A method to estimate the incidence of transfusion reaction for the transfusion-treating disease in Chinese hospital

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Abstract: Though transfusion reaction is directly related to the transfusion component, while in clinic, the transfusion component is related to the disease which the patient caught. As some of the transfusion reactions could be life-threatening, estimating the incidence of transfusion reaction (in this study, allergic and febrile non-haemolytic transfusion reaction only) of some specific categories of diseases is helpful for the clinicians. According to the reported blood use in the specific departments, the number of transfusion patients in these departments could be estimated. By Apriori algorithm the categories of diseases which often encounter the transfusion reaction have been screened. It is found that the diseases which belong to C00-C97, D00-D48, D50-D89, K00-K93, N00-N99 and O00-O99 (ICD-10) often encounter transfusion reaction. The platelet transfusion patients whose diseases belong to C00-C97 would encounter transfusion reaction with the incidence about 1%, which is much higher than the average incidence. The incidence of transfusion reaction of the patients whose diseases belong to K00-K93, with plasma transfusion might be higher than the average incidence, as the lower bound of the incidence equals to the average incidence. Based on this study, it is suggested that attentions should be paid to the patients whose diseases belong to C00-C97 with platelet transfusion to prevent them encountering the allergic transfusion reaction.

Key words: Transfusion reaction; Apriori algorithm; Incidence of transfusion reaction

1 Introduction

Transfusion is a kind of therapeutic procedure performed in hospitalized patients [1]. It is well known that errors in blood transfusion practices can lead to serious consequences for the recipient in terms of morbidity and mortality [2]. The morbidity or mortality caused by transfusion are called adverse

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transfusion reactions or transfusion reactions (TRs). The incidence of transfusion reaction is about 2‰ [3, 4]. Most of the transfusion reactions are related to immune reactions [5]. Allergic and febrile non-haemolytic transfusion reactions (FNHTR) are the most common transfusion reactions which the clinicians often meet. In this study the TRs that belong to allergy or FNHTR are of enough sample size, so in this paper we only focus on these 2 kinds of transfusion reactions.

For clinicians, attentions are paid to the diseases which the patients caught. They make decisions whether the patient needs transfusion treatment according to the patient's condition. As some mechanisms of the TR still remain unknown [6,7], estimating the incidence of transfusion reaction corresponding to some specific categories of diseases is better than judging the incidence of transfusion reactions by the average incidence. This would be helpful for the clinician to prevent the transfusion patients from encountering the transfusion reactions.

Though the number of transfusion patients in the specific categories of diseases is supplied, it could be roughly estimated by the blood use in the departments. The information of the transfusion reaction patients (including the department which they were in, their categories of TRs and diseases, etc) has already been collected in a database. This means that the interval or at least the lower bound of the incidence might be estimated. To screen the specific categories of diseases which often encounter transfusion reaction, the Apriori algorithm [8,9] is used. According to the number of samples which belong to the specific category of diseases screened by Apriori algorithm, the lower bound or interval of the incidence of transfusion reaction of specific category of diseases could be estimated.

2 Materials and methods

2.1 Ethical approval

All patients involve in the study had given written informed consent by participating hospitals. The current project was approved by the review board of the Research Ethics Committee of Institute of Blood Transfusion, Chinese Academy of Medical Sciences and Peking Union Medical College on September 18, 2016 (registration number 2016017).

2.2 Materials

The samples of transfusion reaction patients are supplied by the key laboratory of transfusion adverse reaction. The *Key laboratory of transfusion adverse reactions* (Key laboratory) have been collecting the clinical cases of transfusion reaction. 79 hospitals have joined the key laboratory. Apart from Xizang province, the samples supplied by these hospitals are representative of the entire transfusion reaction patients in the main land of China.

From May 2018 to June 2019, 1255 cases had been collected. In this study the sample size of allergy and FNHTR were large enough for statistical research. Among the 1255 cases, only 839 cases appeared to be allergy or FNHTR. According to the clinical diagnoses, there are 754 confirmed cases. Table 1 shows

the number of transfusion patients and the total quantity of transfusion components.

Table 1: The total quantity of transfusion patient and blood components

	Number	Person time	Red cell	Plasma	BC-PC	Apheresis platelets	Cryoprecipitation
Total	681077	1188380	1264293.85	136100947.38	10315.5	240190.1	1545916.2

The data in table 1 have only supplied the number of transfusion patients while the number of patients who belongs to the specific category of diseases that resulted in transfusion have not been supplied. Estimating the incidence of transfusion reaction needs 2 kinds of information: the number of transfusion patients who belonged to a specific category of diseases, and how many of them showed transfusion reactions. The former has not been supplied, so it needs estimation and the latter has been supplied by the key laboratory. The "Chinese clinical blood use Research Report (2016)" is helpful for the estimation. This report has been completed in 2017, which has shown the proportion of blood use in the departments is shown in table 2.

Table 2: Proportion of blood use in each department

Department	Red cell	Plasma	Platelet	Cryoprecipitation
Internal medicine	24%	27%	48%	15%
Surgery	39%	42%	17%	23%
Gynaecology and obstetrics	6%	3%	4%	3%
ICU	9%	15%	6%	15%
Paediatrics	3%	3%	6%	34%
Others	19%	10%	19%	8%

2.3 Estimation of the number of transfusion patients

Following table 2, estimate the average blood dosage in each of the department first. With the average dosage the number of transfusion patients in each of the department could be estimated. According to the transfusion dosage record supplied by the hospitals, the estimated average transfusion dosage is shown in table 3.

According to table 3 and table 1-2, the number of transfusion patients in each of the department could be estimated in table 4.

Table 4 supplies the base information of the number of transfusion patients. The total number of transfusion patients figured by table 4 is larger than the total number supplied by table 1. The reason is that some patients were transfused by more than one kind of component and some transfusions had been stopped when encountered with acute TRs. These situations lead to the errors of average dosage estimation. The estimated number is larger than the number of person per time in table 1. By calculation, the actual

Table 3: Average dosage estimated in each of the department

Department	Red cell	Plasma	Platelet	Cryoprecipitation
Internal medicine	4.63	1411	3.86	5.02
Surgery	3.92	707	0.11	1.11
Gynaecology and obstetrics	4.17	554	2	9.4
ICU	7.19	1475	6.78	220
Paediatrics	2.54	162	2.86	6.95
Others	4.46	777	4.5	3.14

Table 4: Estimated number of transfusion patients in each of the department

Department	Red cell	Plasma	Platelet	Cryoprecipitation
Internal medicine	65535	26043	31150	46192
Surgery	125784	80852	387145	320324
Gynaecology and obstetrics	18191	7370	5010	4933
ICU	15825	13840	2216	1054
Paediatrics	14932	25203	5255	75627
Others	53860	17516	10576	39386

number of transfusion person per time is 0.85 times of the estimated number of transfusion person per time. Though it is not able to know exact number of transfusion patients who caught the specific disease, the number of transfusion patients in each of the departments has already given the interval of the number of transfusion patients who caught the specific category of the diseases.

2.4 Estimation of the incidence of transfusion reaction

By intuition, some categories of diseases encounter transfusion reaction more frequently. The transfusion component is associated with the patient's condition and the patient's condition is relevant to the disease which the patient caught. The causality is this: the disease which the patient caught resulted in the transfusion component the clinician chose, and the transfusion component and the patient's condition resulted in the transfusion reaction. The causes which result in transfusion reaction form a chain of causality. Each of the TR patients produces a chain of causality.

The transfusion patients are divided into the groups according to the departments' classification in table 2-4. The causes of each of the samples are divided into 4 parts: the disease which the patient caught, the reason for transfusion, the immune history of the patient, the component which the patient was transfused. The information of all samples is supplied by the Key laboratory. Schematic graph of the relation of causes is shown in figure 1

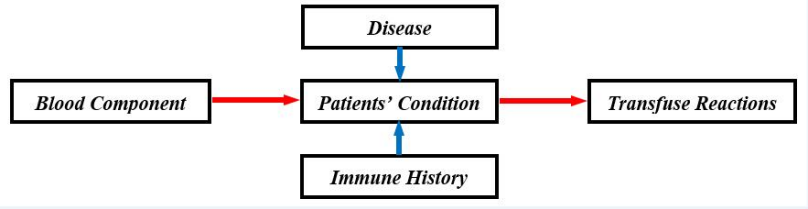

Figure 1: The causality network of transfusion reaction

The support and confidence of the combination of these causes could be figured out by apriori algorithm. The larger the support is, the stronger the association with the disease and the transfusion reaction. Collecting the frequently encountered combination of the causes, it is possible to estimate the incidence of transfusion reaction of a certain category of diseases.

The minimal support in the Apriori algorithm is set as 10^{-4}. This means that as long as a chain of causality is found, this chain of causality is considered to be associated with the transfusion reaction. But in practice we choose the minimum support like this: if the support of the chain of causality is lower than 0.05 in the 4 causes-combination, or 0.04 in the 5 causes-combination, this causality chain is taken into consideration. The reason is that the sample size of transfusion reaction in each of the departments are not as large as the sample size of customers' purchasing behavior. Though a low support of a certain kind of combination might indicate that this could be a causality chain, it is difficult to conclude that this combination is of statistical significance.

3 Results

The estimated incidence of transfusion reaction in each of the departments is shown in tables 5-10. The classification of disease is in accordance with the International Classification of Diseases, 10th revision (ICD-10). By Apriori algorithm, 7 kinds of diseases that would frequently encounter transfusion reaction were found. According to reference [10] (figure 3), the incidence of cancer in China is 2‰. In the internal department, according to the record supplied by the key laboratory, i.e. all the patients had transfusion reaction (allergy or FNHTR), 137 out of 408 patients in total were cancer patients. It could be reasonable to estimate that in the internal department 20% of the patients might be cancer patients. And according to the data supplied by the Key laboratory, in the internal department, nearly 1/3 (33 out of 109) of the patients whose disease belonged to D50-D89 also caught cancer. That is why the upper bound of the incidence of transfusion reaction of the diseases belonged to C00-C99 and D50-D89 would be estimated in the internal department.

Remarks: In table 5, myelosuppression after chemotherapy could result in thrombocytopenia, so the bound of the ATR patients belonged to C00-C97 is estimated as $(64, 89)$. Similarly, the bound for the ATR patients belonged to D50-D89 is $(30, 49)$ (according to table 11). The total number of transfusion patients who were transfused by the specific kind component is shown in table 4. It has been assumed that 20% of the patients in the internal department belong to C00-C93. And as 1/3 of the patients whose diseases

Table 5: The incidence of transfusion reaction in the internal department

ICD	Lower bound of incidence	Upper bound of incidence	Component	Category of reaction
C00-C97	0.0020	0.0143	Platelet	Allergy
D50-D89	0.00096	0.0026	Platelet	Allergy
K00-K93	0.0019	-	Plasma	Allergy

Table 6: The incidence of transfusion reaction in the surgery department

ICD	Lower bound of incidence	Upper bound of incidence	Component	Category of reaction
K00-K93	0.0001	-	Plasma	Allergy
S00-T98	9.89×10^{-5}	-	Plasma	Allergy

Table 7: The incidence of transfusion reaction in the gynaecology and obstetrics department

ICD	Lower bound of incidence	Upper bound of incidence	Component	Category of reaction
D00-D48	0.0001	-	Red cell	FNHTR
N00-N99	0.0001	-	Red cell	FNHTR
O00-O99	0.0001	-	Red cell	FNHTR
D50-D89	0.0001	-	Red cell	Allergy
O00-O99	0.0003	-	Red cell	Allergy
O00-O99	0.0016	-	Plasma	Allergy

Table 8: The incidence of transfusion reaction in the ICU department

ICD	Lower bound of incidence	Upper bound of incidence	Component	Category of reaction
K00-K93	0.0002	-	Red cell	Allergy
K00-K93	0.0004	-	Plasma	Allergy

Table 9: The incidence of transfusion reaction in the paediatrics department

ICD	Lower bound of incidence	Upper bound of incidence	Component	Category of reaction
C00-C97	0.01	-	Platelet	Allergy
D50-D89	0.002	-	Platelet	Allergy

Table 10: The incidence of transfusion reaction in the other department

ICD	Lower bound of incidence	Upper bound of incidence	Component	Category of reaction
C00-C97	0.0001	0.00056	Red cell	FNHTR
D50-D89	0.0001	-	Red cell	FNHTR
N00-N99	0.0001	-	Red cell	Allergy
C00-C97	0.0003	0.001	Plasma	Allergy

belonged to D50-D89 also caught cancer, it could be assumed that $0.3 \times 20\% = 6\%$ of the patients in the internal department belong to D50-D89. In table 7, bleeding would result in anemia (according to table 13), so the bound for the ATR patients belonged to O00-D99 is $(12, 15)$, but the patients who need plasma transfusing in the gynaecology and obstetrics department not all belong to O00-O99. So the upper bound of the incidence could not be estimated. In table 9, the lower bound of the number of cancer patients is estimated by 53. Though according to table 15, bleeding is related to thrombocytopenia, but according to the raw data supplied by the key laboratory, only 1 sample showed both bleeding and thrombocytopenia. In table 10, it is also assumed that 20% of the patients in the department out of the above belong to C00-C93.

The detailed information of the support and the combinations of the causes are shown in tables 11-16 which show the support of the combination of the causes in each of the departments. These tables supply the support information for tables 5-10. According to table 11-16, apart from the gynaecology and obstetrics department, the diseases which belong to C00-C97, K00-K93 and D50-D89 encounter the transfusion reaction frequently. The transfusion components which would most probably cause allergy are platelet and plasma. The component red cell causes FNHTR mainly occurs in the gynaecology and obstetrics department.

The guidelines of transfusion reaction [2,11] have mentioned that immune history especially transfusion history is related to transfusion reaction, the causality chains found in table 11-16 are consistent with that view. The patients whose disease belonged to the classifications C00-C97, D50-D89 or K00-K93 often received transfusion treatment. These diseases result in repeated transfusion treatment may be a cause of transfusion reaction.

Table 11: The support of the combination of the causes in the internal medicine department

Total samples	361	
Combination	Support	Samples
K00-K93, Coagulable abnormality, Plasma, Allergy	0.135734072	49
C00-C97, Myelosuppression, Platelet, Allergy	0.108033241	39
D50-D89, Myelosuppression, Platelet, Allergy	0.083102493	30
C00-C97, Coagulable abnormality, Platelet, Allergy	0.069252078	25
C00-C97, Thrombocytopenia, Platelet, Allergy	0.069252078	25
D50-D89, Thrombocytopenia, Platelet, Allergy	0.052631579	19
K00-K93, Transfusion history, Plasma, Allergy	0.074792244	27
C00-C97, Transfusion history, Platelet, Allergy	0.163434903	59
C00-C97, Transfusion reaction history, Platelet, Allergy	0.066481994	24
C00-C97, Allergy history, Platelet, Allergy	0.063711911	23
D50-D89, Transfusion history, Platelet, Allergy	0.110803324	40
D50-D89, Transfusion history reaction, Platelet, Allergy	0.055401662	20
K00-K93, Coagulable abnormality, Transfusion history, Plasma, Allergy	0.069252078	25
C00-C97, Myelosuppression, Transfusion history, Platelet, Allergy	0.077562327	28
C00-C97, Myelosuppression, Transfusion history reaction, Platelet, Allergy	0.052631579	19
C00-C97, Myelosuppression, Allergy history, Platelet, Allergy	0.052631579	19
D50-D89, Myelosuppression, Transfusion history, Platelet, Allergy	0.060941828	22
D50-D89, Myelosuppression, Transfusion history reaction, Platelet, Allergy	0.04432133	16
C00-C97, Thrombocytopenia, Transfusion history, Platelet, Allergy	0.041551247	15

Myelosuppression means myelosuppression after chemotherapy

Table 12: The support of the combination of the causes in the surgery department

Total samples	126	
Combination	Support	Samples
K00-K93, Coagulable abnormality, Plasma, Allergy	0.079365079	10
S00-T98, Coagulable abnormality, Plasma, Allergy	0.063492063	8

Table 13: The support of the combination of the causes in the gynaecology and obstetrics department

Total samples	40	
Combination	Support	Samples
D00-D48, Anemia, Red cell, Allergy	0.05	2
O00-O99, Anemia, Red cell, Allergy	0.15	6
O00-O99, Coagulable abnormality, Plasma, Allergy	0.175	7
O00-O99, Anemia, Plasma, Allergy	0.05	2
O00-O99, Perioperative blood transfusion, Plasma, Allergy	0.075	3
O00-O99, Bleeding, Plasma, Allergy	0.075	3
D50-D89, Anemia, Red cell, FNHTR	0.05	2
N00-N99, Anemia, Red cell, FNHTR	0.05	2
O00-O99, Anemia, Red cell, FNHTR	0.05	2
D00-D48, Transfusion history, Red cell, Allergy	0.05	2
D00-D48, Transfusion reaction history, Red cell, Allergy	0.05	2
O00-O99, Pregnancy history, Red cell, Allergy	0.075	3
O00-O99, Transfusion history, Plasma, Allergy	0.125	5
O00-O99, Pregnancy history, Plasma, Allergy	0.325	13
O00-O99, Pregnancy history, Red cell, FNHTR	0.075	3
O00-O99, Pregnancy history, Plasma, FNHTR	0.05	2
D00-D48, Anemia, Transfusion history, Red cell, Allergy	0.05	2
D00-D48, Anemia, Transfusion history reaction, Red cell, Allergy	0.05	2
O00-O99, Anemia, Pregnancy history, Red cell, Allergy	0.075	4
O00-O99, Coagulable abnormality, Transfusion history, Plasma, Allergy	0.1	4
O00-O99, Coagulable abnormality, Pregnancy history, Plasma, Allergy	0.15	6
O00-O99, Perioperative blood transfusion, Pregnancy history, Plasma, Allergy	0.075	3
O00-O99, Bleeding, Pregnancy history, Plasma, Allergy	0.05	2

Table 14: The support of the combination of the causes in the ICU department

Total samples	55	
Combination	Support	Samples
K00-K93, Coagulable abnormality, Red cell, Allergy	0.054545455	3
K00-K93, Coagulable abnormality, Plasma, Allergy	0.090909091	5
K00-K93, Transfusion history, Red cell, Allergy	0.054545455	3
K00-K93, Transfusion history, Plasma, Allergy	0.054545455	3
K00-K93, Pregnancy history, Plasma, Allergy	0.054545455	3
K00-K93, Coagulable abnormality, Transfusion history, Plasma, Allergy	0.054545455	3

Table 15: The support of the combination of the causes in the paediatrics department

Total samples	88	
Combination	Support	Samples
C00-C97, Coagulable abnormality, Platelet, Allergy	0.238636364	21
D50-D89, Coagulable abnormality, Platelet, Allergy	0.102272727	9
C00-C97, Thrombocytopenia, Platelet, Allergy	0.170454545	15
C00-C97, Bleeding, Platelet, Allergy	0.204545455	18
C00-C97, Transfusion history, Platelet, Allergy	0.465909091	41
C00-C97, Transfusion reaction history, Platelet, Allergy	0.136363636	12
C00-C97, Allergy history, Platelet, Allergy	0.102272727	9
D50-D89, Transfusion history, Platelet, Allergy	0.159090909	14
C00-C97, Coagulable abnormality, Transfusion history, Platelet, Allergy	0.227272727	20
C00-C97, Coagulable abnormality, Transfusion reaction history, Platelet, Allergy	0.090909091	8
C00-C97, Coagulable abnormality, Allergy history, Platelet, Allergy	0.079545455	7
D50-D89, Coagulable abnormality, Transfusion history, Platelet, Allergy	0.090909091	8
C00-C97, Thrombocytopenia, Transfusion history, Platelet, Allergy	0.079545455	7
C00-C97, Bleeding, Transfusion history, Platelet, Allergy	0.147727273	13
D50-D89, Bleeding, Transfusion history, Platelet, Allergy	0.045454545	4

Table 16: The support of the combination of the causes in the other department

Total samples	84	
Combination	Support	Samples
N00-N99, Anemia, Red cell, Allergy	0.095238095	8
C00-C97, Coagulable abnormality, Plasma, Allergy	0.05952381	5
C00-C97, Anemia, Red cell, FNHTR	0.071428571	6
D50-D89, Anemia, Red cell, FNHTR	0.071428571	6
N00-N99, Pregnancy history, Red cell, Allergy	0.095238095	8
C00-C97, Pregnancy history, Plasma, Allergy	0.05952381	5
C00-C97, Transfusion history, Platelet, Allergy	0.095238095	8
C00-C97, Pregnancy history, Platelet, Allergy	0.095238095	8
C00-C97, Transfusion history, Red cell, FNHTR	0.05952381	5
N00-N99, Anemia, Transfusion history, Red cell, Allergy	0.047619048	4
N00-N99, Anemia, Pregnancy history, Red cell, Allergy	0.083333333	7
C00-C97, Coagulable abnormality, Pregnancy history, Plasma, Allergy	0.05952381	5
C00-C97, Anemia, Transfusion history, Red cell, FNHTR	0.05952381	5
D50-D89, Anemia, Transfusion history, Red cell, FNHTR	0.047619048	4
D50-D89, Anemia, Pregnancy history, Red cell, FNHTR	0.047619048	4

4 Conclusion and Discussion

It has already been discussed in section 3, the diseases which frequently encounter transfusion reaction most probably belong to thees classifications: C00-C97, K00-K93 and D50-D89. According to tables 5-10, the incidence of transfusion reaction is high in the group of cancer patients, especially when the platelet is transfused. In the paediatrics department the cancer patients' transfusion reaction is nearly 10 times of the average incidence. The patients whose disease belonged to the classifications C00-C97, D50-D89 or K00-K93 may received repeated transfusion treatment. These diseases result in repeated transfusion treatment may be a cause of transfusion reaction. This result is consistent with the previous study.

Without mechanism study, the information is extracted from the data base. So attentions should be paid to the cancer patients who need platelet transfusion. So far the samples of the transfusion reaction are not large. If the samples are large enough, the information of transfusion reactions such as transfusion associated circulatory overload, transfusion related acute lung injury etc which might related to some certain kind of disease could be extracted by the similar way. This study only shows a method to estimate the incidence of transfusion reaction. If the information of the number of transfusion patients who belong to the specific kind of disease is known, the estimation would be more accurate.

Competing Interest Statement

The authors have declared no competing interest.

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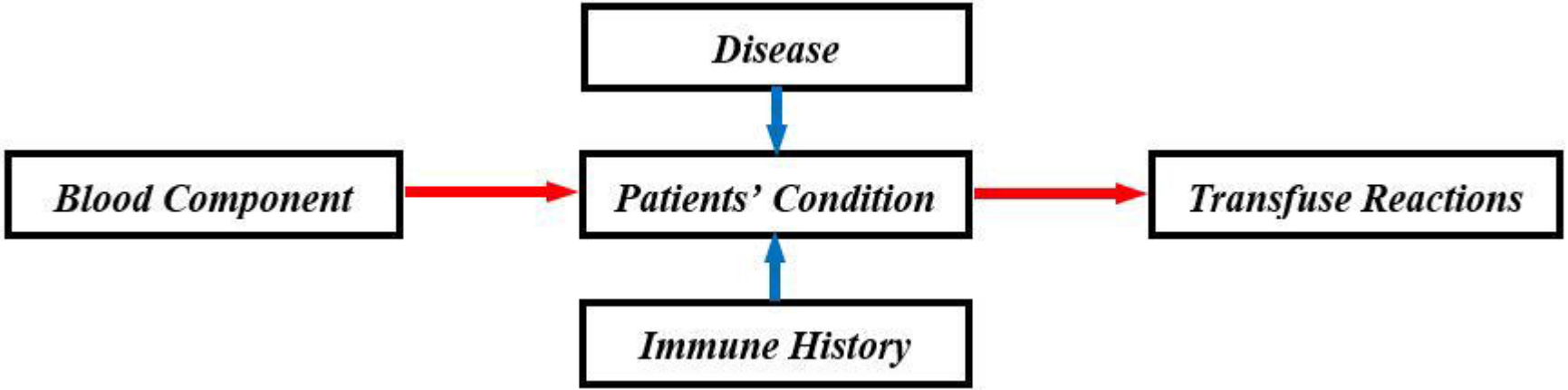
Disease
Blood Component
Patients' Condition
Transfuse Reactions
Immune History