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ORIGINAL RESEARCH

Differential Analysis of Blood Routine Examination Parameters in Patients with Upper Gastrointestinal Bleeding and Lower Gastrointestinal Bleeding

Jun Wang, MM; Houwei Ren, MM; Bin Gu, MM; Yuezhan Zhang, MD

ABSTRACT

Background • This study addresses the critical need for differentiating between upper and lower gastrointestinal bleeding by focusing on blood routine parameters to enhance diagnostic precision.

Objective • This study aims to identify and compare specific blood routine parameters to determine their efficacy in distinguishing between upper and lower gastrointestinal bleeding for improved clinical decision-making.

Methods • This retrospective study analyzed 119 patients with gastrointestinal bleeding (GIB) admitted to our hospital between January 2017 and June 2020. Among them, 86 were diagnosed with upper GIB (UGIB) and 33 with lower GIB (LGIB). After admission, peripheral blood samples were collected for a comprehensive blood routine examination, including white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb), platelet count (PLT), blood urea nitrogen (BUN), creatinine (Cr), and BUN to Cr ratio (BUN/Cr ratio). Differences in blood routine parameters were compared between the UGIB and LGIB groups. Receiver Operating Characteristic (ROC) curve analysis was conducted to assess the efficacy of blood routine examinations in differentiating between UGIB and LGIB.

Results • The study revealed no significant differences in WBC and Cr levels between LGIB and UGIB patients ($P > .05$). However, UGIB patients exhibited statistically lower levels of RBC, Hb, and PLT, along with higher BUN and BUN/Cr ratio levels compared to LGIB patients ($P < .05$). Pearson correlation coefficient analysis indicated an inverse correlation of BUN/Cr with RBC, Hb, and PLT in GIB patients and a positive association between BUN/Cr and BUN ($P < .05$). ROC analysis demonstrated that RBC, Hb, PLT, BUN, and BUN/Cr ratios were effective in distinguishing UGIB from LGIB ($P < .05$).

Conclusions • Blood routine parameters, including RBC, Hb, PLT, BUN, and BUN/Cr ratio, are valuable in differentiating between UGIB and LGIB. These parameters can serve as early evaluation indexes for GIB, facilitating timely intervention and treatment to enhance therapeutic outcomes. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Acute gastrointestinal bleeding (GIB), characterized by symptoms like hematemesis, melena, or hematochezia, remains common in the gastroenterology department.[1] GIB is categorized into upper GIB (UGIB) and lower GIB (LGIB); it poses a high risk of death if not treated promptly and properly.[2] In cases of acute massive GIB, evidence shows annual incidences of approximately 40-150 cases per 100 000 persons for UGIB and 20-27 cases per 100,000 persons for LGIB.[3-5] Acute overt LGIB accounts for about 20% of all GIB cases.[6] Studies report mortality rates of 4.5%-10% for UGIB and 1.9%-2.3% for LGIB.[7-9]

In clinical practice, it is often observed that upper gastrointestinal bleeding (UGIB) classically presents with hematemesis and/or melena,[10,11] while hematochezia mostly indicates bleeding originating from lower gastrointestinal sources (LGIB).[12] Diagnostic tools include esophagogastroduodenoscopy and colonoscopy for UGIB and LGIB, respectively, with capsule endoscopy or arteriography as necessary. Previous studies[13-15] have indicated that LGIB usually stops bleeding spontaneously, requiring no specific treatment in most cases. In contrast, bloody stools in UGIB often necessitate further endoscopy for confirmation.

Today, the swift and accurate differentiation of UGIB from LGIB remains a common and challenging concern for clinicians, particularly when facing patients with hemodynamic instability or those unable to undergo invasive tests promptly.

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In such situations, appropriate diagnostic laboratory tests can prove invaluable in supporting a specific diagnosis, facilitating expedited evaluation, and ensuring precise treatments.[15,16]

Richards, et al.[16] investigated 126 patients with GIB and observed that individuals with UGIB had a significantly higher blood urea nitrogen to creatinine (BUN/Cr) ratio compared to those with LGIB. However, in the study by Ernst, et al.[17] no significant differences were found in blood urea nitrogen (BUN), creatinine (Cr), BUN/Cr ratio, hemoglobin (Hb), and hematocrit between UGIB and LGIB. Hence, the potential of these cost-effective and easily accessible hematologic biomarkers for preliminary differentiation between UGIB and LGIB remains uncertain.

Presently, there is a lack of discussion on the comparative diagnostic efficacy of hematologic variables for distinguishing UGIB from LGIB, and correlation analyses between different hematologic parameters are yet to be explored. Therefore, our study aims to contribute novel evidence regarding the potential diagnostic value of RBC, Hb, platelet counts (PLT), BUN, and the BUN/Cr ratio in distinguishing between UGIB and LGIB. Our findings contribute to addressing the diagnostic gaps in distinguishing between upper and lower gastrointestinal bleeding, thus informing more accurate and timely clinical interventions.

MATERIALS AND METHODS

Study Design

A retrospective study was conducted, and a total of 119 patients experiencing acute hematemesis, melaena, or hematochezia were consecutively enrolled in this study at Taizhou People's Hospital between January 2017 and June 2020. All participants underwent comprehensive endoscopic and/or colonoscopy examinations, except for a subset of cases where hematemesis and liver cirrhosis were confirmed through imaging studies. Finally, 86 cases constituted inpatients with the UGIB group, while the remaining 33 cases constituted inpatients with the LGIB group. The study adhered to the Declaration of Helsinki and received approval from the Ethics Committee of Taizhou People's Hospital.

Inclusion and Exclusion Criteria

The inclusion criteria encompassed: (10 adults aged ≥ 18 years; (2) with symptoms occurring within the last 24 hours; (3) all of whom underwent hematologic variable tests. Exclusion criteria comprised: (1) individuals with hematological diseases, renal insufficiency, acute or chronic inflammatory diseases, cancers, thyroidal dysfunction, acute stroke, acute coronary syndrome, or other trauma-related diseases; (2) pregnant women; (3) patients with symptoms onset beyond 24 hours; (4) those treated with antibiotics or blood transfusion before laboratory tests; and (5) individuals with incomplete clinical data were excluded.

Baseline Data Collection

The collection of patient baseline data involved extracting information from the medical records meticulously maintained at Taizhou People's Hospital.

Evaluation Criteria

Hematologic Variable Tests. Hematologic variable tests were conducted either in the emergency room or upon admission. The SYSMEX XE-2100 hematology analyzer and Hitachi7600 automatic biochemical analyzer were utilized to determine leukocytes, RBC count, Hb, PLT count, BUN, and Cr, respectively.

Endoscopy/Colonoscopy Tests. Within the first 48 hours of hospitalization, comprehensive endoscopy and colonoscopy examinations were conducted to assess and diagnose gastrointestinal conditions.

Analytical Methods. The SYSMEX XE-2100 hematology analyzer and Hitachi7600 automatic biochemical analyzer were employed for hematologic variable measurements. The BUN/Cr ratio was calculated and recorded, with the conversion factors BUN (1 mg/dL = 0.357 mmol/L) and Cr (1 mg/dL = 88.4 μmol/L).

Statistical Analysis

The statistical analysis was performed using SPSS v19.0 (SPSS Inc., Chicago, IL, USA). Count data are expressed as [n (%)], and group comparisons were conducted using the chi-square test. Measurements are presented as ($\bar{x} \pm s$), and inter-group comparisons were made using the independent samples t test. Correlations were assessed through Pearson's correlation coefficient. Prognostic performance was evaluated by constructing receiver operating characteristic (ROC) curves, and the area under the curve (AUC) was calculated. The cutoff value for the above scores was determined from the ROC coordinates, utilizing the score value with the best Youden index (sensitivity + specificity -1). Additional correlation analyses were conducted using Pearson correlation coefficients. A significance level of $P < .05$ was considered statistically significant.

RESULTS

Demographic Characteristics Comparison between Groups

UGIB and LGIB patient groups exhibited no significant differences in age, gender composition, diabetes, hypertension, smoking, drinking, exercise habits, and residence ($P > .05$), refer to Table 1. Among UGIB patients,

Table 1. Comparison of the Levels of Different Variables between the Two Groups of GIB

Variables	UGIB (n=86)	LGIB (n=33)	t/χ^2	*P* value
Age (years)	61.48 ± 13.45	60.82 ± 15.29	0.231	.818
Gender (Male/Female)	55 / 31	17 / 16	1.544	.214
Diabetes Mellitus (Y/N)	15 / 71	5 / 28	0.089	.765
Hypertension (Y/N)	28 / 58	16 / 17	2.596	.107
Smoking (Y/N)	45 / 41	16 / 17	0.141	.708
Drinking (Y/N)	36 / 50	14 / 19	0.003	.956
Exercise Habit (Y/N)	12 / 74	5 / 28	0.028	.867
Place of Residence (urban/rural area)	71 / 15	28 / 5	0.089	.765

Note: Data presented as mean ± standard deviation or frequency. t/χ^2 represents the t value for continuous variables or the chi-square value for categorical variables. P values indicate the significance level of differences between UGIB and LGIB groups.

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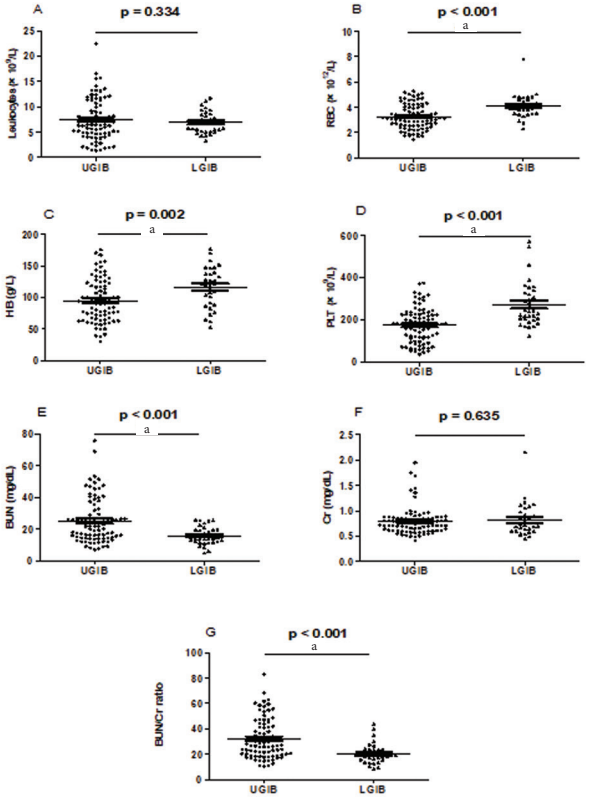
Figure 1. Comparison of Hematologic Variables between UGIB and LGIB Groups. (A) Lymphocytes, (B) Red Blood Cell (RBC) counts, (C) Hemoglobin (HB) levels, (D) Platelet (PLT) counts, (E) Blood Urea Nitrogen (BUN) levels, (F) Creatinine (Cr) levels, (G) BUN/Cr ratio.

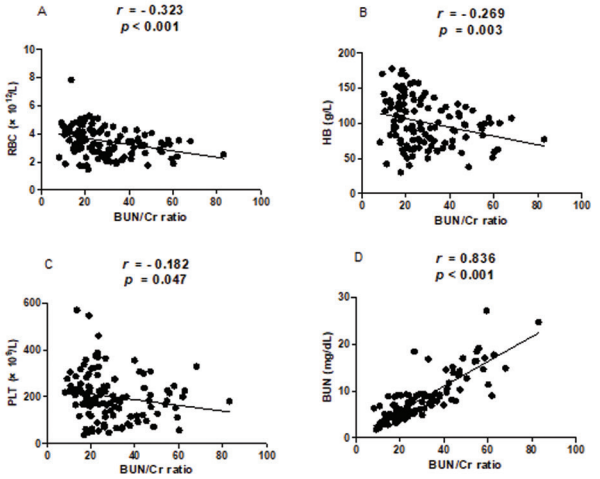


[a]*P* < .001 indicates a highly significant difference between UGIB and LGIB groups.

Note: Data represents mean values. Statistical significance was determined using independent samples *t* test for continuous variables.

Abbreviations: UGIB, Upper Gastrointestinal Bleeding, LGIB, Lower Gastrointestinal Bleeding.

Figure 2. Correlation analysis between hematologic parameters in Gastrointestinal Bleeding (GIB). (A) Correlation of Red Blood Cell (RBC) counts and BUN/Cr ratio, (B) Correlation of Hemoglobin (Hb) levels and BUN/Cr ratio, (C) Correlation of Platelet (PLT) counts and BUN/Cr ratio, (D) Correlation of Blood Urea Nitrogen (BUN) levels and BUN/Cr ratio.



Note: Pearson correlation coefficients were used to analyze the relationships between the indicated variables.

Abbreviation: GIB, Gastrointestinal Bleeding.

29.1% (25 cases) were attributed to peptic ulcers, 39.5% (34 cases) to gastroesophageal varices, and 31.4% (27 cases) to other causes. In the LGIB patient group, 48.5% (16 cases) were associated with colitis/proctitis, 24.2% (8 cases) with colorectal polyps, 9.1% (3 cases) with hemorrhoids, and 18.2% (6 cases) with other causes.

Comparison of Hematologic Variables

The UGIB group exhibited significantly decreased levels of RBC, Hb, and PLT, while BUN and the BUN/Cr ratio were elevated compared to the LGIB group (all $P < .05$). No significant differences were observed in leukocyte counts and Cr between the two groups ($P > .05$). Refer to Figure 1A-1G.

Correlation Analysis of Gastrointestinal Bleeding Parameters

The interrelation between the blood routine parameters that exhibited statistical differences was further explored. Pearson correlation coefficients were employed to assess the associations between RBC count, Hb, PLT count, BUN, and the BUN/Cr ratio in all patients with GIB. Notably, RBC, HB, and PLT levels demonstrated negative correlations with the BUN/Cr ratio of GIB (r = -0.323, $P < .001$; r = -0.269, $P = .003$; r = -0.182, $P = .047$). In contrast, BUN exhibited a positive correlation with the BUN/Cr ratio (r = 0.836, $P < .001$), refer to Figure 2.

Comparison of ROC Curves for Differentiating UGIB and LGIB

The efficacy of RBC count, Hb, PLT count, BUN, and the BUN/Cr ratio in distinguishing between upper UGIB and LGIB was evaluated through ROC curves. The AUC (95% CI) for RBC was 0.746 (0.658 to 0.821); for Hb, it was 0.685 (0.593 to 0.767); for PLT, it was 0.768 (0.682 to 0.841), for BUN it was 0.709 (0.619 to 0.789), and for BUN/Cr ratio it was 0.742 (0.654 to 0.818). All parameters demonstrated excellent results in differentiating between LGIB and UGIB.

The cutoff values, specificity, sensitivity, and Youden index for distinguishing UGIB from LGIB were as follows: RBC: 3.44×10^{12}/L (specificity: 87.88%, sensitivity: 62.79%, Youden index: 0.507). Hb: 100 g/L (specificity: 72.73%, sensitivity: 65.12%, Youden index: 0.378). PLT: 183×10^{9}/L (specificity: 84.85%, sensitivity: 56.98%, Youden index: 0.418). BUN: 25.49 mg/dL (specificity: 96.97%, sensitivity: 37.21%, Youden index: 0.342). BUN/Cr ratio: 24.03 (specificity: 81.82%, sensitivity: 59.30%, Youden index: 0.411). Refer to Figure 3 for a detailed representation of the ROC curves and corresponding diagnostic indices.

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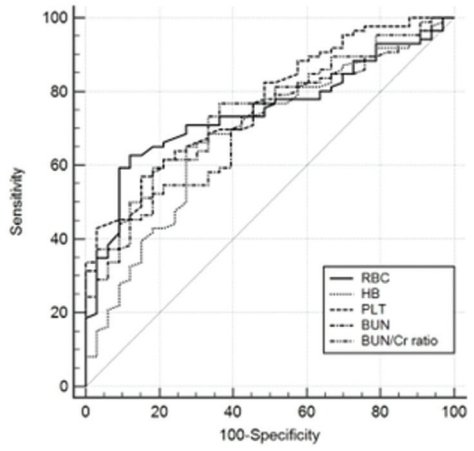
Figure 3. Receiver Operating Characteristic (ROC) analysis for hematologic parameters in distinguishing Upper Gastrointestinal Bleeding (UGIB) from Lower Gastrointestinal Bleeding (LGIB).



Note: RBC (Red Blood Cell counts): AUC: 0.746 (95% CI: 0.658 to 0.821); Cutoff value: 3.44 × 10^{12}/L; Specificity: 87.88%; Sensitivity: 62.79%; Youden index: 0.507. Hb (Hemoglobin): AUC: 0.685 (95% CI: 0.593 to 0.767); Cutoff value: 100 g/L; Specificity: 72.73%; Sensitivity: 65.12%; Youden index: 0.378. PLT (Platelet counts): AUC: 0.768 (95% CI: 0.682 to 0.841); Cutoff value: 183 × 10^{9}/L; Specificity: 84.85%; Sensitivity: 56.98%; Youden index: 0.418. BUN (Blood Urea Nitrogen): AUC: 0.709 (95% CI: 0.619 to 0.789); Cutoff value: 25.49 mg/dL; Specificity: 96.97%; Sensitivity: 37.21%; Youden index: 0.342. BUN/Cr (Blood Urea Nitrogen to Creatinine) Ratio: AUC: 0.742 (95% CI: 0.654 to 0.818); Cutoff value: 24.03; Specificity: 81.82%; Sensitivity: 59.30%; Youden index: 0.411. The AUC represents the accuracy of the diagnostic test, with a higher value indicating better authenticity. Sensitivity and specificity denote the effectiveness of the screening test, while the Youden index combines both measures.

DISCUSSION

GIB is a complex and often life-threatening condition that poses significant challenges in its diagnosis and management. Distinguishing between UGIB and LGIB is crucial for guiding appropriate interventions and optimizing patient outcomes. In this context, hematologic parameters such as RBC count, Hb, PLT count, BUN, and the BUN/Cr ratio have emerged as potential indicators with diagnostic significance.[16,17] Understanding the distinct profiles of these hematologic markers in UGIB and LGIB patients can provide valuable insights into the pathophysiological mechanisms underlying gastrointestinal bleeding.

In this study, we conducted a detailed analysis of these hematologic parameters, exploring their interrelationships and assessing their diagnostic utility in effectively differentiating between UGIB and LGIB. Our study demonstrated a significant reduction in Hb levels within the UGIB group compared to the LGIB group (P = .002). This finding suggests the potential utility of HB as a discriminatory marker between UGIB and LGIB. Additionally, our analysis revealed a parallel trend in RBC count, which exhibited a significant decrease in the UGIB group compared to the LGIB group (P < .001). This parallel reduction in both HB and RBC suggests that RBC levels could similarly serve as discriminators between UGIB and LGIB.

These observations indicate that reduced Hb and/or RBC levels are associated with an increased likelihood of hemodynamic instability and severe bleeding. Additionally, we established a significantly lower PLT count in the UGIB group compared to the LGIB group (P < .001), suggesting that PLT levels could serve as discriminators between UGIB and LGIB. Our findings align with the findings of Ziabari, et al.[18]

However, it is important to note that some prior studies have presented conflicting results.[26] For example, Sittichanbuncha, et al.[19] conducted a study involving 76 GIB patients presenting with hematochezia (30 with UGIB, 43 with LGIB). Their findings indicated no significant difference in PLT count between patients with UGIB and LGIB [(249.13 ± 93.28) × 10^{9}/L vs. (280.51 ± 91.69) × 10^{9}/L, P > .05]. In contrast, our study revealed a significantly lower PLT in the UGIB group compared to the LGIB group (P < .001), supporting PLT as a potential discriminator between UGIB and LGIB.

Furthermore, we observed a significantly higher BUN in the UGIB group compared to the LGIB group (P < .001), suggesting BUN's potential utility in distinguishing UGIB from LGIB. Our findings align with previous clinical evidence that supports the association between elevated BUN levels and upper gastrointestinal bleeding. However, Ernst et al.[20] presented a differing perspective, asserting that there was no significant difference in BUN levels between UGIB and LGIB [(25 ± 18) mg/dL vs. (20 ± 12) mg/dL, P > .05].

In our current investigation, we also observed a significantly higher BUN/Cr ratio in the UGIB group compared to the LGIB group (P < .001). This finding suggests that the BUN/Cr ratio may serve as a useful discriminator between UGIB and LGIB. Our results align with similar conclusions drawn in previous studies.[21]

Moreover, Snook, et al.[22] concluded that the BUN/Cr ratio on admission was significantly higher in UGIB than in LGIB across various estimated blood loss categories. In our investigation, we observed no statistically significant differences in leukocyte and Cr levels between UGIB and LGIB patients, indicating that neither leukocytes nor Cr can effectively differentiate between UGIB and LGIB. However, a study by Tomizawa, et al.[23] reported elevated leukocyte levels in UGIB compared to LGIB patients, presenting a discrepancy with our findings.

Recognizing the established significance of the BUN/Cr ratio in distinguishing UGIB from LGIB, as highlighted in the relevant studies, we conducted Pearson's correlation analyses to explore the relationship between the BUN/Cr ratio and other variables for the first time. Our findings demonstrated a negative correlation between RBC count, Hb, PLT count, and the BUN/Cr ratio in GIB patients, while BUN exhibited a positive correlation (all P < .05). In essence, a patient with lower RBC, HB, PLT, and higher BUN and BUN/Cr ratio was more likely to receive a diagnosis of UGIB.

We discovered that the AUC for distinguishing between UGIB and LGIB was 0.746 for RBC count, 0.685 for Hb, 0.768 for PLT count, 0.709 for BUN, and 0.742 for BUN/Cr ratio. Notably, no significant differences were observed

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between either of the two parameters. This finding implies that RBC, Hb, PLT, BUN, and BUN/Cr ratios all exhibit accurate and reliable diagnostic values in distinguishing UGIB from LGIB. A previous study[24] also supported our findings to some extent, reporting AUC, specificity, and threshold values for Hb and BUN as 0.615, 93.0%, 21.0 mg/dL and 0.619, 80.7%, 8.7 g/dL, respectively.

The precise reason for the inconsistent conclusions remains elusive, and we hypothesized that it could be attributed to variations in factors such as the onset-to-admission interval, etiological composition ratios, and varying sample sizes. Despite these inconsistencies with prior studies, our findings underscore the importance of these hematologic parameters in enhancing the accuracy of distinguishing between UGIB and LGIB.

Study Limitations

While our study provides valuable insights, it is essential to acknowledge its limitations. Firstly, a more rigorous design is imperative for this retrospective analysis. Secondly, expanding the sample size is crucial to enhance the generalizability of our findings. Thirdly, the sample exhibits heterogeneity, including variations in onset-to-admission intervals and etiological components. To support and validate our conclusions, larger and more homogeneous samples derived from multicenter studies are warranted.

CONCLUSION

In conclusion, our study demonstrates the remarkable efficacy of blood routine parameters, including RBC count, Hb, PLT count, BUN, and BUN/Cr ratio, in distinguishing UGIB from LGIB. The findings propose the potential utilization of these hematologic markers as early evaluation indices for GIB in future clinical settings. This not only enhances the precision of differentiating between UGIB and LGIB but also holds promise for facilitating timely interventions and improving overall treatment outcomes for affected patients. The robust effects observed in our study emphasize the clinical relevance of these routine blood parameters in advancing diagnostic and therapeutic approaches for GIB.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHORS' CONTRIBUTIONS

Yuezhan Zhang designed the research, Jun Wang drafted and revised the manuscript, Houwei Ren and Bin Gu collected and analyzed the data, and All authors read and approved the final submitted manuscript.

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