Retrospective Cohort Study of Neonatal Blood Transfusion in China

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Abstract

Background: Blood transfusion treatment is extremely important for newborns—but the threshold of neonatal blood transfusion is not same in different countries, which may be due to differences in regions, races and nationalities, as well as medical conditions and treatment methods. Up to now, there are not enough clinical studies and prospective follow-up to determine the suitable threshold for Chinese newborns. Therefore, it is important to establish a retrospective and prospective multicenter cohort study to evaluate whether the blood transfusion scheme is suitable for newborns in China.

Methods: This is a retrospective cohort study of neonatal blood transfusion and prospective follow-up from January 1, 2017 to June 30, 2021, aim to evaluate the effect of restricted and unrestricted blood transfusion on neonatal health. Diagnosis and blood transfusion data of 5,669 newborns between January 1, 2017 and June 30, 2018 from 46 hospitals in China were analyzed through retrospective study and followed up for 1w, 1m and 3y after discharge. The variable data of newborns and their mothers was collected in this cohort study with 280 variables and 2.98 million data volumes including in the database. The primary outcome index of the study was death, and the secondary outcome index was complications during hospitalization, hospitalization time, NICU hospitalization days and hospitalization expenses.

Discussion: The groups were grouped by birth weight, and each group was defined as a restricted and unrestricted cohort according to the Recommended Program for Neonatal Blood Transfusion (5th Edition), and evaluate applicability of this scheme for Chinese newborns based on outcome indicators. According to the neonatal treatment data, a appropriate neonatal blood transfusion threshold and neonatal blood transfusion program for China would be determined.

Contributions To The Literature

- This is a retrospective cohort study of neonatal blood transfusion and prospective follow-up from January 1, 2017 to June 30, 2021, aim to evaluate the effect of restricted and unrestricted blood transfusion on neonatal health.
- The variable data of newborns and their mothers was collected in this cohort study with 280 variables and 2.98 million data volumes including in the database. The primary outcome index of the study was death.
- The mortality rate of restricted blood transfusion in < 1500g group was significantly higher than that in the non-restricted blood transfusion group. The threshold of this group was not applicable to Chinese newborns. The mortality rate of restricted blood transfusion in > 2500g group is lower than that in the non-restricted blood transfusion group. This threshold treatment scheme shows great valuable in newborn protection and will be verified in combination with long-term effects.

Background

Neonatal blood transfusion is used for treatment of neonatal anemia caused by various reasons, neonatal thrombocytopenia and coagulation dysfunction related diseases. Newborns, a special group, have imperfect hematopoietic system and rapid disease changes. Blood transfusion treatment is extremely important for newborns, especial very low birth who suffer undeveloped hematopoietic system and rapid disease changes. with blood transfusion rate as high as over 80% during hospitalization^[1-5]. And gestational age is inversely proportional to the number of blood transfusions^[6]. However, improper blood transfusion treatment also brings risks. For example, excessive blood transfusion can lead to iron load, heavy circulatory load, intraventricular hemorrhage and adverse reactions of blood transfusion^[7-11]. Insufficient blood transfusion treatment will affect neonatal development and therapeutic effect disease treatment, and could lead to apnea, neurodysplasia or poor weight gain^[12]. Therefore, it is extremely important to determine the threshold of neonatal blood transfusion treatment. The research results show that a small group of countries including Britain, the United States and Australia have formulated neonatal blood transfusion programs^[6, 13-15], but the threshold of neonatal blood transfusion is not same in different countries, which may be due to differences in regions, races and nationalities, as well as medical conditions and treatment methods^[16]. The neonatal blood transfusion program standardized the protocol of neonatal blood transfusion treatment, but it also brings hidden dangers. Especially for VLBW infants, a large number of studies have reported that strict blood transfusion threshold will increase the incidence of severe neurology in newborns, reduce long-term brain volume, increase the incidence of periventricular leukomalacia and a series of complications of intraventricular hemorrhage^[17]. At present, doctors in China is still relying on clinical experience or referring to foreign programs for treatment. The recommended threshold for neonatal blood transfusion treatment in China is still from the fifth edition of Practical Neonatology. Up to now, there are not enough clinical studies and prospective follow-up to determine the suitable threshold for Chinese newborns. Therefore, it is important to establish a retrospective and prospective multicenter cohort study to evaluate whether the blood transfusion scheme is suitable for newborns in China.

It has been reported that different blood transfusion thresholds should be adopted for newborns with different weights, and a higher threshold should be carried out in unrestricted blood transfusion for newborns with very low weights, so as to ensure the development of their nervous system. More and more studies showed that the adverse effects of restricted blood transfusion on newborns have inconsistent results, especially for low birth weight infants and newborns with severe disease^[18-22]. In addition, due to the physiological decline of hemoglobin level of newborns after birth, it is more difficult to judge physiological anemia or pathological anemia of newborns^[23]. There are many factors should be taken into consideration in newborns' blood transfusion, especially for low birth weight infants, including disease type, weight, assisted breathing mode, gestational age at birth, clinical signs, threshold of blood transfusion treatment, blood transfusion volume and selection of blood products [and so on](#). Previous cohort studies were carried out in other countries and regions with fewer observation variables and smaller sample size, which only reflected the local neonatal blood transfusion and prognosis. The indicators involved in reflecting the variables within the group are not comprehensive enough. Most of the studies focus on the threshold of blood transfusion treatment, the occurrence of adverse reactions of blood transfusion and growth and development. Previous investigations barely include infusion volume and blood products for newborns in cohort studies. It has been reported that the total amount of blood infused in low birth weight infants is related to necrotizing

enterocolitis(NEC) associated blood transfusion. Infants within 32 weeks or with a weight lower than 1500g have been recommended to take blood transfusion on 15ml/kg volume instead of calculating with traditional formula^[10]. Some researchers believe that using irradiated red blood cells for VLBW newborns can reduce the occurrence of transfusion-related graft host disease (TA-GVHD), but a large amount of irradiated red blood cells could increase the risk of hyperkalemia^[24, 25]. The use of washed red blood cells and less white red blood cells has been taken into consideration as well, which might be beneficial in reducing anticoagulant-preservative exposure and cytomegalovirus infection in newborns^[26, 27]. Therefore, it is necessary to establish a multicenter cohort study in China with variables comprehensively reflect the individual blood transfusion treatment and long-term effects of newborns in order to establish a neonatal blood transfusion program suitable for China.

So far, there is no cohort study of neonatal blood transfusion programs in China. In order to fill this gap, we established a multicenter retrospective and prospective study cohort to observe the treatment status, clinical symptoms, signs and other variables of transfused newborns during hospital, and prospective follow-up for 1 week, 1 month and 3 years after discharge. The cohort involves 5,669 newborns with blood transfusion from 46 hospitals in China of 7 regions and 21 provinces, each case contained 280 variables, with a total of 2.98 million variables. The main objective of this cohort study include, 1) To determine the downward trend of hemoglobin level in hospitalized newborns with time and the physiological changes of neonatal hemoglobin, 2) The groups were grouped by birth weight, and each group was defined as a restricted and unrestricted cohort according to the Recommended Program for Neonatal Blood Transfusion (5th Edition), and evaluate applicability of this scheme for Chinese newborns based on outcome indicators, 3) According to the neonatal treatment data, a appropriate neonatal blood transfusion threshold and neonatal blood transfusion program for China would be determined. This study was approved by the Ethics Committee of the Institutional Evaluation Committee of Shaanxi Provincial People's Hospital (NO: 2020-R001).

Methods

Who is in the cohort?

In this study, the neonatal blood transfusion cohort was established to provide evidence-based medical basis for formulating the treatment plan or guideline of neonatal blood transfusion in China. The diagnosis and treatment data of inpatients with blood transfusion was from 46 hospitals in 21 provinces of China. A multi-center retrospective and prospective study method was carried out to systematically investigate the blood transfusion of newborns in China.

A unified spreadsheet was used to collect data in Forty-six hospitals covering 21 provinces and cities (Beijing, Gansu, Guangdong, Guangxi, Guizhou, Hebei, Henan, Heilongjiang, Hubei, Jilin, Jiangxi, Liaoning, Inner Mongolia, Shandong, Shanxi, Shaanxi, Sichuan, Xinjiang, Yunnan, Zhejiang, Chongqing, shown in Fig. 1). The data spreadsheet is unified and integrated in Shaanxi Provincial People's Hospital, the responsible unit of this project, for unified collation and analysis. The database included 5669 hospitalized newborns with blood transfusion from January 2017 to June 2018. There are 280 variables in each case, including newborn mother information and newborn blood transfusion treatment information, The maternal variables include the address where the child's mother is located, hospital, age, delivery mode, multiple births, pregnancy times, parity times, and maternal complications. The neonatal variables include the baseline data of the child: gender, date of birth, date of admission, date of discharge, birth weight, birth length, birth head circumference, admission weight, Apgar score (1-5-10), and newborn admission-associated diseases (15 kinds); Blood test indexes: newborn blood type, routine blood indexes (10 test points), liver function indexes (5 test points), coagulation indexes (5 test points) and blood gas indexes (10 test points); Treatment and observation indicators: surgical operation (8 kinds), delivery room resuscitation methods (9 kinds), ventilator application (3 kinds), postpartum umbilical cord clamping time, blood transfusion treatment, infusion time, infusion volume, blood transfusion products (10 kinds of blood products), blood transfusion adverse events (8 kinds), clinical manifestations after blood transfusion (4 directions), iatrogenic blood loss evaluation (< 1500g), exchange transfusion treatment, exchange transfusion components, exchange transfusion volume, exchange transfusion blood type; Outcome indicators: discharge weight, hospitalization days (days), hospitalization expenses (yuan), stay in NICU days (days), main diagnosis of discharge (14 kinds), outcome of children (cure and improvement, transfer to hospital, death), complications during hospitalization (12 kinds), causes of death (9 kinds), discharge follow-up (1W/1M) and Bailey Infant Development Scale evaluation at 3 years old^[28]. The Bailey Scale is divided into three scales: 1) Intelligence Scale (163 items) 2) Exercise Scale (81 items) 3) Social Behavior. (Table 1)

Among 5669 newborns with blood transfusion, 625 newborns with exchange transfusion treatment, 848 newborns with simple plasma transfusion, 43 newborns with simple platelet transfusion, 22 newborns with simultaneous platelet and plasma transfusion and 210 newborns with incomplete data were excluded, and 1.8 million data of 3921 newborns with red blood cell transfusion were analyzed (shown in Fig. 2).

In this cohort study, 3921 newborns infused with red blood cells were divided into three groups according to their birth weight, namely < 1500g, 1500-2500g, and ≥ 2500g. Transfusion intervention was performed according to the threshold of neonatal blood transfusion in the fifth edition of Practical Neonatology among each group, and the Hb value of newborns before the first blood transfusion was detected. The Hb lower than the threshold was defined as restricted blood transfusion group, and the Hb higher than the threshold was defined as non-restricted blood transfusion group. Therefore, we established three groups of neonatal blood transfusion cohorts by different weights.

We established a retrospective cohort of 3,921 neonates with red blood cell transfusion from January 1, 2017 to June 30, 2018 with 1.8 million valid data. This cohort is a relatively large neonatal blood transfusion cohort, and the newborns in this cohort are followed up after discharge and prospectively expanded.

Blood sampling

Among the 280 variables observed, we collected 5 blood transfusion time points and transfusion methods, and included more blood index detection points, so as to evaluate the blood transfusion effect in time and effectively. Blood samples are collected and tested according to strict guidelines. Blood routine index test has been taken with 10 results after admission. Liver function test and coagulation function test indexes were included in the results of 5 tests after

admission. The indexes of blood gas test were included in the results of 10 times after admission. If the detection time point of the neonate is less than the set number of times, all results are included.

Sub-studies collecting clinical data

Among the 5,669 cases, 3,921 cases of red blood cell infusion were used for cohort study. The other 625 newborn exchange transfusion cases were included in a sub-research project to explore appropriate exchange transfusion treatment schemes. The information of clinical medication was included in this sub-project research, such as blue light therapy, phenytoin sodium and albumin use. The plasma transfusion group of 1677 cases include plasma transfusion alone, simultaneous plasma and red blood cell transfusion, and simultaneous plasma and platelet transfusion, which will further explore for clinical application scheme of plasma in this sub-project study.

How often have they been followed up?

Since the neonatal blood transfusion database has been established in 2017, 5,669 cases were included. New records of 280 variables were updated after hospital discharge, and cohorts were established according to weights and recommended thresholds for newborns. The first statistical analysis of data will include the variables during hospitalization and the follow-up results of 1 week and 1 month after discharge, i.e. The retrospective follow-up time lasted until July 30, 2018. The survival of all newborns was followed up from 1 week to 1 month after discharge. After that, all cases were followed up for 3 years, and the long-term effects on growth and development were evaluated by Bailey Scale. Cohort participants were considered reaching their follow-up endpoints if they satisfied one of the following: 1) individual death of newborns; 2) Newborns lost follow-up within 3 years of age.

Discussion

In the three cohorts with different weights, the distribution of mothers' baseline age, delivery mode, multiple births, parity, pregnancy times and accompanying complications is basically the same (Table 2), which reflects the matching choice of baseline characteristics of newborn mothers. The baseline characteristics of newborns in the three groups are basically the same in sex, birth weight, birth length, birth head circumference, admission weight, Agpar score, and the number of concomitant diseases. The < 1500 g group has differences in Agpar score 5min, 10min and ventilator use. There are differences in gender, birth length, admission weight and ventilator use in the 1500-2500 g group. The birth weight, Agpar score and ventilator use were different in the ≥ 2500 g group. This reflects the matching selection of neonatal baseline characteristics (Table 3).

The investigation of blood transfusion treatment in < 1500g group showed that compared with the non-restrictive transfusion group, the restrictive transfusion group had lower levels of Hb at the time of admission and hospitalization. The number of infusions and the average total infusion volume were larger in the restricted transfusion group, but the average infusion volume per infusion was the same between the two groups (Table 4). Among the secondary outcome indicators, the restricted transfusion group had fewer costs. The main outcome indicators showed that there was a statistical difference between the two groups. The implementation of this standard significantly increases the risk of death. The mortality rate in restricted infusion group (11.41%) was higher than that in non-restricted infusion group (5.12%). According to the analysis of treatment, secondary outcome indicators and death, the threshold of < 1500g neonatal blood transfusion scheme is not suitable to Chinese neonatal population, and a better blood transfusion scheme should be established in combination with the long-term effect evaluation results (Table 5,6).

The study of blood transfusion treatment in the 1500-2500g group suggested that compared with non-restrictive transfusion group, restrictive transfusion group had lower levels of Hb at the time of admission, hospitalization and discharge. There was no difference in other blood transfusion treatments between the two groups. Among the secondary outcome indicators, the restricted transfusion group had fewer hospitalization time, NICU time, and hospital costs, and there was no difference in complications during hospitalization between the two groups. The mortality rate of restricted infusion group (3.53) was lower than that of unrestricted infusion group (4.71)(Table 5,6), but there was still no statistical significance between the two groups. According to the above results, it is also necessary to further explore a more ideal blood transfusion scheme.

Blood transfusion treatment in ≥ 2500 g group suggest that compared with non-restrictive transfusion group, restrictive transfusion group had lower levels of Hb at the time of admission, hospitalization and discharge. There was no significant difference between the two groups in the treatment methods of transfusion of red blood cells, plasma and platelets. Among the secondary outcome indicators, the restricted transfusion group had fewer hospitalization time and hospital costs. The death outcome of the two groups showed that the mortality rate of restricted infusion group (3.02) was significantly lower than that of non-restricted infusion group (9.55)(Table 5,6). Combined with the above analysis results, the blood transfusion threshold adopted by this group is a more appropriate blood transfusion scheme, and then the results should be verified with the long-term effect results.

What are the main strengths and weaknesses?

The establishment of neonatal blood transfusion cohort in China has important implications. First of all, this is the first neonatal blood transfusion cohort study established in China. At present, China's neonatal blood transfusion guidelines still follow foreign blood transfusion guidelines, so there is no research report on the neonatal blood transfusion threshold in this country. The cohort includes neonatal blood transfusion cases from 46 hospitals in 21 provinces and cities in China, which can provide representative characteristics of the Chinese neonatal population. Secondly, newborns are a special group with complex and changeable diseases. The cohort established in this study covers 280 variable data, which is the study with the largest number of variables known in the world. It includes the baseline data of both mother and newborn, all the information of newborn blood transfusion treatment, as well as the main treatment methods and comprehensive laboratory indicators during hospitalization. The database enables a comprehensive observation of newborns. It provides a reliable data in determine the best blood transfusion threshold of newborns. Third, the data is large in volume. According to the birth weights of newborns,

three groups of neonatal blood transfusion cohorts were established. Fourthly, the end point of the cohort was 3-year-old newborns, and the Bailey scale was used to evaluate the long-term effect of blood transfusion on their growth and development.

This cohort study has some limitations. First, the cohort is based on retrospective data, so there are differences in the amount of cases and baseline data between restricted blood transfusion group and unrestricted blood transfusion group. Secondly, the observation outcome index in this paper only includes the follow-up study of 1 week and 1 month after discharge, and the real endpoint is the long-term effect evaluation table from prospective to 3-year-old exit, so only preliminary observation results are obtained. Thirdly, due to the different on the geographical location and economic situation, party of data was lost in the final export, but the large sample in this study could make up partly. An adjustment will be made in the inappropriate blood transfusion scheme and establish a blood transfusion threshold scheme that meets the needs of Chinese newborns.

Abbreviations

VLBW : very low birth weight

NEC : necrotizing enterocolitis

TA-GVHD : transfusion-related graft host disease

Declarations

Ethical Approval and Consent to participate

Ethical approval for the study was obtained from the institutional review board of People's Hospital of Shaanxi Province (No: 2020-R001)

Consent for publication

Not applicable

Availability of data and materials

We warmly welcome the cooperation for the cohort study of neonatal blood transfusion in China and make full use of the data. Since the research is still undergoing and the information used in this study relate to personal privacy, the database cannot be open in the public domain for free, but researchers interested in collaboration and further information are welcome to contact the corresponding authors via email [yjc65@sina.com].

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Tables

Table 1 Data collection of neonatal blood transfusion cohort: variables of neonatal mother and neonatal groups

Mother variable	Neonatal variable			
	Baseline	Blood test index	Treatment and observation indicators	Outcome indicator
Provinces	Gender	Neonatal blood group	Operation (8 species)	Discharge weight
Name of hospital	Date of birth	Routine blood index (10 times test) (RBC/HB/HCT/WBC/PLT)	Resuscitation Methods in Delivery Room (9 species)	Hospitalization days (days)
Age	Date of admission	Liver function index (5 times test) (TBIL/DBIL/ALT/TP)	Ventilator application (Yes/No)	Hospitalization expenses
Mode of delivery (Natural delivery/ Midwifery/Cesarean section)	Date of discharge	Coagulation index (5times test) (APTT/PT/INR/FIB)	Postpartum umbilical cord clipping time(0-30s/1-60s/1-2min/2min/unknown)	Days in NICU (days)
Number of births (1/ ≥2)	Birth weight	Blood gas index (10 times test) (PH/PO2/PCO2/LAC)	Blood transfusion treatment (time/volume/type(15 blood products))	Main diagnosis of discharge (14 species)
Pregnancy times (1/2/≥3)	Birth length		Adverse events of blood transfusion (8 species)	Outcome (cure and improvement/transfers/death)
Parity(1/2/≥3)	Birth head circumference		Adverse events of blood transfusion (8 species)	Complications (12 species)
Maternal complication (11 species)	Admission weight		Evaluation of curative effect after blood transfusion(4 species)	Causes of death (9 species)
	Agpar score (1-5-10)		Evaluation of curative effect after blood transfusion(4 species)	Follow-up after discharge (1W/1M/3Y)
	Neonatal Admission Accompanying Diseases (15 species)		Exchange transfusion therapy (time/volume/blood products /blood type)	Bailey scale

Maternal complication (11 species) = 1 no 2 respiratory system disease 3 circulatory system disease 4 digestive system disease 5 blood disease 6 childbirth disease 7 reproductive system infection 8 Maternal and infant blood type incompatibility 9 uterine disease 10 placental comorbidities 11 other diseases. Neonatal Admission Accompanying Diseases (15 species) = 1 premature infant 2 low birth weight infant 3 sepsis 4 neonatal necrotizing colitis 5 neonatal bleeding 6 neonatal hemolysis 7 neonatal hyperbilirubinemia (non-immune factor) 8 neonatal anemia 9 thrombocytopenia 10 neonatal disseminated intravascular bleeding 11 neonatal pneumonia 12 birth asphyxia 13 neonatal bronchopulmonary dysplasia 14 neonatal respiratory distress syndrome 15 other neonatal diseases. Operation (8species) = 1 no 2 PICC 3 umbilical vein catheterization 4 blood exchange 5 lumbar puncture 6 blue light irradiation 7 cardiovascular surgery 8 other operations. Resuscitation Methods in Delivery Room (9 species)= 1 normobaric oxygen therapy 2 balloon pressurized oxygen therapy 3 endotracheal intubation balloon pressurized oxygen therapy 4 chest compressions 5 trachea cannula 6 epinephrine 7 volume expansion 8 naloxone 9 unknown. Type(15 blood products) =1 red blood cell (leukocyte-filtered, irradiated) 2 red blood cell (non-leukocyte-filtered, irradiated) 3 red blood cell (non-leukocyte-filtered, nonirradiated) 4 red blood cell (irradiated) 5 red blood cells (leukocyte-filtered) 6 fresh frozen plasma 7 fresh frozen plasma (virus inactivated) 8 frozen plasma 9 apheresis platelets (leukocyte-filtered) 10 apheresis platelets (non-leukocyte-filtered) 11 cryoprecipitate 12 whole blood 13 CMV antibody testing of blood products (positive) 14 CMV antibody testing of blood products (negative) 15 CMV antibody testing of blood products (unknown). Adverse events of blood transfusion (8 species) = 1 hemolysis reaction 2 coagulation dysfunction 3 circulation overload 4 metabolic disorder 5 acute necrotizing enterocolitis 6 hypothermia 7 hypocalcemia 8 acute lung injury. Evaluation of curative effect after blood transfusion(4 species) = color of skin, mental state, feeding, heart rate reduction(1 obvious, 2 improved, 3 normal, 4 no change). Main diagnosis of discharge (14 species)=1 premature infant 2 low birth weight infant 3 sepsis 4 neonatal necrotizing colitis 5 neonatal bleeding 6 neonatal hemolysis 7 neonatal hyperbilirubinemia (non-immune factor) 8 thrombocytopenia 9 neonatal disseminated intravascular bleeding 10 neonatal pneumonia 11 neonatal asphyxia 12 neonatal bronchopulmonary dysplasia

13 neonatal respiratory distress syndrome 14 other neonatal diseases. Complications (12 species)= 1 none 2 retinopathy of prematurity 3 acute necrotizing enterocolitis 4 chronic bronchopulmonary dysplasia 5 intracranial hemorrhage 6 neonatal periventricular leukomalacia 7 cholestasis syndrome 8 hepatitis 9 neurodevelopmental disorder 10 neonatal encephalopathy 11 coagulation dysfunction 12 others. Causes of death (9 species) = 1 sepsis 2 pulmonary hemorrhage 3 pneumonia 4 respiratory distress syndrome 5 asphyxia 6 bronchopulmonary dysplasia 7 hypoxic ischemic encephalopathy 8 neonatal necrotizing enterocolitis 9 others.

Table 2 Basic demographic characteristics of mothers in the neonatal blood transfusion cohort

		< 1500g			1500-2500g			≥ 2500g		
		0	1	P	0	1	P	0	1	P
Total (n)		674	643		1104	297		1025	178	
Age		30 (19-44)	30 (18-42)	0.194	30 (16-45)	30 (18-47)	0.659	30 (17-44)	30 (14-44)	0.658
Mode of delivery	Natural delivery	110	471	0.755	345	111	0.076	443	77	0.486
	Midwifery	4	8		12	5		21	4	
	Cesarean section	148	574		747	181		560	97	
	Unknown	1	1		0	0		1	0	
Number of births	Single fetus	166	734	0.062	771	215	0.324	962	164	0.773
	Multiple births	92	309		321	78		48	7	
	Unknown	5	11		12	4		15	7	
Pregnancy times	1	68	387	0.012	375	107	0.312	345	64	0.640
	2	85	302		304	90		331	55	
	3 times or more	94	318		374	92		332	54	
	Unknown	16	47		51	8		17	5	
Parity	1	112	484	0.282	447	143	0.065	474	89	0.600
	2	121	450		522	119		462	66	
	3 times or more	21	77		96	28		71	18	
	Unknown	9	43		39	7		18	5	
Number of mothers with complications (n)		117	453	0.009	401	118	0.944	276	39	0.149

Table 3 Basic demographic characteristics of newborns in the neonatal blood transfusion cohort

		< 1500g			1500-2500g			≥ 2500g		
		0	1	P	0	1	P	0	1	P
Total (n)		263	1054		1104	297		1025	178	
Gender	Male	148	552	0.257	626	189	0.032	610	107	0.892
	Female	115	502		478	108		415	71	
Birth weight M(max, min)		1235 (530-1490)	1226 (630-1498)	0.817	1813 (1500-2480)	1760 (1500-2490)	0.147	3025 (2500-5500)	3175 (2500-8600)	0.002
Birth length M(max, min)		38 (27-54)	38 (29-53)	0.486	43 (28-60)	43 (32-53)	0.017	50 (32-57)	50 (42-56)	0.044
Head circumference M(max, min)		28 (21-47)	28 (18-40)	0.992	30 (21-41)	30 (21-49)	0.766	34 (23-48)	34 (31-44)	0.043
Admission weight M		1265	1250	0.684	1870	1750	0.001	3040	3100	0.291
Agpar score (M)	1min	8	8	0.179	9	8	0.084	9	9	0.007
	5min	9	9	0.005	9	9	0.050	10	9	0.012
	10min	10	9	0.023	10	10	0.192	10	10	0.010
Total number of diseases associated M(max, min)		4 (0-10)	4 (0-11)	0.414	4 (0-14)	4 (0-12)	0.149	2 (0-8)	2 (0-6)	0.531
Number of cases of ventilator application n (%)		219 (83.27)	720 (68.31)	0.000	571 (51.72)	177 (59.60)	0.033	285 (27.83)	74 (41.34)	0.000

Table 4 Treatment of blood transfusion by restricted blood transfusion and non-restricted blood transfusion

		< 1500g			1500-2500g			≥ 2500g		
		0	1	P	0	1	P	0	1	P
Hb level	Admissions (M)	109	157	0.000	133	165	0.000	110	159	0.000
	Minimum during hospitalization (M)	82	95	0.000	94	111	0.000	94	121	0.000
	Discharge(M)	111	117	0.150	116	126	0.000	121	134	0.000
Red blood cell infusion	Number of infusions (M)	2	2	0.000	1	1	0.351	1	1	0.798
	Average total infusion volume (mL)	60	50	0.000	46	44	0.147	60	60	0.131
	Average infusion volume per infusion (mL)	26	27	0.843	35	31	0.000	50	50	0.015
	Mean infusion per kilogram of body weight (mL)	10	10	0.867	9	9	0.064	8	8	0.239
Plasma infusion	Number of infusion cases (%)	53 (20.15)	289 (27.42)		126 (11.41)	143 (48.15)		140 (13.66)	56 (31.46)	
	Number of infusions (M)	1	2	0.113	1	2	0.039	1	2	0.200
	Average total infusion volume (mL)	30	34	0.998	47	57	0.146	71	93	0.023
	Average infusion volume per infusion (mL)	20	20	0.053	30	28	0.142	50	50	0.051
	Mean infusion per kilogram of body weight (mL)	9	8	0.022	8	8	0.803	7	8	0.240
Plt infusion	Number of infusion cases (%)	13 (4.94)	35 (3.32)		24 (2.17)	12 (4.04)		30 (2.93)	9 (5.06)	
	Number of infusions (M)	1	1	0.161	1	1	0.577	1	1	0.805
	Average total infusion volume (mL)	28	23	0.388	40	38	0.987	60	80	0.429
	Average infusion volume per infusion (mL)	20	20	0.809	35	31	0.688	58	50	0.582
	Mean infusion per kilogram of body weight (mL)	9	9	0.971	10	9	0.945	9	8	0.756

Table 5 Analysis of main outcome indicators of neonatal blood transfusion

		< 1500g					1500-2500g					≥ 2500g				
		0	1	OR	CI	P	0	1	OR	CI	P	0	1	OR	CI	P
Total number (n)		263	1054				1104	297				1025	178			
Death	Total	30	54	0.416	0.260	0.666	< 0.05	39	14	1.374	0.735	2.569	> 0.05	31	17	3.0
	N (%)	(11.41)	(5.12)					(3.53)	(4.71)					(3.02)	(9.55)	
	During hospitalization	11	25					8	5					9	6	
	N (%)	(4.18)	(2.37)					(0.72)	(1.68)					(0.88)	(3.37)	
	Follow-up for 1 week	15	22					20	7					17	8	
	N (%)	(5.7)	(8.37)					(1.81)	(2.36)					(1.66)	(4.49)	
	Follow-up for 1 month	4	7					11	2					5	3	
	N (%)	(1.52)	(2.66)					(1.00)	(0.67)					(0.49)	(1.69)	

Table 6 Analysis of secondary outcome indicators of neonatal blood transfusion

	< 1500g			1500-2500g			≥ 2500g		
	0	1	P	0	1	P	0	1	P
Hospitalization days (M)	38	40	0.074	22	26	0.002	10	14	0.000
NICU hospitalization days (M)	30	29	0.547	9	16	0.000	0	0	0.186
Hospitalization expenses (Yuan, M)	53954	68573	0.000	36727	51365	0.000	17891	22959	0.022
Number of complicated diseases in hospital (M)	1	1	0.217	1	1	0.121	1	1	0.712

Figures

Figure 1

A unified spreadsheet was used to collect data in Forty-six hospitals covering 21 provinces and cities (Beijing, Gansu, Guangdong, Guangxi, Guizhou, Hebei, Henan, Heilongjiang, Hubei, Jilin, Jiangxi, Liaoning, Inner Mongolia, Shandong, Shanxi, Shaanxi, Sichuan, Xinjiang, Yunnan, Zhejiang, Chongqing, shown in Fig. 1).

Figure 2

Among 5669 newborns with blood transfusion, 625 newborns with exchange transfusion treatment, 848 newborns with simple plasma transfusion, 43 newborns with simple platelet transfusion, 22 newborns with simultaneous platelet and plasma transfusion and 210 newborns with incomplete data were excluded, and 1.8 million data of 3921 newborns with red blood cell transfusion were analyzed (shown in Fig. 2).

Supplementary Files

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- [SupplementaryFigure1.tif](#)