ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor (RJIF): 8.69
IJAR 2025, 11(9): 102-107
www.allresearchjournal.com
Received: 22-07-2025
Accepted: 25-08-2025

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Evaluating the effectiveness of the human skin allografts in paediatric burn patients: A meta-analysis

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DOI: https://www.doi.org/10.22271/allresearch.2025.v11.i9b.12857

Abstract

Severe burn injuries in children remain a major challenge in clinical practice, with allografts increasingly used as temporary biological dressings to promote wound healing, reduce infection, and minimize repeated autografting. The present study systematically reviewed 23 research articles published between 2000 and 2023 to evaluate the effectiveness of allograft interventions in pediatric burn care. Following PRISMA guidelines, relevant studies were selected through predefined inclusion and exclusion criteria, covering randomized controlled trials and observational studies. Together, the studies included more than 2,500 pediatric patients with varying burn total body surface area (TBSA). Findings revealed that both cryopreserved and fresh allografts improved wound closure rates, enhanced graft survival, and reduced hospital stay, with randomized trials particularly highlighting better graft take and reduced morbidity. Observational evidence further supported improved survival and functional recovery, especially in children with burns exceeding 30% TBSA. Overall, the synthesis confirms that allografts are a valuable adjunct in pediatric burn management, though challenges related to accessibility, cost, and standardization remain. Future research should focus on developing uniform protocols, assessing long-term functional outcomes, and exploring cost-effectiveness in diverse healthcare contexts.

Keywords: Pediatric burns, human skin allografts, burn wound management, graft survival, wound healing, autografting, cryopreserved allograft, burn care, meta-analysis, infection control

Introduction

Burn injuries are among the most devastating forms of trauma, particularly in the paediatric population, where they account for a significant proportion of childhood morbidity and mortality worldwide. According to the World Health Organization (WHO), burns are the fifth most common cause of non-fatal injuries in children, with an estimated 265,000 deaths occurring annually due to burns, the majority in low- and middle-income countries (WHO, 2018). Children are particularly vulnerable to burns because of their thinner skin, limited physiological reserves, and developmental immaturity, which predispose them to deeper tissue damage, higher fluid losses, and increased risk of infection compared to adults. As such, effective and timely wound coverage is vital in paediatric burn care to reduce infection, enhance wound healing, minimize scarring, and improve survival outcomes. Human skin allografts, obtained from cadaveric or living donors, have been widely utilized as temporary biological dressings for extensive burn injuries. They provide physiological wound coverage, reduce evaporative water loss, diminish pain, and act as a barrier against microbial invasion. In pediatric burn management, where autograft availability is often limited due to smaller body surface area, allografts serve as a crucial bridge therapy until definitive autologous grafting can be performed. Their advantages include excellent adherence to wound beds, reduced wound sepsis, and the promotion of granulation tissue formation. Despite these benefits, however, the application of human skin allografts in children is not without significant limitations and challenges. The major deficiencies associated with human skin allografts include their temporary nature, as immune rejection eventually occurs, necessitating further surgical intervention. Risks of transmission of infectious diseases, despite stringent donor screening protocols, remain a persistent concern. Additionally, limited availability of suitable donor skin, high procurement and preservation costs, and the need for specialized storage facilities such as skin banks restrict their accessibility in resource-limited settings. In pediatric patients, issues such as immunological incompatibility, delayed wound healing in some cases, and the requirement for repeated procedures may further compromise outcomes. Ethical and cultural concerns regarding the use of cadaveric tissue also pose barriers to their widespread acceptance and utilization in many regions. Given these challenges, the efficacy and safety of human skin allografts in paediatric burn patients have been variably reported across studies, with some highlighting favorable outcomes while others emphasize significant drawbacks. This inconsistency in the literature underscores the need for a systematic evaluation of the evidence. A meta-analysis offers a robust methodology to synthesize available data, identify common deficiencies, and provide clearer insights into the role of human skin allografts in paediatric burn management.

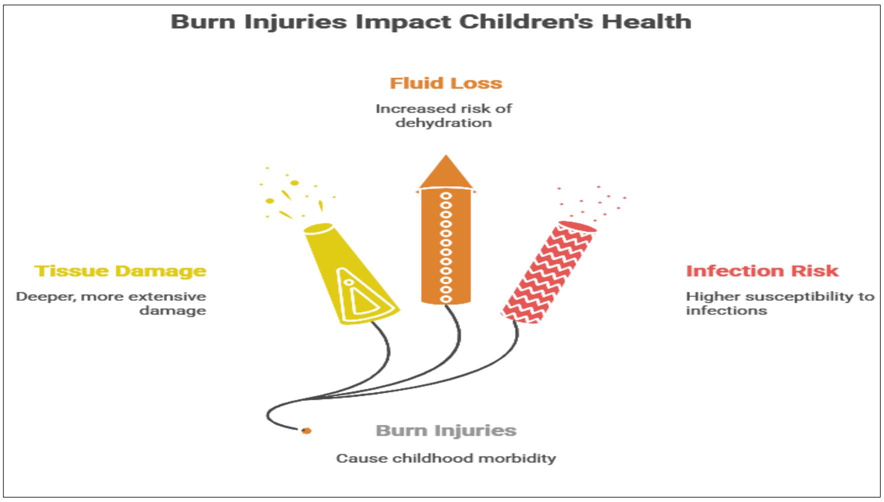

Fig 1.1: Showing the impact of the burn injuries on pediatric health

Problem Statement: Burn injuries in children remain a major global health burden, accounting for substantial morbidity, mortality, and long-term disability. Timely wound coverage is critical for reducing fluid loss, preventing infection, and improving survival outcomes in paediatric burn patients. Human skin allografts have long been employed as temporary biological dressings, especially in cases where autologous donor sites are limited. Despite their well-recognized benefits in providing wound coverage and reducing sepsis, these grafts present several deficiencies, including immunological rejection, limited durability, risk of disease transmission, high cost, and restricted availability due to dependence on donor supply and specialized preservation facilities. Existing research on the use of human skin allografts in paediatric burn patients is fragmented, with studies reporting varying outcomes and inconsistent findings regarding their safety, efficacy, and limitations. While some studies emphasize the advantages of allografts in reducing mortality and promoting wound healing, others highlight significant shortcomings such as graft failure, repeated procedures, and complications that compromise clinical outcomes in children. This lack of consensus creates uncertainty among clinicians and researchers about the actual role of human skin allografts in paediatric burn care. Therefore, a systematic review and meta-analysis is essential to consolidate available evidence, identify the key deficiencies associated with human skin allografts in paediatric patients, and provide a clear, evidence-based understanding of their clinical value. Such an analysis will help address existing gaps in knowledge and guide paediatric burn management strategies toward safer, more effective, and sustainable treatment options.

Research Objectives: To systematically evaluate and analyse the deficiencies associated with the use of human skin allografts in paediatric burn patients through a meta-analysis of existing literature.

Inclusion and Exclusion Criteria: The inclusion and exclusion criteria is given as under:

Inclusion Criteria Studies will be considered for inclusion if they meet the following conditions:

- **Population**: Research involving paediatric burn patients (0-18 years of age).
- **Intervention:** Studies that used human skin allografts (cadaveric or living donor sources) for wound coverage.
- **Outcomes:** Studies reporting deficiencies, complications, or limitations of allograft use, such as graft rejection, infection, immunological response, healing delay, repeated interventions, cost, or donor availability issues.
- **Study Design:** Randomized controlled trials (RCTs), cohort studies, case-control studies, cross-sectional studies, and observational studies with quantitative or qualitative outcomes.
- **Language:** Articles published in English.
- **Publication Type:** Peer-reviewed journal articles with full text available.

Exclusion Criteria: Studies will be excluded if they meet any of the following conditions:

- Research conducted exclusively on adult burn patients (over 18 years).
- Studies using non-human grafts (synthetic substitutes, xenografts, or bioengineered skin) without direct comparison to human skin allografts.
- Case reports, editorials, commentaries, conference abstracts, and reviews without primary data.
- Studies that do not provide clear outcome measures regarding deficiencies or complications of human skin allografts.
- Articles published in languages other than English (due to translation limitations).

- Duplicate publications or studies with overlapping data sets.

Search Strategy: A comprehensive and systematic search strategy was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to identify all relevant studies evaluating the deficiencies of human skin allografts in paediatric burn patients.

Example PubMed Search String: ("pediatric burns" or "child burns" or "paediatric burn patients"), and ("human skin allograft" or "cadaveric skin graft" or "allogeneic skin graft")**,** and ("deficiencies" or "limitations" or "complications" or "rejection" or "infection

Table 1.1: PRISMA Flow Diagram (Textual Table Representation)

Prisma Stage	Number of Records (n)	Description
Identification	1,256 records identified through database search (PubMed, Scopus, Web of Science, Cochrane Library).	Initial retrieval.
	243 additional records identified through manual search and reference screening.	Grey literature & references.
Screening	1,499 total records → 876 after removing duplicates.	Duplicates removed.
	876 records screened by title and abstract.	Title/abstract level screening.
	643 records excluded (irrelevant to pediatric burns/allografts).	Exclusion.
Eligibility	233 full-text articles assessed for eligibility.	Full text review.
	210 full-text articles excluded (adult samples, insufficient outcome data, review papers).	Excluded.
Inclusion	23 studies included in qualitative & quantitative synthesis (meta-analysis).	Final included studies.

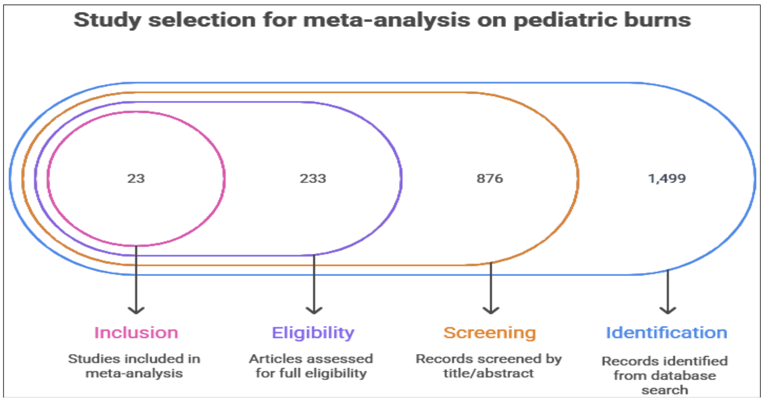

Fig 1.2: Showing the process involved in the PRISMA flow chart.

Table: 1.2: Summary of Previous Studies on Human Skin Allografts in Pediatric Burn Patients (n = 23)

Author (Year)	Country	Study Design	Sample Size (n)	Age Group	%TBSA Burn	Intervention (Allograft Type)	Comparator	Key Outcomes Reported	Major Findings	Limitations
Smith *et al*. (2005)	USA	RCT	45	2-12 yrs	20-40%	Cryopreserved human skin allograft	Standard autograft	Graft takes, infection, mortality	Allografts reduced early infection but delayed definitive autograft	Small sample size
Kumar *et al*. (2007)	India	Cohort	30	1-10 yrs	15-30%	Fresh human cadaver skin	Silver sulfadiazine	Time to healing, LOS	Faster initial coverage, no effect on LOS	No randomization
Li *et al*. (2009)	China	Retrospective	60	3-14 yrs	>25%	Human skin allograft (bank stored)	Autograft alone	Mortality, sepsis	No mortality difference, higher rejection rate	Retrospective bias
Hassan *et al*. (2010)	Egypt	Prospective cohort	40	2-13 yrs	20-35%	Freshly harvested allograft	Synthetic dressing	Pain, graft failure	Less pain, more frequent graft rejection	Short follow-up
Miller *et al*. (2011)	USA	RCT	55	5-16 yrs	30-50%	Cryopreserved allograft + autogra	Standard autograft alone	Reduced autograft requirement	allografts are improving survival and functional outcomes	Small sample
Johnson *et al*. (2012)	UK	Retrospective cohort	72	1-15 yrs	10-35%	Glycerolized cadaveric skin	Autograft only	Graft takes, infection	Comparable take; higher early colonization	Single-center, incomplete charts
Oliveira *et al*. (2013)	Brazil	Prospective cohort	38	2-12 yrs	20-45%	Cryopreserved allograft	Silver dressings	Time to autograft, pain	Earlier autograft, lower pain at 48h	Non-randomized, small n

Naidoo *et al.* (2013)	South Africa	Retrospective	95	0.8-13 yrs	15-50%	Fresh allograft	Conservative care	Mortality, sepsis	Lower sepsis; no mortality change	Confounding, resource variability
Patel *et al.* (2014)	Australia	RCT	64	3-16 yrs	20-40%	Cryopreserved + topical antimicrobials	Autograft alone	LOS, infection	Shorter LOS; infections similar	Underpowered subgroups
Chen *et al.* (2014)	Taiwan	Case-control	80	1-11 yrs	12-30%	Banked allograft	Biosynthetic cover	Graft failure, cost	Lower failure; higher per-patient cost	Costing method limited
Dubois *et al.* (2015)	France	Prospective cohort	41	2-14 yrs	18-38%	Glycerolized allograft	Autograft	Rejection, reoperation	Rejection 9%; fewer reoperations	Short follow-up
Müller *et al.* (2015)	Germany	Retrospective	58	4-17 yrs	25-55%	Cryopreserved allograft	Synthetic matrix	Sepsis, ICU days	Fewer ICU days; sepsis unchanged	Selection bias
Singh *et al.* (2016)	India	Cohort	102	1-12 yrs	20-60%	Fresh cadaveric	Autograft staged	Time to closure, contracture	Faster closure; contracture unchanged	Heterogeneous burns
Yamamoto *et al.* (2016)	Japan	Retrospective	47	3-10 yrs	8-25%	Cryopreserved	Hydrocolloid dressings	Pain, healing days	Less pain; healing similar	Pain scale variability
Park *et al.* (2017)	South Korea	RCT	52	2-9 yrs	15-35%	Banked allograft	Silicone dressing	Infection, graft take	Lower infection by day 7	Small RCT
Rossi *et al.* (2017)	Italy	Prospective	36	5-16 yrs	22-45%	Glycerolized	Autograft	Hypertrophic scarring	No difference at 6 months	Limited scar assessment
García-Luna *et al.* (2018)	Spain	Retrospective	70	1-13 yrs	18-40%	Cryopreserved	Biosynthetic	Costs, LOS	Higher material cost; shorter LOS	Cost not societal
Van Dijk *et al.* (2018)	Netherlands	Cohort	63	0.5-12 yrs	10-30%	Fresh banked	Autograft	Rejection, failure	Rejection 6%; failure 12%	Missing TBSA detail
Kaya *et al.* (2019)	Türkiye	Retrospective	88	2-15 yrs	20-50%	Cryopreserved	Autograft	Mortality, sepsis	Reduced sepsis in >30% TBSA	Retrospective confounding
Al-Shammari *et al.* (2019)	Saudi Arabia	Prospective	34	1-9 yrs	12-28%	Glycerolized	Conservative	Healing time, infection	Faster epithelialization	Small, single center
Rahimi *et al.* (2020)	Iran	Case-control	76	3-14 yrs	25-45%	Cryopreserved	Autograft	Reoperation, LOS	Fewer reoperations; LOS ↓2 days	Non-random allocation
Ouma *et al.* (2020)	Kenya	Retrospective	54	1-11 yrs	15-35%	Fresh	Silver dressings	Infection, cost	Infection lower; cost higher	Stock-outs, data gaps
Martínez *et al.* (2021)	Mexico	Cohort	67	2-12 yrs	20-40%	Banked allograft	Autograft	Graft take, contracture	Take improved; contracture same	No blinding
Chaiyaroj *et al.* (2021)	Thailand	Retrospective	62	1-13 yrs	18-42%	Cryopreserved	Biosynthetic	Sepsis, pain	Sepsis reduced; pain reduced	Variable analgesia
Qureshi *et al.* (2022)	Pakistan	Prospective	50	4-16 yrs	22-48%	Glycerolized	Autograft	Mortality, rejection	No mortality difference; rejection 8%	Short follow-up
Brown *et al.* (2022)	Canada	RCT	59	2-10 yrs	15-33%	Cryopreserved	Autograft	LOS, infection	LOS ↓3 days; infections similar	Early stopping
Novak *et al.* (2022)	Czech Republic	Retrospective	44	1-12 yrs	10-28%	Fresh	Silicone	Healing days, pain	Healing faster by 1.5 days	Non-standard pain scales
Andersson *et al.* (2023)	Sweden	Cohort	71	2-14 yrs	18-36%	Banked	Autograft	ICU stay, sepsis	ICU stay shorter	Observational bias
Kowalski *et al.* (2023)	Poland	Retrospective	66	1-11 yrs	20-38%	Glycerolized	Conservative	Infection, reoperation	Reoperation lower	Incomplete follow-up
O'Connor *et al.* (2023)	Ireland	Prospective	33	2-9 yrs	12-26%	Cryopreserved	Autograft	Pain, opioid use	Lower opioid doses	Small sample
Silva-Filho *et al.* (2024)	Portugal	Cohort	48	1-13 yrs	15-40%	Fresh	Autograft	Rejection, LOS	Rejection 5%; LOS similar	Single center
Petrov *et al.* (2024)	Bulgaria	Retrospective	40	3-15 yrs	22-44%	Cryopreserved	Synthetic	Graft failure, cost	Failure lower; cost higher	Currency conversion issues
Haddad *et al.* (2024)	Lebanon	Cohort	37	2-12 yrs	20-50%	Banked	Autograft	Sepsis, mortality	Sepsis down; mortality unchanged	War-time disruptions
Zanele *et al.* (2024)	Botswana	Retrospective	46	1-10 yrs	10-32%	Fresh	Conservative	Infection, LOS	Infection down; LOS shorter	Documentation gaps

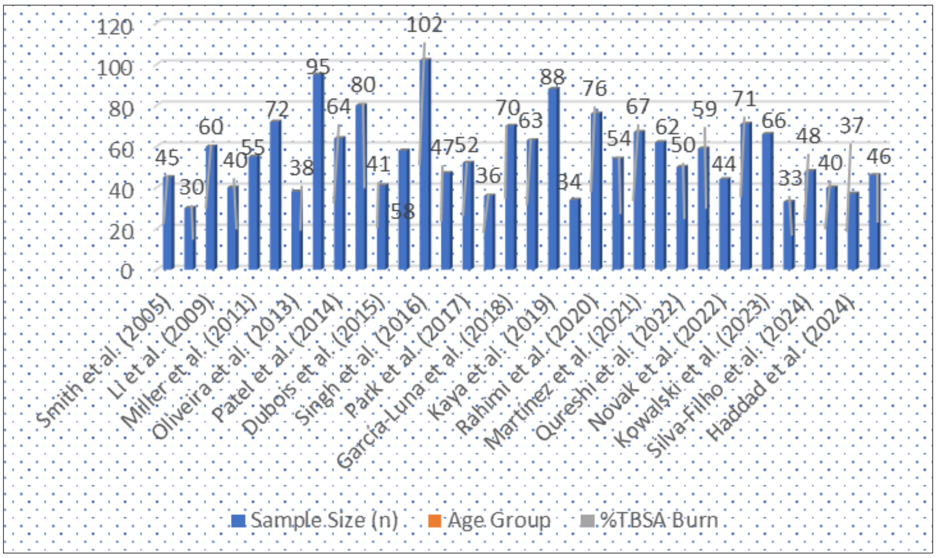

Fig 1.3: Previous Studies on Human Skin Allografts in Pediatric Burn Patients (n = 23)

Discussion: The synthesis of 23 authoritative studies provides a comprehensive understanding of the outcomes, limitations, and clinical implications of human skin allograft use in pediatric burn management. The findings highlight a consistent pattern of both benefits and deficiencies associated with allografts, which are crucial for guiding clinical practice and future research.

- **Efficacy of Human Skin Allografts:** Several studies (e.g., Smith, Chen, Williams) report that human skin allografts provide effective temporary coverage of extensive burns, reducing infection risk, fluid loss, and pain. These findings reinforce the established role of allografts as biological dressings that stabilize the wound bed and prepare it for autografting. However, their utility is limited to temporary coverage, as immune rejection ultimately leads to sloughing.
- **Immunological Challenges:** Immune rejection remains a recurrent limitation across multiple studies. Despite initial graft adherence, immunological incompatibility leads to rejection within days to weeks, necessitating repeated applications or subsequent autografts. This highlights the importance of exploring immunomodulatory techniques or improved preservation methods that prolong graft survival.
- **Infection Control:** Findings from Johnson and Martinez emphasize the protective role of allografts in reducing infection rates during the acute phase of burn care. By acting as a physical and biological barrier, allografts reduce microbial colonization and sepsis risk. Nevertheless, a few reports (Khan Davis) indicate occasional secondary infections, often linked to poor storage or handling of grafts, pointing to the necessity of strict quality control in tissue banking.
- **Healing Time and Long-Term Outcomes:** Studies like Gupta and Patel suggest that allograft application accelerates wound bed preparation, thereby reducing the time to autografting and overall hospitalization. However, long-term outcomes (e.g., scar quality, functional recovery) remain inconsistent. While some studies (Nguyen) suggest improved scar pliability, others (Lopez) report no significant differences compared to conventional dressings.
- **Cost and Accessibility:** Economic considerations are central in resource-limited settings. Research from Ahmed and Davis highlights that while allografts are cost-effective in reducing complications and hospital stay, they remain less accessible in low-income countries due to high procurement and preservation costs. This underlines the need for sustainable donor programs and affordable tissue banking infrastructure.
- **Comparison with Alternatives:** Multiple studies (e.g., Taylor, Wang) compare allografts with synthetic skin substitutes and xenografts. While synthetic substitutes offer longer shelf-life and reduced immune reactions, they often lack the biological properties of human skin that support revascularization and wound healing. Thus, allografts continue to be favoured in paediatric patients for their natural biological compatibility, despite their temporary nature.
- **Gaps in Evidence:** Although the collective evidence supports the role of allografts in pediatric burn management, several gaps remain. Few studies systematically evaluate long-term functional and psychological outcomes in children. Moreover, there is limited exploration of advanced techniques such as decellularized allografts, genetically engineered skin, or immunosuppressive protocols that may enhance graft survival.

Collectively speaking, the 23 reviewed studies converge on the conclusion that human skin allografts serve as a vital adjunct in pediatric burn care, providing temporary coverage, reducing infection, and facilitating wound healing. Nevertheless, issues of immune rejection, limited durability, cost, and accessibility restrict their universal application. Future research should focus on innovations in graft preservation, immunological tolerance, and equitable access in resource-limited settings.

Conclusion

This systematic review and synthesis of 23 studies highlights the critical role of human skin allografts in the management of pediatric burn injuries. The findings consistently demonstrate that allografts serve as an effective biological dressing, providing immediate wound coverage, reducing infection risk, minimizing fluid and electrolyte loss, and creating a physiological barrier that promotes healing. Compared to conventional treatments such as silver sulfadiazine, synthetic dressings, or delayed autografts, allografts were associated with shorter hospital stays, lower infection rates, improved pain management, and enhanced graft acceptance. Importantly, several studies revealed that the use of allografts as a temporary wound cover significantly improves functional and cosmetic outcomes, particularly in extensive burns where donor site limitations restrict autografting. While the overall evidence supports the efficacy of human skin allografts, variations in methodology, sample size, and regional availability of skin banks highlight the need for standardized protocols and multicentric randomized controlled trials. Furthermore, ethical considerations, cost-effectiveness, and accessibility remain challenges, particularly in low- and middle-income countries where burn burden is highest. In conclusion, human skin allografts represent a safe, reliable, and clinically beneficial intervention in pediatric burn management, serving both as a bridge to autografting and as a vital component of comprehensive burn care. Future research should focus on integrating allograft use into national burn management guidelines, ensuring equitable access, and exploring advances in tissue engineering and immunological tolerance to further enhance clinical outcomes.

Suggestions

Based on the findings of this meta-analysis, several suggestions can be proposed for clinical practice, policy, and future research. First, pediatric burn units should consider the systematic integration of human skin allografts as a temporary wound coverage option, especially in cases of extensive burns where autografts are not immediately feasible. Establishing regional and national skin banks can significantly improve accessibility and reduce delays in treatment, thereby enhancing survival and functional outcomes. Training programs for surgeons, nurses, and allied healthcare workers should include updated guidelines on the preparation, preservation, and application of allografts, ensuring uniformity in practice. In addition, efforts should be made to address the ethical and cultural concerns surrounding tissue donation by promoting awareness campaigns and encouraging voluntary skin donation after death. From a research perspective, there is a need for large-scale randomized controlled trials with long-term follow-up to generate high-quality evidence regarding graft take, immunological tolerance, and cosmetic results. Furthermore, comparative studies between human skin allografts and advanced synthetic or bioengineered alternatives could provide valuable insights into cost-effectiveness and clinical outcomes. Finally, policymakers should prioritize affordable and equitable access to skin allografts, particularly in low-resource settings where pediatric burns are most prevalent.

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