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Management of refined and personalized newborn blood specimen collection

Hui-Bin Huang [a,1], Yu-Bin Lin [a,1], Jin-Hua Chen [b,1], Min Zhu [a], Li-Jin Chen [a], Wang Ye [a], Lin-Hua Luo [a], Hui-ming Ye [a,*]

[a] Department of Laboratory Medicine, Fujian Key Clinical Specialty of Laboratory Medicine, Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen, Fujian, China
[b] Department of Clinical Laboratory, Fujian Provincial hospital, Shengli Clinical Medical College of Fujian Medical University, 350001, Fujian, China

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ABSTRACT

Background: Iatrogenic blood loss is an important cause of neonatal anemia. In this study, a spreadsheet tool was developed to reduce blood collection, providing a new idea for the prevention of iatrogenic blood loss in newborns.
Methods: Based on hematocrit, minimum test volume and dead volume, a new tool was to calculate the minimum blood collection volume and the number of containers required for the test portfolio. We collected data from October 2022 to October 2023 from Xiamen Maternal and Child Health Hospital for analysis and validation.
Results: During this year, there were 16,434 patients and 13,696 plasma/serological samples in the neonatology department. Among them, there were 8 test combinations of greater than 1%, and 9490 samples in total. According to the hospital manual, the recommended amount of blood collection is 27,534 ml and 9490 containers. Through the analysis of this tool, total blood collection was 8864.77 ml, marked qnantity of upward containers (closest level to the calculated blood collection volume) was 10301 ml, and the amount of containers was 8835, which decreased by 67.8%, 62.58% and 6.9% respectively. Besides, if the hematocrit information cannot be obtained in advance and the high hematocrit is calculated as 0.8, the recommended amount of blood collection is 14334.3 ml, and the marked amount of the upward container markering is 17340 ml, decreasing by 47.9% and 37.02% respectively.
Conclusion: We have developed an auxiliary tool that can manage neonatal blood specimen collection in a fine and personalized way and can be applied among different laboratory instruments by parameters modification.

1. Introduction

Newborn anemia is one of the major diseases that endanger the health of newborns. Mild anemia can affect growth and development, severe anemia can cause organ hypoxia damage, even shock and death, and long-term anemia can affect cardiac function, immune function, and intellectual development, leading to growth retardation, susceptibility to infectious diseases, and increased risk

* Corresponding author.
E-mail address: yehuiming@xmu.edu.cn (H.-m. Ye).
[1] Co-first author: Hui-Bin Huang, Yu-Bin Lin and Jin-Hua Chen equally contributed to this study.

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of mortality [1].

The study found that the severity of anemia is positively correlated with the degree of iatrogenic blood loss, and the increase in iatrogenic blood loss is positively correlated with transfusion requirements. In about one-fourth of laboratories, blood collection exceeds the needs of routine diagnosis and treatment, and these necessary blood tests are the main cause of iatrogenic anemia [2]. According to multiple studies, diagnostic tests are the most common cause of iatrogenic anemia in newborns [3–5], especially in premature infants in neonatal intensive care units (NICUs) [6]. Even though only a small amount of blood is taken for analysis each time, a 1 mL blood sample may account for over 1% of their total blood volume [7], because the blood volume of newborns is approximately 85–105 mL per kilogram. The total blood loss can be equivalent to 15%–30% of the premature infant's circulating blood volume, leading to a decrease in the newborn's blood volume and thereby increasing the risk of anemia [8]. Therefore, reducing unnecessary testing blood volume becomes extremely important.

The laboratory sample collection manual is the primary basis for standardized sample collection in most hospitals. Since sample volume requirements for individual tests or the most common test combinations are only involved in sample collection, the minimum laboratory detection volume determined is often set based on the following criteria: first, completing any required test combination with one blood drawing; second, leaving enough sample volume for repeat analysis; and finally, when performing plasma/serum testing, the collection volume requirement must accommodate the possibility of a high hematocrit level. The blood volume is extremely precious in newborns, especially premature and very low birth weight infants, so we have developed a "minimum blood volume" tool. It can be set in a personalized way according to different instruments, accurately calculate the minimum blood collection volume and container quantity required for any project combination for special patients, in order to minimize iatrogenic blood loss. Subsequently, we conducted a statistical analysis on the benefits of the tool to the neonatology department over the past year.

2. Methods

2.1. Spreadsheet tool development

The "minimum test volume" of an inspection instrument refers to the smallest quantity or concentration of a substance that the instrument can reliably detect or measure. Generally, a smaller minimum detectable limit indicates higher sensitivity of the instrument. The "dead space volume" of an instrument typically refers to the space or components within the internal volume of the instrument that are not involved in sample analysis. These areas may include pipes, connectors, valves, etc., which do not come into contact with the sample or affect the sample analysis process. Therefore, the "dead volume" needs to consider the volume retained during the sample flow process.

The minimum test volume and dead space volume are determined primarily by the instrument itself and result from the combined influence of various factors. Instrument manufacturers typically provide relevant indicators and parameters in technical specifications. We obtained the minimum detectable limit and dead volume required for relevant instrument detection projects from instrument manufacturers.

Then, we developed an Excel tool integrating this information with patient hematocrit and sample container type. This tool was developed by informatics methods such as designing data structure, selecting appropriate functions and formulas, establishing data input interface, performing calculations and analysis, and adding visualizations. Our tool provides an interface where patient hematocrit can be entered, and the desired test items selected. Since plasma yields 15–20% more than serum at the same hematocrit [9, 10], the formula for calculating serum volume is: Serum volume = Whole blood volume *HCT* 0.8. It can automatically analyze the minimum required sample blood volume and minimum number of containers needed.

Additionally, since different laboratory instruments have varying minimum test volume and dead space volume, we can apply our tool into different laboratories by adjusting two parameters within the tool.

2.2. Comparison of the amount of blood drawn and the number of containers

To determine the potential impact of implementing this tool on changes in blood collection volume, all serum/plasma sample data from the neonatology department of Xiamen Maternal and Child Health Hospital were collected for comparative analysis over one year. The top eight combinations of projects were selected based on quantity, each accounting for more than 1% of the total, for comparison. They were divided into three groups. The first group represented the recommended volume according to the sample collection manual. The recommended blood collection volume for the eight project combinations was calculated based on the sample collection manual. The second group represented the recommended volume according to the tool. Blood collection volume was calculated in a personalized way based on the patient's hematocrit value obtained from the complete blood count on the day of collection.The third group represented the volume rounded up to the nearest container marking. Since it is unlikely that sample collection personnel would collect blood to the milliliter precision recommended by the tool in actual practice, additional analysis was conducted. It was found that the containers used in the research hospital were marked at five levels: 1 ml, 2 ml, 3 ml, 4 ml, and 5 ml. The recommended blood collection volume from the tool was rounded up to the nearest container marking.

Additionally, since some patients were undergoing their first test and neonatal hematocrit fluctuates with increasing age, it was not possible to accurately obtain the hematocrit data for the day of collection in advance. The reference range for neonatal hematocrit in our laboratory was 0.47–0.67. The highest hematocrit included in the samples was 0.75. Aas hematocrit increased, the required blood collection volume also increased. An additional calculation was performed using a high hematocrit value of 0.8 to validate the superiority of the tool.

This study was reviewed and approved by the Ethics Committee of the Xiamen Maternal and Child Health Hospital (approval number: KY-2024-032-K01).

3. Results

Fig. 1 displays some functions of the tool. Clinicians can select projects based on specific patient conditions, input the hematocrit, and obtain the minimum blood collection volume and the minimum number of blood collection tubes required for the patient. Different laboratories can personalize modifications based on the minimum detection volume and dead space volume of different instruments for application. This tool can calculate the minimum test volume and the minimum number of blood collection containers that is more accurately than the commonly used sample collection manuals in hospitals.

We collected a total of 46,922 blood samples from 16,434 patients in the neonatology department over one year. Among these, there were 13,696 plasma/serum samples. Among the samples, we screened out eight test combinations of more than 1%, totaling 9490 samples, representing 69.29% of the total, as shown in Fig. 2. According to the hospital's sample collection manual, the recommended total blood collection volume was 27,534 ml, distributed among 9490 containers. Through tool analysis, the recommended total blood collection volume was 8864.77 ml, reducing by 67.8%. Marked qnantity of upward containers (the level closest to the tool's blood collection volume recommendation) was 10,301 ml, reducing by 62.58%, as shown in Table 1.

Since some patients underwent their first test without prior hematocrit information, and neonatal hematocrit fluctuated with increasing age, obtaining the hematocrit data for the day of collection in advance was not possible. Additionally, a high hematocrit value of 0.8 was used for further analysis. A total blood collection volume of 14,334.3 ml recommended by the tool represented a reduction of 47.9%. Marked qnantity of upward containers was 17,340 ml, reducing by 37.02%. Collection of these samples in 8835 containers recommended by the tool reduced by 6.9%, as shown in Table 2. We observed a significant decrease in blood collection volume and the number of blood collection containers after applying this tool, as depicted in Fig. 3.

4. Discussion

Currently, preventive measures to reduce iatrogenic anemia in newborns mainly focus on increasing the use of point-of-care testing (POCT), reducing discarded blood at the start of phlebotomy, and standardizing medical protocols such as minimizing unnecessary tests. However, methods for precisely calculating blood collection volumes to reduce the amount of blood drawn are scarce [11]. In routine communication between the laboratory and clinical departments, we found common issues regarding the minimum test volume for certain test combinations and found that whether the number of blood collection containers can be reduced. For instance, in neonatology, especially for critically ill newborns, very low birth weight infants, and preterm infants, laboratory staff often struggle to provide timely and accurate answers due to variations in patient hematocrit levels and the complexity of different test combinations. Iatrogenic anemia is a significant cause of anemia in newborns [11]. Currently, most laboratories cannot accurately and rapidly calculate the specific minimum sample volume required for various test combinations.

Based on the clinical problems identified, in this study, a new informatics tool was explored, developed and validated for analyzing blood collection volumes in clinical practice. This tool integrates data such as test projects, hematocrit values of the samples, minimum detection limits of laboratory instruments, and instrument dead space volumes to calculate the minimum blood collection volume required for various test combinations in a fine-grained and personalized manner. It aims to reduce blood sample wastage and assist in improving the diagnosis and treatment effectiveness of newborns. Additionally, by adjusting the parameters within the tool, the model provided by this tool can be applied to different laboratory instruments, offering a novel approach to refined blood collection in the future.

	0.70	←HCT	
Select the project	Yellow tube	Serum sample size (μL)	Dead space volume (ul)
	Liver function	200	100
	Biochemical full set	320	100
	blood lipids	180	100
	Kidney function	160	200
	K+、Na+、Cl-、Ca2+、Mg2+、P、Glu	160	100
	TSH、T3、T4	300	100
	Lac	150	100
	TRUST+TP	300	100
	HBsAg、anti-HBs、HBeAg、anti-HBe、anti-HBc	450	100
	HBsAg、anti-HBs、HBeAg、anti-HBe、anti-HBc、HIV、TP、TRUST	700	100
	Anti-Mycoplasma pneumoniae antibodies	80	100
	Cytokines	100	100
	Autoimmune antibody panels	150	100
	ALT	30	100
	CK	50	300
	AST	30	100
	Total number of tubes	5	
	Total serum amount of the selected item	1680	100
	the actual amount of blood is actually needed	3051.43	

Fig. 1. Partial screenshot of the spreadsheet tool.

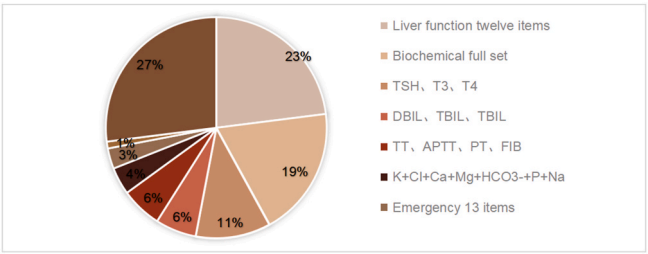

Fig. 2. The number of neonatal pediatrics test portfolios ranked top 8 in the past year.

Table 1
According to the calculation of hematocrit on the same day, the recommended amount of collection manual, tool and upward container in 9490 tests of neonatal pediatric patients in the past year.

project	number	the hospital collection manual recommended (ml)	Tools recommended (ml) (the same day HCT)	Up to the container marking (ml)
Liver function twelve items	2658.00	7974.00	2537.18	2761.00
Biochemical full set	2567.00	7701.00	2701.81	2942.00
TSH、T3、T4	1353.00	4059.00	1324.07	1465.00
DBIL、TBIL、TBIL	815.00	2445.00	653.00	868.00
TT、APTT、PT、FIB	766.00	1532.00	598.64	828.00
K + Cl + Ca + Mg + HCO3- + P + Na	825.00	2475.00	463.01	632.00
Emergency 13 items	336.00	1008.00	461.97	627.00
TT、APTT、PT、FIB、D-D、FDP	170.00	340.00	125.08	178.00
total	9490.00	27534.00	8864.77	10301.00

Table 2
Hematocrit is calculated at 0.8. the recommended amount of collection manual, tool and upward container in 9490 tests of neonatal pediatric patients in the past year.

project	number	the hospital collection manual recommended (ml)	Tools recommended (ml) (The HCT was 0.8)	Up to the container marking (ml)
Liver function twelve items	2658.00	7974.00	3322.50	5316.00
Biochemical full set	2567.00	7701.00	5134.00	5134.00
TSH、T3、T4	1353.00	4059.00	2570.70	2706.00
DBIL、TBIL、TBIL	815.00	2445.00	570.50	815.00
TT、APTT、PT、FIB	766.00	1532.00	1532.00	1532.00
K + Cl + Ca + Mg + HCO3- + P + Na	825.00	2475.00	495.00	825.00
Emergency 13 items	336.00	1008.00	369.60	672.00
TT、APTT、PT、FIB、D-D、FDP	170.00	340.00	340.00	340.00
total	9490.00	27534.00	14334.30	17340.00

Compared to traditional sample collection manuals, this tool in our study assisted physicians in reducing blood sample collection volume in the neonatal population by up to 67.8%. However, during practical implementation, we encountered two issues. Firstly, experienced blood collection personnel couldn't precisely draw the recommended blood collection volume suggested by the tool. Moreover, the current markings on the containers used in hospitals are lack of precision. Therefore, further analysis was performed based on the nearest container marking. Despite this, blood collection volume could still be reduced by 62.58%. Secondly, some patients underwent their first test without prior hematocrit information. Therefore, simulated verification of the tool's superiority was conducted with a high hematocrit value of 0.8. Even with this adjustment, the tool recommended a total blood collection volume of 14,334.3 ml, representing a reduction of 47.9%, and rounding up to the nearest container marking, it amounted to 17,340 ml, a decrease of 37.02%.

In our study, to overcome insufficient precision on blood collection tubes, blood collection personnel used syringes with accurate graduations to collect blood and then transferred it to blood collection tubes. However, applying negative pressure during the collection process could cause hemolysis, and the lack of anticoagulants in the syringes could lead to clotting during the transfer, resulting in a significant increase in the rate of sample rejection. Given these challenges, we propose that if manufacturers could accurately indicate the markings on the containers, this technical improvement could bring even greater benefits in reducing blood collection volume in newborns. Additionally, for coagulation function screening projects, the ratio of anticoagulant to blood must be

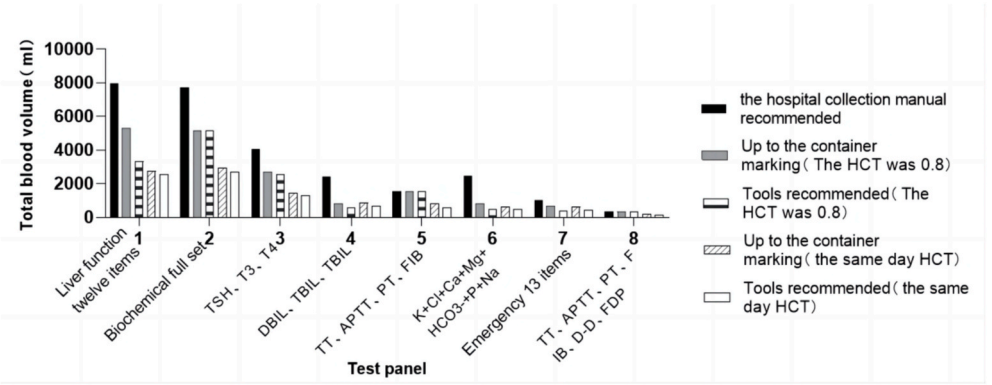

Fig. 3. omparison of recommended volume of different project collection manuals, recommended amount of tools and recommended amount of blood collected up the container.

maintained within a certain range. Therefore, when the amount of anticoagulant in the collection tube is fixed, the required blood volume cannot be altered. Hence, if manufacturers of blood collection containers could provide tubes with different amounts of anticoagulant for selection, the blood volume required for our coagulation-related projects might further decrease. Another limitation of this tool is that it calculates the blood collection volume required for a single test, meaning that if a sample needs to be reanalyzed or additional tests are requested clinically, blood collection needs to be performed again.

In conclusion, the blood collection volume assistance tool developed in this study can help clinicians obtain minimum blood collection by precise and personalized calculation based on Hematocrit levels when there were Neonatal patients with very low blood volume, thus minimizing iatrogenic anemia resulting from venous blood collection. By modifying tool parameters such as instrument minimum detection limits and dead space volumes, this tool's model can be applied to different laboratories, offering a new direction for preventing iatrogenic anemia.

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Ethical approval

This study was reviewed and approved by the Ethics Committee of the Xiamen Maternal and Child Health Hospital (approval number: KY-2024-032-K01).

CRediT authorship contribution statement

Hui-Bin Huang: Writing – review & editing, Writing – original draft, Methodology, Data curation. **Yu-Bin Lin:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Data curation. **Jin-Hua Chen:** Writing – review & editing, Writing – original draft, Methodology, Data curation. **Min Zhu:** Validation, Supervision, Data curation, Conceptualization. **Li-Jin Chen:** Supervision, Data curation, Conceptualization. **Wang Ye:** Supervision, Data curation, Conceptualization. **Lin-Hua Luo:** Investigation, Formal analysis, Data curation, Conceptualization. **Hui-ming Ye:** Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.plabm.2024.e00408.

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