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Original Article

Enhancing blood transfusion safety through extended Rh matching in preparation for electronic crossmatch in Hezhou

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ABSTRACT

This study aims to prepare an electronic crossmatch (ECM) system in Hezhou People's Hospital and to evaluate its clinical applicability based on ABO/RhD and extended Rh antigen matching. A retrospective analysis was conducted on 36 196 transfusion records from 2022 to 2024. ABO and Rh blood typing were performed using the gel card method on a fully automated analyzer. An ABC grading standard was established to evaluate Rh phenotype compatibility as follows: Grade A (complete match of C, c, E, e antigens), Grade B (avoidance of introducing new antigens), and Grade C (priority matching of strongly immunogenic antigens). The ECM system preparation involved three key steps: (1) consolidating all ABO/RhD and RhCE phenotyping results into a standardized digital database; (2) developing an ABC grading algorithm and applying it to previous transfusion records; and (3) validating the algorithm against historical transfusion outcomes. The results demonstrated 100% concordance for ABO/RhD matching. The overall Rh phenotype matching rate was 64.32%, with CCee (59.08%) and CcEe (28.43%) being the most prevalent phenotypes. Among the matched phenotypes, Grade A accounted for 84.05%, Grade B for 4.47%, and Grade C for 11.48%. The study suggests that the donor-recipient blood group database provides a solid data foundation and facilitates the establishment of the ECM system within the hospital. The high Grade A matching rate demonstrates its strong supply reliability and safety, offering an effective and efficient alternative to traditional serological crossmatching. This study presents a feasible approach to promote the implementation of ECM in primary-level hospitals.

Keywords: electronic crossmatch, supply assurance, Rh phenotype, graded matching, transfusion safety

INTRODUCTION

Electronic crossmatch (ECM) is an intelligent blood compatibility testing method developed in modern transfusion medicine based on computer information technology and blood group serology principles[1]. This technology enables automation and precision in blood group compatibility judgment by constructing a standardized blood group database for donors and recipients, combined with algorithmic models for systematic analysis of blood group antigen-antibody systems. Its core principle lies in digitizing conventional serological test results and rapidly comparing the blood group data of recipients and

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donors against predefined blood group serological rules to identify potential compatibility risks[2–3]. Compared with traditional manual crossmatch, ECM significantly reduces the risk of transfusion-related adverse events resulting from operational errors or blood group misidentification by minimizing the human intervention step[4]. At the data processing level, this technology relies on experimental data such as blood group genotyping and antibody screening, in conjunction with the theoretical framework of blood group serology, to systematically analyze interactions between red blood cell (RBC) surface antigens and plasma antibodies. ECM, as a significant milestone in the development of modern transfusion technology, has been widely used for decades in regions such as Europe, the United States, and Hong Kong, China, due to its advantages in efficiency, safety, and resource conservation. Its core process entails directly assigning compatible blood through a computer system after confirming the recipient's ABO/RhD blood group and a negative irregular antibody screen, bypassing cumbersome serological crossmatching procedures[5].

However, the promotion of ECM in China remains at an early stage, facing multiple challenges related to regulatory frameworks, technological infrastructure,, and clinical awareness[6]. Current internationally accepted ECM guidelines primarily emphasize ABO and RhD compatibility. However, numerous studies have shown that in clinical transfusion, alloimmunization caused by other Rh blood group system antigens (such as C, c, E, e) have surpassed anti-D as a leading cause of hemolytic transfusion reactions and ineffective transfusion[7]. Rh antibodies account for up to 68% of all antibodies in Chinese transfusion recipients, with anti-E exhibiting the highest detection rate (41%–56%), underscoring the necessity of extended Rh phenotype matching[8].

This work addressed this situation by conducting an innovative investigation in Hezhou region of southern China, integrating the fundamental requirements of ECM with matched transfusion for clinically significant Rh system antigens. This study aims to quantitatively evaluate the level of supply assurance and safety tiers achievable with an extended matching strategy, thereby providing essential regional practical experience and data support for the forthcoming implementation of ECM.

MATERIALS AND METHODS

Data source

Retrospective data were collected from all clinical transfusion records at the Department of Transfusion Medicine, Hezhou People's Hospital, between January 1, 2022, and December 31, 2024. Inclusion criteria: negative patient antibody screen; positive RhD status in both patient and blood bag; valid ABO blood group detection (A, O, AB, or B) for both. Exclusion criteria: positive patient antibody screen; recent transfusion history (< 72 hours); samples of unsatisfactory quality (*e.g.*, hemolysis, clots). This study was approved by the Ethics Committee of Hezhou People's Hospital (Approval No. HZ-2023-015). All sample information was anonymized to ensure privacy protection.

ABO and Rh blood typing

ABO and Rh blood typing were performed by the gel card method on a fully automated analyzer (Model: AISEN120; Yantai Aidekang Biotechnology Co., Ltd., Yantai, Shandong, China) according to the manufacturer's instructions for use. The following reagents were employed: Rh Phenotype Card (Batch Nos. 202201013, 202311008, and 202402014; Jiangsu LIBO Medicine Biotechnology Co., Ltd., Jiangyin, Jiangsu, China); ABO RhD + Reverse Grouping Card (Batch Nos. 202203008, 202312006, and 202406015; Jiangsu LIBO Medicine Biotechnology Co., Ltd.); Coombs (Anti-IgG+C_3d) Card (Batch Nos. 202203014, 202310001, and 202401016; Jiangsu LIBO Medicine Biotechnology Co., Ltd.). All reagents were utilized within their specified validity periods and in accordance with the provided instructions.

Data processing and screening flow

The format and column names of the three-year data tables were standardized, misaligned data were corrected, and year identifiers were added. Records were rigorously selected in which the patient's antibody screen was negative, the patient was RhD positive with a valid ABO blood group, and the blood bag was RhD positive with a valid ABO blood group and complete Rh phenotype data. The ABO blood group matching status of all records was assessed to ensure basic compatibility. The screened data were then graded based on the concordance of RhCE antigens (C, c, E, e) between donors and recipients (***Table 1***).

Statistical analysis

Data analysis was performed using SPSS (version 26.0, IBM Corp., Armonk, NY, USA). In descriptive statistics, a multidimensional analysis was conducted on patient ABO blood group distribution, Rh

Table 1 **Rh antigen matching grading**

Grade	Basic principle	Matching requirement	Safety assessment
A	Complete match	Donor and recipient have four identical RhCE antigens (C, c, E, e).	Safe
B	Avoidance of new antigens	Donor does not introduce any RhCE antigen absent in the recipient (*e.g.*, recipient CCEe → donor CCEE/CCee).	Generally safe
C	Prioritization of strongly immunogenic antigens	Priority matching based on immunogenicity (E > C > c > e)	Requiring careful monitoring

phenotype distribution, diagnosis distribution, blood usage department distribution, ABC grading distribution for blood group matching, and blood usage volume. Categorical variables were compared using the chi-square test. A *P*-value less than 0.05 was considered statistically significant.

RESULTS

Patient blood group distribution characteristics

Following data consolidation, 36 196 valid records were obtained for the period from 2022 to 2024. Analysis of these valid transfusion records revealed distinct distribution patterns in patient blood groups. As shown in ***Table 2***, the ABO blood group distribution was as follows: type O, 16 652 cases (46.01%); type A, 9072 cases (25.06%); type B, 8879 cases (24.53%); and type AB, 1593 cases (4.40%). This distribution pattern aligns with established norms for Chinese populations, with type O being predominant and type AB the least frequent. Notably, ABO compatibility between donors and recipients was achieved in 100% of cases, satisfying the fundamental prerequisite for ECM implementation.

Table 2 **Patient ABO blood group distribution**

ABO blood group	Patient count	Percentage (%)	Blood bag matching status [*n* (%)]
O	16 652	46.01	16 648 (100)
A	9072	25.06	9072 (100)
B	8879	24.53	8879 (100)
AB	1593	4.40	1593 (100)

Regarding Rh phenotypes (***Table 3***), two phenotypes predominated in the patient population: CCee accounted for 21 384 cases (59.08%), and CcEe for 10 289 cases (28.43%), together comprising 87.51% of all patients. Less common phenotypes included ccEE (1847 cases, 5.10%) and other variants (2676 cases, 7.39%). The overall Rh phenotype matching rate was 64.32%, with minimal variation across phenotype subgroups (range: 63.80%–65.12%). The high proportion of CCee individuals (E antigen-negative) explains the elevated risk of E antigen mismatch during transfusion, as these recipients are susceptible to alloimmunization against the E antigen when exposed to E-positive donor blood.

Table 3 **Distribution of major Rh phenotypes in patients**

Rh phenotype	Patient count	Percentage (%)	Matching rate (%)
CCee	21 384	59.08	64.21
CcEe	10 289	28.43	64.55
ccEE	1847	5.10	65.12
Other	2676	7.39	63.80

Patient disease diagnosis and blood usage department distribution

Table 4 presents the diagnostic profile of transfused patients. The three most frequent diagnoses requiring transfusion were thalassemia major (2068 cases, 17.31%), upper gastrointestinal hemorrhage (1560 cases, 13.06%), and gastrointestinal hemorrhage (1368 cases, 11.45%). The substantial proportion of patients with thalassemia, who require chronic transfusion support, highlights the importance of long-term alloimmunization risk management in this population.

Table 4 **Patient disease diagnoses**

Diagnosis	Count	Percentage (%)
Thalassemia major	2068	17.31
Upper gastrointestinal hemorrhage	1560	13.06
Gastrointestinal hemorrhage	1368	11.45
Decompensated liver cirrhosis	673	5.63
Chronic renal failure	596	4.99
Acute upper gastrointestinal hemorrhage	580	4.85
Severe anemia	567	4.75
Myelodysplastic syndrome	505	4.23
Acute myeloid leukemia	494	4.13
Heart failure	440	3.68
Supportive therapy for malignancy	391	3.27
Neonatal respiratory distress syndrome	364	3.05
Abnormal uterine bleeding	354	2.96
Acute leukemia	336	2.81
Severe pneumonia	333	2.79
Community-acquired pneumonia, non-severe	287	2.40
Post-chemotherapy myelosuppression	270	2.26
Anemia	261	2.18
Iron deficiency anemia	251	2.10
Liver malignancy	249	2.08

Analysis of departmental blood utilization revealed that the Intensive Care Unit (ICU) had the highest demand, accounting for 8233 transfusions (26.29%), followed by the Hematology Department with 4155

transfusions (13.27%) (***Table 5***). Collectively, critical care areas (ICU and EICU) accounted for 33.7% of all transfusions, reflecting the concentration of severely ill patients necessitating emergent blood support.

Table 5 **Blood usage department distribution**

Department	Count	Percentage (%)
ICU	8233	26.29
Hematology department	4155	13.27
EICU	2320	7.41
Digestive disease center	2144	6.85
Infectious diseases department	1916	6.12
Pediatrics ward II	1555	4.97
Orthopedics & sports medicine	1202	3.84
Hepatobiliary & pancreatic surgery	1077	3.44
Orthopedic Trauma	1046	3.34
Cardiothoracic vascular surgery II	992	3.17
Gastrointestinal surgery	890	2.84
Gynecology ward	858	2.74
Pediatrics ward I	803	2.56
Burn and plastic surgery	794	2.54
Nephrology & rheumatology	730	2.33
Neurosurgery ICU	652	2.08
Neurology I	590	1.88
Obstetrics	529	1.69
Urologic surgery	417	1.33
Spine & joint surgery	412	1.32

ICU: intensive care unit. EICU: emergency intensive care unit.

Donor-recipient blood group ABC grading matching and blood usage volume

Application of the ABC grading system to all transfusion records revealed that Grade A (complete Rh antigen match) was achieved in 30 423 cases (84.05%), demonstrating that the Hezhou blood supply system can provide fully Rh-matched blood products for the vast majority of transfusions (***Table 6***). Grade B (avoidance of introducing new Rh antigens) accounted for 1617 cases (4.47%), while Grade C (priority matching of strongly immunogenic antigens) comprised 4156 cases (11.48%).

The analysis of annual data revealed consistent patterns in the ABC grading distribution from 2022 to 2024 (***Table 7***). Grade A proportion ranged from 82.85% to 86.08%, Grade B from 4.16% to 4.63%, and Grade C from 9.76% to 12.58%. Although the proportion of Grade C showed a slight increase in 2023 (12.58%) compared to 2022 (9.76%), potentially reflecting changes in donor availability or patient case mix, the overall stability suggests consistent operation of the blood supply system. The proportion of Grade A matches was stable across the three years (86.08% in 2022, 82.85% in 2023, and 83.51% in 2024), with no significant temporal trend (χ^2 = 3.42, df = 2, P = 0.18) (***Table 7***).

Table 6 **Statistics of donor-recipient blood group ABC grading matching**

Grade	Record count	Percentage (%)	Clinical significance	Safety assessment
A	30 423	84.05	Rh antigen complete match	Safe
B	1617	4.47	Avoidance of introducing new antigens	Generally safe
C	4156	11.48	Major antigen mismatch	Requiring caution

Table 7 **Annual trend of donor-recipient blood group ABC grading matching [*n* (%)]**

Year	Grade A	Grade B	Grade C	Total
2022	9359 (86.08)	452 (4.16)	1061 (9.76)	10 872
2023	10 478 (82.85)	578 (4.57)	1591 (12.58)	12 647
2024	10 586 (83.51)	587 (4.63)	1504 (11.86)	12 677

χ^2 for trend = 3.42; P = 0.18.

To further elucidate the clinical context of Rh antigen matching, we performed a stratified analysis of ABC grade distribution across the five most prevalent diagnostic categories requiring transfusion (***Table 8***). Across all five diagnostic categories, Grade A (complete Rh antigen match) remained the predominant matching outcome, with proportions ranging from 79.40% to 85.60%. The distribution of ABC grades varied significantly across the five major diagnostic categories (χ^2 = 89.70, df = 8, P < 0.001). Patients with thalassemia exhibited the highest proportion of Grade C (16.30%), reflecting that chronically transfused patients are at greater risk of E antigen mismatch.

Table 8 **Distribution of ABC grades by major diagnostic categories [*n* (%)]**

Diagnosis	Grade A	Grade B	Grade C	Total
Thalassemia major	1642 (79.40)	89 (4.30)	337 (16.30)	2068
Upper gastrointestinal hemorrhage	1332 (85.38)	70 (4.49)	158 (10.13)	1560
Gastrointestinal hemorrhage	1171 (85.60)	61 (4.46)	136 (9.94)	1368
Decompensated liver cirrhosis	568 (84.40)	31 (4.61)	74 (11.00)	673
Chronic renal failure	507 (85.07)	27 (4.53)	62 (10.40)	596

χ^2 = 89.70; df = 8; P < 0.001.

The distribution of blood usage volume per patient is illustrated in ***Fig. 1***. The majority of patients (53.88%) required 2 units of RBCs, which may be derived from two different donors.

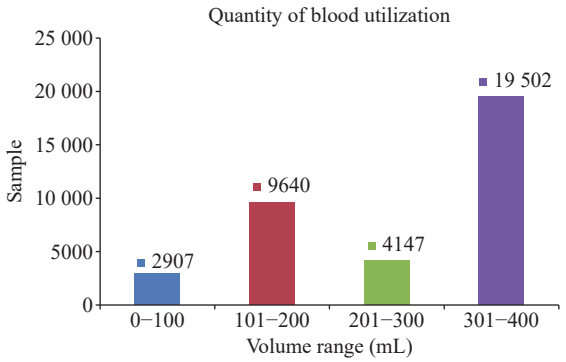

Fig. 1 **Distribution of patient blood usage volume (2022–2024)**

DISCUSSION

At the time of this study, Hezhou People's Hospital was in the developmental and validation phase of establishing an ECM system; complete clinical implementation of ECM activation had not yet been achieved. The present retrospective analysis of 36 196 transfusion records served as the foundational data platform for system development. Through this work, three essential steps were completed: (1) consolidation of all historical ABO/RhD and RhCE types into a standardized donor-recipient database; (2) development and retrospective application of the ABC grading algorithm; and (3) validation of its stratification capability against historical outcomes. Integration with the Hospital Information System (HIS) and Laboratory Information System (LIS) is currently in progress, with full ECM implementation scheduled for 2026. Therefore, the present study reports on the preparation and validation phase rather than on a completed clinical implementation.

The ABO blood group distribution of patients (***Table 2***) was as follows: type O, 46.01%; type A, 25.06%; type B, 24.53%; and type AB, 4.40%, which is consistent with the ABO blood group distribution pattern observed in southern Chinese populations[9]. Among the Rh phenotypes presented in ***Table 3***, CCee (59.08%) and CcEe (28.43%) were the most predominant, together accounting for 87.51% of the total. This distribution aligns with several recent large-scale domestic studies, offering a critical foundation for the optimal configuration of Rh phenotypes in clinical blood inventory management[10].

The clinical transfusion records from Hezhou (***Table 6***) showed that the matching rates for both ABO and RhD blood groups reached 100%, meeting the prerequisites for ECM. The overall Rh phenotype matching rate in this study was 64.32%, which objectively reflects the polymorphism characteristics of the Rh blood group system in the patient population of Hezhou and the challenges it poses for clinical matching. Specifically, the high frequency of the CcEe phenotype (28.43%) in patients, which expresses a full set of RhCE antigens, allows for precise matching by avoiding the transfusion of blood carrying new RhCE antigens when these individuals are recipients, significantly reducing the risk of alloimmunization. However, the CCee phenotype accounted for a high proportion (59.08%), indicating a high proportion of E antigen-negative individuals in this population, which increases the risk of anti-E antibody production. This distribution pattern is a key factor affecting the overall Rh matching rate and highlights the importance of strengthening E antigen matching management in blood supply[11]. These findings provide a scientific basis for regional blood inventory optimization and the development of personalized transfusion strategies. As shown in ***Fig. 1***, 53.88% of patients required 2 units of blood. This necessitates querying the blood group database to ensure sufficient phenotype-matched blood products whenever possible[12]. The system must support multiple donor queries per recipient to maintain uniform matching quality, particularly concerning E and other immunogenic antigens. It has been demonstrated that large electronic datasets from multiple hospitals could predict the potential transfusion needs and improve transfusion practice[13].

The 84.05% Grade A complete Rh match rate demonstrates that the regional blood supply can support fully Rh-matched transfusions in the vast majority of cases, providing strong feasibility evidence for ECM with extended matching. The stability of Grade A proportions from 2022 to 2024 indicates consistent quality of the blood inventory system. The significant variation in Grade C across diagnostic categories, with the highest proportion observed in thalassemia (16.30%), emphasizes the need for tailored matching strategies for multi-transfused patients. These individuals face an increased risk of cumulative antigen exposure, and prioritizing them for Grade A or B units would reduce long-term alloimmunization. Furthermore, the distribution structure indicates that the ABC grading system can effectively distinguish donor-recipient combinations at different levels of immunization risk, enabling refined management of transfusion matching strategies[14] and providing a feasible evaluation framework for improving clinical transfusion safety.

From the perspective of supply assurance capability, ***Table 7*** indicates that the proportion of

Grade A crossmatches remained stable within the range of 82.85% to 86.08%. The stability in Grade A proportions from 2022 to 2024 indicates consistent quality of the blood inventory system. ***Table 4*** encompasses a wide spectrum of diagnoses, reflecting the diversity of clinical transfusion needs. This breadth provides a solid data foundation and an operational basis for the routine application of ECM and the rapid issuance in emergency settings. Actual operational data demonstrate that in emergency transfusion scenarios, the automatic screening and matching of blood *via* the ECM system can markedly reduce blood issuance time from the tens of minutes required for traditional serological crossmatching to just a few minutes, greatly enhancing rescue efficiency and highlighting the important value of informatized and intelligent transfusion management in clinical emergency care[15].

Compared with international recommendations (*e.g.*, AABB, BCSH) that focus on ABO/RhD and negative antibody screen, the proposed ABC grading adds a quantitative dimension of "matching degree" assessment, making supply safety both measurable and manageable[16–17]. However, the 11.48% of Grade C matches still poses a non-negligible immunization risk. Therefore, we recommend a stratified management strategy that includes: (1) electronic flagging of Grade C combinations; (2) strengthened post-transfusion antibody monitoring (*e.g.*, at 72 hours and 4 weeks); and (3) prioritization of Grade A or B blood for chronically transfused recipients.

The current study has several limitations, primarily its retrospective design and the lack of systematic prospective hemovigilance data on delayed hemolytic reactions or *de novo* alloantibody formation following Grade C transfusions. The real-world clinical outcomes of ABC-guided matching versus traditional crossmatching require prospective comparison. Furthermore, the database currently covers a single center; therefore, multi-center validation and the integration of uniform RhCcEe typing into routine practice are necessary to establish a regional intelligent blood supply system. It is noteworthy that some blood centers have employed an electronic transfusion reaction reporting system for effective hemovigilance based on the frequency and nature of transfusion reactions[18]. Future endeavors should focus on promoting multi-center validation and establishing a real-time warning system to achieve closed-loop management encompassing "precise matching – efficient supply – safe transfusion".

In conclusion, the constructed donor-recipient database and the validated ABC grading system provide a robust and replicable foundation for ECM establishment and implementation in Hezhou. The high complete match rate and stable supply indicators confirm that ECM with extended Rh matching is advantageous, feasible, and safe. Future efforts will focus on prospective controlled trials, the development of a real-time automated ABC warning system, and deep integration with HIS/LIS to realize closed-loop, precise, intelligent, and sustainable transfusion management.

Author contributions

Conceptualization, Shanchang Chen and Hongjun Gao; Methodology, Shanchang Chen and Hongjun Gao; Software, Yanxia Mo and Hongjun Gao; Validation, Yu Zhong and Renming Huang; Formal Analysis, Yanxia Mo and Yu Zhong; Investigation, Renming Huang; Resources, Jikai Zhou, Yuxiang Huang, Miaoli Hu, Xiang Lu, Yan Tan, Pingping Guo, Yan Liu, and Fangfang Chen; Data Curation, Renming Huang; Writing – Original Draft Preparation, Shanchang Chen, Yanxia Mo, and Hongjun Gao; Writing – Review & Editing, Hongjun Gao and Shanchang Chen; Visualization, Yanxia Mo and Yu Zhong; Supervision, Shanchang Chen; Project Administration, Shanchang Chen; Funding Acquisition, Shanchang Chen and Hongjun Gao.

Ethics statement

Not applicable.

Informed consent statement

Not applicable.

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Declaration of competing interest

The authors declared no conflict of interests.

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