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ORIGINAL RESEARCH ARTICLE

Frequency and Risk Factors of Red Cell Alloimmunization in Transfused Patients with Sickle Cell Disease and Sickle Cell–β Thalassemia: A Three-Year Retrospective Study from a Tertiary Care Centre.

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Abstract

Background: Red cell alloimmunization is a clinically significant complication of repeated transfusions in sickle haemoglobinopathies. Comparative data from eastern India remain limited.

Objectives: To determine the frequency of alloimmunization in transfused patients with sickle cell disease (SCD) and SCD with β-thalassemia, and to identify associated demographic and transfusion-related risk factors.

Materials and Methods: A retrospective observational study was conducted at KIMS, Bhubaneswar, from October 2022 to October 2025. A total of 148 patients (131 SCD, 17 SCD+β-thalassemia) with a clearly recorded indirect Coombs test (ICT) result were analysed. Demographic and transfusion data were retrieved from blood bank registers. Statistical analysis included chi-square, Fisher's exact, Mann-Whitney U tests, and binary logistic regression.

Results: The overall alloimmunization frequency was 12.2% (18/148). Rates were 11.5% in SCD and 17.6% in SCD+β-thalassemia ($p = 0.437$). Alloimmunization increased significantly with transfusion burden, from 2.3% after one transfusion to 31.6% beyond ten transfusions ($\chi^2 = 10.23$, $p = 0.017$). On multivariable regression, age was the only independent predictor (OR = 1.045/year, 95% CI 1.008–1.085, $p = 0.018$).

Conclusion: Alloimmunization affects approximately one in eight transfused patients with sickle haemoglobinopathies at this centre. Transfusion burden and age are the principal determinants. Extended antigen phenotyping and prophylactic Rh/Kell matching are strongly recommended, particularly for patients anticipated to receive more than five lifetime transfusions.

Key words: Alloimmunization, sickle cell disease, SCD-β thalassemia, indirect Coombs test, red cell transfusion, transfusion safety, haemoglobinopathy, India

1 | INTRODUCTION

Sickle cell disease (SCD) and sickle cell–β thalassemia are autosomal recessive haemoglobinopathies characterised by structurally abnormal or quantitatively deficient haemoglobin, resulting in chronic haemolytic anaemia, vaso-occlusive crises, and progressive end-organ injury. India bears a disproportionate share of the global burden, with an estimated prevalence of approximately 1.17% (nearly 1.2 million affected individuals), concentrated predominantly among tribal communities of central, eastern, and peninsular India. Odisha ranks among the states with the

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highest disease prevalence in the country, making it a region of particular clinical and public health relevance for haemoglobinopathy research (1, 2).

Recurrent red blood cell (RBC) transfusions remain a cornerstone of management in both SCD and SCD–β thalassemia, indicated for acute anaemia, splenic sequestration, stroke prevention, and perioperative cover. However, repeated exposure to donor erythrocyte surface antigens that differ from those of the recipient carries a well-recognised risk of red cell alloimmunization — the formation of antibodies directed against foreign blood group antigens (3). Once developed, alloantibodies can render future crossmatching difficult, prolong time to compatible blood provision, precipitate acute or delayed haemolytic transfusion reactions, and, in the most severe cases, prove life-threatening. Published alloimmunization rates in multi-transfused SCD patients vary widely across settings — from below 5% in some Indian centres to more than 30% in highly transfused Western cohorts — differences attributable to transfusion burden, recipient–donor antigen disparity, and the extent of pre-transfusion phenotype matching employed (4–8).

Despite its clinical significance, comparative data on alloimmunization between SCD and SCD–β thalassemia patients from eastern India remain sparse. The present study was therefore designed with three primary objectives: to determine the overall frequency of red cell alloimmunization among transfused patients with SCD and SCD–β thalassemia at a tertiary referral centre in Odisha, to compare alloimmunization rates between the two disease subgroups; and to identify demographic and transfusion-related risk factors independently associated with alloimmunization, with a view to informing institutional transfusion safety protocols.

2 | MATERIALS AND METHODS

Study Design and Setting

This was a retrospective observational study conducted at the Department of Transfusion Medicine, Kalinga Institute of Medical Sciences (KIMS), Bhubaneswar, Odisha, India, over a three-year period from October 2022 to October 2025. KIMS is a tertiary care multispeciality hospital serving a large catchment area of tribal and semi-urban populations in Odisha and neighbouring states, regions with a well-documented high burden of sickle haemoglobinopathies. Hospital transfusion records, blood bank registers, and electronic patient files were reviewed systematically to identify eligible cases. The study was carried out in accordance with institutional ethical guidelines and the Declaration of Helsinki; patient identifiers were anonymised prior to analysis.

Study Population

Inclusion Criteria

Patients were considered eligible if they had a confirmed diagnosis of sickle cell disease (HbS) or sickle cell disease with β-thalassemia (HbS/β-thalassemia), had received at least one packed red blood cell transfusion at KIMS during the study period, and had a documented indirect Coombs test (ICT) result in the transfusion database. The diagnosis was established using haemoglobin electrophoresis (at both alkaline and acid pH) or high-performance liquid chromatography (HPLC), with genetic testing used for confirmation where available, as recorded in the medical records.

Exclusion Criteria

Patients with sickle cell trait (HbAS), other haemoglobinopathies unrelated to HbS, or those whose ICT result was absent, unclear, or technically invalid were excluded from the primary analysis. Records with incomplete demographic data were flagged separately and excluded from multivariate modelling. Applying these criteria, 159 non-blank records were initially retrieved; seven patients with sickle cell trait or a non-qualifying diagnosis and four with missing or equivocal ICT results were excluded, yielding a final primary analysis cohort of 148 patients.

Data Collection

A standardised data extraction sheet was used to collect the following variables from the transfusion register and clinical case notes: (i) patient demographics — age at time of transfusion and biological sex; (ii) haematological diagnosis — SCD or SCD with β-thalassemia; (iii) transfusion history — total number of red cell units received (cumulative lifetime count) and dates of transfusion episodes; and (iv) antibody screening status — result of the most recent

pre-transfusion ICT recorded during the study window. Transfusion counts were subsequently categorised into four exposure groups: 1 transfusion, 2–5 transfusions, 6–10 transfusions, and more than 10 transfusions; records with no retrievable transfusion count were classified as unknown and excluded from exposure-specific analyses.

Alloimmunization Assessment — Indirect Antiglobulin (Coombs) Test

Antibody screening was performed in the blood bank laboratory prior to each transfusion episode using the indirect antiglobulin test (IAT), in accordance with standard operating procedures. Briefly, patient serum was incubated with group O reagent red cells at 37 °C, followed by the addition of polyspecific anti-human globulin (anti-IgG/anti-C3d). Visible agglutination after centrifugation was recorded as a positive result. Any patient with at least one positive ICT result during the study period was classified as alloimmunized (ICT-positive). Where antibody identification panels were performed, specificities were recorded; however, antibody identification was not available for all positive cases and its systematic analysis fell outside the scope of this study (9, 10).

Statistical Analysis

All analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Age and transfusion count were tested for normality using the Shapiro-Wilk test; both were non-normally distributed and are therefore summarised as median (interquartile range, IQR) alongside mean ± standard deviation (SD). Categorical variables were compared between ICT-positive and ICT-negative groups using Pearson's chi-square test or Fisher's exact test, as appropriate (expected cell count < 5). Continuous variables were compared using the Mann-Whitney U test. Odds ratios (OR) with 95% confidence intervals (CI) were calculated for categorical predictors. To identify independent predictors of alloimmunization, binary logistic regression was performed incorporating age (continuous), disease group, and gender as covariates; model fit was assessed by McFadden's pseudo R^2, Akaike Information Criterion (AIC), and the log-likelihood ratio (LLR) test. A two-tailed p-value of less than 0.05 was considered statistically significant throughout. No correction for multiple comparisons was applied, as all analyses were pre-specified and exploratory in nature.

3 | RESULTS

Study Population and Demographic Profile

After excluding seven patients with sickle cell trait/other haemoglobinopathies and four with missing indirect Coombs test (ICT) results, the final analysis included 148 patients with a confirmed diagnosis of sickle cell disease (SCD) or SCD with β-thalassemia. The demographic and baseline clinical characteristics are summarised in Table 1 and Figure 1 . Age was non-normally distributed (Shapiro-Wilk W = 0.933, p < 0.001); median (IQR) is therefore reported as the primary measure of central tendency alongside mean ± SD. The cohort was predominantly young and male, with a mean age of 23.5 ± 13.3 years (median 20, IQR 15–30; range 1–64 years). Males constituted 60.1% of participants and the 11–20 year age group was the largest age stratum (n = 52, 35.1%), consistent with the predominance of paediatric and young adult presentations of sickle haemoglobinopathies at a tertiary referral centre.

Age was non-normally distributed (Shapiro-Wilk p < 0.001); median (IQR) is the primary central tendency measure. Patients with sickle cell trait (n = 7) and unclear ICT results (n = 4) were excluded from the primary analysis.

Patients with SCD+β-thalassemia were notably younger than those with SCD (mean 14.1 ± 6.2 vs. 24.8 ± 13.4 years), reflecting the earlier onset and greater frequency of transfusion requirements in compound heterozygous disease. The disease group distribution is illustrated below.

Distribution of Transfusion Exposure

The distribution of cumulative transfusion exposure is presented in **Table 2**. Transfusion counts were highly right-skewed, with a median of 2.5 (IQR 1–6) and a range extending to 1,012 transfusions in a single SCD+β-thalassemia patient on regular exchange transfusion therapy; mean ± SD (21.0 ± 98.1) is therefore of limited descriptive value, and median is reported preferentially. The single-transfusion group was the largest (29.1%), followed by the 2–5 group (33.8%), collectively accounting for 63% of

the cohort. Patients with >10 transfusions, though fewer in number (n = 19), exhibited the highest alloimmunization rate (31.6%).

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (N = 148)

Characteristic	Category	n (%)	Mean ± SD (years)	Median (IQR)	Range
Total	—	**148 (100%)**	23.5 ± 13.3	20 (15–30)	1–64
Age Group	0–10 years	22 (14.9%)	—	—	—
	11–20 years	52 (35.1%)	—	—	—
	21–30 years	37 (25.0%)	—	—	—
	31–40 years	22 (14.9%)	—	—	—
	41–50 years	6 (4.1%)	—	—	—
	>50 years	9 (6.1%)	—	—	—
Gender	Male	89 (60.1%)	22.7 ± 13.9	19 (13–30)	—
	Female	58 (39.2%)	24.9 ± 12.3	23 (16–32)	—
	Unknown	1 (0.7%)	—	—	—
Disease Group	Sickle Cell Disease	131 (88.5%)	24.8 ± 13.4	22 (17–32)	1–64
	SCD + β-Thalassemia	17 (11.5%)	14.1 ± 6.2	15 (11–19)	3–27

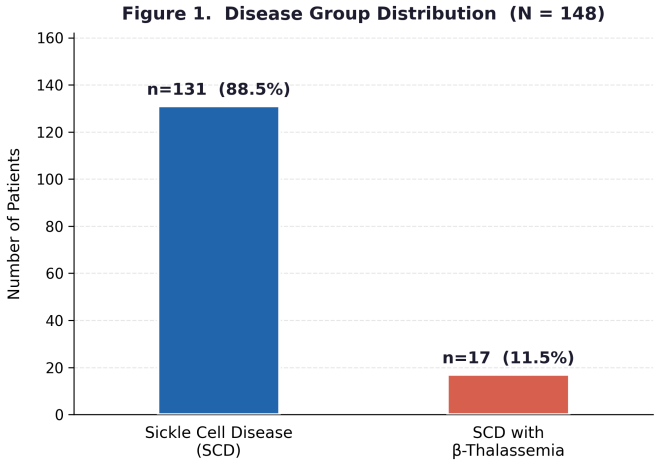

Fig. 1: Distribution of study participants by disease group (N = 148)

Table 2. Distribution of Participants by Transfusion Exposure Group

Transfusion Exposure Group	n (%)	ICT-Positive	ICT-Negative	Alloimmunization (%)
1 transfusion	43 (29.1%)	1	42	2.3%
2–5 transfusions	50 (33.8%)	9	41	18.0%
6–10 transfusions	14 (9.5%)	2	12	14.3%
>10 transfusions	19 (12.8%)	6	13	31.6%
Unknown/Not recorded	22 (14.9%)	0	22	0.0%†
Total	**148 (100%)**	**18**	**130**	**12.2%**

†The unknown group was excluded from chi-square testing of the exposure–alloimmunization association. Transfusion count (continuous): median 2.5 (IQR 1–6), range 1–1,012.

Overall Frequency of Alloimmunization

Of 148 patients with a clearly recorded ICT result, 18 were alloimmunized (ICT-positive), yielding an overall alloimmunization frequency of 18/148 (12.2%). The overall frequency and descriptive comparison between ICT-positive and ICT-negative groups are presented in Table 3. ICT-positive patients were older (mean 29.8 ± 14.7 years) and had a significantly higher cumulative transfusion burden

(median 5, IQR 3–15) compared to ICT-negative patients (mean 22.7 ± 12.9 years; median transfusion count 2, IQR 1–5). Transfusion count was the only continuous variable that differed significantly between the two groups (Mann-Whitney U = 1,405, p = 0.002), underscoring cumulative antigen exposure as the principal driver of sensitisation.

Table 3. Overall Frequency of Alloimmunization and Descriptive Comparison by ICT Status

Parameter	ICT-Positive (n = 18)	ICT-Negative (n = 130)	Total (n = 148)	p-value
Frequency, n (%)	**18 (12.2%)**	130 (87.8%)	148	—
Age, mean ± SD	**29.8 ± 14.7**	22.7 ± 12.9	23.5 ± 13.3	0.065†
Age, median (IQR)	26 (18–38)	20 (15–29)	20 (15–30)	—
Transfusion count, median (IQR)	**5.0 (3.0–15.0)**	2.0 (1.0–5.0)	2.5 (1.0–6.0)	**0.002†**
Gender: Male, n (%)	9 (50.0%)	80 (61.5%)	89 (60.1%)	0.441‡
Gender: Female, n (%)	9 (50.0%)	49 (37.7%)	58 (39.2%)	—
SCD, n (%)	15 (83.3%)	116 (89.2%)	131 (88.5%)	0.437‡
SCD + β-Thal, n (%)	3 (16.7%)	14 (10.8%)	17 (11.5%)	—

†Mann-Whitney U test (non-parametric; age non-normally distributed by Shapiro-Wilk). ‡Fisher's exact test. Bold values indicate statistical significance (p < 0.05). Age difference between ICT+ and ICT− groups approached but did not reach significance (p = 0.065).

Alloimmunization Frequency by Disease Group

The alloimmunization rate was 11.5% among patients with SCD and 17.6% among those with SCD+β-thalassemia, as shown in Table 4. Despite the numerically higher rate in the SCD+β-thalassemia subgroup, Fisher's exact test revealed no statistically significant difference (OR = 0.60, 95% CI 0.15–2.41, p = 0.437). The absence of significance is likely attributable to the small SCD+β-thalassemia sample (n = 17), which limits statistical power. The comparison is illustrated in Figure 2 below.

Table 4. Alloimmunization by Disease Group

Disease Group	Total (n)	ICT-Positive	ICT-Negative	Alloimmunization (%)	OR (95% CI)	p-value
Sickle Cell Disease	131	15	116	**11.5%**		—
SCD + β-Thalassemia	17	3	14	**17.6%**	0.60 (0.15–2.41)	0.437
Total	**148**	**18**	**130**	**12.2%**	—	—

Fisher's exact test; two-tailed. OR < 1 indicates lower odds in SCD+β-thalassemia vs. SCD (reference); confidence interval crosses 1.0, confirming non-significance. The small SCD+β-thalassemia sample (n = 17) limits statistical power.

Association of Alloimmunization with Demographic Variables

The associations of alloimmunization with age group and gender are presented in Table 5. A descriptive trend of increasing alloimmunization frequency with advancing age was observed — rising from 4.5% in the 0–10 year group to 33.3% in the 41–50 year group — but the chi-square test was not statistically significant ($\chi^2 = 5.90$, df = 5, p = 0.316). Similarly, female patients had a higher alloimmunization rate (15.5%) than males (10.1%), but this difference did not achieve significance (Fisher's exact, OR = 0.61, 95% CI 0.23–1.63, p = 0.441). Although neither variable achieved statistical significance, the consistent pattern of higher rates in older patients and females suggests biological plausibility — older patients accumulate more heterologous antigen exposures, while females may be sensitised via pregnancy in addition to transfusion.

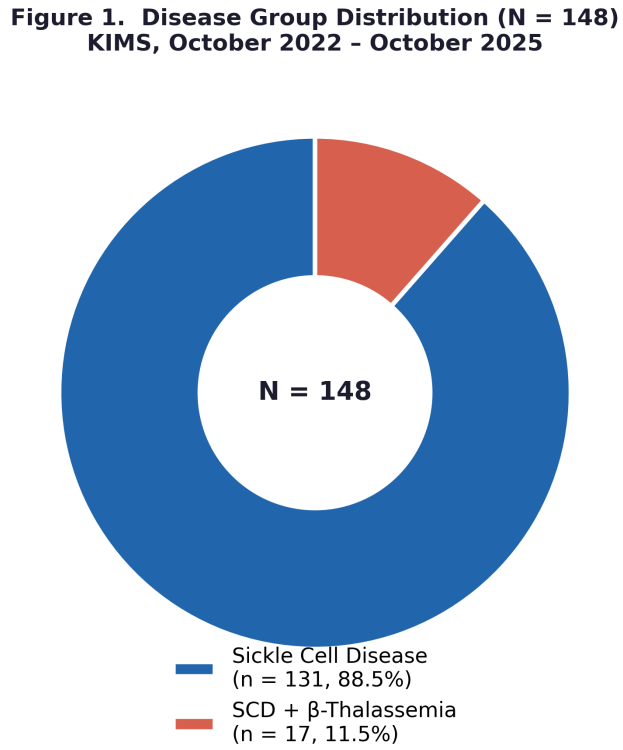

Fig. 2: Comparison of alloimmunization frequency by disease group

Chi-square for age group had ≥2 cells with expected count < 5; interpret with caution. Mann-Whitney U used for age as a continuous variable. OR for gender: female vs. male as reference.

3.1 | Alloimmunization Trend with Increasing Transfusion Exposure

A clear and statistically significant dose-response relationship was identified between transfusion exposure and alloimmunization, as detailed in Table 6 and illustrated in Figure 3 below. Alloimmunization frequency increased from 2.3% after a single transfusion to 18.0% after 2–5, 14.3% after 6–10, and 31.6% after more than 10 transfusions (chi-square = 10.23, df = 3, p = 0.017), representing a 13.7-fold higher alloimmunization rate in heavily transfused patients (>10 units) compared to first-time recipients. This significant association was confirmed by both categorical (p = 0.017) and continuous (Mann-Whitney U, p = 0.002) analyses, providing robust, converging evidence that cumulative transfusion burden is the strongest modifiable risk factor for red cell alloimmunization in this cohort.

Chi-square excludes the unknown/unrecorded group (n = 22). Fold-increase calculated relative to the single-transfusion reference group. Both categorical and continuous analyses confirm a significant association.

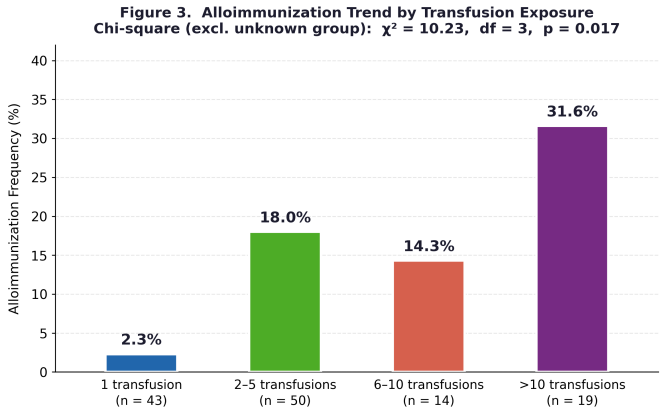

Fig. 3: Trend of alloimmunization frequency with increasing transfusion exposure

Table 5. Association of Alloimmunization with Demographic Variables

Variable	Category	ICT+ (n)	ICT− (n)	Total	% Positive	Test (Statistic)	p-value
Age Group (years)						Chi-square (χ^2=5.90, df=5)	**0.316**
	0–10	1	21	22	4.5%		
	11–20	6	46	52	11.5%		
	21–30	3	34	37	8.1%		
	31–40	4	18	22	18.2%		
	41–50	2	4	6	33.3%		
	>50	2	7	9	22.2%		
	ICT+ age: mean ± SD	29.8 ± 14.7	—	—	—	Mann-Whitney U = 1,485	0.065
	ICT− age: mean ± SD	—	22.7 ± 12.9	—	—		
Gender						Fisher's exact	**0.441**
	Male	9	80	89	10.1%	OR = 0.61 (0.23–1.63)	
	Female	9	49	58	15.5%		

Table 6. Association Between Transfusion Exposure and Alloimmunization

Transfusion Exposure	ICT+ (n)	ICT− (n)	Total	% Positive	Fold-Increase vs. "1"
1 (reference)	1	42	43	2.3%	1.0×
2–5	9	41	50	18.0%	7.8×
6–10	2	12	14	14.3%	6.2×
>10	6	13	19	31.6%	**13.7**×
Unknown (excluded)	0	22	22	0.0%	—
Overall (known groups)	**18**	**108**	**126**	**14.3%**	—
Chi-square	χ^2 = 10.23	df = 3	—	—	**p = 0.017**
Mann-Whitney U (continuous)	Median 5 (IQR 3–15)	Median 2 (IQR 1–5)	—	U = 1,405	**p = 0.002**

Multivariable Logistic Regression — Independent Predictors of Alloimmunization

To identify independent predictors of alloimmunization, binary logistic regression was performed incorporating age (continuous), disease group, and gender as covariates (Table 7 and figure 4). After multivariable adjustment, age was the only statistically significant independent predictor (OR = 1.045 per year, 95% CI 1.008–1.085, p = 0.018), indicating a 4.5% incremental increase in the odds of alloimmunization for each additional year of age. Disease group (SCD+β-thalassemia vs. SCD) and gender (female vs. male) did not achieve statistical significance after adjustment (p = 0.108 and p = 0.257, respectively). The wide confidence interval for disease group (OR = 3.52, 95% CI 0.76–16.29) reflects insufficient power from the small SCD+β-thalassemia sample (n = 17).

Binary logistic regression, maximum likelihood estimation; n = 148. Bold row = statistically significant predictor (p < 0.05). Pseudo R^2 (McFadden) = 0.066 indicates modest but detectable model fit. OR > 1 = increased odds of alloimmunization; 95% CI not crossing 1.0 confirms significance for age only.

Each dot represents one patient, jittered slightly to prevent overplotting. The blue S-curve is the logistic regression fit and the shaded band is the 95% confidence interval. The probability of alloimmunization rises steadily with age, consistent with the significant independent age effect in multivariable regression (OR = 1.045/year, 95% CI 1.008–1.085, p = 0.018). Alloimmunized patients (clustered at y = 1.0) are visibly more common at older ages, while the 0–10 year group sits almost entirely at y = 0.

Panel B — Age vs. Transfusion Count by Alloimmunization Status

ICT-positive (alloimmunized) patients are shown as

Table 7. Binary Logistic Regression — Predictors of Alloimmunization (N = 148)

Predictor	β Coefficient	Odds Ratio (OR)	95% CI	Wald z	p-value
Constant	−3.575	—	—	−4.95	<0.001
Age (per 1 year)	**+0.044**	**1.045**	**1.008–1.085**	**2.36**	**0.018**
Disease (SCD+β-Thal vs. SCD)	+1.258	3.519	0.760–16.292	1.61	0.108
Gender (Female vs. Male)	+0.602	1.825	0.645–5.165	1.13	0.257
Model fit	Pseudo R^2 = 0.066	AIC = 110.3	BIC = 122.3	LLR p = 0.064	—

Figure 4. Scatter Analysis — Predictors of Red Cell Alloimmunization (N = 148)

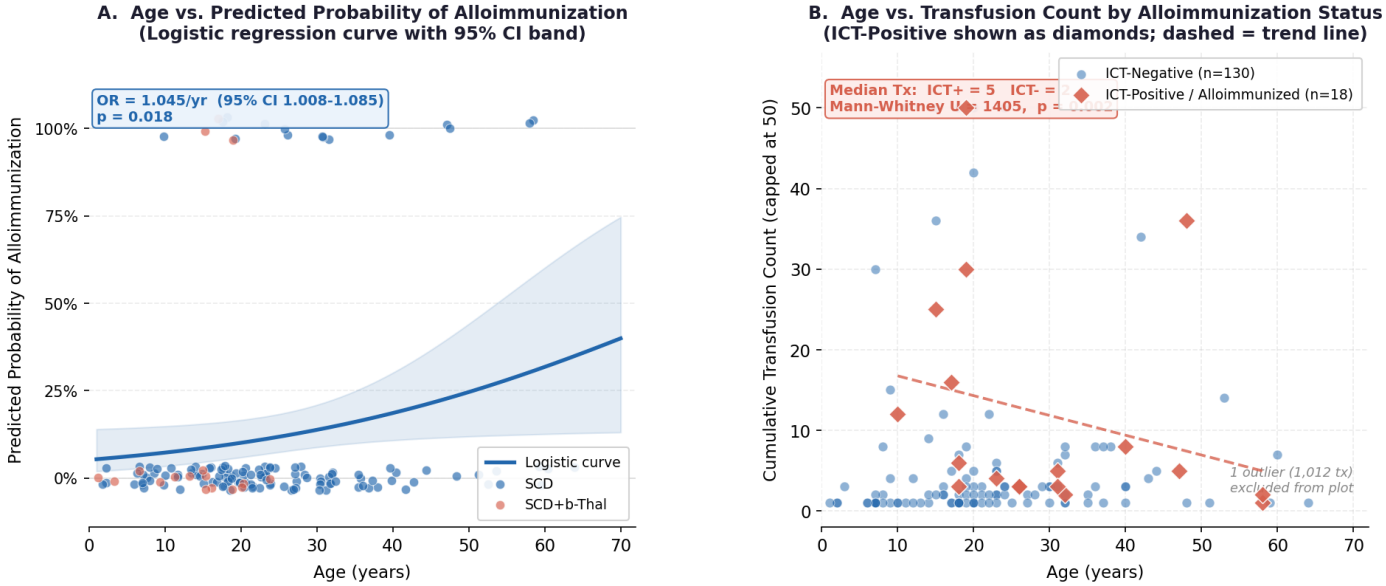

Fig. 4: Scatter Analysis — Predictors of Red Cell Alloimmunization (N = 148)

red diamonds; ICT-negative patients as blue circles. The dashed red trend line through alloimmunized patients shows a positive association between older age and higher transfusion burden. The median transfusion count was 5 (IQR 3–15) in alloimmunized vs. 2 (IQR 1–5) in non-alloimmunized patients (Mann-Whitney U = 1,405, p = 0.002), confirming transfusion exposure as the strongest single predictor of red cell alloimmunization in this cohort. One extreme outlier (1,012 transfusions in an SCD+β-thalassemia patient on exchange transfusion) was excluded from the plot for visual clarity but retained in all statistical analyses.

4 | DISCUSSION

The present study recorded an overall red cell alloimmunization frequency of 12.2% (18/148) among transfused patients with sickle cell disease (SCD) or SCD with β-thalassemia at a tertiary centre in southern India. This figure falls within the broad range reported from comparable Indian settings. Jariwala et al., in a retrospective analysis from Gujarat, documented alloimmunization rates of approximately 7–10% in multiply transfused SCD and β-thalassemia patients, while a study from western Odisha recorded 13.64% in SCD alone (11, 12). At the global level, a recent systematic review encompassing 19 SCD studies (3,867 patients) reported a pooled mean alloimmunization prevalence of 14% (95% CI 10–19%), and an equivalent meta-analysis for thalassemia yielded 13% (95% CI 10–15%). The current finding of 12.2% therefore aligns reasonably well with both Indian benchmarks and the broader international literature, suggesting that the immunological burden of alloimmunization in this population is neither trivially low nor exceptionally high (13, 14).

The numerically higher alloimmunization rate observed in the SCD+β-thalassemia subgroup (17.6% vs. 11.5% in pure SCD) did not achieve sta-

tistical significance (p = 0.437), a result attributable primarily to the small size of the compound heterozygous cohort (n = 17). A comparative study from Gujarat similarly found that β-thalassemia patients carried a modestly greater sensitisation risk than SCD patients, an observation linked to their typically earlier onset of regular transfusion and higher lifetime unit exposure. The inability to confirm this difference statistically in the current data underlines the need for a larger multicentre cohort that recruits sufficient numbers of SCD+β-thalassemia cases to achieve adequate power (15, 16).

The most robust finding in this study was the dose-response relationship between cumulative transfusion burden and alloimmunization, with rates rising from 2.3% after a single transfusion to 31.6% in patients who had received more than ten units (χ^2 = 10.23, p = 0.017; Mann-Whitney U, p = 0.002). This gradient closely mirrors observations from Sippert et al. in Brazil, who demonstrated a stepwise increase in alloimmunization proportional to lifetime transfusion count in SCD patients, and from the Blood journal review by Yazdanbakhsh et al., which noted that cumulative transfusion number is one of the most consistently replicated risk factors across diverse populations (17, 18). A study from Pakistan on multiply transfused thalassemia patients similarly identified number of red cell units transfused per year as the dominant predictor in multivariate analysis (OR 0.927, 95% CI 0.888–0.968) (19).

Age emerged as the only independent predictor in multivariable logistic regression (OR 1.045/year, p = 0.018), likely acting as a surrogate for cumulative antigenic exposure over a longer transfusion history rather than reflecting an intrinsic age-related immunological susceptibility. Gender did not independently predict alloimmunization after adjustment (p = 0.257), though the directionally higher rate in females (15.5% vs. 10.1% in males) is consistent with published literature attributing additional sensitisation risk in women to pregnancy-related alloexposure. A large Brazilian cohort and the recent 2025 meta-analysis both identified female sex as a significant risk factor in several included studies, reinforcing this biological plausibility even where individual studies lack power to confirm it (20, 21).

Taken together, these data reinforce the clinical imperative of extended red cell phenotyping at first presentation and prophylactic antigen matching — at minimum for Rh (C, c, E, e) and Kell systems — particularly for patients anticipated to require more than five lifetime transfusions. The finding that alloimmunization risk exceeds 30% beyond ten transfusions provides a pragmatic, evidence-based threshold to guide institutional policy at centres where comprehensive phenotype matching remains resource-constrained.

5 | CONCLUSION

This study established a red cell alloimmunization frequency of 12.2% among transfused patients with sickle cell disease or SCD with β-thalassemia at a tertiary centre in southern India. Cumulative transfusion burden was the single most significant predictor, with alloimmunization exceeding 31% in patients receiving more than ten units — a 13.7-fold increase over first-time recipients. Age independently predicted alloimmunization on multivariable analysis, likely reflecting lifetime antigen accumulation. These findings advocate for pre-transfusion red cell phenotyping and prophylactic antigen matching, particularly for Rh and Kell systems, in all patients anticipated to require repeated transfusions, as a cost-effective institutional strategy to reduce sensitisation and future transfusion-related complications.

6 | FUNDING STATEMENT

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest Statement

The authors declare no conflicts of interest, financial or otherwise, relevant to this study.

7 | ETHICAL APPROVAL

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki (revised 2013) and approved by the Institutional Ethics Committee of Kalinga Institute of Medical Sciences (KIMS), Bhubaneswar, Odisha, India. Patient data

were fully anonymised prior to analysis; informed consent was waived given the retrospective nature of the study.

Data Availability Statement

The de-identified dataset supporting the findings of this study is available from the corresponding author upon reasonable request and subject to institutional data-sharing policies.

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