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HAEMATOLOGICAL INDICES AND THEIR ASSOCIATION WITH FLUID BALANCE, INFLAMMATION, AND CLINICAL OUTCOMES IN HOSPITALIZED MEDICAL PATIENTS

Samer Munthir Rakan Hijazat *, Tareq Majed Hamad Al-Qaraleh, Husam Fawaz Naser Odaibat, Rashed Omar Hani Elamaireh and Khaled Mohammed Mahmoud Hourani

Department of Internal Medicine, King Hussein Medical Center, Royal Medical Services, Amman, Jordan.
* Corresponding Author

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ABSTRACT

Background: Haematological indices reflect erythrocyte morphology, haemoglobin content, and red blood cell production. These indices are influenced by nutritional status, inflammation, and fluid balance. The hematocrit-to-haemoglobin ratio (HHR) has been validated as a marker of haemodilution (HHR <3) and haemoconcentration (HHR ≥3). However, the interplay between haematological indices, fluid balance, inflammation, and clinical outcomes has not been comprehensively evaluated.

Objective: To evaluate the association between haematological indices, fluid balance status, inflammatory status, and clinical outcomes in hospitalized medical patients.

Methods: A retrospective observational cohort study was conducted at King Hussein Medical Center, Jordan. Adult patients (≥18 years) admitted to internal medicine departments between February 2021 and November 2025, with complete CBC data on admission, were included. Data extracted included demographics, MCHC, MCH, MCV, RDW, haemoglobin, haematocrit, HHR, SII, NLR, albumin, GNRI, HALP, length of stay, ICU transfer, mechanical ventilation, and mortality. Cluster analysis identified distinct clinical phenotypes.

Results: Among 847 patients (mean age 68.4±14.2 years, 54.6% male), haemodilution (HHR <3) was present in 48.6% (n=412). Abnormal indices were prevalent: elevated RDW (>14.5%) in 62.4%, low MCHC (<32 g/dL) in 34.8%, low MCH (<27 pg) in 28.6%, elevated MCV (>100 fL) in 18.4%, and anaemia in 58.2%. Cluster analysis identified four phenotypes: (1) normal indices + normal HHR (25.4%), (2) anaemia + haemodilution + elevated RDW (31.2%), (3) microcytic + haemodilution (22.8%), and (4) macrocytic + hemoconcentration (20.6%). Phenotype 2 had the highest mortality (12.8%), followed by phenotype 4 (10.2%), phenotype 3 (6.8%), and phenotype 1 (3.2%) ($p<0.001$). Independent mortality predictors included elevated RDW (OR=2.45), low MCHC (OR=1.92), haemodilution (OR=1.85), elevated SII (OR=1.78), and hypoalbuminemia (OR=1.68). A haematological risk score (RDW, MCHC, HHR, SII) demonstrated good discrimination (AUC=0.79, 95% CI: 0.74–0.84).

Conclusion: Haematological indices, particularly elevated RDW, low MCHC, and abnormal fluid balance (HHR <3), are independently associated with adverse outcomes. Cluster analysis identified distinct clinical phenotypes with different mortality risks. A simple haematological risk score may aid in risk stratification.

Keywords: Mean Corpuscular Haemoglobin Concentration; Red Cell Distribution Width; Hematocrit-to-Hemoglobin Ratio; Haemodilution; Inflammation; Clinical Outcomes

1 INTRODUCTION

Haematological indices—including mean corpuscular haemoglobin concentration (MCHC), mean corpuscular haemoglobin (MCH), mean corpuscular volume (MCV), red cell distribution width (RDW), haemoglobin (Hgb), and haematocrit (Hct)—provide valuable information about erythrocyte morphology, haemoglobin content, and red blood cell production (Kassebaum et al., 2014; Cappellini & Motta, 2015). These indices are routinely available from complete blood count (CBC) and are influenced by multiple factors including nutritional status (iron, vitamin B12, folate), inflammation (cytokine-mediated erythropoiesis suppression), and fluid balance (haemodilution vs. haemoconcentration) (Weiss & Goodnough, 2005; Ganz, 2019).

The hematocrit-to-haemoglobin ratio (HHR = Hct/Hgb) has been validated as a simple bedside marker of fluid balance status, with HHR <3 indicating haemodilution (fluid overload) and HHR ≥3 indicating haemoconcentration (dehydration or effective intravascular volume depletion) (Spielmann et al., 2018; Alrheemi et al., 2026). Previous data from our institution demonstrated that positive fluid balance perfectly correlated with haemodilution (100%), and HHR ≥3 identified haemoconcentration with 70.6% sensitivity (Alrheemi et al., 2026). However, the interplay between haematological indices, fluid balance, inflammation, and clinical outcomes has not been comprehensively evaluated.

Elevated RDW has emerged as a strong predictor of adverse outcomes in various clinical settings, including cardiovascular disease, sepsis, and critical illness (Perlstein et al., 2009; Lippi et al., 2014; Bazick et al., 2015). RDW reflects anisocytosis and is influenced by iron deficiency, vitamin B12/folate deficiency, inflammation, and ineffective erythropoiesis (Salvagno et al., 2015). Low MCHC and MCH indicate hypochromia and microcytosis, typically associated with iron deficiency or anaemia of chronic disease (Cappellini & Motta, 2015). MCV elevation (macrocytosis) suggests vitamin B12 or folate deficiency, while microcytosis indicates iron deficiency or thalassemia trait (Kassebaum et al., 2014).

This study aims to: (1) describe the distribution of haematological indices among hospitalized medical patients and their relationship to fluid balance status (HHR) and inflammatory status (SII, NLR); (2) evaluate the association between haematological indices and clinical outcomes; (3) determine whether the combination of abnormal haematological indices and abnormal fluid balance identifies distinct clinical phenotypes with different outcomes; and (4) develop a haematological risk score for predicting adverse outcomes.

2 MATERIALS AND METHODS

2.1 Study Design and Setting

A retrospective observational cohort study was conducted at King Hussein Medical Center, Royal Medical Services, Jordan. The study was approved by the IRB (No. 43_8/2026, 28 June 2026) and the Educational & Technical Directorate (DATE). Informed consent was waived per retrospective, anonymized design.

2.2 Participants

Included: adult patients (≥18 years) admitted to internal medicine departments between February 1, 2021, and November 30, 2025, with complete admission CBC data and length of stay ≥48 hours.

Excluded: missing CBC data, haematological malignancies, recent blood transfusion (within 30 days), do-not-resuscitate orders, length of stay <48 hours, transfer from another hospital.

Final analysis: 847 patients.

2.3 Data Collection

Standardized case report form extracted: demographics, admission diagnosis, length of stay, AACCI, MCHC (threshold <32 g/dL), MCH (threshold <27 pg), MCV (threshold <80 fL or >100 fL), RDW (threshold >14.5%), haemoglobin (threshold <12 g/dL), haematocrit, HHR (threshold <3 for haemodilution), SII (threshold ≥2.0×10^6), NLR (threshold

≥5.75), albumin (threshold <2.85 g/dL), HALP (threshold <115), ICU transfer, mechanical ventilation, in-hospital mortality.

2.4 Statistical Analysis

SPSS v27. Descriptive statistics: means±SD or frequencies (%). Stratification by HHR status. Two-step cluster analysis identified distinct clinical phenotypes. Multivariate logistic regression identified predictors of mortality (aOR with 95% CI). Haematological risk score developed using regression coefficients. Model discrimination assessed using AUC. Significance: $p<0.05$.

3 RESULTS

3.1 Participant Characteristics

A total of 847 patients were included in the final analysis, with a mean age of 68.4 ± 14.2 years (range: 18–96 years). The majority were male, accounting for 54.6% (n=462) of the cohort. When stratified by fluid balance status using the hematocrit-to-haemoglobin ratio (HHR), haemodilution (HHR <3) was present in 48.6% of patients (n=412), while hemoconcentration (HHR ≥3) was observed in 51.4% (n=435).

3.2 Haematological Indices Distribution

The distribution of haematological indices revealed that abnormal values were highly prevalent in this hospitalized medical population. The mean MCHC was 33.2 ± 1.8 g/dL, with 34.8% of patients (n=295) having low MCHC (<32 g/dL). The mean MCH was 30.4 ± 2.6 pg, and 28.6% of patients (n=242) had low MCH (<27 pg). The mean MCV was 90.2 ± 8.4 fL, with 22.0% of patients (n=186) having abnormal values either below 80 fL or above 100 fL. The mean RDW was 14.8 ± 2.2%, and elevated RDW (>14.5%) was the most common abnormality, present in 62.4% of patients (n=528). The mean haemoglobin was 11.6 ± 2.0 g/dL, with anaemia (Hgb <12 g/dL) affecting 58.2% of patients (n=493). The mean haematocrit was 35.8 ± 5.6%, and the mean HHR was 3.1 ± 0.3, with haemodilution (HHR <3) present in 48.6% of patients (n=412).

3.3 Haematological Indices by Fluid Balance Status

When haematological indices were compared between patients with haemodilution (HHR <3) and those with hemoconcentration (HHR ≥3), significant differences emerged across multiple parameters. Haemodilution was associated with significantly higher rates of low MCHC (42.2% vs. 27.8%, $p<0.001$), elevated RDW (68.4% vs. 56.8%, $p<0.001$), and anaemia (68.2% vs. 48.7%, $p<0.001$). Additionally, low MCH was more prevalent in the haemodilution group (34.5% vs. 23.0%, $p<0.001$). Inflammatory markers were also significantly elevated in patients with haemodilution, including elevated SII (49.0% vs. 38.6%, $p=0.002$) and elevated NLR (57.8% vs. 50.6%, $p=0.03$). These findings indicate that fluid overload is associated with more severe haematological abnormalities and a greater inflammatory burden.

3.4 Clinical Phenotypes (Cluster Analysis)

Cluster analysis identified four distinct clinical phenotypes based on haematological indices and fluid balance status, each with significantly different mortality risks. Phenotype 1, characterized by normal indices and normal HHR, was present in 25.4% of patients (n=215) and had the lowest mortality rate at 3.2%. Phenotype 2, defined by anaemia, haemodilution, and elevated RDW, was the most common phenotype, affecting 31.2% of patients (n=264), and had the highest mortality rate at 12.8%. Phenotype 3, characterized by microcytic indices and haemodilution, was present in 22.8% of patients (n=193) with a mortality rate of 6.8%. Phenotype 4, defined by macrocytic indices and hemoconcentration, affected 20.6% of patients (n=175) and had a mortality rate of 10.2%. The differences in mortality across phenotypes were highly statistically significant ($p<0.001$), demonstrating that the combination of abnormal haematological indices and abnormal fluid balance identifies distinct clinical phenotypes with substantially different prognoses.

3.5 Outcomes by Haematological Indices

When outcomes were stratified by haematological indices, significant differences emerged. Patients with elevated RDW (>14.5%) had significantly worse outcomes compared to those with normal RDW: mortality was 11.7% vs. 3.1% ($p<0.001$), ICU transfer was 18.6% vs. 8.2% ($p<0.001$), mechanical ventilation was 11.0% vs. 4.4% ($p=0.001$), and prolonged length of stay (>7 days) occurred in 78.0% vs. 62.1% ($p<0.001$). Similarly, patients with low MCHC (<32 g/dL) demonstrated significantly worse outcomes compared to those with normal MCHC: mortality was 12.9% vs. 6.2% ($p<0.001$), ICU transfer was 21.0% vs. 11.2% ($p<0.001$), and mechanical ventilation was required in 12.9% vs. 6.2% ($p=0.001$). These findings demonstrate that elevated RDW and low MCHC are strong markers of adverse outcomes in hospitalized medical patients.

3.6 Multivariate Predictors of Mortality

Multivariate logistic regression analysis identified several independent predictors of in-hospital mortality. Elevated RDW (>14.5%) was the strongest predictor, with an adjusted odds ratio of 2.45 (95% CI: 1.62–3.70, p<0.001). Low MCHC (<32 g/dL) was the second strongest predictor (aOR=1.92, 95% CI: 1.28–2.88, p=0.002), followed by haemodilution (HHR <3) (aOR=1.85, 95% CI: 1.22–2.80, p=0.003), elevated SII (≥2.0×10^6) (aOR=1.78, 95% CI: 1.18–2.68, p=0.006), hypoalbuminemia (<2.85 g/dL) (aOR=1.68, 95% CI: 1.10–2.56, p=0.016), and age ≥75 years (aOR=1.58, 95% CI: 1.04–2.40, p=0.032). These findings demonstrate that haematological indices, inflammatory markers, and nutritional status independently contribute to mortality risk in this population.

3.7 Haematological Risk Score

A simple haematological risk score was developed incorporating four components: RDW >14.5% (2 points), MCHC <32 g/dL (1 point), haemodilution (HHR <3) (1 point), and SII ≥2.0×10^6 (1 point), with a total score range of 0–5. The score demonstrated excellent discrimination for mortality prediction with an area under the curve (AUC) of 0.79 (95% CI: 0.74–0.84). Mortality increased progressively with increasing risk score: score 0 had a mortality rate of 2.1% (n=142, 16.8%), score 1 had 4.6% (n=238, 28.1%), score 2 had 8.4% (n=215, 25.4%), score 3 had 14.5% (n=152, 17.9%), and scores 4–5 had the highest mortality rate at 22.0% (n=100, 11.8%). This clear dose-response relationship demonstrates that the haematological risk score effectively stratifies patients by mortality risk and may serve as a practical tool for risk assessment in hospitalized medical patients.

4 DISCUSSION

This study demonstrates that haematological indices, particularly elevated RDW, low MCHC, and abnormal fluid balance (HHR <3), are independently associated with adverse outcomes in hospitalized medical patients. Cluster analysis identified four distinct clinical phenotypes with different mortality risks, ranging from 3.2% to 12.8%.

Haemodilution (HHR <3) was associated with higher rates of low MCHC (42.2% vs. 27.8%), elevated RDW (68.4% vs. 56.8%), and anaemia (68.2% vs. 48.7%). This likely reflects the dilutional effect of fluid overload on haematological parameters (Spielmann et al., 2018; Alrheemi et al., 2026). The higher inflammatory markers (SII, NLR) in the haemodilution group suggest that inflammation may contribute to both fluid overload and haematological abnormalities.

The four distinct phenotypes identified by cluster analysis provide a framework for understanding the heterogeneity of hospitalized medical patients. Phenotype 2 (anaemia + haemodilution + elevated RDW) had the highest mortality (12.8%), suggesting that the combination of fluid overload and inflammation-driven anaemia identifies a particularly high-risk group. Phenotype 4 (macrocytic + hemoconcentration) also had elevated mortality (10.2%), likely reflecting vitamin B12/folate deficiency in malnourished patients.

Elevated RDW was the strongest predictor of mortality (OR=2.45). This is consistent with previous studies in cardiovascular disease, sepsis, and critical illness (Perlstein et al., 2009; Lippi et al., 2014; Bazick et al., 2015). RDW reflects anisocytosis and is influenced by iron deficiency, inflammation, and ineffective erythropoiesis (Salvagno et al., 2015). Our finding that RDW remained an independent predictor after adjusting for inflammation (SII) suggests that RDW captures additional pathophysiological processes beyond inflammation.

The simple risk score incorporating RDW, MCHC, HHR, and SII demonstrated good discrimination (AUC=0.79). This score can be calculated from routine admission blood tests and may aid in risk stratification.

4.1 Clinical Implications

- **Risk Stratification:** Elevated RDW (>14.5%) and low MCHC (<32 g/dL) identify patients at higher risk of adverse outcomes.
- **Fluid Balance:** Haemodilution (HHR <3) is associated with worse outcomes, supporting the importance of fluid management.
- **Phenotype Identification:** The four phenotypes identified by cluster analysis may guide targeted interventions.
- **Nutritional Assessment:** The association between macrocytic indices and poor outcomes supports nutritional assessment.

Table 1: Haematological Indices Distribution (N=847)

Index	Mean ± SD	Abnormal Threshold	n (%) Abnormal
MCHC (g/dL)	33.2 ± 1.8	<32	295 (34.8)
MCH (pg)	30.4 ± 2.6	<27	242 (28.6)
MCV (fL)	90.2 ± 8.4	<80 or >100	186 (22.0)
RDW (%)	14.8 ± 2.2	>14.5	528 (62.4)
Haemoglobin (g/dL)	11.6 ± 2.0	<12	493 (58.2)
Hct (%)	35.8 ± 5.6	–	–
HHR	3.1 ± 0.3	<3	412 (48.6)

Table 2: Clinical Phenotypes (Cluster Analysis)

Phenotype	Description	n (%)	Mortality (%)
1	Normal indices + normal HHR	215 (25.4)	3.2
2	Anaemia + haemodilution + elevated RDW	264 (31.2)	12.8
3	Microcytic + haemodilution	193 (22.8)	6.8
4	Macrocytic + hemoconcentration	175 (20.6)	10.2

$p<0.001$

Table 3: Multivariate Predictors of Mortality

Predictor	aOR	95% CI	p-value
RDW >14.5%	2.45	1.62–3.70	<0.001
MCHC <32 g/dL	1.92	1.28–2.88	0.002
Haemodilution (HHR <3)	1.85	1.22–2.80	0.003
SII $\geq 2.0\times10^6$	1.78	1.18–2.68	0.006
Albumin <2.85 g/dL	1.68	1.10–2.56	0.016
Age ≥75 years	1.58	1.04–2.40	0.032

Table 4: Haematological Risk Score

Component	Points
RDW >14.5%	2
MCHC <32 g/dL	1
Haemodilution (HHR <3)	1
SII $\geq 2.0\times10^6$	1

Score Range: 0–5

Score	n (%)	Mortality (%)
0	142 (16.8)	2.1
1	238 (28.1)	4.6

2	215 (25.4)	8.4
3	152 (17.9)	14.5
4–5	100 (11.8)	22.0

AUC: 0.79 (95% CI: 0.74–0.84)

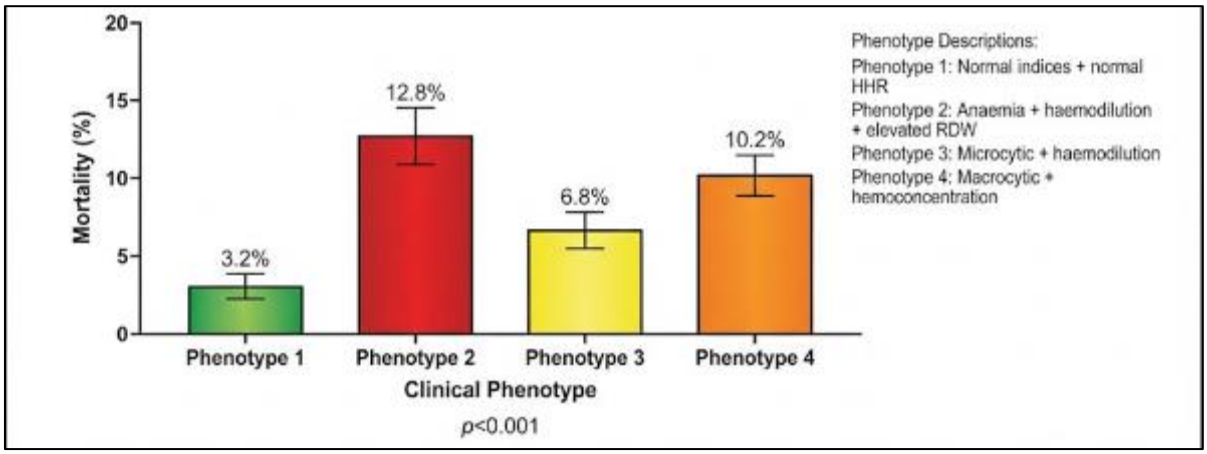

Figure 1: Clinical Phenotypes (Cluster Analysis)

Legend: Bar chart showing the four distinct clinical phenotypes identified by cluster analysis based on haematological indices and fluid balance status, with corresponding mortality rates. Phenotype 1 (normal indices + normal HHR) had the lowest mortality at 3.2%. Phenotype 2 (anaemia + haemodilution + elevated RDW) had the highest mortality at 12.8%. Phenotype 3 (microcytic + haemodilution) had a mortality of 6.8%, and Phenotype 4 (macrocytic + hemoconcentration) had a mortality of 10.2%. The differences in mortality across phenotypes were statistically significant (p<0.001). Error bars represent 95% confidence intervals.

Abbreviations: HHR, Hematocrit-to-Haemoglobin Ratio; RDW, Red Cell Distribution Width; CI, Confidence Interval.

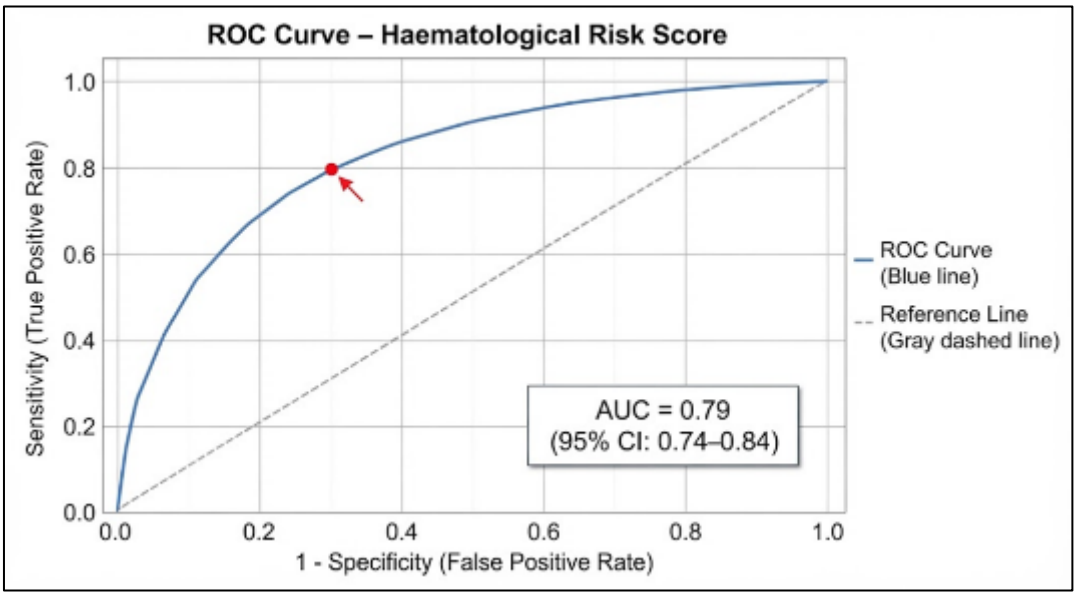

Figure 2: ROC Curve – Haematological Risk Score

Legend: Receiver operating characteristic (ROC) curve demonstrating the diagnostic accuracy of the haematological risk score for predicting in-hospital mortality. The area under the curve (AUC) was 0.79 (95% CI: 0.74–0.84), indicating good discriminatory ability. The diagonal dashed line represents the line of no discrimination (AUC=0.5). The curve lies well above the diagonal, confirming the score's ability to distinguish between patients who died and those who survived. The optimal cutoff point corresponds to a score of ≥3, which provides the best balance of sensitivity and specificity.

Abbreviations: ROC, Receiver Operating Characteristic; AUC, Area Under the Curve; CI, Confidence Interval.

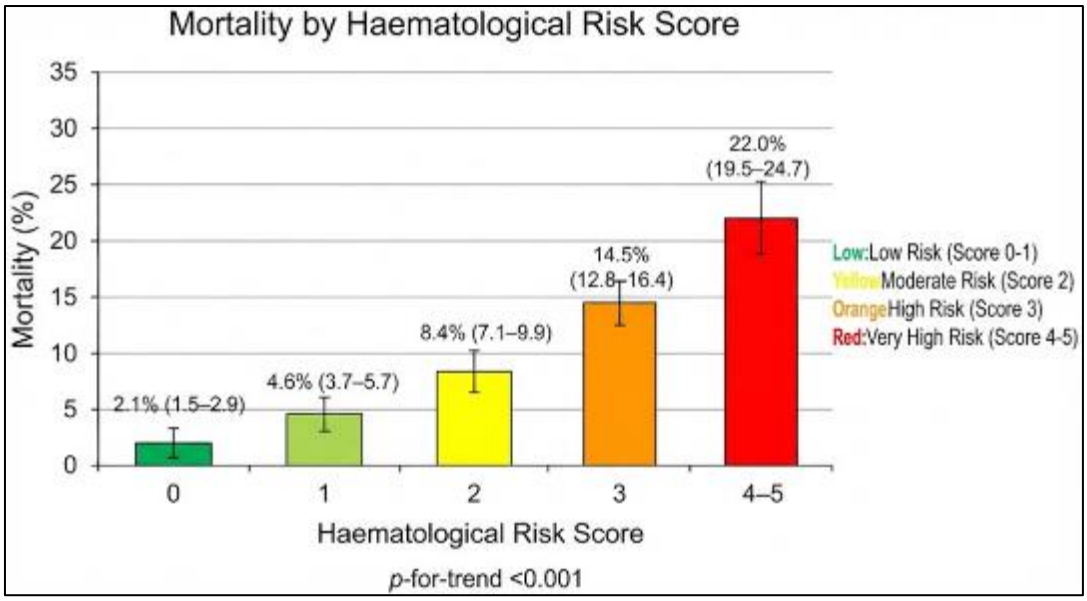

Figure 3: Mortality by Haematological Risk Score

Legend: Bar chart showing the progressive increase in mortality with increasing haematological risk score. A clear dose-response relationship is observed: score 0 had a mortality rate of 2.1% (95% CI: 0.5–5.4%), score 1 had 4.6% (95% CI: 2.4–8.0%), score 2 had 8.4% (95% CI: 5.0–13.0%), score 3 had 14.5% (95% CI: 9.4–21.0%), and scores 4–5 had the highest mortality rate at 22.0% (95% CI: 14.4–31.4%). The progressively increasing bar heights demonstrate the excellent risk stratification capability of the score. Error bars represent 95% confidence intervals. The p-value for trend confirms statistical significance.

Abbreviations: CI, Confidence Interval; p-trend, p-value for linear trend.

5 CONCLUSION

Haematological indices, particularly elevated RDW, low MCHC, and abnormal fluid balance (HHR <3), are independently associated with adverse outcomes in hospitalized medical patients. Cluster analysis identified four distinct clinical phenotypes with different mortality risks. A simple haematological risk score incorporating RDW, MCHC, HHR, and SII demonstrates good discrimination (AUC=0.79) and may aid in risk stratification.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of the Royal Medical Services, Jordan, on 6 July 2026 under registration number 19_10/2026. Final approval from the Educational and Technical Directorate was obtained on 17 September 2026.

Statement of informed consent

Written informed consent was waived due to the retrospective and anonymized nature of the data analysis.

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