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ORIGINAL ARTICLE

Platelet Lipidome Characteristics of Adverse Reactions Associated with Irradiated Aphaeresis Platelets Transfusion in Children

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SUMMARY

Background: **In clinical practice, we have observed that compared with red blood cells and plasma, platelet transfusion is more likely to cause transfusion adverse reactions, especially in children. Platelets may suffer different degrees of structural and biochemical damage during processing and preservation, and the lipid components contained in platelets may have a significant impact on the generation of transfusion adverse reactions. Therefore, the objective of this study is to identify the key bioactive lipid components that cause adverse blood transfusion reactions especially allergic rash and to explore ways to reduce the adverse transfusion reactions caused by irradiated aphaeresis platelets.**

Methods: **Platelet antibodies were determined in 15 children with rash after transfusion and 15 children with no adverse transfusion reactions, then lipid composition was analyzed by mass spectrometry. The Thermo UHPLC-Q Exactive HF-X Vanquish Horizon system compared differential lipid composition using GraphPad version 8.3.0 for statistical analysis and Pearson's correlation coefficient analysis.**

Results: **Platelet antibodies were negative in the allergic transfusion reaction (ATR) group. Among the platelet lipid components, PE (18:3/18:2) and TG (18:1/18:2/24:1) were up-regulated, whereas SM (d17:1/18:1), SM (d17:1/18:3) were significantly down-regulated in the no-AR group. Furthermore, the enrichment analysis of the KEGG pathway of differential lipids indicated that cholesterol metabolism has the most significant diversity.**

Conclusions: **The data suggests that the content of PE (18:3/18:2), TG (18:1/18:2/24:1), SM (d17:1/18:1), SM (d17:1/18:3) in platelets can prospectively predict transfusion-related allergic reactions in children. It is possible to improve platelet products by changing the lipid component of platelets to improve platelet transfusion efficiency.**
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KEYWORDS

platelet lipidome, irradiated aphaeresis platelets (IAPs), children, allergic transfusion reaction (ATR)

LIST OF ABBREVIATIONS

PE - phosphatidylethanolamine
TG - triacylglycerol
SM - Sphingomyelin
IAPs - irradiated aphaeresis platelets
ATR - allergic transfusion reaction
TA-GVHD - transfusion-associated graft versus host disease

DAMPS - damage-associated molecular patterns
TRALI - transfusion-related acute lung injury
AR - adverse reaction
PC - platelet concentration
SDA-PC - single donor apheresis - platelet concentrates
FA - fatty acids
GL - glycerolipids
GP - glycerophospholipids
SP - sphingolipids
ST - sterols lipids
PR - prenol lipids
SL - saccharolipids
PK - polyketides.

INTRODUCTION

Blood transfusion is a life-saving medical intervention, yet it carries inherent risks of adverse reactions, which range from mild symptoms to life-threatening complications. Therapeutic platelet transfusion serves dual prophylactic and hemostatic purposes in clinical practice. With global demographic aging and the escalating prevalence of hematological pathologies, platelet demand has surged significantly, particularly among patients undergoing hematological and oncological therapies [1,2]. Although platelet transfusion is a safe treatment, recipients may experience several adverse reactions, including mild and severe adverse reactions, during or after the transfusion [3,4]. Among these, allergic transfusion reactions (ATRs) represent one of the most common types of non-hemolytic transfusion reactions. ATRs occur in approximately 1 - 3% of all transfusions, with manifestations varying from localized urticaria and pruritus to systemic anaphylaxis [5]. Severe allergic reactions, though rare (affecting 1 in 20,000 - 50,000 transfusions), can lead to hypotension, bronchospasm, and even death if not promptly managed. The pathophysiology of ATRs is primarily driven by IgE-mediated hypersensitivity to donor plasma proteins, though non-IgE mechanisms involving cytokine release or complement activation may also contribute [6,7].

While standardized protocols have reduced the frequency of severe ATRs, critical knowledge gaps persist. The interplay between donor-specific factors (e.g., plasma composition, storage lesions) and recipient immune status (e.g., atopy, IgA deficiency) remains poorly characterized.

Furthermore, the lack of reliable biomarkers for predicting or diagnosing ATR hinders personalized prevention. Existing therapies, such as IgE-targeted biologics, show promise but require validation in transfusion settings. A deeper understanding of the immunopathological cascades, coupled with innovations in blood component processing and recipient screening, is essential to minimize risks and optimize transfusion safety.

Addressing these challenges demands interdisciplinary research integrating immunology, transfusion medicine, and systems biology to unravel the intricate mechanisms governing ATR development and prevention [8-10].

The complexity of ATRs stems from multifaceted etiological factors. First, the mechanisms underlying allergic reactions are heterogeneous. IgE-mediated responses are triggered by allergens in donor blood, such as soluble antigens (e.g., drugs, food-derived proteins) or immunoglobulin aggregates. Non-IgE pathways, including activation of mast cells and basophils by cytokines (e.g., histamine, tryptase) or complement fragments, further complicate the clinical picture. Second, ATRs directly compromise transfusion efficacy [11]. Mild reactions often necessitate transfusion interruption, delaying critical therapy, while severe reactions may render the patient ineligible for future transfusions, exacerbating anemia or coagulopathy [12]. Third, life-threatening anaphylaxis poses significant risks, particularly in immunocompromised or critically ill patients. Fourth, current preventive strategies, such as premedication with antihistamines or corticosteroids, leukoreduction, and washed blood components - only partially mitigate risks, highlighting gaps in mechanistic understanding. Finally, despite advances, the precise molecular pathways driving ATRs remain elusive, particularly in cases where no specific allergen is identified, suggesting roles for novel mediators like extracellular vesicles or microRNAs or other components in donor blood [13].

Here, we intend to evaluate the lipidome differences between platelets that cause allergic transfusion reactions and normal platelets in children, we aim to search markers related to lipid metabolism which can predict adverse blood transfusion reactions and, thus, reduce the incidence of adverse blood platelet transfusion reactions in children. In this study, we investigated the characteristics of platelet lipidome associated with anaphylaxis after platelet transfusion irradiation in children. By exploring the lipid profile of platelets, this study is designed to uncover potential biomarkers or lipid signatures that may predispose pediatric patients to severe allergic reactions. Understanding these lipidomic alterations can provide insight into the underlying mechanisms of allergic reactions and inform safer platelet transfusion practices in clinical settings. By elucidating the lipidomic factors involved in anaphylaxis, the ultimate goal of this study is to improve the safety and efficiency of platelet transfusion therapy in pediatric patients.

MATERIALS AND METHODS

Inclusion of patients and isolation of platelets

Fifteen patients with allergic rash following irradiated aphaeresis platelets (IAPs) transfusion, and fifteen age- and gender-matched patients without adverse transfusion reaction following IAP transfusion from West China Second University Hospital, Sichuan University were enrolled. The study was approved by the Ethics

Committees (Sichuan University), was performed in accordance with the Declaration of Helsinki, and each study participant or their legally authorized representative gave written informed consent for platelet preparation.

The patient's blood bag was returned to the blood bank within 24 hours after completing the transfusion, remaining IAP supernatants were collected after centrifugation (2,379g, 5 minutes), aliquoted, and stored at -80°C for future HLA, HPA analysis, and mass spectrometry use.

Platelet antibody test

Platelet antibody was detected using the MASPAT kit (Sanquin Regents, K1360), following these steps: First take out the MASPAT microplate with the specific number of wells needed from its packaging. The remaining unused wells should be kept with the desiccant in the plastic bag. Using a plastic pipette, dispense 1 drop (50 µL) of donor platelet concentrate into the designated wells (for the patient's serum, positive and negative controls of the MASPAT). Subsequently, spin the microplate at 50 rcf for 5 minutes without braking to fix the platelets to the wall surfaces. Afterward, discard any loose platelets by manually rinsing the wells three times with 150 µL of PBS/Tween 0.005%. The wash solution should be added dropwise using a multichannel pipette. Decant PBS/Tween between washes by inverting and flicking. Add 2 drops (100 µL) MASPAT LISS to each well. Add 1 drop (50 µL) of MASPAT positive or negative control to the appropriate wells. Add 50 µL of the patient's serum into the wells that have the donor platelet monolayers. Mix the contents on a microplate shaker for 10 seconds at a speed of 800 rpm (using a Sarstedt TPM-2 shaker). Then, let the microplate sit at a temperature of 37°C for 30 minutes with the microplate sealed to prevent evaporation. After incubation, pour off the contents and manually rinse the wells five times with 150 µL of PBS/Tween, following the same procedure as in step 4. After washing, promptly add 50 µL of MASPAT anti-IgG reagent to each well. Then, add 50 µL of MASPAT Indicator Red Cells to each well. Gently shake the plate. Centrifuge the microplate at 200 rcf for 5 minutes without using the brake. Finally, the reactions can be observed either macroscopically or with an automatic reader [14].

Mass spectrometry

The analysis of the sample was conducted using liquid chromatography-tandem mass spectrometry (LC-MS/MS) on a Thermo Scientific UHPLC-Q Exactive HF-X Vanquish Horizon platform, equipped with an Accucore C30 column measuring 100 mm in length and 2.1 mm in diameter with a particle size of 2.6 µm; the system was sourced from Thermo, USA. The testing was performed at Majorbio Bio-Pharm Technology Co. Ltd (Shanghai, China).

Differential metabolites analysis

Perform an analysis of variance on the matrix file after completing the data preprocessing stage. Use the R package ropls (Version 1.6.2) for conducting principal component analysis (PCA) and orthogonal partial least squares discriminant analysis (OPLS-DA). Validate the model's robustness through a 7-cycle cross-validation process. Additionally, conduct Student's t-tests and fold difference analyses. The determination of markedly distinct metabolites relies on the Variable Importance in Projection (VIP) scores derived from the OPLS-DA model and the p-values obtained from Student's t-tests, where metabolites are deemed significantly different if their VIP scores exceed 1 and their p-values are below 0.05. Consolidate the differentially expressed metabolites between the two groups and incorporate them into their corresponding biochemical pathways by conducting metabolic enrichment and pathway analysis with the aid of database searches (KEGG, http://www.genome.jp/kegg/). These metabolites can be classified according to the pathways they participate in or the roles they fulfill. Enrichment analysis generally assesses whether a set of metabolites is enriched at a particular functional node. This approach shifts from examining individual metabolites to evaluating a collection of them. Employ scipy.stats (a Python package) to ascertain the statistical significance of pathway enrichment using Fisher's exact test.

Statistical analysis

Following the UPLC-MS/MS analysis, the initial data were transferred to LipidSearch software (Thermo, CA, USA) for the detection, alignment, and identification of lipid peaks. Identification of lipids was achieved through MS/MS fragment analysis. The mass tolerance for both precursor ions and fragment ions was configured to 10 parts per million (ppm). The m-score threshold for display was established at 2.0, and quality grades A, B, C, and D were utilized as criteria for the identification quality filter. The preprocessing phase yielded a data matrix that included lipid classes, retention times (RT), mass-to-charge ratios (m/z), and peak intensities. The dataset was then analyzed using the free online services provided by the Majorbio Cloud platform (cloud.majorbio.com) [15].

RESULTS

Clinical Characteristics

A total of 30 IAPs were included in this study, including 15 normal control IAPs and 15 induced IAPs (Table 1). The main clinical presentation of all patients was allergic rash. Table 1 reports the clinical and demographic characteristics of platelet transfusion patients. All the included numerical variables were judged to be non-normal distribution after the normality test and were described by the median (quartile). There were no substantial variations detected between the patient group

Table 1. Clinical and demographic characteristics of subjects.

	AR patients (n = 15)	No-AR patients (n = 15)	p-value
Demographics			
Age (Days)	3,285.00 [2,190.00, 4,197.50]	2,920.00 [1,717.50, 3,832.50]	0.428
Gender (male), n (%)	7 (46.7)	9 (60.0)	0.714
BMI	16.07 [14.29, 16.77]	16.44 [15.50, 17.81]	0.206
Death(n)	1	0	/
Laboratory tests (before transfusion）			
CRP (mg/L)	20.00 [1.85, 52.65]	2.90 [0.40, 7.20]	0.104
PLT (× 10^9/L)	19.00 [17.00, 26.00]	20.00 [15.00, 35.00]	0.868
MPV (FL)	11.00 [10.30, 11.15]	11.00 [10.80, 11.55]	0.391
WBC (× 10^9/L)	1.10 [0.65, 2.30]	1.50 [0.85, 3.50]	0.633
Neutrophils (%)	21.40 [1.80, 51.60]	22.40 [9.15, 74.00]	0.29
Lymphocyte (%)	66.70 [31.00, 92.10]	38.00 [5.55, 73.20]	0.085
NLR	0.32 [0.02, 1.84]	0.36 [0.20, 9.29]	0.206
SP	96.00 [91.50, 102.00]	93.00 [88.50, 113.00]	0.852
DP	55.00 [51.50, 62.50]	57.00 [49.50, 65.00]	0.917
Thrombotic events (n)	0	0	/

All numerical variables are judged to be non-normal distributions after normality tests and are described by the median (quartile).
CRP high-sensitivity C-reactive protein, PLT platelet, MPV mean platelet volume, WBC white blood cell, NLR neutrophil-to-lymphocyte ratio, SP systolic pressure, DP diastolic pressure.

Table 2. Comparison of adverse reaction rates by component type, 2019 - 2023.

Component type	RBC	FFP	PLT	CRYO	Total
AR Cases	250	316	636	1	1,203
Transfusion man-time	58,038	35,788	21,806	1,027	116,659
AR Rate (%)	0.43	0.88	2.92	0.10	1.03

AR adverse reaction, RBC red blood cell, FFP fresh frozen plasma, CRYO cryoprecipitate.

Table 3. Comparison of adverse reaction rates by component type, 2019 - 2023.

Component type	RBC (%)	FFP (%)	PLT (%)	CRYO (%)	Total (%)
FNHTR	98 (39.20%)	26 (8.23%)	68 (10.69%)	0 (0%)	192 (15.96%)
Allergic	139 (55.60%)	288 (91.14%)	558 (87.74%)	1 (100%)	986 (81.96%)
AHTR	6 (2.40%)	1 (0.32%)	0 (0.00%)	0 (0%)	7 (0.58%)
Others	7 (2.80%)	1 (0.32%)	10 (1.57%)	0 (0%)	18 (1.50%)
Total	250 (100%)	316 (100%)	636 (100%)	1 (100%)	1,203 (100%)

FNHTR non-hemolytic transfusion reaction, AHTR acute hemolytic transfusion reaction.

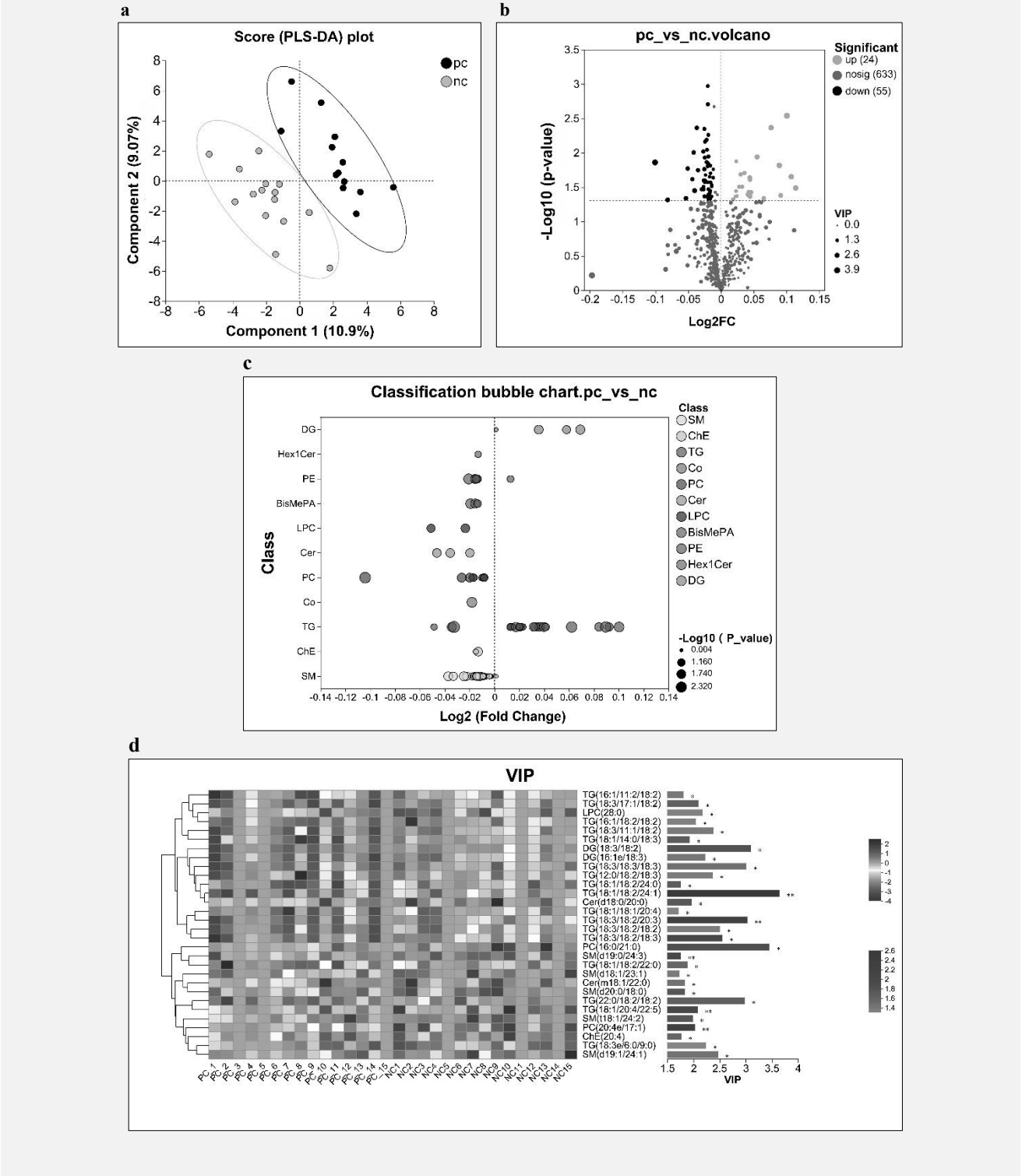

Figure 1. Platelet lipidome. A Partial Least Squares Discriminant Analysis (PLS-DA) scores plot based on the AR/no-AR classification. B Volcano plot of lipidomics for platelets (upregulated lipids, grey vs. downregulated lipids, black) in ESI+ionization mode. C Lipid group bubble plot for the AR vs. NC group.

(Different dots in the figure represent a metabolite, the horizontal coordinate is the multiple change value of the expression difference of metabolites between the two groups, that is, Log2 (fold-change), the vertical coordinate represents the subclass classification of lipids, and different colors represent different classifications). D) VIP Heatmap of the top different features in lipidomics. The right side of Figure D is the metabolite VIP bar chart. The bar's length signifies the metabolite's contribution to the disparity between the two groups; a longer bar denotes a more pronounced difference. The color of the bar reflects the statistical significance of the metabolite's variation between the two sample groups (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

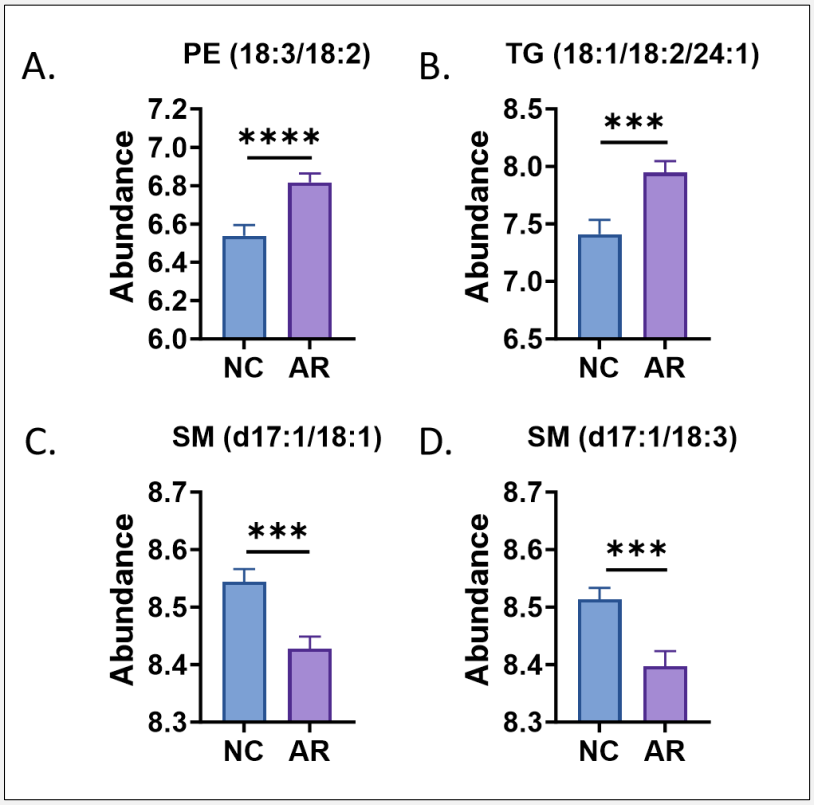

Figure 2. Variation of a number of the lipid classes in AR patients compared to NC.

A PE (18:3/18:2). B TG (18:1/18:2/24:1). C SM (d17:1/18:1). D SM (d17:1/18:3). Results are reported as columns (mean ± SEM).

and the control group across all the included statistical indicators.

Platelet transfusion resulted in the highest adverse transfusion reaction rate

We analyzed the incidence of transfusion adverse reactions of different blood products (red blood cells, platelets, plasma, cryoprecipitates) transfused in our hospital from 2019 to 2023 (Table 2). Among them, the incidence of transfusion adverse reactions from platelet transfusion was 2.92%, red blood cell transfusion was 0.43%, and that of plasma transfusion was 0.88%. By comparing the incidence of different types of transfusion adverse reactions, the highest proportion of platelet transfusion allergic reactions was 87.74%, followed by non-hemolytic fever reaction at 10.69%, and the proportion of other transfusion adverse reactions was 1.57% (Table 3). In the past five years, the rate of adverse reactions caused by platelet transfusion in our hospital has been the highest, and the allergic rash is the main one. Therefore, we should focus on adverse reactions related to platelet transfusion allergy and explore appropriate methods to reduce the occurrence of adverse reactions to improve the transfusion efficiency in pediatric patients. It has been reported that various lipid compounds produced during platelet storage can affect the transfusion effect of platelets, and there is a correlation with adverse reactions. In children, the component of blood products known as plasma is regarded as a significant contributor to the development of transfusion-related adverse reactions, including conditions like allergic transfusion reaction (ATR) and febrile non-hemolytic transfusion reactions (FNHTR) [16].

No matter which type of platelet product is used for blood transfusion, biological response regulators are released, especially inflammatory molecules that accumulate throughout the processing of the platelet product, including collection, preparation, filtration, preparation for infusion of platelet concentration (PC), and storage [17]. In this study, we focused on the differences between IAPs that cause adverse transfusion reactions and normal IAPs. We concentrated on differential lipids and pathways to find ways to improve IAP transfusion outcomes.

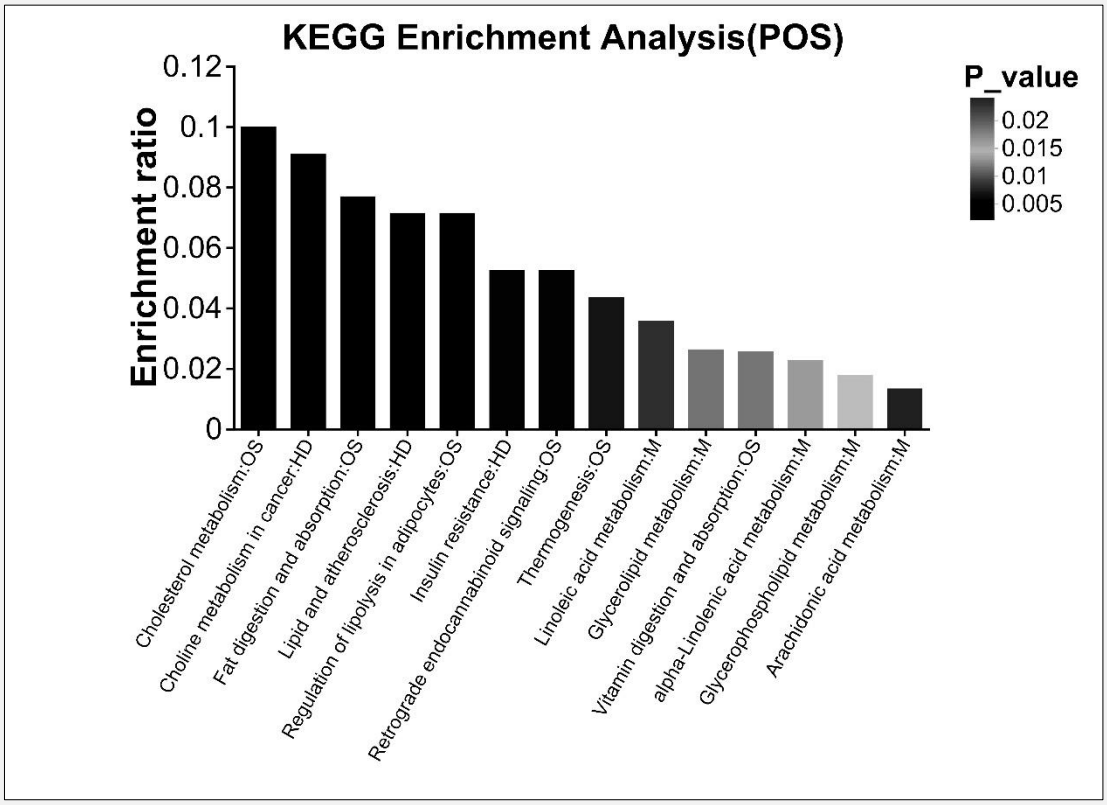

Figure 3. KEGG pathway enrichment map of differential metabolic set.

A The horizontal axis denotes the pathway names, while the vertical axis indicates the enrichment rate, which is the proportion of metabolites enriched in the pathway to the total number of metabolites annotated in the pathway within the background data. A higher ratio indicates a higher level of enrichment. p-value or FDR < 0.001 is marked with ***, p-value or FDR < 0.01 is marked with **, and p-value or FDR < 0.05 is marked with *.

Platelet lipidome

First, we conducted platelet antibody detection [including anti-HLA-I (HLA-A, B, C) and anti-HPA (HPA-1, 2, 3, 4, 5, 15 antibodies] using solid phase agglutination method on the collected IAPs that caused allergic reactions. We found none of the donor platelets that caused allergic reactions had platelet allo-antibodies, so antibody-related immune interference could be excluded (SF1.A). Then we conducted a lipidomic analysis of platelets to identify the correlation between individuals with AR and those without AR by ESI-MS/MS using methods validated and described previously. To characterize the differences, projections to latent structures-discriminant analysis (PLS-DA) plots were generated (Figure 1A). The PLS-DA charts indicate a clear separation between the AR and no-AR groups. The volcano plot reveals that 30 distinct metabolites exhibited significant abundance changes between the negative control (NC) and platelet concentration (PC) groups, with 55 lipids being downregulated and 24 being upregulated (Figure 1B, the detailed information in supplementary data).

Lipidomic analysis of adverse reaction (AR) and no-adverse reaction (no-AR) IAPs was performed by LC-MS. Then, we classified the LIPID metabolites according to the LIPID category. The classification bubble chart (Figure 1C) shows the different multiples of AR compared with no-AR group. Other dots in the figure represent a metabolite, and the horizontal axis represents the fold change in the differential expression of metabolites between the two groups, i.e. Log2 (fold-change). The ordinate represents the lipid subclass classification, the different colors represent the various classifications, and the size of the bubble indicates the significance of the difference. It can be seen that according to lipid classification, PS, PE, TG, PC, and SM are the main differential lipid molecules in AR group compared with no-AR group.

Then we conducted a classification analysis of differential lipids. According to VIP heat map, lipids with the most obvious differences between the two groups were concentrated in TG, DG, PC, TG, and SM (Figure 1D). Then, we analyzed the lipid content of these subclasses of differential lipids, and the results showed that under the cationic mode phosphatidylethanolamine [PE (18:3/18:2)] and triacylglycerol [TG (18:1/18:2/24:1)] were up-regulated (Figure 2A, B), whereas sphingomyelin [SM (d17:1/18:1)] and sphingomyelin [SM (d17:1/18:3)] were significantly down-regulated (Figure 2C, D).

Enrichment of KEGG pathway in differential metabolic set

Using the LC-MS method, we compared the lipidome of platelets in the AR and no-AR groups, and finally, we analyzed the correlation between the metabolic pathways of differential lipid enrichment (Figure 3A), as shown in the KEGG pathway enrichment map of differential metabolic set. The x-axis displays the names of the pathways, while the y-axis shows the enrichment rate, representing the proportion of metabolites in the pathway that are enriched relative to the total metabolites annotated for that pathway in the background dataset (p-value or FDR < 0.001 is marked with ***, p-value or FDR < 0.01 is marked with **, and p-value or FDR < 0.05 is marked with *). The KEGG pathway enrichment analysis showed that the pathways of cholesterol metabolism, choline metabolism in cancer, fat digestion and absorption signaling were found to be distinct between platelets with AR and those without AR. Interestingly, cholesterol metabolism exhibits the most significant diversity, which suggests that the level of cholesterol metabolism in the donor may be related to the occurrence of adverse reactions.

DISCUSSION

Transfusion-related adverse reactions (TARs) represent a critical concern in transfusion medicine, encompassing a spectrum of immune-mediated and non-immune complications. Broadly categorized, TARs include allergic reactions, febrile non-hemolytic transfusion reactions (FNHTRs), hemolytic reactions, transfusion-related acute lung injury (TRALI), and transfusion-associated circulatory overload (TACO). Among these, allergic reactions and FNHTRs account for most non-infectious complications, with reported incidences ranging from 0.1% to 3% depending on blood product type and patient susceptibility [18]. The pathogenesis of these reactions is closely linked to donor-derived bioactive substances within blood components. For instance, plasma proteins such as immunoglobulins, cytokines, and histamine-releasing factors in platelet concentrates are primary mediators of allergic reactions, while leukocyte-derived cytokines in red blood cell (RBC) or platelet units often trigger FNHTRs [19]. Notably, the risk profile varies significantly across blood products: platelet transfusions exhibit the highest TAR rates (1 - 5%), followed by plasma (0.5 - 3%) and RBCs (0.2 - 1%), whereas cryoprecipitate demonstrates minimal reactivity due to its low plasma content [20]. Patient-specific factors further modulate susceptibility, with multiparous women, patients with IgA deficiency, or those receiving frequent transfusions (e.g., hematologic malignancy patients) showing heightened predisposition to allergic or anaphylactoid responses [21].

In this study, we analyzed 2019 - 2023 transfusion data from our institution, revealing distinct patterns in TAR epidemiology. Platelet transfusions demonstrated the highest adverse reaction rate at 2.92%, significantly exceeding those of RBCs (0.43%), plasma (0.88%), and cryoprecipitate (statistically negligible). Allergic reactions dominated platelet-associated TARs (87.74%), primarily manifesting as urticarial eruptions, followed by FNHTRs (10.69%) and rare miscellaneous events (1.57%, Table 3). This aligns with global reports attributing platelet reactivity to its unique composition: high plasma volume (≥ 50 mL/unit), elevated histamine and cytokine levels from storage lesions, and donor-specific IgE/IgG antibodies against recipient antigens. The observed 5-year prevalence underscores platelets as the highest-risk product, particularly for hypersensitivity manifestations. Comparatively, RBC-associated TARs showed lower allergenic potential (0.43%), likely reflecting leukoreduction practices and limited plasma carryover. Plasma reactions (0.88%), though less frequent than platelets, frequently involved severe anaphylaxis due to prekallikrein activator or kinin system activation. Notably, our hematology/oncology cohort exhibited disproportionate TAR susceptibility (72% of all cases), emphasizing the compounding effects of repeated transfusions, immunosuppression, and endothelial dysfunction in this population [7]. These findings reinforce the necessity for risk stratification protocols, particularly for platelet recipients with atopic histories or prior transfusion reactions.

Recently, bioactive lipids were reported as biomarkers of adverse reactions associated with apheresis platelet concentrate transfusion. We propose that a decrease in lysophosphatidylcholine and an increase in lysophosphatidic acid can prospectively predict severe adverse transfusion reactions. The analysis of platelet lipid composition in the AR and no-AR groups was conducted through mass spectrometry, revealing 15 lipids with significant differences between the groups. Among those lipids, PE (18:3/18:2) and TG (18:1/18:2/24:1) were up-regulated, whereas SM (d17:1/18:1) and SM (d17:1/18:3) were significantly down-regulated.

Lipids are not only a key component of our daily diet, but also a source of energy and nutrients necessary to maintain human health. Specific lipid molecules are known as bioactive lipids because of their biological activity and positive effects on health, such as phosphoinositide, sphingolipid, cholesterol, and arachidonic acid etc. They are generally considered to play an im-

portant role in regulating cell proliferation, metabolic activity, organelles function, endocytosis, autophagy, stress response, apoptosis and senescence [22,23]. Ethanolamine is the head group of PE and other lipid molecules, which is commonly found in every cell of the human body. At the same time, it is also present in body fluids [22]. In healthy cells, PE resides predominantly in the lumen surface of endothelial cells. Meanwhile, PE is a cofactor in the anticoagulant mechanism. In addition to being the body's main form of energy storage, TG is involved in regulating the rate of oxidation of fatty acids, the content of free fatty acids in plasma, the synthesis of other lipid molecules, and the metabolic processes of lipoproteins. The concentration of TG is a key indicator to assess the health status of an individual. *In vivo*, the synthesis and breakdown of triglycerides is the core part of energy metabolism. They are not only a reserve and supply source of energy, but also participate in the construction of cellular structures and regulate the properties of biofilms. The concentration of TG in plasma is affected by physiological factors, such as gender, age, diet, and lifestyle (exercise) [24-26]. Therefore, there will be differences in plasma TG of different blood donors. Sphingomyelin (SM) is the precursor substance of ceramide, contributing to the geometrical stability of the cell membranes. Interestingly, the longevity of the human family seems to be linked to the presence of certain more unusual SM species. Over the past few years, the association between SM and cholesterol (Chol) has been scrutinized, predominantly within the framework of the "lipid raft" hypothesis [27-29]. The addition of SM to cells increased cholesterol biosynthesis and affected LDL binding to cell surface receptors and subsequent internalization. We found the expression of SM (d17:1/18:1) and SM (d17:1/18:3) was down-regulated among the lipids that caused adverse blood transfusion reactions, moreover, we conducted a metabolomic analysis of differential lipids' metabolic profile.

The KEGG annotation analysis showed that the majority of the changed metabolites were associated with cholesterol metabolism. SM is usually the only fully saturated phospholipid in the cell membrane (except for trans-double bonds of long-chain bases), so cholesterol prefers to interact with SM [27]. The combination of the differential lipid metabolic pathways we screened were mainly concentrated in cholesterol metabolism. We considered that it is possible to improve the occurrence of adverse blood transfusion reactions by increasing the amount of SM in platelets.

In summary, the varying degrees of lipid metabolism and the presence of long-chain polyunsaturated fatty acids (PUFAs) in donor platelets may be key factors contributing to differences in adverse transfusion reactions. These bioactive lipids play an extremely important role in the metabolism of organisms. However, there are few studies investigating the impact of lipid content on platelet transfusion. Therefore, on the one hand, it is possible to consider improving platelet products by adding certain bioactive lipids such as SM (d17:1/18:1) and SM (d17:1/18:3), on the other hand, the content monitoring of PE (18:3/18:2) and TG (18:1/18:2/24:1) can be used as a screening method for blood products before blood transfusion and providing suggestions for pre-transfusion management of children at the same time, such as formulating a blood donor screening plan (recent diet and cholesterol intake survey of blood donors) to reduce the incidence of adverse blood transfusion reactions.

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Data Availability Statement:
The corresponding author will provide the data supporting the study's findings upon reasonable request.

Ethical Approval Statement:
The Ethics Committee of the Second West China University Hospital, Sichuan University (2020051) approved this study.

Patient Consent Statement:
IAPs were obtained from the Blood Bank of West China Second University Hospital, Sichuan University with 30 volunteers enrolled between August 2023 to October 2023 giving their informed consent.

Declaration of Interest:
The authors state that they have no relevant conflicts of interest.

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