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ORIGINAL ARTICLE

A Meta Analysis of RBC Alloimmunization in Transfused Sickle Cell and Thalassemia Patients in Saudi Arabia

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SUMMARY

Background: **Alloimmunization to red blood cells (RBCs) presents a significant challenge in blood transfusion for individuals afflicted with sickle cell disease (SCD) and thalassemia. However, there is a scarcity of data regarding the prevalence of RBC alloimmunization in such patients in Saudi Arabia. To address this gap, a comprehensive meta-analysis was undertaken to ascertain the rate of RBC alloimmunization in SCD and thalassemia patients who receive regular transfusions in Saudi Arabia.**

Methods: **A systematic search and subsequent meta-analysis, following PRISMA guidelines, were carried out. We meticulously combed through six prominent scientific databases, including PubMed, Web of Science, SCOPUS, EMBASE, MEDLINE, and Google Scholar, up to July 20, 2023, to identify pertinent English-language articles. Data were meticulously extracted from the selected studies. The meta-analysis adopted a random-effects model and included subgroup analyses to delineate the RBC alloimmunization rates specifically for SCD and thalassemia patients receiving regular transfusions. Heterogeneity was assessed through Cochran's Q and I^2 tests. The study protocol was registered under PROSPERO, with the code CRD42023440761.**

Results: **Our comprehensive search yielded a total of 983 articles, with 12 meeting the criteria for the final analysis, encompassing a total of 1,811 SCD and thalassemia patients. The collective RBC alloimmunization rate across all the eligible articles for patients with SCD and thalassemia who received regular transfusions in Saudi Arabia was determined to be 18.2%. Subgroup analysis, comprising nine articles, indicated that the RBC alloimmunization rate among SCD patients was 18.6%, while analysis of six articles revealed that the rate among thalassemia patients stood at 19.5%.**

Conclusions: **This meta-analysis underscores that the RBC alloimmunization rate in SCD and thalassemia patients who regularly receive transfusions in Saudi Arabia stands at 18.2%. Considering these findings, it is essential to prioritize extended phenotyping prior to transfusion to significantly reduce the risk of RBC alloimmunization.**

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Supplementary Data

Table S1. PRISMA recommendations checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	**1**	**Identify the report as a systematic review, meta-analysis, or both.**	**1**
ABSTRACT			
Structured summary	**2**	**Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.**	**2**
INTRODUCTION			
Rationale	**3**	**Describe the rationale for the review in the context of what is already known.**	**3, 4**
Objectives	**4**	**Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).**	**4**
METHODS			
Protocol and registration	**5**	**Indicate if a review protocol exists, if and where it can be accessed (e.g. web address), and, if available, provide registration information, including registration number.**	**4**
Eligibility criteria	**6**	**Specify study characteristics (e.g. PICOS, length of follow-up) and report characteristics (e.g. years considered, language, publication status) used as criteria for eligibility, giving rationale.**	**5**
Information sources	**7**	**Describe all information sources (e.g. databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.**	**4**
Search	**8**	**Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.**	**4**
Study selection	**9**	**State the process for selecting studies (i.e. screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).**	**5**
Data collection process	**10**	**Describe method of data extraction from reports (e.g. piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.**	**5**
Data items	**11**	**List and define all variables for which data were sought (e.g. PICOS, funding sources) and any assumptions and simplifications made.**	**5**
Risk of bias in individual studies	**12**	**Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.**	**6**
Summary measures	**13**	**State the principal summary measures (e.g. risk ratio, difference in means).**	**6, 7**
Synthesis of results	**14**	**Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g. I^2) for each meta-analysis.**	**6, 7**
Risk of bias across studies	**15**	**Specify any assessment of risk of bias that may affect the cumulative evidence (e.g. publication bias, selective reporting within studies).**	**6, 7**
Additional analyses	**16**	**Describe methods of additional analyses (e.g. sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.**	**6, 7**

Table S1. PRISMA recommendations checklist (continued).

Section/topic	#	Checklist item	Reported on page #
RESULTS			
Study selection	**17**	**Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.**	**7**
Study characteristics	**18**	**For each study, present characteristics for which data were extracted (e.g. study size, PICOS, follow-up period) and provide the citations.**	**7, 8**
Risk of bias within studies	**19**	**Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).**	**10**
Results of individual studies	**20**	**For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.**	**9 - 12**
Synthesis of results	**21**	**Present results of each meta-analysis done, including confidence intervals and measures of consistency.**	**7 - 13**
Risk of bias across studies	**22**	**Present results of any assessment of risk of bias across studies (see item 15).**	**10**
Additional analysis	**23**	**Give results of additional analyses, if done (e.g. sensitivity or subgroup analyses, meta-regression [see item 16]).**	**10**
DISCUSSION			
Summary of evidence	**24**	**Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g. healthcare providers, users, and policy makers).**	**13**
Limitations	**25**	**Discuss limitations at study and outcome level (e.g. risk of bias), and at review-level (e.g. incomplete retrieval of identified research, reporting bias).**	**14 - 15**
Conclusions	**26**	**Provide a general interpretation of the results in the context of other evidence, and implications for future research.**	**13 - 14**
FUNDING			
Funding	**27**	**Describe sources of funds for the systematic review and other support (e.g. supply of data), role of funders for the systematic review.**	**16**

From: Moher D, Liberati A, Tetzlaff J, Altman DG; The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009;6(7):e1000097. doi:10.1371/journal.pmed1000097.
For more information, visit: www.prisma-statement.org.

Table S2. PubMed search strategy.

Search	Query	Hits *
#1	(red blood cells[MeSH Terms]) OR (alloimmunization[MeSH Terms]) OR (thalassemia[MeSH Terms]) OR (sickle cell disease[MeSH Terms])	119
#2	(red blood cells[Title/Abstract]) OR (erythrocytes[Title/Abstract])) OR (blood[Title/ Abstract]) OR (alloimmunization[Title/Abstract]) OR (transfusion[Title/Abstract]) OR (transfusion[Title/Abstract]) OR (multiple transfusions of blood[Title/Abstract]) OR (transfusion of blood[Title/Abstract]) OR (thalassemia[Title/Abstract]) OR (thalassemias[Title/Abstract]) OR (sickle cell disease[Title/Abstract]) OR (sickle cell anaemia[Title/Abstract]) OR (sickle cell anemia[Title/Abstract] OR (SCD[Title/Abstract]) OR (Saudi Arabia[Title/Abstract] OR (Saudi community[Title/Abstract]) OR (Saudi society[Title/Abstract])	286
#3 (#1 AND #2)	(red blood cells[MeSH Terms]) OR (alloimmunization[MeSH Terms]) OR (thalassemia[MeSH Terms]) OR (sickle cell disease[MeSH Terms]) AND red blood cells[Title/Abstract]) OR (erythrocytes[Title/Abstract]) OR (blood[Title/Abstract]) OR (alloimmunization[Title/Abstract]) OR (transfusion[Title/Abstract]) OR (transfusion[Title/Abstract]) OR (multiple transfusions of blood[Title/Abstract]) OR (transfusion of blood[Title/Abstract]) OR (thalassemia[Title/Abstract]) OR (thalassemias[Title/Abstract]) OR (sickle cell disease[Title/Abstract]) OR (sickle cell anaemia[Title/Abstract]) OR (sickle cell anemia[Title/Abstract] OR (SCD[Title/Abstract]) OR (Saudi Arabia[Title/Abstract] OR (Saudi community[Title/Abstract]) OR (Saudi society[Title/Abstract])	214

*** Date of search: July 20, 2023.**