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Leukocyte reduction filters (bed line) as an alternative source of leukodepleted Packed Red Cells (PRC)

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ABSTRACT

Background: Leukocyte contamination in blood components is associated with febrile non-haemolytic transfusion reactions, alloimmunization, and immunomodulation. Leukoreduction can be performed pre-storage or post-storage, yet universal leukodepletion increases operational cost. Identifying effective and feasible filtration methods is therefore critical, particularly for facilities supplying leukoreduced components only to high-risk patients. This study evaluates the effectiveness of bedside leukocyte-reduction filters as an alternative source of leukodepleted packed red cells (PRC-LD).

Methods: An analytical quantitative study was conducted from January to May 2025 using 43 fresh whole-blood donations processed into PRC units. All components were prepared via closed-system centrifugation, ABO/Rh typing, crossmatching, and transfusion-transmissible infection screening (HIV, HBsAg, HCV, syphilis). Leukoreduction was performed using RC2VAE bedside filters (Transmedic). Total leukocyte counts were measured before and after filtration using a Sysmex hematology analyzer (LoB 0.00×10^3/µL; LoD 0.01×10^3/µL; LoQ 0.03×10^3/µL). Hemoglobin concentration and leukocyte counts were compared using paired statistical testing.

Results: Bedside filtration produced a marked leukocyte reduction in all PRC units. Mean pre-filter leukocyte count was $3.20 \pm 1.19\times10^3$/µL, decreasing to $0.03 \pm 0.02\times10^3$/µL post-filter ($p < 0.05$), achieving residual leukocyte levels $<1\times10^6$/unit in accordance with PMK No. 91/2015 and AABB standards. Hemoglobin levels showed no significant change before versus after filtration (14.63 ± 1.6 g/dL vs 13.68 ± 1.4 g/dL; $p = 0.76$), indicating minimal red-cell loss during the procedure. These findings confirm that bedside filters provide effective leukoreduction comparable to conventional pre-storage systems.

Conclusion: Leukocyte-reduction bedside filters significantly reduce leukocyte levels in PRC without compromising hemoglobin concentration, making them a viable alternative for producing leukodepleted blood components, particularly in settings where universal leukoreduction is not feasible.

Keywords: Leukodepleted, Packed Red Cells, Leukoreduction, Blood Transfusion.
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INTRODUCTION

Indonesia faces a substantial clinical burden due to a large population requiring repeated transfusions. Patients with thalassemia who depend on regular transfusion therapy, along with the expanding hemato-oncology group needing diverse blood component support, represent the majority of this demand. Many of these individuals eventually develop alloimmunization against red cell, platelet, or HLA antigens throughout their transfusion course. This condition generates significant immunohematological challenges in providing adequate blood component therapy, particularly platelet support in refractory cases. Consequently, the use of leukoreduced blood components becomes critically important for these patient groups.[1] The higher the frequency of transfusions administered, the greater the likelihood of adverse reactions.

In order to limit such reactions, various strategies have been implemented by modifying the processing of blood components and blood products. The application of leukodepleted Packed Red Cells (PRC) has been recognized as effective in reducing transfusion-related reactions because these units contain minimal leukocytes and plasma.[2] Leukodepleted components are defined as products with leukocyte concentrations reduced to 1×10^6 per unit according to national regulations (PMK RI No. 91/2015).[3] In line with this, the American Association of Blood Banks (AABB) requires that leukocyte-reduced RBC units contain $<5\times10^6$ residual leukocytes. Pre-storage filtration has been shown to decrease the incidence of febrile non-haemolytic transfusion reactions (FNHTR), especially in thalassemia patients.[4] Among the available methods to enhance transfusion safety, leukocyte filtration remains the most widely adopted due to its simplicity, efficiency, and rapid processing. It is now incorporated into transfusion safety policies in several countries.[2]

Leucodepletion is capable of achieving a 99.99% leukocyte removal rate, thereby improving the shelf-life and safety of blood components.[5] It also ensures leukocyte levels below $<1\times10^6$ per unit according to European standards.[6] Current techniques

include both pre-storage and post-storage leukocyte reduction. The effectiveness of filtration can be increased by utilizing bedside leukocyte filters in a closed system either before storage or immediately after, by connecting them to satellite bags using a Sterile Connecting Device (SCD). In contrast, in-line leucodepletion filters blood products directly during processing, followed by centrifugation to obtain pre-storage leukodepleted units.[5]

Therefore, the purpose of this study is to quantitatively evaluate the leukocyte-reduction performance of bedside leukoreduction filters by comparing pre- and post-filtration leukocyte counts in Packed Red Cell (PRC) units, and to determine whether these filters consistently achieve the regulatory threshold for leukodepleted blood components.

METHODS

This study was carried out in a voluntary blood bank setting, where all blood units were obtained exclusively from healthy individuals who donated blood on a voluntary basis. Donors who contributed to the pool of available blood units were between 20 and 40 years of age, representing the typical adult donor population. The research was conducted over five months, from January to May 2025. A total of 43 Packed Red Cell (PRC) units were included, each designated for leukodepletion analysis. Only freshly collected blood units were processed to ensure that leukocyte integrity and component quality were not affected by prolonged storage prior to filtration.

All blood components underwent preparation using standard procedures, which involved centrifugation and component separation within a closed collection system to prevent contamination and maintain product sterility. Before leukoreduction was initiated, whether by direct connection to the filter or prior to filtration, each PRC unit underwent routine immunohematological testing. This included ABO blood grouping, RhD typing, and compatibility testing through crossmatching with the intended recipient's sample. These steps were performed to ensure that filtration did not interfere with downstream transfusion compatibility.

All units were also screened for transfusion-transmissible infections as part of standard blood-bank safety protocols. Screening was conducted using chemiluminescent immunoassay (CLIA) techniques for HIV, hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV), and syphilis, ensuring that only infection-negative units proceeded to leukodepletion.

Leukoreduction was performed using RC2VAE bedside leukocyte-reduction filters manufactured by Transmedic. These filters were attached to the PRC units in a closed manner according to manufacturer specifications to minimize environmental exposure and maintain sterility. For analytical assessment, total leukocyte concentrations were measured both before and after filtration using a Sysmex hematology analyzer. The analyzer provided high-sensitivity measurements, with a limit of blank (LoB) of 0.00×10^3/µL, a limit of detection (LoD) of 0.01×10^3/µL, and a limit of quantitation (LoQ) of 0.03×10^3/µL, enabling accurate enumeration of residual leukocytes at very low concentrations. All leukocyte values were documented systematically in the laboratory register before and after the leukoreduction procedure to ensure traceability and facilitate comparative analysis.

RESULTS

Filtration of Packed Red Cell (PRC) units demonstrated a clear reduction in leukocyte content. Prior to bedside leukodepletion, the mean leukocyte count was $3.20 \pm 1.19 \times 10^3$/µL. Following filtration, leukocyte values decreased substantially to $0.03 \pm 0.02 \times 10^3$/µL, and the difference was statistically significant ($p < 0.05$). The leukocyte value distribution shown in Figure 1 confirms consistent achievement of near-zero leukocyte levels in the majority of samples. Hemoglobin levels measured before and after filtration showed no significant change. The mean hemoglobin concentration decreased minimally from 14.63 ± 1.6 g/dL to 13.68 ± 1.4 g/dL, with no statistically significant difference ($p = 0.76$) (Table 1). This indicates that the leukodepletion process did not cause substantial red cell loss. Across the 43 PRC units examined, the filtration procedure consistently produced leukodepleted components that met the expected reduced leukocyte thresholds. Technical factors such as flow rate and temperature were noted to influence filtration performance and require careful control to maintain consistent leukocyte reduction outcomes.

DISCUSSION

Leukodepleted PRC is produced through whole-blood processing followed by centrifugation and filtration within 48 hours, with the aim of reducing leukocyte content to $\leq1\times10^6$ per unit, as required in regulated transfusion practice.[3] Pre-storage leukodepletion is well documented to decrease febrile non-haemolytic transfusion reactions (FNHTR), particularly in thalassemia patients who undergo repeated transfusions.[7] The present findings, showing a significant decline in leukocyte counts after bedside filtration, reinforce the established role

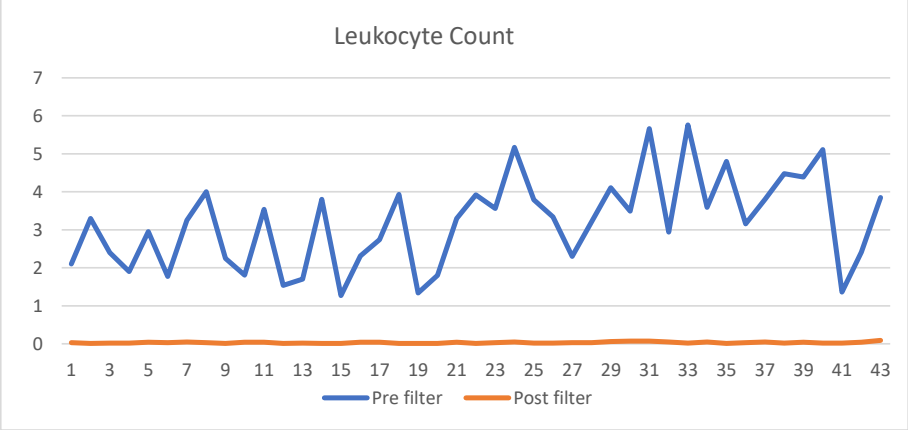

Figure 1. Leukocyte Pre and Post filter.

Table 1. Haematological parameters (routine blood) before and after bedsite leucodepletion

Parameters	Before Bedsite Filter Leukodepleted	After Bedsite Filter Leukodepleted	p
Hemoglobin (g/dl) (mean ± SD)	14.63 ± 1.6	13.68 ± 1.4	0.76
Leukocyte (x10^3/µL) (mean ± SD)	3.20 ± 1.19	0.03± 0.02	<0.05*

*Statistically significant if p-value is less than 0.05

of leukocyte filtration as an effective method for producing leukocyte-poor components. This aligns with global practices where leukocyte filtration has been adopted due to its simplicity, speed, and high efficiency in enhancing transfusion safety.[2]

The significant difference between pre- and post-filtration leukocyte levels observed in this study is consistent with results reported by With et al., who found that conventional PRC units frequently retained unacceptable leukocyte concentrations. In contrast, all leukodepleted PRC units met high-quality standards.[9] The ability of the filter to achieve near-zero residual leukocyte levels in a large proportion of samples suggests adequate performance of the integrated filtration system. Factors such as flow rate, filtration pressure, and temperature are known to influence filtration efficiency and therefore require standardization to ensure reproducibility across batches. Validation of residual leukocyte measurement is essential, as recommended in transfusion regulatory guidelines.[3]

The decrease in leukocyte counts without a corresponding drop in hemoglobin supports the functional benefit of leucodepletion, which not only minimizes cellular contaminants but also preserves the therapeutic value of PRC. This is important because accumulation of donor leukocytes contributes to cytokine buildup, alloimmunization, and an increased risk of FNHTR, particularly in chronically transfused populations.[7-10] The broader advantages of PRC leucodepletion, such as reduced risk of viral transmission, immunomodulation, and alloimmunization, have been emphasized in previous reports.[9] Despite these benefits, limitations remain, including the cost and time requirements associated with filtration.

Additionally, variability in filtration outcomes among studies may be attributed to differences in filter types and their respective manufacturing characteristics. Limited published data on filter performance underscores the need for comparative studies assessing different pre-storage leukoreduction devices. Such research is particularly relevant for low- and middle-income settings where universal leukoreduction is not yet feasible. Consideration of operational factors, such as flow dynamics, filtration pressure, and ambient temperature, should be incorporated in future evaluations to optimize filtration outcomes.

CONCLUSION

This study demonstrated that bedside leukoreduction using RC2VAE filters significantly reduced leukocyte counts in all 43 Packed Red Cell (PRC) units, as evidenced by a p-value < 0.05. The post-filtration leukocyte levels achieved were consistently below the ≤1×10^6 per unit threshold required for leukodepleted components. These findings indicate that the leukodepleted PRC produced at the Blood Transfusion Unit of Bayu Asih Hospital meets the national quality standard stipulated in PMK No. 91/2015 and confirms the effectiveness of bedside filters as a reliable method for preparing high-quality leukoreduced blood components.

ETHICAL CONSIDERATION

Ethical approval from Bayu Asih Hospital and informed consent were obtained. The author attests that all human subjects undertaken as part of research from which this manuscript is derived comply with the regulations of the institution and generally accepted guidelines governing such work. The Author warrants that this manuscript contains no violation of any existing copyright or other third-party right or any material of an obscene, indecent, or otherwise unlawful nature and that, to the best of their knowledge, the manuscript does not infringe the rights of others. Written consent was obtained from all subjects before their enrollment.

CONFLICT OF INTEREST

The author warrants that any financial interests, direct or indirect, that exist or may be perceived to exist for individual contributors in connection with this manuscript have been disclosed in the covering letter.

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AUTHOS CONTRIBUTIONS

R.H. contributed to the study conception and design, data collection, data analysis, interpretation of findings, drafting of the manuscript, and approval of the final version for submission.

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