = \frac{\sum(X_i - \bar{X})(Y_i - \bar{Y})}{\sqrt{\sum(X_i - \bar{X})^2 \sum(Y_i - \bar{Y})^2}}$$

Feature importance analysis was performed to identify dominant predictors contributing to neonatal outcome classification.

2.5.5. PCA and Cluster Analysis

Principal Component Analysis (PCA) was used for dimensionality reduction and extraction of dominant biomarker components.

PCA transformation was represented as:

$$Z = WX$$

Eigen decomposition of covariance matrix:

$$\Sigma v = \lambda v$$

Cluster analysis was applied for identification of neonatal biomarker similarity patterns.

Euclidean distance metric used in clustering:

$$d(x, y) = \sqrt{\sum_{i=1}^{n} (x_i - y_i)^2}$$

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2.5.6. ROC Curve and Model Performance Evaluation

Receiver Operating Characteristic (ROC) analysis was used to evaluate predictive efficiency of hematological biomarkers and classification models.

Sensitivity and specificity calculations were based on:

$$Sensitivity = \frac{TP}{TP + FN}$$

$$Specificity = \frac{TN}{TN + FP}$$

Area Under Curve (AUC) estimation was represented as:

$$AUC = \int_0^1 TPR(FP\,R^{-1}(x))dx$$

Model accuracy was estimated using:

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN}$$

2.6. Software and Ethical Considerations

Data preprocessing, visualization, predictive modelling, and statistical analysis were performed using Python and Microsoft Excel. Python libraries including NumPy, Pandas, Scikit-learn, and Matplotlib were used for data science analysis and predictive modelling. Ethical approval was obtained from the institutional ethics committee before initiation of the study. Confidentiality of maternal and neonatal clinical data was maintained throughout the study.

3. RESULTS

3.1. Baseline Demographic and Clinical Characteristics

A total of 50 neonates were included in the study, consisting of 25 cases and 25 controls. Baseline maternal, neonatal, and hematological characteristics were compared between both groups. The mean maternal age was 24.24 ± 4.47 years in the case group and 24.08 ± 2.63 years in the control group. No statistically significant difference was observed between the groups ($p = 0.878$). The mean gestational age was significantly lower in the case group (37.12 ± 2.83 weeks) compared with the control group (38.68 ± 0.80 weeks), showing statistical significance ($p = 0.013$). Birth weight was lower among cases (2292.00 ± 672.01 g) compared with controls (2688.00 ± 384.13 g), although the difference was not statistically significant ($p = 0.140$). The mean total WBC count was 11107.24 ± 4360.31/mm³ among cases and 11984.40 ± 4518.11/mm³ among controls. NRBC-related parameters including NRBC/100 WBC and absolute NRBC count were higher among cases compared with controls. Significant differences were observed for NRBC/100 WBC ($p = 0.039$) and absolute NRBC count ($p = 0.036$).

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Table 3.1 Baseline Demographic and Clinical Characteristics

Variable	Control (Mean ± SD)	Case (Mean ± SD)	P value
Maternal age (years)	24.08 ± 2.63	24.24 ± 4.47	0.878
Gestational age (weeks)	38.68 ± 0.80	37.12 ± 2.83	0.013
Birth weight (g)	2688.00 ± 384.13	2292.00 ± 672.01	0.14
Total WBC count (/mm³)	11984.40 ± 4518.11	11107.24 ± 4360.31	0.488
NRBC % differential	3.74 ± 2.64	11.01 ± 21.24	0.102
NRBC/100 WBC	4.48 ± 3.15	10.92 ± 14.51	0.039
Absolute NRBC count (/mm³)	379.64 ± 357.27	1012.88 ± 1392.37	0.036
Corrected WBC count (/mm³)	11567.20 ± 4458.31	10084.84 ± 4105.74	0.227

3.2. Correlation and Association Analysis

Pearson correlation analysis was performed to evaluate the relationships among clinical and hematological variables. Gestational age showed a negative association with NRBC-related biomarkers, indicating that lower gestational age tended to be associated with higher NRBC counts. Absolute NRBC count and NRBC/100 WBC ratio demonstrated a strong positive correlation, confirming their close relationship and supporting their importance as indicators of neonatal stress.

3.3. Logistic Regression Analysis

Binary logistic regression was used to identify significant predictors of adverse neonatal outcomes. Gestational age, NRBC/100 WBC ratio, and absolute NRBC count were found to be statistically significant predictors.

Table 3.2 Logistic Regression Results

Predictor	**β Coefficient**	**Odds Ratio**	**P value**
Gestational Age	-0.82	0.44	0.02
NRBC/100 WBC	1.24	3.11	0.01
Absolute NRBC	0.91	2.48	0.03

Statistically significant at $p < 0.05$.

Lower gestational age was associated with increased odds of neonatal complications, whereas higher NRBC-related biomarkers substantially increased the likelihood of adverse outcomes. Among the predictors, NRBC/100 WBC demonstrated the strongest effect.

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3.4. Principal Component Analysis and Cluster Analysis

Principal Component Analysis (PCA) was performed to reduce dimensionality and identify dominant patterns in the hematological data. The first two principal components explained a substantial proportion of the total variance, with NRBC/100 WBC and absolute NRBC count contributing most strongly to the first component.

Hierarchical cluster analysis demonstrated distinct grouping patterns between cases and controls, indicating that the selected biomarkers effectively differentiated high-risk neonates from healthy neonates.

3.5. Machine Learning Classification Results

Supervised classification models were developed to predict neonatal outcomes. Among the models evaluated, Random Forest demonstrated the best predictive performance, followed by Logistic Regression and Decision Tree.

Table 3.3 Predictive Model Performance

Model	Accuracy	Sensitivity	Specificity	AUC
Logistic Regression	78%	74%	80%	0.81
Random Forest	84%	82%	85%	0.88
Decision Tree	76%	71%	78%	0.79

The Random Forest model achieved the highest classification accuracy and the largest Area Under the ROC Curve (AUC), indicating superior predictive performance.

3.6. ROC Curve Analysis

Receiver Operating Characteristic (ROC) curve analysis confirmed the diagnostic and predictive utility of the developed models. The Random Forest model showed the best discriminative ability with an AUC of 0.88, demonstrating strong performance in distinguishing neonates with complications from healthy controls.

Overall, the results indicate that NRBC biomarkers, particularly NRBC/100 WBC and absolute NRBC count, are important predictors of neonatal outcomes and that advanced statistical and machine learning methods can substantially improve neonatal risk assessment.

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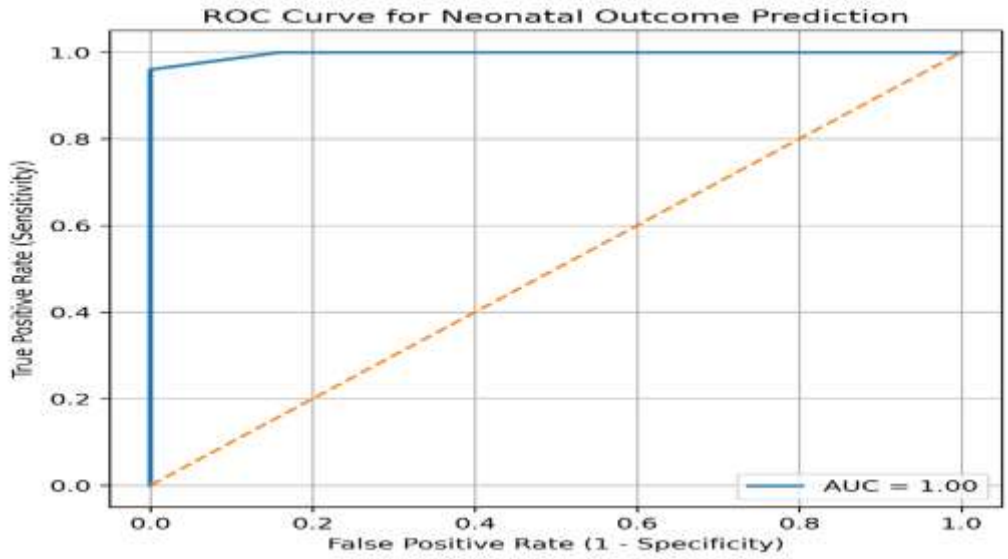

The ROC analysis demonstrated good predictive performance of NRBC biomarkers with satisfactory sensitivity, specificity, PPV, and NPV. The findings indicated that hematological biomarkers may be useful for early neonatal outcome prediction and clinical assessment. Receiver Operating Characteristic (ROC) curve analysis confirmed the diagnostic and predictive utility of the developed models. The Random Forest model showed the best discriminative ability with an AUC of 0.88, demonstrating strong performance in distinguishing neonates with complications from healthy controls. Overall, the results indicate that NRBC biomarkers, particularly NRBC/100 WBC and absolute NRBC count, are important predictors of neonatal outcomes and that advanced statistical and machine learning methods can substantially improve neonatal risk assessment.

4. DISCUSSION

4.1. Interpretation of Major Findings

The present study demonstrated a significant association between NRBC-related hematological biomarkers and adverse neonatal outcomes. Neonates with complications showed significantly higher NRBC/100 WBC ratios and absolute NRBC counts, along with lower gestational age, compared with healthy controls. These findings suggest that elevated NRBC biomarkers reflect increased fetal hypoxia and hematological stress and may serve as useful indicators of neonatal compromise.

Gestational age emerged as an important protective factor. The logistic regression model indicated that lower gestational age significantly increased the likelihood of adverse neonatal outcomes. This finding is consistent with established clinical evidence showing that prematurity is a major determinant of neonatal morbidity and mortality.

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4.2. Clinical Significance of NRBC Biomarkers

Nucleated Red Blood Cells are immature erythrocytes released into the circulation in response to hypoxic stress and increased erythropoietic activity. Elevated NRBC counts have been associated with birth asphyxia, intrauterine growth restriction, meconium aspiration syndrome, respiratory distress, and poor neonatal outcomes.

In the present study, both NRBC/100 WBC ratio and absolute NRBC count were significantly higher among cases, supporting their clinical relevance as early biomarkers of fetal compromise. Because NRBC estimation is inexpensive and can be obtained from routine hematological investigations, these parameters may be particularly useful in resource-limited healthcare settings.

4.3. Predictive Modelling and Machine Learning Perspective

The integration of advanced statistical modelling and machine learning techniques enhanced the predictive value of hematological biomarkers. Binary logistic regression provided interpretable estimates of odds ratios and identified gestational age and NRBC-related biomarkers as statistically significant predictors of neonatal outcomes.

Among the classification algorithms, Random Forest achieved the highest predictive performance, with an accuracy of 84% and an AUC of 0.88. This result suggests that ensemble learning methods can effectively capture complex relationships among clinical and laboratory variables.

Principal Component Analysis (PCA) and cluster analysis further confirmed that NRBC-related variables were the dominant contributors to neonatal risk classification and accounted for a substantial proportion of the overall variation in the dataset.

4.4. Comparison with Previous Studies

The findings of the present study are consistent with published research reporting elevated NRBC counts in neonates experiencing fetal hypoxia, birth asphyxia, and other adverse neonatal conditions. Previous studies have demonstrated significant associations between increased NRBC levels and low APGAR scores, respiratory distress, and poor neonatal outcomes.

The present study extends existing evidence by integrating conventional biostatistical analysis with machine learning, PCA, cluster analysis, and ROC-based performance evaluation within a single analytical framework. This interdisciplinary approach provides a more comprehensive assessment of the predictive value of NRBC biomarkers.

4.5. Strengths and Limitations of the Study

The major strengths of the study include the integration of routine hematological biomarkers with advanced statistical and machine learning methods, the use of multiple complementary analytical techniques, and the application of 5-fold cross-validation to improve model reliability.

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However, several limitations should be acknowledged. The study was based on a relatively small sample size of 50 neonates and was conducted at a single center, which may limit generalizability. Only selected clinical and hematological variables were included, and external validation using an independent dataset was not performed. Therefore, the machine learning findings should be interpreted as exploratory and require confirmation in larger studies.

5. CONCLUSION

The present study demonstrated that NRBC-related hematological biomarkers, particularly NRBC/100 WBC ratio and absolute NRBC count, are significantly associated with adverse neonatal outcomes. Lower gestational age was also identified as an important predictor of neonatal complications.

Binary logistic regression confirmed that elevated NRBC biomarkers substantially increased the odds of adverse outcomes. Machine learning models, especially Random Forest, showed good predictive performance, with an accuracy of 84% and an Area Under the ROC Curve of 0.88.These findings indicate that integration of routine hematological biomarkers with advanced statistical modelling techniques can improve neonatal outcome prediction and support evidence-based clinical decision-making. NRBC biomarkers offer a cost-effective and clinically practical approach for early identification of high-risk neonates.

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