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INCIDENTAL LYMPHOCYTOSIS IN ACCEPTED BLOOD DONORS: EXPOSING THE SUBCLINICAL VIRAL FOOTPRINT AND THE CASE FOR UNIVERSAL LEUKOREDUCTION IN ENDEMIC REGIONS

Transfusion Medicine

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ABSTRACT

Background: In resource-limited blood centers, pre-donation infectious screening relies heavily on a verbal questionnaire and checking basic vitals. This approach often fails to identify donors who are in the subclinical or convalescent phases of a viral illness. While mandatory serology covers specific transfusion-transmitted infections (TTIs), the baseline prevalence of reactive leukocyte states in the "healthy" donor pool remains unquantified. This study evaluates the prevalence of incidental lymphocytosis in accepted donors to assess the hidden hemovigilance risks of transfusing reactive lymphocytes. **Materials and Methods:** We conducted a retrospective, cross-sectional analysis of 2,155 automated complete blood counts (CBC) from prospective, asymptomatic blood donors at Hind Institute of Medical Sciences, Lucknow. Data from a 3-part automated hematology analyzer were evaluated for total leukocyte counts, relative lymphocyte percentages, and specific algorithmic machine flags. **Results:** The healthy donor cohort (predominantly young adult males) exhibited a normal mean total leukocyte count of 8.57 × 10^9/L. However, relative lymphocytosis (Lymphocyte > 40%) was incidentally identified in 24.55% (n=529) of the donor population. Crucially, 20.28% of the total cohort had this reactive lymphoid shift hidden within a strictly normal total WBC count. The automated analyzer successfully flagged "Lymph increased" in 245 individual donor evaluations. **Conclusion:** Nearly one-quarter of accepted blood donors in our demographic carry a silent viral footprint, characterized by relative lymphocytosis. Harvesting blood from donors with an active, reactive lymphoid lineage poses severe, undocumented hemovigilance risks, including the transfusion of inflammatory cytokines and intracellular passenger viruses to vulnerable recipients. These findings expose the severe limitations of symptom-based donor screening and strongly advocate for the implementation of universal leukoreduction in tropical endemic zones.

KEYWORDS

Blood Donors, Lymphocytosis, Hemovigilance, Transfusion Safety, Leukoreduction, Viral Endemicity, Automated Hematology Analyzer.

INTRODUCTION

Ensuring that a blood donation is safe for the recipient involves much more than just screening for HIV, Hepatitis B and C, and Syphilis.[1] Regulatory guidelines, including those from the National AIDS Control Organization (NACO) in India, utilize strict donor selection criteria combining a medical history questionnaire with physical vitals.[1,17] The questionnaire is specifically designed to defer donors who have recently suffered from infectious diseases, aiming to prevent the collection of blood during a viral window period or a state of systemic inflammation.[4]

However, symptom-based questionnaires are inherently flawed. Prospective donors frequently hide or underreport minor upper respiratory tract infections or vague febrile episodes to avoid being deferred.[2,3] Furthermore, in the highly endemic tropical zones of North India, seasonal outbreaks of Dengue, Chikungunya, Influenza, and asymptomatic Hepatitis expose the population to a constant barrage of viral pathogens.[5,6,7]

When an individual recovers from these endemic viruses, they carry a prolonged "convalescent footprint" in their peripheral blood. This typically manifests as relative lymphocytosis and the presence of reactive lymphocytes, which can persist for weeks after clinical symptoms have completely vanished.[16] Current blood bank screening protocols, which rely heavily on haemoglobin estimation, are completely blind to these subclinical cellular shifts. The donor denies symptoms, passes the temperature check, clears the haemoglobin test, and donates blood.

Transfusing blood products derived from donors in a convalescent or subclinical viral state carries massive, undocumented haemovigilance risks. These units contain a high mass of reactive passenger lymphocytes. Not only can these lymphocytes act as Trojan horses for latent intracellular viruses such as Cytomegalovirus (CMV) or Epstein-Barr Virus (EBV),[8,9] but they are also highly metabolically active. They secrete pro-inflammatory cytokines into the plasma supernatant during refrigerated storage (storage lesions), which serves as a primary trigger for Febrile Non-Haemolytic Transfusion Reactions (FNHTR) in the recipient.[10,11,12]

This study aims to quantify the true prevalence of incidental relative lymphocytosis within a large pool of asymptomatic, accepted blood donors in Uttar Pradesh. By evaluating these subclinical leukocyte dynamics using a standard 3-part cell counter, we aim to expose the limitations of current pre-donation screening and provide a data-driven rationale for the implementation of universal leukoreduction.[13]

Materials and Methods

Study Design and Population

We ran a retrospective, observational study using pre-donation lab data from the blood center at Hind Institute of Medical Sciences, Lucknow. The dataset included 2,155 consecutive peripheral venous blood samples from prospective voluntary and replacement blood donors. Every single individual in this dataset had successfully passed the initial verbal medical history screening (denying any recent fever, antibiotic use, or infectious symptoms) and met basic physiological criteria (normal temperature, blood pressure, and pulse).

Laboratory Analysis and Data Cleaning

Samples were drawn in standard EDTA vacutainers prior to donation and processed using a fully automated 3-part differential hematology analyzer. We extracted the Total White Blood Cell count (WBC), Relative Lymphocyte Percentage (Lymph%), Relative Granulocyte Percentage (Gran%), and specific automated interpretive flags (e.g., "Lymph increased").

To ensure the statistical integrity of the data, we applied a strict biological plausibility filter to remove automated machine artifacts (like false spikes caused by micro-clots or platelet clumping). Samples with physiologically impossible parameters were excluded, leaving us with a clean, highly valid cohort of 2,155 donors.

Statistical Analysis

Data were tabulated to calculate frequencies, means, and standard percentages. We specifically cross-tabulated the lymphocyte percentages against the total WBC counts to identify donors who had hidden viral shifts without overt leukocytosis.

RESULTS

Baseline Leukocyte Demographics of the Donor Pool The analyzed donor cohort (N = 2,155) was primarily composed of young adult

males, perfectly reflecting the standard demographic profile of blood donors in the Indian subcontinent (Table 1).

Table 1: Socio-Demographic Characteristics of the Accepted Blood Donors

Variables	Frequency (n)	Percentage (%)
Total Valid Cohort (N)	2,155	100.0
Age Group (Years)		
18 – 25	801	37.2
26 – 35	926	43.0
36 – 45	347	16.1
> 45	81	3.7
Gender		
Male	2,105	97.7
Female	50	2.3

Looking at the total leukocyte count, the overall profile of the accepted donor cohort was remarkably normocellular. As shown in Table 2, the vast majority of accepted donors (84.55%) had a strictly normal total WBC count, with the cohort mean sitting comfortably at 8.57 ± 2.52 × 10^9/L.

Table 2: Total Leukocyte Count (WBC) Distribution in Accepted

WBC Parameter	Frequency (n)	Percentage (%)
Total Cohort Evaluated	2,155	100.0
Leukopenia (WBC < 4.0 × 10^9/L)	13	0.60
Normal WBC (4.0 - 11.0 × 10^9/L)	1,822	84.55
Leukocytosis (WBC > 11.0 × 10^9/L)	320	14.85
Mean WBC ± SD	8.57 ± 2.52	-

The Burden of Incidental Lymphocytosis Despite the normal absolute WBC baseline and the fact that these donors reported excellent clinical health, breaking down the leukocyte differential revealed a massive underlying shift toward the lymphoid lineage (Table 3). Relative lymphocytosis (Lymph% > 40%) was identified in a staggering 24.55% of the entire prospective donor cohort.

Even more concerning from a screening perspective, the vast majority of these lymphoid shifts were completely hidden. Out of the total cohort, 20.28% (n=437) of donors had relative lymphocytosis occurring concurrently with a strictly normal total WBC count.

Table 3: Prevalence of Leukocyte Differential Shifts and the "Silent" Viral Footprint

Differential Parameter	Frequency (n)	Percentage of Total Cohort (%)
Total Cohort Evaluated	2,155	100.0
Lymphocyte Sub-classification		
Normal Lymphocytes (20 - 40%)	1,605	74.48
Lymphocytopenia (< 20%)	21	0.97
Relative Lymphocytosis (> 40%)	529	24.55
-- Lymphocytosis with Normal Total WBC	437	20.28
-- Lymphocytosis with Leukocytosis (WBC > 11)	92	4.27
Mean Lymphocyte % ± SD	34.44 ± 8.37	-

Diagnostic Utility of Automated Analyzer Flags Our data showed that a standard 3-part hematology analyzer successfully flagged these subclinical immunological shifts right at the pre-donation phase without needing a manual smear review (Table 4). The machine generated a "Lymph increased" flag in 245 individual donor evaluations, providing a direct, actionable alert to the blood bank staff.

Table 4: Frequency of Automated WBC Algorithmic Analyzer Flags

Automated Machine Alert (WBC Message)	Frequency (n)	Indication
Lymph increased	245	Suggestive of viral etiology / convalescence
Gran increased	18	Suggestive of bacterial etiology / inflammation

DISCUSSION

The core finding of this study is the remarkably high prevalence (24.55%) of incidental, relative lymphocytosis in an asymptomatic, questionnaire-cleared blood donor cohort. This data demonstrates that depending on verbal screening alone leaves a massive gap in donor haemovigilance.[2,3]

Exposing the "Viral Baseline" in Blood Donors Under normal physiological conditions, a healthy adult leukocyte differential is granulocyte-dominant.[16] However, our data shows that one out of every four healthy blood donors in Uttar Pradesh presents to the blood bank with an inverted or heavily lymphoid-skewed differential. Because donors with overt fever either self-defer or are excluded by temperature checks, this massive **24.55%** of our cohort represents the "convalescent tail" of local endemic outbreaks, such as Dengue or seasonal respiratory viruses.[5,6] These donors have clinically recovered from a mild viral infection but continue to carry a highly reactive immune profile in their peripheral blood.

What makes this phenomenon particularly dangerous is its subclinical nature. Table 3 shows that 20.28% of our accepted donors had high relative lymphocytes while maintaining a perfectly normal absolute WBC count. If a medical officer only reviews the total WBC number, the donor will be erroneously cleared.

The Transfusion Danger of Reactive Lymphocytes When whole blood is collected from a donor with an active, reactive lymphoid lineage, the resulting blood components, especially Packed Red Blood Cells (PRBCs) and Random Donor Platelets (RDPs), are heavily burdened with passenger lymphocytes.

Transfusing these reactive lymphocytes into immunocompromised recipients (such as oncology patients or neonates) poses severe risks. Beyond the rare but fatal risk of Transfusion-Associated Graft-Versus-Host Disease (TA-GVHD),[17] these specific lymphocytes act as cellular vectors for latent viruses like CMV.[8,9] Furthermore, reactive lymphocytes are metabolically hyperactive and actively secrete pro-inflammatory cytokines (such as IL-1, IL-6, and TNF-alpha) into the plasma during storage.[11,12] Transfusing this unit effectively delivers a concentrated dose of cytokines, explaining why these specific units frequently trigger FNHTR on the wards.[10]

Operational Implications: The Case for Universal Leukoreduction Currently, blood centres utilizing standard manual screening are entirely blind to this phenomenon and are routinely collecting and transfusing these lymphoid-heavy units. Our data strongly suggests that isolated relative lymphocytosis is too prevalent (nearly 25%) to be utilized as a strict deferral criterion; deferring all such donors would precipitate a severe regional blood shortage.

Instead, these findings serve as definitive epidemiological proof that advanced component processing is required. The high prevalence of convalescent viral profiles in the North Indian donor pool mandates an urgent transition toward universal pre-storage leukoreduction.[13,14] Utilizing pre-storage leukoreduction filters physically removes these reactive passenger lymphocytes and their associated cytokine generating capacity from the product, effectively neutralizing the risk posed by this endemic immunological baseline.[15] Additionally, Transfusion Medicine officers should actively monitor the "Lymph increased" flags generated by standard 3-part analysers (flagged 245 times in our study) to identify high-risk units that necessitate targeted leukoreduction or washing before being issued to paediatric or oncology patient.

CONCLUSION

Symptom-based donor questionnaires are simply not enough to catch subclinical or convalescent viral states in highly endemic regions. Almost a quarter of visually healthy, accepted blood donors in Uttar Pradesh carry a silent viral footprint in the form of relative lymphocytosis. Harvesting blood from this highly reactive pool poses serious, undocumented risks to vulnerable recipients. These findings highlight the critical necessity of universal leukoreduction to safeguard the blood supply in tropical endemic zones and prove that basic 3-part automated analyzers are an essential tool for modern donor triage.

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