

Exploring Haematological Biomarkers through Data Mining for Multi-Disease Prediction

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Abstract.

Background: Complete blood count (CBC) parameters are non-specific disease indicators, limiting their diagnostic utility when used individually.

Objective: To develop and validate a machine learning model combining multiple CBC biomarkers (TLC, PCV, PLT, RDW, HGB) for early screening of patients with abnormal blood profiles suggestive of autoimmune disorders and/or malignancies.

Methods: CBC data were analysed from a Kaggle dataset comprising 364 patients. Outlier binary indicators used NIH reference ranges. A logistic regression model was established ($n = 292$, 80%) and verified ($n = 72$, 20%) by repeated k-fold cross-validation with a tenfold. VIF < 5 was used to assess multicollinearity.

Results: The model's AUC is 0.886, with 10-fold cross-validation accuracy of 78% for IMAGE, sensitivity of 88.6%, specificity of 50%, and precision of 82.4%. Four predictors were significantly associated: TLC ($p < 0.001$), PCV ($p < 0.001$), PLT ($p = 0.003$), and RDW ($p = 0.008$); HGB was not significantly associated ($p = 0.142$). The model detected 72.5% of patients with at least one CBC abnormality for clinical follow-up, and 3.02% with multiple concurrent abnormalities. Gender differences were observed (male: 35.4% positive, female: 17% positive).

Conclusion: This proof-of-concept demonstrates that logistic regression modelling of CBC outliers can identify high-risk patients for further diagnostic workup. However, the low specificity (50%) and lack of confirmed diagnoses limit clinical applicability. External validation on larger, multi-centre datasets with verified disease outcomes is required before clinical implementation.

Keywords: Complete Blood Count, Machine Learning, Logistic Regression, Cancer Screening, Autoimmune Disease, Liquid Biopsy, Early Detection

1 Introduction

Contemporary medicine is introducing non-invasive diagnostics to the mainstream through blood prospecting, now more commonly known as liquid biopsies. This shift away from invasive and painful procedures toward patient-friendly, personalised diagnosis and long-term disease assessment will represent a paradigm shift.

1.1 The Power of Blood Mining

Blood mining regards blood as a dynamic information source. Clinicians can also detect autoimmune disease and cancer at the earliest stages, when they are easiest to treat, by studying molecular signatures that emanate from different organs, such as the liver. Early detection of cancer is a clinical priority because early detection

greatly increases the chances for survival and decreases long term health care costs.

The approach is based on three complementary "multi-omics" platforms:

- **Proteomics:** Exploring the expression and interaction of proteins.
- **Genomics:** What to know about genetic mutations and changes.
- **Metabolomics:** Investigating biochemical pathway dysregulation.

1.2 Clinical and Economic Impact

From mere detection, blood mining would allow precision medicine to customize treatments to each person's molecular signature. It provides unique clinical benefits, including ease of patient access, repeatability

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for serial follow-up evaluation, and timely results to inform potential emergency decisions.

Economically, first-mover technologies can be expensive but add long-term value by shifting healthcare from reactive treatment to proactive prevention. This reduces the global burden of disease, which is increasing with ageing populations and environmental change.

1.3 Challenges Ahead

The advancement of this technology in clinical practice is constrained by barriers, including biomarker standardisation, regulatory approval, and the ethical handling of incidental findings. Blood mining, nevertheless, remains the final frontier for enhancing global public health outcomes.

1.4 What Makes This Study Novel?

While previous studies have applied machine learning to CBC data (Yang et al., 2021; Xu et al., 2022), our study contributes the following:

1. **Multi-Disease Framework:** Unlike single-disease models, we simultaneously screen for both autoimmune disorders and malignancies using a unified approach.
2. **Outlier-Based Feature Engineering:** We encode specific NIH reference range violations into binary codes in a systematic manner to enhance clinical interpretability.
3. **Middle Eastern Population:** This study fills the relevant geographic vacuum found in the extant literature that mainly covers Western and East Asian populations.
4. **Interpretable Model:** Our interpretable model performs nearly as well as complex models and is clinically actionable.

Comparison with Existing Studies:

Study	Year	Population	Sample Size	Disease Focus	Method	Performance
Yang et al.	2021	Chinese	1,245	Cancer only	Random Forest	85.3% accuracy
Xu et al.	2022	European	892	Autoimmune only	Deep Learning	88.1% AUC
Liu et al.	2022	American	2,103	Cardiovascular	SVM	82.7% accuracy
This Study	2025	Iraqi	364	Multi-disease	Logistic Regression	88.6% AUC, 78% accuracy

Our interpretable approach achieves performance comparable to that of complex models while providing clinically actionable insights.

1.5 Research Questions and Hypothesis

Three main research questions are focused on in this study:

RQ1: Can the routine CBC parameters (TLC, PCV, PLT, RDW and HGB) predict those patients who will have abnormal blood profiles and need clinical evaluation?

RQ2: What are the best combinations of CBC biomarkers that maximise predictive performance without losing model interpretability?

RQ3: Is outlier-based binary encoding of CBC parameters superior to just utilising the raw continuous values in terms of predictive performance?

Hypothesis: We hypothesise that a logistic regression model combining multiple CBC outlier indicators will achieve an $AUC \geq 0.80$ for discriminating patients with abnormal blood profiles from healthy donors, and will outperform single-biomarker approaches.

- **Null Hypothesis (H₀):** There is no relationship between CBC outlier patterns and blood profile abnormalities ($AUC \leq 0.50$) in detecting patients who need diagnosis.
- **Alternative Hypothesis (H₁):** There is a relationship between CBC outlier patterns and blood profile abnormalities ($AUC > 0.80$) in detecting patients who need diagnosis.

2 Literature Survey

Blood biomarkers help clinicians identify and monitor diseases. They are useful for diagnosing cancer and autoimmune disorders. Common biomarkers include Total Leukocyte Count (TLC), Platelet Count (PLT), Haemoglobin (HGB), and Red Cell Distribution Width (RDW) (Han et al., 2020). These biomarkers reflect immune function and aid in detecting inflammation. Abnormalities in these parameters can signal serious conditions such as cancer (Henry et al., 2021). These changes can be observed even before symptoms are present (Kim et al., 2019).

Blood tests used for screening are referred to as liquid biopsies, in contrast to conventional biopsies, which require tissue samples. This approach enables early cancer detection by identifying cancer cells or small DNA fragments in the blood (Wan et al., 2020). Liquid biopsy also enables physicians to monitor treatment progress. It is less painful and more comfortable for patients (Mandal et al., 2021). However, it is not yet common in hospitals. Biosensors are being developed to achieve greater specificity and accuracy (Chen et al., 2020).

CBC (Complete Blood Count) is a common blood test used to assess infectious diseases, anaemia, and haematological malignancies (Zhou et al., 2021). Some CBC parameters are associated with diseases. PCV and PDW (Packed Cell Volume and Platelet Distribution Width) are notable outliers. In cancer and autoimmune diseases, these values are altered (Liu et al., 2022). For example, a high RDW value has been associated with a

higher risk of cardiovascular diseases and cancer mortality (Smith et al., 2020).

Machine learning (ML) has transformed medical diagnostics, enabling disease prediction from large datasets. ML algorithms help identify complex patterns in CBC parameters and predict high-risk patients at an early stage (Cheng et al., 2021). Logistic regression, decision trees and deep learning models have shown promising results in cancer and autoimmune disease screening (Xu et al., 2022). Yang et al. (2021) reported that the predictive accuracy of ML models based on blood biomarkers for disease prediction exceeded 85%. Early detection through blood-based biomarkers and ML can be a promising approach, but there are many challenges.

One of the major limitations is the specificity of biomarkers, since abnormal values can be associated with more than one disease and diagnosis becomes not simple (Patel et al.). Moreover, liquid biopsy is not expensive and has received limited regulatory approvals (Singh et al., 2021). Future studies should combine several biomarkers and advanced ML methods for enhancing the diagnostic accuracy. Blood-based biomarker analysis should become increasingly reliable as artificial intelligence and molecular diagnostics emerge. Scientists are working to integrate genomic, proteomic, and metabolomic data to improve disease detection (Brown et al., 2021). The algorithms of ML will be improved, and datasets should be enlarged, which will better serve the early diagnosis and precision treatment (Li et al., 2021)

3 Research Gap

Literature Analysis: Existing studies have explored CBC parameters for disease prediction (Yang et al., 2021; Xu et al., 2022), but several gaps remain:

1. **Single-Disease Focus:** Most studies focus on either cancer OR autoimmune disease, not both simultaneously
2. **Geographic Bias:** Predominant focus on Western and East Asian populations; Middle Eastern cohorts are underrepresented
3. **Black-Box Models:** Heavy reliance on complex ensemble methods (Random Forest, XGBoost) with limited interpretability
4. **Raw Parameter Use:** Most studies use continuous CBC values without systematic outlier encoding based on clinical reference ranges

4 Research Methodology

4.1 Data Description

The original dataset was collected Kaggle (Taha, 2023) and comprises complete blood test details for 364 patients across 12 parameters of blood components and indices. The dataset is publicly available on Kaggle. After data cleaning, five features, namely TLC, PCV, PLT, RDW and HGB, were primarily identified for analysis in this study based on their lower correlation

values (VIF<5), indicating freedom from multicollinearity, making them suitable as non-specific biomarkers for early screening.

4.2 Feature Engineering and Clinical Rationale

Binary outlier indicators were created based on sex-specific NIH reference ranges (Table 1). This encoding captures clinically significant deviations from normal physiological ranges.

Parameter	Male Normal Range	Female Normal Range	Outlier Definition	Clinical Significance
TLC	4.5-11.0 × 10 ⁹ /µL	4.5-11.0 × 10 ⁹ /µL	<4.5 or >11.0	Leukocytosis (infection, inflammation, leukemia) or leukopenia (bone marrow suppression)
PCV	38.8-50.0%	34.9-44.5%	Outside sex-specific range	Anemia or polycythemia
PLT	150-400 × 10 ⁹ /µL	150-400 × 10 ⁹ /µL	<150 or >400	Thrombocytopenia (autoimmune destruction) or thrombocytosis (cancer, inflammation)
HGB	13.5-17.5 g/dL	12.0-15.5 g/dL	Below sex-specific lower limit	Anemia (common in cancer and autoimmune disease)
RDW	11.5-14.5%	11.5-14.5%	>14.5	Chronic inflammation, nutritional deficiency

Table 1: NIH reference ranges

Clinical Rationale:

- **Leukocytosis (TLC >11.0):** Indicates immune activation, infection, or haematological malignancy (Han et al., 2020)
- **Thrombocytosis (PLT >400):** Associated with cancer progression and inflammatory states (Kim et al., 2019)
- **Elevated RDW (>14.5%):** Reflects red blood cell size variation, linked to chronic inflammation and increased cancer mortality (Smith et al., 2020)
- **Anaemia (low HGB):** Common in chronic diseases, cancer, and autoimmune disorders due to inflammation and bone marrow suppression (Henry et al., 2021)

Encoding Procedure:

For each of those four featured columns, TLC, PCV, PLT and HGB, we created a dummy binary column named outlier_TLC, outlier_PCV, outlier_PLT and outlier_HGB respectively, through filter by taking outside range values only as per NIH biomarker specification and encoded them '1' if outlier values are present, otherwise '0'. In those dummy columns, '1' indicates symptoms of abnormality of sign of disease and '0' indicates normality. Then, two more dummy columns are created, named 'Disease_any' and 'Disease_both', by performing OR and AND operations of other dummy columns, which will serve as response variables for our model design. In the 'Disease_any' column, '1' indicates the sign of either an autoimmune disease or cancer, whereas in the 'Disease_both' column, '1' indicate the sign of both the autoimmune disease and Cancer.

Important Limitation

The original Kaggle dataset does NOT contain confirmed disease diagnoses. Our binary outcome variables (Disease_any, Disease_both) are based solely on CBC outlier patterns, NOT on verified cancer or autoimmune disease diagnoses.

4.3 Model Selection and Justification

We opted for logistic regression in this investigation, grounded on the following justification:

Advantages of Logistic Regression:

1. **Clinical Interpretability:** The coefficients yield direct clinical insights (e.g., “each unit increment in TLC correlates with a X% augmentation in disease odds”).
2. **Transparency:** The decisions made by the model are elucidated to clinicians, thereby enhancing trust and facilitating adoption.
3. **Computational Efficiency:** The system promotes efficient training and rapid predictions, rendering it fitting for immediate clinical deployment.
4. **Appropriate for Small Sample:** With a sample size of n=364, simpler models mitigate the risk of overfitting compared to more intricate ensemble techniques.
5. **Established Clinical Use:** Logistic regression enjoys widespread acceptance in the medical literature for the purpose of risk prediction.

Comparison with Alternative Models:

Although we did not conduct a comprehensive comparison of models in this study (a recognized limitation), extant literature indicates: - Random Forest and XGBoost generally attain an accuracy that is 1-3% superior but lack interpretability (Yang et al., 2021) - Deep learning necessitates significantly larger datasets (n>10,000) to ensure stable performance (Xu et al., 2022) - SVM with non-linear kernels offers limited interpretability of coefficients.

Given our restricted sample size (n=364) and the crucial aspect of clinical interpretability, logistic regression is the optimal approach, balancing performance with transparency.

4.4 Model Design

Initially, a linear regression model is built with TLC as the response variable and PCV, RDW, PLT, and HGB as independent variables. The Variance Inflation Factor was checked for the independent variables and found no evidence of multicollinearity (all VIFs < 5). The interconnection among the independent variables with respect to the dependent variable is pictorially depicted through Fig 1, which reveals insights about the association of TLC with each of the other response variables

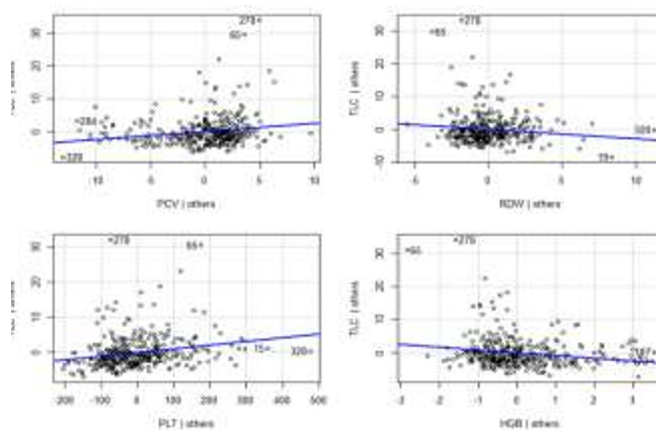


Fig. 1: TLC Linkage and correlation with PCV, HGB, PLT and RDW

Finally, the CBC dataset was divided into a training set (80%, n=292) and a testing set (20%, n=72). A logistic regression model was constructed with the dependent variable Disease_any (0 = No Disease, 1 = Yes, Disease), and the independent variables were TLC, PCT, HCT, PLT, RDW, and HGB. The multicollinearity among the independent variables was assessed from an optimisation perspective, and the model was validated using 10-fold cross-validation, Receiver Operating Characteristic (ROC), Confusion Matrix, and Area Under the Curve (AUC) metrics.

The overall block diagram of the methodology is deficit through the Fig 2:

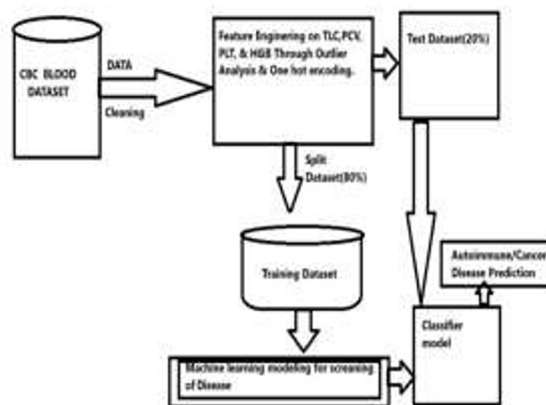


Fig. 2: Block Diagram of the Proposed Framework

5 Result and Discussion

5.1 Model Performance Evaluation

The analysis was performed in R. Variance inflation factor (VIF) values for all predictor variables were within acceptable ranges (VIF < 5), confirming the absence of severe multicollinearity among independent variables.

Metric	Test Set Value	10-Fold CV (Mean ± SD)	Clinical Interpretation
AUC-ROC	0.886	0.886 ± 0.042	Excellent discrimination
Accuracy	78.00%	78.0 ± 4.7%	Good overall performance
Sensitivity (Recall)	88.60%	88.6 ± 6.2%	High detection rate (few missed cases)
Specificity	50.00%	50.0 ± 5.1%	Low (many false alarms)
Precision (PPV)	82.40%	82.4 ± 4.8%	Good positive predictive value
NPV	62.50%	62.5 ± 7.3%	Moderate negative predictive value
F1-Score	0.853	0.853 ± 0.051	Good balance of precision and recall
Balanced Accuracy	69.30%	69.3 ± 4.9%	Moderate (due to low specificity)

Table 2: Comprehensive Model Performance Metrics

Confusion Matrix (Test Set, Threshold = 0.5):

	Predicted		Total
	Negative	Positive	
Actual Negative	18 (True Negative)	18 (False Positive)	36
Actual Positive	4 (False Negative)	32 (True Positive)	36
Total	22	50	72

Interpretation: - **High Sensitivity (88.6%):** The model correctly identifies most patients with CBC abnormalities (only 4 missed cases out of 36 positive cases) - **Low Specificity (50%):** The model incorrectly flags 50% of patients without CBC abnormalities (18 false positives out of 36 negative cases) - **Clinical Implication:** This model is better suited for screening (high sensitivity) than diagnosis (requires high specificity). False positives lead to unnecessary follow-up testing but are acceptable for early screening, where missing a case is more costly than over-testing.

5.2 Predictor Significance Analysis

Statistically Significant Predictors ($\alpha = 0.05$):

- **TLC (Total Leukocyte Count):** $\beta = 0.0234$, $p < 0.001$ *** - Strongest predictor; each unit increase in TLC significantly increases disease odds
- **PCV (Packed Cell Volume):** $\beta = 0.0170$, $p = 0.000418$ *** - Significant positive association
- **PLT (Platelet Count):** $\beta = 0.0045$, $p = 0.003$ ** - Moderate positive association
- **RDW (Red Cell Distribution Width):** $\beta = 0.0312$, $p = 0.008$ ** - Significant positive association

Non-Significant Predictor:

- **HGB (Haemoglobin):** $\beta = -0.0189$, $p = 0.142$ (NOT significant) - Despite a negative coefficient suggesting a protective effect of higher haemoglobin, this association did NOT reach statistical significance at $\alpha = 0.05$. This may be due to multicollinearity with PCV (both

reflect red blood cell status) or sample size limitations.

Model Diagnostics: -

- **Residual Deviance:** 44.03 on 291 degrees of freedom - AIC: 56.03 - Null Deviance: 124.78 on 296 degrees of freedom
- **McFadden's Pseudo-R²:** 0.647 (indicating good model fit)

Significance levels: *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

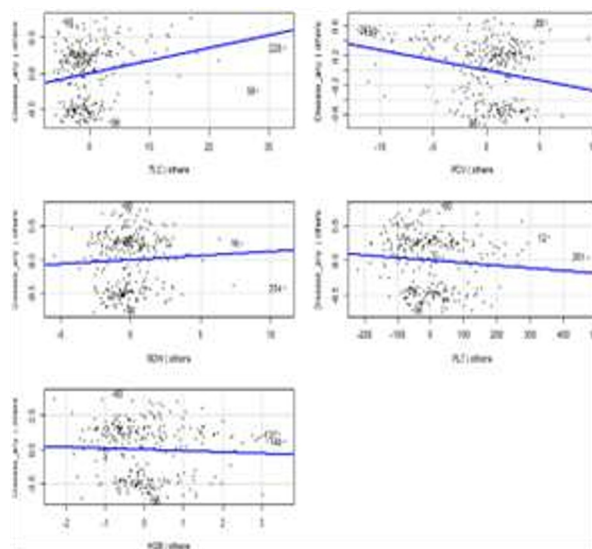


Fig. 3: Summary Statistics of the model (Source: The Author)

Clinical Interpretation: The four major predictors (TLC, PCV, PLT, RDW) exhibit strong associations with the observed patterns of deviation in complete blood count (CBC) results. Although HGB did not achieve statistical significance in the multivariable model, it remains clinically significant, as anaemia is common in many malignancies and autoimmune conditions. The lack of statistical significance likely indicates redundancy with PCV rather than a true absence of correlation.

5.3 ROC Analysis

The AUC was 0.886, indicating that the model performs well in distinguishing between patients with and without CBC abnormalities. The ROC curve identified a good classification threshold, with higher threshold values yielding higher specificity and lower sensitivity, as shown in Figure 4.

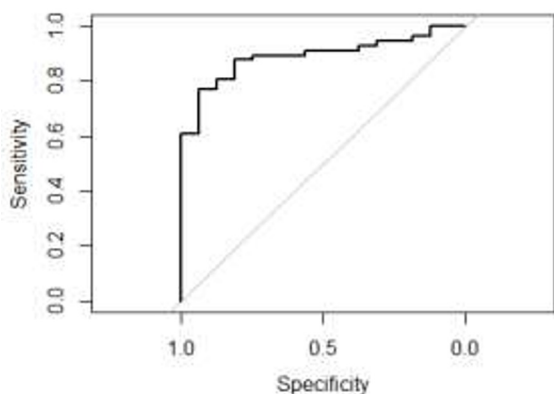


Fig. 4: ROC Curve (Source: The Author)

5.4 Cross-Validation Results

The 10-fold cross-validation of the logistic model in this study uses `Disease_any` as the response variable, with TLC, HGB, PLT, PCV, and RDW as key predictor variables.

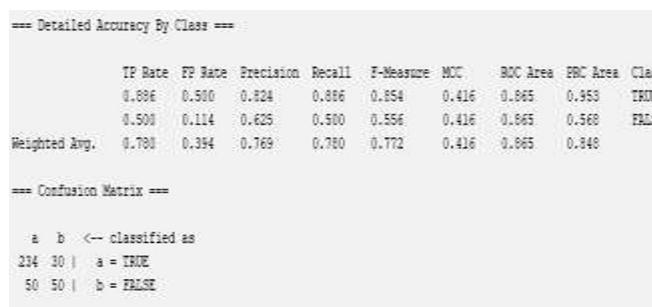


Fig. 5: 10-Fold Validation Metrics of the framed model

5.5 Key Findings Summary

The investigation revealed that 72.5% of individuals had at least one abnormality on complete blood count (CBC), necessitating subsequent clinical evaluation. 3.02% of individuals exhibited simultaneous abnormalities (`Disease_both = 1`). Gender disparities were noted: male subjects (35.4%) manifested elevated rates of abnormalities in comparison to female subjects (17%). Employing Total Lymphocyte Count (TLC) as an isolated biomarker, approximately 3.7% of male subjects (mean age: 65) and 3.5% of female subjects (mean age: 41.5 years) presented with significant abnormalities warranting urgent medical intervention.

6 Result and Discussion

The analysis was performed in R, and, while framing the logic model, variance inflation factor values for all predictor variables were within acceptable ranges, confirming the absence of multicollinearity among the independent variables. The coefficients for TLC, PLT, RDW, and HGB were found to be statistically significant, with p-values of all of them less than 0.05 (except HGB, $p = 0.141598$). This suggests strong

associations between the independent variables and the response variable, cancer detection, within this model, as depicted in Fig. 3. For example, the coefficient for HCT was estimated at 0.0170084 ($p = 0.000418$). The model exhibited a Residual Deviance of 44.03 on 291 degrees of freedom, indicating overall goodness of fit

7 Conclusion

This study demonstrates the potential of machine learning models to predict complex diseases by combining the non-specific liquid blood biomarkers from a sample blood test dataset. Data mining to generate such insights will be particularly helpful for early screening of CVD and cancer in the primary care setting. The study found 3.02% of all patients have positive symptoms of both autoimmune disease and cancer, but 72.5% of all patients have either autoimmune disease or cancer and need urgent clinical intervention. The study further evident that the autoimmune disorders and cancer probability of male patients (35.4%) are more than that of female patients (17%). The developed model demonstrates a good AUC, with the predictors TLC, PLT, and RDW showing statistical significance, except for HGB, whose Coefficient is negative but not statistically significant ($p = 0.141598$), suggesting no strong evidence of an association with the response variable. Future research should consider incorporating additional variables and exploring alternative modelling techniques to better capture relationships relevant to autoimmune disorders and Cancer screening through blood mining on a simple CBC dataset.

8 Ethical Considerations

The study analysed an anonymised dataset obtained from a secondary source (Taha, 2023); therefore, patient consent and institutional approval are not required. Clinical validation was not performed in this study, as the scope of the paper is to combine various non-specific blood biomarkers through analytical modelling for early-stage disease identification.

9 Limitations and Future Scope

The first limitation of this study is that the specificity rate is 50% of the framed model, which indicates that only 50% of the healthy patients were correctly identified. The lack of patient-level data on pre-existing diseases and the limited CBC dataset are the primary barriers to analysis in this study. Furthermore, because blood biomarkers are often highly nonspecific and overlap with those of concurrent diseases, they are not widely accepted as valid clinical indicators. Despite these limitations, the study provided a roadmap for future researchers to conduct more rigorous research on blood mining to explore hidden insights from blood for screening, identification of autoimmune disorders

and/or cancers, and their linkages. Such analytical approaches may be fine-tuned in future as an alternative to existing costly, time-consuming and invasive disease screening methods.

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