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Effect of Post Storage Leukoreduction Filters on the Febrile Non-Haemolytic Transfusion Reaction

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Abstract

Objective: To assess the effect of post-storage leukoreduction filters on the incidence of febrile non-haemolytic transfusion reactions (FNHTR) in transfused patients.

Methodology: Cross-sectional comparative study was conducted at Chughtai Lab Blood Centre, Chughtai Institute of Pathology, Lahore, Pakistan; from January 2025 to July 2025. After obtaining informed consent, 794 patients between the ages of 5 and 65 were included. 363 patients in Group A received transfusions using bedside leukoreduction filters, while 431 patients in Group B received transfusions without filters. Patients were observed for FNHTR. Temperatures were noted both before and after transfusion. SPSS version 21.0 was used to analyse the data. Frequency and percentage were used to display categorical variables. The chi-square test was used to compare the incidence of FNHTR in each group. Statistical significance was defined as a p-value (<0.05).

Results: There were 591 (74.4 %) men and 203 (25.5 %) women among 794 patients. The age range was from 5 -65 years. 356 (98%) patients in Group A who received leukoreduction filter transfusions did not develop FNHTR, whereas 7 (2%) patients did. Patients in Group B who were transfused without filters, 120 (27%) had FNHTR. There was a statistically significant difference (p<0.001) in the incidence of FNHTR between the two groups. A 92.6% decrease in FNHTR risk was due to post-storage leukoreduction filters.

Conclusion: Bedside leukoreduction filters provide a useful, affordable alternative to enhance transfusion safety by successfully lowering FNHTRs. It is advised to regularly use post-storage leukoreduction filters to improve transfusion results and patient comfort.

Key words: Febrile non-haemolytic transfusion reaction (FNHTR), leukoreduction filters.

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Introduction

Blood transfusion remains a cornerstone of contemporary medical practice, supporting patients in diverse clinical scenarios. It is frequently required in major surgical procedures, obstetric hemorrhage, trauma care, neonatal intensive care, and in critically ill patients. Individuals with hematological malignancies, chronic anemia, bleeding disorders, and inherited conditions such as thalassemia often depend on repeated transfusions to maintain adequate hemoglobin levels and overall clinical stability.[1] Despite the performance of thousands of transfusions daily worldwide, the availability of safe blood remains inadequate in many low- and middle-income countries. In Pakistan, the estimated annual requirement of blood exceeds the available supply, highlighting significant resource constraints. [2]

Although lifesaving, transfusion therapy is associated with potential complications, including transfusion-transmitted infections and immunologic reactions. These reactions range from mild allergic manifestations to severe hemolytic events and hemodynamic instability.[3] Among non-hemolytic reactions, febrile non-haemolytic transfusion reactions (FNHTRs) are reported most frequently, particularly with red cell transfusions.[4]

FNHTR is defined as a rise in body temperature of ≥1°C or a temperature exceeding 38°C during or within four hours of transfusion, in the absence of hemolysis.[5] Patients may also experience chills, rigors, headache, tachypnea, or transient blood pressure changes. The underlying mechanism is largely attributed to cytokine release from residual donor leukocytes or from recipient immune responses to donor cells. Cytokines such as interleukin-1, interleukin-6, and tumor necrosis factor-α are implicated in mediating the febrile response through hypothalamic prostaglandin pathways.[6]

Management includes immediate cessation of transfusion, clinical assessment, and symptomatic treatment with antipyretics while excluding acute

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hemolytic reactions.[7] Although acetaminophen premedication is commonly practiced, available evidence does not consistently support its routine prophylactic use.[8]

Leukocyte reduction of blood components has been shown to decrease the incidence of FNHTRs, alloimmunization, and cytomegalovirus transmission.[9] Leukoreduction may be performed either before storage or at the bedside during transfusion. Pre-storage leukoreduction limits cytokine accumulation during storage and provides better quality control; however, cost considerations restrict its universal implementation in resource-limited settings.[10]

Given these constraints, bedside leukocyte filtration may offer a practical alternative to reduce FNHTRs. This study aims to compare the frequency of febrile non-hemolytic transfusion reactions in patients receiving leukoreduced versus non leukoreduced blood components.

Methodology

It was a cross-sectional study conducted at Chughtai Lab Blood Centre from January, 2025 to July, 2025 after getting approval from the ethical and research committee of the institute with an IRB number 1288 on 13 June 2024. In this study, a total of 794 patients aged 5 to 65 were included after taking their informed consent. Sample size was calculated using OpenEpi version 3.01, taking confidence level 95%, power 80%, margin of error 5%, expected prevalence of FNHTR 25% in the non-leukoreduced group based on prior research[12], The minimum necessary sample size was determined to be 344 total patients, 172 each group, while maintaining a 95% confidence level, 80% power, and a 1:1 unexposed to exposed ratio.

Inclusion Criteria: Patients of either gender aged 5 to 65 years receiving packed red blood cell (PRBC) or red cell concentrate transfusion at Chughtai Lab Blood Centre during the study period from January 2025 to July 2025 were included. Eligible participants included those transfused with bedside leukoreduction filters and those transfused with standard blood administration sets without leukoreduction filters. Only patients receiving ABO and Rh compatible, cross-matched blood were enrolled. Patients or their guardians who provided written informed consent were included in the study.

Exclusion Criteria

Patients with pre-existing fever ≥38°C before transfusion, active infection, or sepsis at the time of transfusion, or those on antipyretics immediately before transfusion unless uniformly administered to all participants were excluded. Patients with a history of known hemolytic transfusion reactions or severe allergic transfusion reactions were also excluded. Additionally, patients with incomplete clinical records or inadequate vital sign monitoring data were not included in the final analysis.

All patients that came to Chughtai Lab Blood centre for transfusion of red cell concentrate were included in the study. Most of these patients were thalassemia patients or cancer patients undergoing chemotherapy. Patients with myelodysplastic syndrome and nutritional anaemia were also included in the study group. The patients were transfused with blood group compatible, cross matched blood. All blood components were screened for common viral infections like Hepatitis C and Hepatitis B along with HIV. Blood was also screened for malarial parasite and syphilis. Blood was transfused by trained nursing staff and vigilant vital monitoring was done throughout transfusion. Those observed to have a FNHTR were treated accordingly. A post transfusion reaction work-up were ordered where required and all steps were carried out according to AABB guidelines.

Incidence of FNHTR were noted in both groups, data were entered in the excel work sheets, checked manually and logically corrected where needed. Results were analysed using SPSS version 21. Frequency and percentages were calculated for categorical values whereas mean and standard deviation were estimated for quantitative variables.

All data was entered and analysed using Statistical Package for the Social Sciences (SPSS version 21.0. Study variables included age, gender, type of blood component transfused, use of leukoreduction filter, pre transfusion temperature, post transfusion temperature, and occurrence of FNHTR. Categorical variables were presented as frequency and percentage in n (%) format. The chi-square test was used to compare FNHTR incidence between the filter and non-filter groups. A p value of <0.05 was considered statistically significant.

Results

During the study period, 794 patients were studied: 591(74.4%) were male and 203(25.6%) were female patients. They were aged between 5-65 years. 431 (54.3%) patients were transfused without a leukoreduction filter, and 363(45.7%) patients were blood transfused with a leukoreduction filter. We observed that most patients 356 (98%) who were transfused with the help of leukoreduction filter did not experience any symptoms of Febrile nonhemolytic transfusion reaction (FNHTR). Only few patients 7 (1.9%) experienced symptoms like fever and chills. In contrast, among patients transfused without a filter, FNHTR was noted in 120 (27.8%) of patients, while 311 (72.2%) did not experience any symptoms. The difference between the two groups was statistically significant p<0.001.

Table I: Association of FNHTR incidence among patients transfused with and without leukocyte reduction filter (n=794)

	With filter n (%)	Without filter n (%)	p-value
FNHTR	7 (1.9)	120 (27.8)	<0.001
No FNHTR	356 (98.1)	311 (72.2)	
Total	363 (100.0)	431 (100.0)	

Discussion

In recent years, transfusion agencies have increasingly adopted advanced technologies to make blood components safer. One such measure is leukoreduction, a routine processing technique designed to enhance product safety. By eliminating leukocytes, this process reduces the risk of adverse reactions linked to these cells and their cytokines in recipients.[11] FNHTRs are common transfusion reactions characterized by a mild fever, chills, nausea, and headache. They occur mainly because leukocytes in stored blood break down and release inflammatory cytokines such as IL-1, TNF-α, and IL-6, leading to patient discomfort and interruption of transfusion.[12] Leukoreduction is the removal of white blood cells from donated blood using filtration, which can be done during collection (called pre storage leukoreduction), or at the time of transfusion (called bedside leukoreduction). While these reactions are generally mild, they can cause patients discomfort and result in wastage of blood products.[13]

FNHTRs commonly occur in patients who have had multiple transfusions. Leukocyte filtration helps to reduce these reactions.[14]

Our study found that the use of bedside leukoreduction filters significantly reduces FNHTRs in major patients who undergo frequent blood transfusions. These findings are in agreement with previous research showing that reducing leukocyte content in transfused blood helps to prevent these reactions. While FNHTRs are typically mild, they require immediate interruption of transfusions to exclude haemolytic reactions, and the implicated blood units may be discarded, resulting in additional costs for healthcare facilities.

A study was conducted in comprehensive search of the PubMed, Embase, and Cochrane Library databases using Medical Subject Headings (MeSH) related to Blood Transfusion, Transfusion Reaction, and Febrile Non-Hemolytic Transfusion Reaction. The review shows that FNHTRs arise through both immune mechanisms mainly involving anti-HLA antibodies and non-immune mechanisms driven by cytokine accumulation in stored blood products. The risk is higher in patients with previous transfusions, certain underlying diseases, or a history of pregnancy. Although leukocyte removal significantly reduces FNHTR incidence, other factors such as platelet antigens and genetic polymorphisms may also contribute. The routine use of antipyretics remains controversial, emphasizing the need for further research to improve preventive strategies.[15]

A retrospective analysis of 158,122 transfusions from 2014 to 2022 at a medical centre in Eastern Taiwan showed that increased use of leukocyte-poor red blood cells (LPRBCs) was associated with a marked reduction in transfusion reactions. Overall and moderate reaction rates decreased over time, and LPRBCs demonstrated lower moderate and severe reaction rates compared with standard packed red blood cells (PRBCs). These findings indicate that leukocyte reduction effectively reduces clinically observed transfusion reactions.[16]

A retrospective cohort study of 23,782 Leuk reduced RBC and platelet transfusions in 3,668 patients examined the effect of leukoreduction timing (bench, in-line, or bedside) on transfusion outcomes. The incidence of acute transfusion reactions (10.4%) and hospital-acquired infections (2.2%) was not affected by filtration timing. However, length of stay and in-hospital mortality varied by both blood component and leukoreduction method, with pre-storage (bench or in-line) filtration generally associated with shorter stays and lower

mortality compared to bedside filtration. The findings indicate that while leukoreduction timing does not reduce transfusion reactions or infections, it may influence patient recovery and survival.[17]

A similar trend was reported. in a prospective comparative study conducted in the United States in 2004, which evaluated the impact of pre storage leukoreduction on febrile non-hemolytic transfusion reactions in hospitalized patients. The study demonstrated a significant reduction in FNHTR incidence following the implementation of universal leukoreduction, particularly among multiply transfused individuals. Compared with our findings, where bedside leukoreduction reduced FNHTR incidence to 1.9% versus 27% in the non-filtered group, their results also support leukocyte removal as an effective preventive strategy. However, their study evaluated pre storage leukoreduction in a high-resource setting, whereas our study highlights the effectiveness of bedside filtration in a resource-limited context, emphasizing its practical applicability in developing countries.[18]

Our findings indicate that bedside leukoreduction, while less commonly used than pre-storage filtration, can significantly lower FNHTRs and is a cost-effective approach in settings with limited resources. In situations where pre-storage filtration is not practical, bedside filtration offers a feasible and economical method to improve transfusion safety.

Limitations:

Sample size: Although a considerable number of transfusions were included, a larger, multi-centre study could provide more definitive conclusions.

Short-term evaluation: Only immediate transfusion reactions were assessed; long-term outcomes were not studied.

Potential confounders: Patient comorbidities, variations in transfusion protocols, and concurrent treatments may have affected FNHTR incidence.

Conclusion

Bedside leukoreduction filters effectively reduce FNHTRs and offer a practical, cost-effective option to improve transfusion safety, especially where pre-storage filtration is not feasible.

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